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VIDEO-ASSISTED THORACIC SURGERY

EDITORS: JIANXING HE, DIEGO GONZALEZ-RIVAS, ALAN D. L. SIHOE

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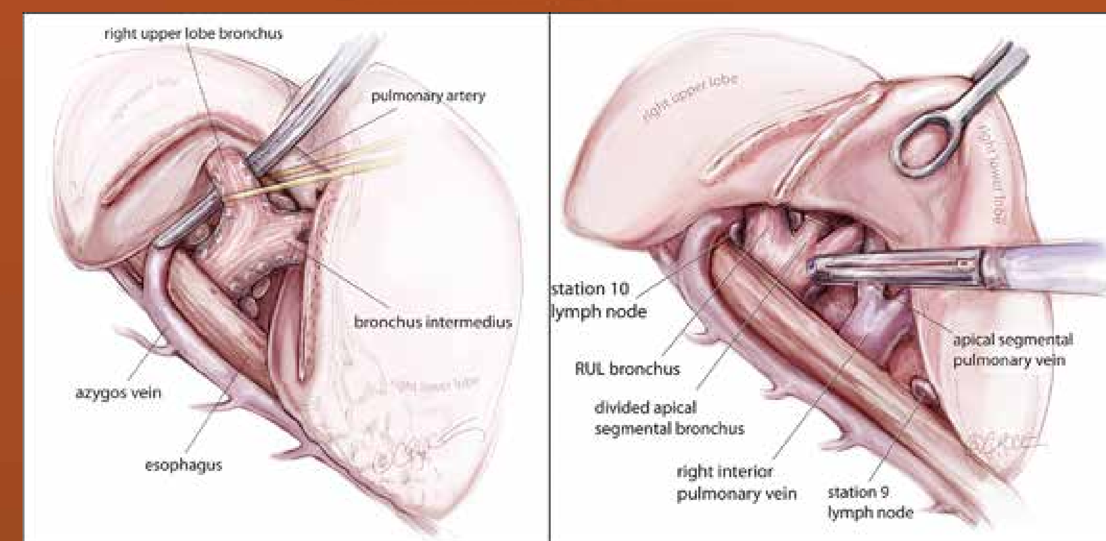
HONORARY EDITOR: JIE HE

EDITORS: JIANXING HE, DIEGO GONZALEZ-RIVAS, ALAN D. L. SIHOE

ASSOCIATE EDITORS: SHUGENG GAO, DOMINIQUE GOSSOT, RENE H. PETERSEN, GAVIN M. WRIGHT, JANG-MING LEE



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Jianxing He, Diego Gonzalez-Rivas, Alan D. L. Sihoe

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Contributors

HONORARY EDITOR

Jie He
Department of Thoracic Surgical Oncology, Cancer Institute & Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College; National Cancer Center, Beijing 100021, China

EDITORS

Jianxing He
Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China; Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China

Diego Gonzalez-Rivas
Department of Thoracic Surgery, Coruña University Hospital, Coruña, Spain; Minimally Invasive Thoracic Surgery Unit (UCTMI), Coruña, Spain

Alan D. L. Sihoe
Division of Cardiothoracic Surgery, Department of Surgery, The Li Ka Shing Faculty of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong 999077, China

ASSOCIATE EDITORS

Shugeng Gao
Department of Thoracic Surgical Oncology, Cancer Institute & Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College; National Cancer Center, Beijing 100021, China

Dominique Gossot
Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France

Rene H. Petersen
Department of Cardiothoracic Surgery, Copenhagen University Hospital, Rigshospitalet, Denmark

Gavin M. Wright
St Vincent's Hospital, Melbourne, Australia; University of Melbourne Department of Surgery, St Vincent's Hospital, Melbourne, Australia; Division of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

Jang Ming Lee
Department of Thoracic Surgery, National Taiwan University Hospital, Taiwan.

AUTHORS

Su C. Ang
Department of Cardiothoracic Surgery, St George Hospital, Sydney, Australia

Sofina Begum
St. James's University Hospital, Leeds, UK

Mark F. Berry
Department of Surgery, Division of Thoracic Surgery, Duke University Medical Center, Durham, North Carolina, USA

Deborah Black
Faculty of Health Sciences, University of Sydney, Sydney, Australia

Matthew J. Bott
Division of Thoracic Surgery, Washington University School of Medicine, St. Louis, Missouri, USA

Emmanuel Brian
Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France

Ayesha S. Bryant
Division of Cardiothoracic Surgery, University of Alabama at Birmingham, Birmingham, AL 35294, UK

Bryan M. Burt
Division of Thoracic Surgery, Stanford University School of Medicine, Stanford, USA

Christopher Cao
The Systematic Review Unit, The Collaborative Research (CORE) Group, Sydney, Australia; The Baird Institute for Applied Heart and Lung Surgical Research, Sydney, Australia; Department of Cardiothoracic Surgery, St George Hospital, Sydney, Australia

Fiona M. Carnochan
Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK

Philip W. Carrott Jr
Department of Surgery, University of Michigan, Ann Arbor MI, USA

DuyKhanh P. Ceppa
Division of Cardiothoracic Surgery, Indiana University School of Medicine, Indianapolis, Indiana, USA

Robert J. Cerfolio
Division of Cardiothoracic Surgery, University of Alabama at Birmingham, Birmingham, AL 35294, UK

David Chandrakumar
The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia

Jin-Shing Chen
Division of Thoracic Surgery, Division of Experimental Surgery, Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

Hanzhang Chen
Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China; Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China

Ya-Jung Cheng
Department of Anesthesiology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

Traves Crabtree
Division of Thoracic Surgery, Washington University School of Medicine, St. Louis, Missouri, USA

Fei Cui
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou, China

Thomas A. D'Amico
Department of Surgery, Duke University Medical Center, Durham, NC 27710, USA

Maria Delgado Roel
Complejo Hospitalario Universitario A Coruna, La Coruna, Spain

Todd L. Demmy
Department of Thoracic Surgery Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA

Qinglong Dong
Department of Anesthesiology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China

Joel Dunning
Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK

Makoto Endoh
Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Ricardo Fernandez
Department of Thoracic Surgery, Coruña University Hospital, Coruña, Spain

Eva Fieira
Department of Thoracic Surgery, Coruña University Hospital, Coruña, Spain

Ludovic Fournel
Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France

Diego Gonzalez-Rivas
Department of Thoracic Surgery, Coruña University Hospital, Coruña, Spain; Minimally Invasive Thoracic Surgery Unit (UCTMI), Coruña, Spain

Dominique Gossot
Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France

Madalina Grigoroiu
Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France

Zhihua Guo
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

Sunil Gupta
The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia

Jennifer M. Hanna
Department of Surgery, Duke University Medical Center, Durham, NC 27710, USA

Henrik Jessen Hansen
Department of Cardiothoracic Surgery, Copenhagen University Hospital, Rigshospitalet, Denmark

Jianxing He
Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China; Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China

Mark W. Hennon
Department of Thoracic Surgery, Roswell Park Cancer Institute, Buffalo, NY, USA; Department of Surgery, State University of New York at Buffalo, Buffalo, NY, USA

Hsao-Hsun Hsu
Division of Thoracic Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

Jun Huang
Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China; Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China

Ming-Hui Hung
Department of Anesthesiology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan

Takashi Inoue
Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Gening Jiang
Department of Thoracic Surgery, Shanghai Pulmonary Hospital of Tongji University, Shanghai 200433, China

David R. Jones
Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Hirohisa Kato
Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Tunc Lacin
Department of Thoracic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Jingpei Li
Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China; Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China

Lixia Liang
Department of Anesthesiology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China

Chen-Sung Lin
Faculty of medicine, School of Medicine, National Yang-Ming University, Taipei 112, Taiwan; Division of Thoracic Surgery, Department of Surgery, Taipei Hospital, Ministry of Health and Welfare, New Taipei City, Taiwan; Division of Thoracic Surgery, Department of Surgery, Koo-Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

Chao-Yu Liu
Faculty of medicine, School of Medicine, National Yang-Ming University, Taipei 112, Taiwan; Division of Thoracic Surgery, Department of Surgery, Far Eastern Memorial Hospital, New Taipei City, Taiwan; Division of Thoracic Surgery, Department of Surgery, Koo-Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

Chia-Chuan Liu
Faculty of medicine, School of Medicine, National Yang-Ming University, Taipei 112, Taiwan; Division of Thoracic Surgery, Department of Surgery, Koo-Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

Jun Liu
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou, China

Lunxu Liu
Department of Cardiovascular and Thoracic Surgery, West China Hospital, Sichuan University, Chengdu 610041, China

Deruo Liu
Department of Thoracic Surgery, China and Japan Friendship Hospital, Beijing 100029, China

Con Manganas
Department of Cardiothoracic Surgery, St George Hospital, Sydney, Australia

Antonio E. Martin-Ucar
Department of Thoracic Surgery, Nottingham University Hospitals NHS Trust, Nottingham, UK

Robert J. McKenna Jr
Division of Thoracic Surgery, Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, California, USA

Jian-Dong Mei
Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China

Takahiro Mimae
Department of Surgical Oncology, Hiroshima University, Hiroshima, Japan

John D. Mitchell
General Thoracic Surgery, Division of Cardiothoracic Surgery, University of Colorado School of Medicine, Aurora, Colorado, USA

Yoshihiro Miyata
Department of Surgical Oncology, Hiroshima University, Hiroshima, Japan

Jacob R. Moremen
Division of Cardiothoracic Surgery, Indiana University School of Medicine, Indianapolis, Indiana, USA

Haruhiko Nakayama
Department of Thoracic Surgery, Kanagawa Cancer Center, Yokohama, Japan

Charles Neveu
Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France

Hiroyuki Oizumi
Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Morihito Okada
Department of Surgical Oncology, Hiroshima University, Hiroshima, Japan

Sakae Okumura
Department of Thoracic Surgery, Cancer Institute Hospital, Tokyo, Japan

Jonathan D. Oparka
Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, Edinburgh, UK

Kostas Papagiannopoulos
St. James's University Hospital, Leeds, UK

Bernard J. Park
Division of Thoracic Surgery, Hackensack University Medical Center, 30 Prospect, Avenue, Suite 5636, Hackensack, NJ 07601, USA

Guilin Peng
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

René Horsleben Petersen
Department of Cardiothoracic Surgery, Copenhagen University Hospital, Rigshospitalet, Denmark

Kevin Phan
The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia

Qiang Pu
Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China

Yuan Qiu
Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China; Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China

Jennifer M. J. Richards
Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK

Mitsuaki Sadahiro
Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Dmitrii Sekhniaidze
4Thoracic Surgery Department, Regional Oncological Center, Tyumen, Russian

Wenlong Shao
Department of Cardiothoracic Surgery, the First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

Chih-Hsun Shih
Faculty of medicine, School of Medicine, National Yang-Ming University, Taipei 112, Taiwan; Division of Thoracic Surgery, Department of Surgery, Koo-Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

Joseph B. Shrager
Division of Thoracic Surgery, Stanford University School of Medicine, Stanford, USA

Harmik J. Soukiasian
Division of Thoracic Surgery, Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, California, USA

Scott J. Swanson
Department of Thoracic Surgery, Brigham and Women's Hospital, Boston, Massachusetts, USA

David H. Tian
The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia

Alper Toker
Department of Thoracic Surgery, Istanbul Medical School, Istanbul University, Istanbul, Turkey

Betty C. Tong
Division of Cardiothoracic Surgery, Duke University, Durham, North Carolina, USA

Yasuhiro Tsutani
Department of Surgical Oncology, Hiroshima University, Hiroshima, Japan

Nestor Villamizar
Department of Thoracic Surgery, Brigham and Women's Hospital, Boston, Massachusetts, USA

William S. Walker
Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK

Wei Wang
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

Hanghang Wang
Division of Thoracic Surgery, Duke University Medical Center, Durham, North Carolina 27705, USA

Qun Wang
Department of Thoracic Surgery, Shanghai Zhongshan Hospital of Fudan University, Shanghai 200032, China

Zheng Wang
Department of Thoracic Surgery, Shenzhen People's Hospital, Shenzhen 518020, China

Hikaru Watarai
Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Gavin M. Wright
Director of Surgical Oncology, St Vincent's Hospital, Melbourne, Australia; Clinical Associate Professor, University of Melbourne Department of Surgery, St Vincent's Hospital, Melbourne, Australia; Thoracic Surgical Lead, Division of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

Zhi-Lan Xiao
Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China

Xinguo Xiong
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

Xin Xu
Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China; Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China

Zhiqiang Xu
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

Tristan D. Yan
The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia; Department of Cardiothoracic Surgery, Royal Prince Alfred Hospital, University of Sydney, Sydney, Australia

Jen-Ting Yang
Department of Anesthesiology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

Chi-Fu Jeffrey Yang
Department of Surgery, Duke University Medical Center, Durham, North Carolina, USA

Weiqiang Yin
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

Masahiro Yoshimura
Department of Thoracic Surgery, Hyogo Cancer Center, Akashi, Japan

Rym Zaimi
Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France

Xin Zhang
Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

Zhihua Zhu
Department of Thoracic Oncology, Cancer Center of Sun Yat-Sen University, Guangzhou 510060, China

Executive Copy Editor

Emily M. Shi

Executive Typesetting Editor

Chuyuan Xie

Preface

The world in the early 1990s was a very different place. Phones tended to be connected to the wall, and encouraged people to talk instead of making conversation redundant. A computer network that connected the entire globe was the stuff of science-fiction movie nightmares starring a former Austrian body-builder. Cardiac surgeons still had a comfortable near-monopoly on coronary therapy, untroubled by cardiologists waving catheters.

This was the world into which Video-Assisted Thoracic Surgery (VATS) was born.

When VATS – and especially VATS for major lung resection – was first pioneered, it immediately came under incredible resistance and even outright hostility. The thoracic surgery 'establishment' was largely content with the open thoracotomy, and conservative voices threw scepticism, scorn and scolding at the new kid on the block. In lieu of any good clinical evidence on either side, the debate nonetheless was vociferous and vicious. As the dust settled, VATS gradually gained a toehold in the specialty, and was grudgingly acknowledged as an 'alternative' approach but only for 'selected' patients and conditions.

In the quarter of a century since the painful birth of this approach, VATS has soared to previously unimaginable heights. VATS has arguably revolutionized thoracic surgery more than any other minimally invasive approach in any other surgical specialty. Thanks to the intrepid work of the VATS pioneers, a considerable body of clinical data has been accumulated illustrating the safety, versatility and advantages of this minimal access approach. Today, VATS has completely shed its previous identity as an 'alternative', and is now entrenched firmly as the mainstream strategy for almost every conceivable operation in the human chest. Moreover, official guidelines have increasingly recommended VATS as the *preferred* option for most operations, including curative resection for lung cancer.

In this era, when patients have virtually limitless access to the latest medical information in the palm of their hands, the appreciation and demand for VATS is ubiquitous. The public and their physicians are becoming increasingly aware that a minimally invasive surgical approach is not just a matter of feeling less pain or going home sooner: it may have potentially significant benefits for their treatment outcomes. VATS today is therefore no longer a 'luxury' for the practicing thoracic surgeon, but an essential element of his/her operative repertoire.

This book collects some of the finest articles on the state-of-the-art in VATS. The authors are a virtual who's who in thoracoscopic surgery: experts from around the globe who are not only experienced masters in the operating room, but also amongst the finest teachers and advocates of the technique. The articles span everything from the theory and basic principles, through the technical details of each procedure, to the tips and tricks that will help in troubleshooting with difficult cases.

A special feature of this book is the attention paid to the emerging trends in minimally invasive surgery: sublobar resection, robot-assisted surgery, Uniportal surgery, novel anesthetic approaches, and so on. Regardless of the huge strides VATS has made over the last 20-odd years, thoracic surgery remains challenged by advances in other fields of chest medicine (including stereotactic body radiation therapy and many other disruptive technologies). The perspectives provided in this book on some of the evolving directions in VATS may prove highly significant in determining the future of our specialty.

It is the aim of this book to ultimately provide the reader with an authoritative, up-to-date, and comprehensive reference to this core component of modern thoracic surgery. For the beginner, this should be the ideal place to learn the fundamentals of the technique. For the experienced surgeon, this will serve as clinical companion and benchmark for the approach. It is sincerely hoped that whoever reads this book will continue the practice and development of VATS, and further the remarkable success story well into the future!

Jianxing He
Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China;
Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China;
Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China

Alan D. L. Sihoe
Division of Cardiothoracic Surgery, Department of Surgery, The Li Ka Shing Faculty of Medicine,
The University of Hong Kong, Queen Mary Hospital, Hong Kong 999077, China

"And of strong wines I drank boldly, as drink they who seek after pleasure and are brave" Konstantinos Kavafis (1863-1933), Greek poet

The development of thoracoscopic procedures have more than one-hundred years of history. In the year 1910, the Swedish physician Hans Christian Jacobaeus described the first thoracoscopic procedure to release adherences in patients suffering from tuberculosis. Using a simple candle as a light source, Jacobaeus peered through the rigid tube to look inside the chest cavity. He used this direct thoracoscopy technique to lyse adhesions in order to collapse the lungs. This technique was adopted throughout Europe in the early decades of the 20th century. However, for many years this procedure was relegated only to diagnostics and minor therapeutic procedures.

It is only in the last two decades that interest in minimally invasive thoracic surgery was renewed by two key technological improvements: (1) The development of endoscopic cameras offering a panoramic view instead of the previous tunnel-like vision; and (2) the availability of new endoscopic instruments like the linear mechanical stapler. From these advances, Video-Assisted Thoracic Surgery (VATS) was born. In the year of 1992 Giancarlo Roviaro revolutioned the thoracic surgery by performing the first anatomic lung resection through small incisions while looking at a screen and with no rib spreading. He went from an aggressive open surgery to a minimally invasive procedure to operate lung cancer. He was criticized for many years by the more traditional surgeons who claimed that this approach was not an oncological procedure. This new approach was a threat for traditional surgeons because it was a completely different way to operate, not easy to learn, with a loss of 3D vision, lack of sense of touch and dexterity and a totally different instrumentation. In the history of medicine and mankind in general, every innovation has been followed by a first phase of restriction and refusal by the hand of the more conservative minds. However, good ideas finally settle in thanks to determination, hard work and dedication. A road full of obstacles is sometimes the best stimulus to grow, improve and develop new ideas.

In the following years, the progress of VATS was slow with constant critics until studies showing clear benefits of VATS over open surgery started to be published. From that point on, the technique spread throughout the world and variations of the technique, in terms of number and placement of incisions, surgical approaches and new surgical instruments used started to emerge. Despite this, there was a common consensus for thoracoscopic major resections: no rib spreading, a maximum of 6-8 cms for the access incision, anatomic resection of the hilum and systematic lymph node dissection (identical to an open thoracotomy).

Thanks to the improvements and experience gained through the last years, nowadays thoracic surgical procedures, whether minor or major, easy or advanced cases, can be performed by VATS, therefore resulting in less pain, shorter hospital stay and with excellent surgical outcomes. .The evolution of VATS is an ongoing process and challenges to the role of a VATS lobectomy will never cease to emerge. The information available on internet, live surgery events and experimental courses has contributed to the rapid learning of minimally invasive surgery during the last decade. While initially slow to catch on, the traditional multi-port approach has evolved into a single-port (uniportal approach) that mimics open surgical vantage points while utilizing a non-rib-spreading, non-thoracotomy micro-incision. The early period of uniportal VATS development was focused on minor procedures until the second phase uniportal VATS started in 2010 with the development of the technique for major pulmonary resections. In only a period of 5 years, experts have been able to apply uniportal VATS technique to encompass more complex procedures such as bronchial sleeve, vascular reconstructions or carinal resections. In contrast, non-intubated and awake thoracic surgery techniques, described since the early history of thoracic surgery, peaked in the decades before the invention of the double lumen endotracheal tube and has failed to gain widespread acceptance following its re-emergence over a decade ago thanks to the improvements in video-assisted thoracoscopic techniques.

It's interesting to realize that from the first thoracoscopic procedure done over more than a century ago, the biggest developments have taken place in the last 2 decades and especially in the last 5 years. Several factors are responsible for this: Internet has provided an invaluable platform to share knowledge. The creation of specialized websites to which videos can be uploaded and scientific journals that include videos have contributed enormously to the dissemination and learning of minimally invasive techniques. The development of modern endostaplers or specifically adapted surgical instrumentation for thoracoscopic procedures have been also other key factors for the growth of video-assisted surgery interest in the latest years. At the same time, advancements in the technology of ultra-high definition cameras, 3D systems or other precise robotic systems have contributed to the progressive adoption of the minimally invasive surgery throughout the globe. Next to this, it is logic to think that this new and revolutionizing way of operating the thorax has found its place among the so-called “Playstation generation”. Having been born and grown up in the midst of computers and videogames has probably facilitated the fast adoption of these techniques by the newer generations.

This book offers a magnificent compilation of several articles published in the last years showing the different techniques described by some of the greatest specialists in the field of minimally invasive surgery. The topics included range from conventional VATS or robotic surgery to uniportal VATS, as well as emerging techniques such as non-intubated or subxiphoid approaches. Keeping in mind that the medical oncology advances at a neck-breaking speed through the development of new chemotherapy, with lesser toxicity and major effectiveness as well as radio therapeutic techniques such as the SBRT; the role of a surgeon is to offer the patient the best oncologic procedure with the least surgical aggressiveness and anaesthetics.

However, in order to evolve and to improve surgical techniques towards less invasive procedures, change is necessary. This only happens when we are outside of our comfort zone, requiring sacrifice and a special dedication. As Charles Darwin said… “It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is the most adaptable to change”. In our professional life sometimes we reach a road crossing where we must chose between something novel, unknown but very attractive or continue down the road of tradition and security. Following the latter will provide tranquillity and security but will limit our evolution and prevent us from offering our patients something better At the same time, it is a dangerous road by falling into routine and monotony of the profession. When we chose to follow a new road, adopt or develop a new technique, a door to the future opens up Uncertain but with new horizons and chances of improvement.

We live in a moment in thoracic surgery where VATS and robotic approaches are creating new opportunities for collaboration with the industry to push the boundaries on minimally invasive surgery. During the last years a rapid progress in instrument design and technology have brought developments of narrower and more angulated endostaplers, sealing devices for vessels and adapted and refined thoracoscopic instruments. We truly believe in the use of the least invasive techniques combined with modern naked 3D image systems, wireless cameras and future improved robotic technology to perform major pulmonary resections. The digital technology will facilitate the adoption of minimally invasive surgery worldwide in the next coming years.

Diego Gonzalez-Rivas, MD, FECTS
Director Uniportal VATS training program
Shanghai Pulmonary Hospital, Tongi University

Considering the contents of this textbook about Video-Assisted Thoracic Surgery, we could not believe these techniques were born only 20 years ago in the head and hands of a few pioneers. Indeed, most of the chapters deal with very advanced procedures, most of them being hardly conceivable just a few years ago.

The first part of this book comprises many articles about technical aspects of lobectomies and segmentectomies. The full range of approaches is covered, from the popular anterior approach described by the Copenhagen team to the posterior one, initially described in Edinburg, and to single port surgery whose interest is rising, especially in China. As none of these various approaches have proved to be superior to the others, the reader will benefit from all theses different technical descriptions and choose his/her own way. Although lobectomy remains the best surgical treatment for non small cell lung cancer, at least in terms of survival, there is a growing interest for sublobar resections. The reason is that we do operate more and more elderly patients, or patients with a limited pulmonary function and/or presenting with a second carcinoma several years after a lobectomy. In addition, with the development of lung cancer screening programs, more and more ground glass opacities and small nodules will be detected. As the morbidity of thoracoscopic segmentectomies is low, compared to an open approach,these techniques will compete not only with lobectomies but with non surgical treatments such as SBRT or radiofrequency. Eventually, at the end of the first section, 3 different chapters demonstrate that an appropriate lymph node dissection can be performed thoracoscopically, showing once again that VATS major pulmonary resections are oncologically sound.

The second section reports advanced procedures who are only mastered by a few experts, such as sleeve or double sleeve lobectomies. But there is no doubt that - thanks to experience and technological advances - these techniques will be accepted in a near future.

In the third section, the issue of robotically assisted thoracic surgery is treated. At this time, it is still hard to know whether the robot is a competitor for VATS or a helpful tool in the arsenal of minimally invasive thoracic surgery. The robot is anyway a challenger for conventional VATS, pushing thoracic surgeons to increase the accuracy and safety of their procedures and to foresee new technical solutions.

Finally, all these challenging techniques have their complications, some of them being dramatic and even life threatening, as recently reported by a european survey. Knowing these complications, especially the vascular ones, is essential to prevent them and anticipate their management. Complications also raise the issue of teaching and of the learning curve which are tackled in this book.

In total, thanks to the efforts of Drs Jinxing He, Diego Gonzalez-Rivas and Alan D. L. Sihoe, all surgeons wishing embarking in this new era of thoracic surgery, will find a lot of information in this book.

Dominique Gossot
Head of Thoracic Surgery Department
Institut Mutualiste Montsouris
Paris, France

Preface

With the evolution of modern technology and surgical technique, video-assisted thoracic surgery (VATS) has been widely accepted as an effective surgical approach for treating various thoracic diseases. It has been demonstrated feasible for performing various thoracic surgical procedures including lobectomy, segmentectomy and bronchoplasty. Also there is always a challenge existing for the standardization of VATS procedures. It is now acceptable for the VATS to be performed with multi-port, single-port or even robotic-assisted approaches. I am happy to know that the AME Publishing Company will publish a text book for the VATS procedures. It no doubt can provide the readers a short-cut to approach these diversified as well as technical-demanding surgical procedures from reading the clinical experiences provided by the experts of this field in the world.

Jang-Ming Lee, MD, PhD
Professor and Chief
Division of Thoracic Surgery
Department of Surgery
National Taiwan University Hospital

Preface

The development and refinement of Video-Assisted Thoracic Surgery has undergone a tremendous improvement over the last decade and the initial sceptics have vanished. This remarkable book: "Video-Assisted Thoracic Surgery" is comprised of contributions by the most accomplished minimal invasive thoracic surgeons internationally and contains important and precious information for the thoracic community.

René Horsleben Petersen, MD
Chief Thoracic Surgeon
Department of Cardio-thoracic Surgery RT 2.15.2
Copenhagen University Hospital, Rigshospitalet
Blegdamsvej 9, Copenhagen 2100 Ø Denmark

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Surgical atlas of thoracoscopic lobectomy and segmentectomy

Tristan D. Yan[1,2]

[1]The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia; [2]Department of Cardiothoracic Surgery, Royal Prince Alfred Hospital, University of Sydney, Sydney, Australia

Correspondence to: Tristan D. Yan, MBBS, MS, MD, PhD, FRACS, Professor of Cardiovascular and Thoracic Surgery. Macquarie University Hospital, 2 Technology Place, Sydney, Australia. Email: tristanyan@annalscts.com.

Abstract: Thoracoscopic lobectomy or segmentectomy via the posterior approach is a safe, reliable and reproducible technique. It was first developed by Mr. William Walker from Edinburgh in 1992. The main advantages of the posterior approach include: (I) easy access to posterior hilum and segmental bronchi; (II) safe dissection, as the tips of the instruments are coming towards the operating surgeon; and (III) complete ipsilateral lymph node clearance.

Keywords: Video-assisted thoracoscopic surgery (VATS); thoracoscopic; minimally invasive surgery; lobectomy; segmentectomy

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Video-assisted thoracoscopic surgery (VATS) is a well-established technique for major pulmonary resections (1). Since the first procedure was performed more than 20 years ago, the operative approach and instrumentation have matured. In 2007, CALGB 39802 trial established the most authoritative and accepted definition of the VATS lobectomy technique, i.e., 4-8 cm access incision, totally endoscopic approach, without rib spreading and individual anatomical dissection and division of pulmonary vein, artery and bronchus (2). Compared to open surgery, the minimally invasive approach has a number of benefits especially in the immediate post-operative period (3). A recent meta-analysis of propensity score matched patients demonstrated significantly lower incidences of overall complications, prolonged air leak, pneumonia, atrial arrhythmias and renal failure, as well as shorter hospitalization compared to open thoracotomy (4). This study further consolidated the benefits of VATS and offered the highest clinical evidence on this topic.

The posterior approach was first developed by Mr. William Walker from Edinburgh in April 1992. In contrast to the anterior approach, the main differences in techniques of the posterior approach include: (I) the surgeons stand posterior to the patient; (II) the utility incision is made at the 6th or 7th intercostal space anterior to latissimus dorsi muscle, instead of the 4th intercostal space; (III) the camera port is made through the auscultatory triangle, instead of lower anterior incision; and (IV) the order of dissection is from posterior to anterior, by opening up the fissure first to identify and isolate pulmonary arterial branches. The main advantages of the posterior approach include: (I) easy access to posterior hilum; (II) lymph nodes are clearly visualized; and (III) tips of the instruments are coming towards the camera, which allows safer dissection. The fact that the posterior hilum can be clearly seen greatly facilitates dissection of the segmental bronchial branches and pulmonary arteries. Hence, the posterior approach offers great advantages for VATS segmentectomy.

Preoperative considerations

I have adopted VATS resection as the preferred surgical strategy of choice for all cases of peripheral lung carcinoma of 7 cm or less in diameter and for suitable benign disease. Lobectomy and anatomic segmentectomy are standard procedures. It is possible to utilize VATS techniques in patients with more advanced disease such as moderate chest wall or pericardial involvement and, rarely, for pneumonectomy in patients with low bulk hilar involvement. However, with the trend towards lung conservation strategies, we now reserve pneumonectomy for individuals in whom bronchovascular reconstruction is not feasible.

Baseline pulmonary function is assessed by using a combination of spirometry and CO transfer factors. Additionally, selected patients undergo exercise testing. Cardiological assessment is carried out as relevant to the individual patient. Echocardiography assessment of pulmonary (PA) pressure is undertaken in patients at risk of pulmonary hypertension (PAP >45 mmHg). Few patients are declined surgery on the basis of poor pulmonary function data (e.g., both FEV_1 and FVC <35%) (1). In addition to a contrast-enhanced computed tomography scan of the head, chest, abdomen and pelvis, positron emission tomography-CT (PET-CT) with 18F-fluordeoxyglucose (^{18}F-FDG) is performed in all patients with bronchogenic carcinoma under consideration for resection. In patients considered suitable for lobectomy or segmentectomy, the VATS approach is attempted in all patients meeting size and stage criteria. The only absolute contraindications are those patients in whom the pleural cavity is obliterated on radiological grounds or who clearly have very proximal disease requiring a pneumonectomy. The requirement for sleeve lobectomy is a significant relative contraindication, but not absolute.

Operative techniques

Anesthesia and positioning

Following induction of anesthesia, the patient is positioned in the lateral decubitus position. The hands are placed unsupported in the "prayer" position in front of the face and the operating table is manipulated to extend the thorax laterally opening up the intercostal spaces. As soon as the double lumen endotracheal tube is confirmed to be in the correct position, whilst the patient is still in the anaesthetic room, ventilation is switched to the contralateral lung to optimize deflation of the lung that is to be operated upon. Suction is occasionally used if the lung does not deflate readily. The respiratory rate can be increased to 20 breaths/min or more in order to reduce the tidal volume and hence the degree of mediastinal excursion due to ventilation. This provides a more stable operating field. Central lines or urinary catheters are rarely used, but always use an arterial line and large bore venous cannulae.

The paravertebral catheter is inserted as soon as the chest cavity is entered, under thoracoscopic guidance. This is used for perioperative analgesia in preference to epidural anaesthesia and it remains in place for 48 hours. Furthermore, a patient-controlled pump is supplied to the patient for post-operative analgesia. The positioning of the surgical, anaesthetic and nursing teams and the equipment is illustrated in *Figure 1*. The surgeon and their assistants stand at the patient's back with the screen directly across the table and the scrub nurse obliquely opposite.

Instrument

I prefer a zero degree 5 mm high definition STORZ video thoracoscope, as it provides a single axis view allowing easy correction of orientation. A combination of endoscopic and standard open surgical instruments is used. Lung retraction and manipulation are performed using ring-type sponge-holding forceps. Long artery dissection forceps (30 cm) with or without mounted pledgets are employed for blunt dissection, which are particularly useful for exposing the PA at the base of the oblique fissure, cleaning structures and clearing node groups. A range of curved forceps and an endodissector are used gently as probes to create a passage between the lung parenchyma and major hilar structures. A right-angled dissector or long curved artery forceps is used to dissect out and pass slings around pulmonary arteries and veins. Endoscopic clips are used to ligate small vessels whilst large vessels and lung parenchyma are divided using endoscopic stapling devices to ensure haemostasis and aerostasis. Both endoscopic shears and specific VATS Metzenbaum type scissors to be helpful. The latter have the advantage of curved blade ends, which reduce the risk of vascular injury.

Incision

Three access ports are used and port position is standard irrespective of the lobe or segment to be removed (*Figure 2*). A 3-4 cm utility port site incision is made in the sixth or seventh intercostal space (whichever is the wider). The camera is temporarily introduced through this port to facilitate safe creation of a 0.5 cm incision posteriorly in the auscultatory triangle at the point nearest to the upper end of the oblique fissure. The anterior hilum dissection is not essential for the posterior approach. However, for completeness of this article, it is important to understand the segmental anatomy of the pulmonary veins viewed from the anterior hilum. The pulmonary veins are the most anterior structures in the hilum (*Figure 3*). Their tributaries

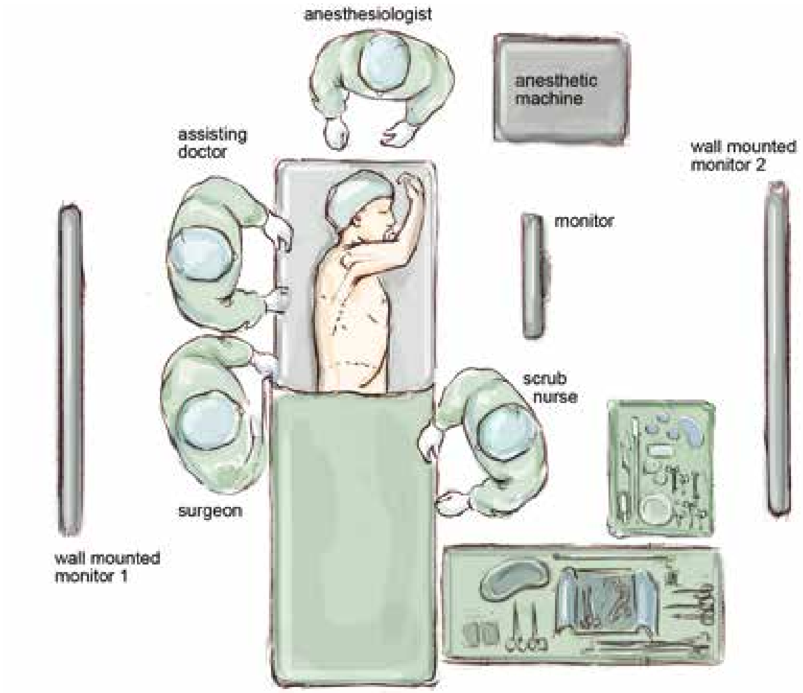

Figure 1 The positioning of the surgical, anaesthetic and nursing teams and the equipment for thoracoscopic surgery.

Figure 2 Standardized incisions for the posterior approach.

are also anterior to the segmental arteries and bronchi. The interlobar vein often traverses between the upper and lower lobes in the oblique and then the upper and middle lobes in the horizontal fissure before joining the superior pulmonary vein in the hilum. In majority of cases, the middle lobe vein drains into the right superior pulmonary vein.

A port is inserted to accommodate the camera, which is positioned in the auscultatory triagle for the remainder of the procedure. A further 1 cm port is created in the mid-axillary line level with the upper third of the anterior utility port. The anterior and posterior ports lie at opposite ends of the oblique fissure. A video-imaged thoracoscopic assessment is performed to confirm the location of the lesion, establish resectability and exclude unanticipated disease findings that might preclude resection. If the lesion is small or cannot be palpated easily, sound knowledge of segmental anatomy is crucial for determining the location of the lesion within the segment(s) of the respective lobe.

The 'landmark' lymph node

The first step is to identify the PA within the central section of the oblique fissure. In some patients the PA is immediately visible, but in the majority of cases, the PA is revealed by separating the overlying pleura using blunt dissection with mounted pledgets. If the fissure does not open easily or is fused, an alternative approach utilizing a fissure-last dissection should be considered. Once the PA has been identified, the sheath of the artery is grasped with a fine vascular clamp or long artery forceps and an endoscopic dissector is used to enter the sheath defining the anterior

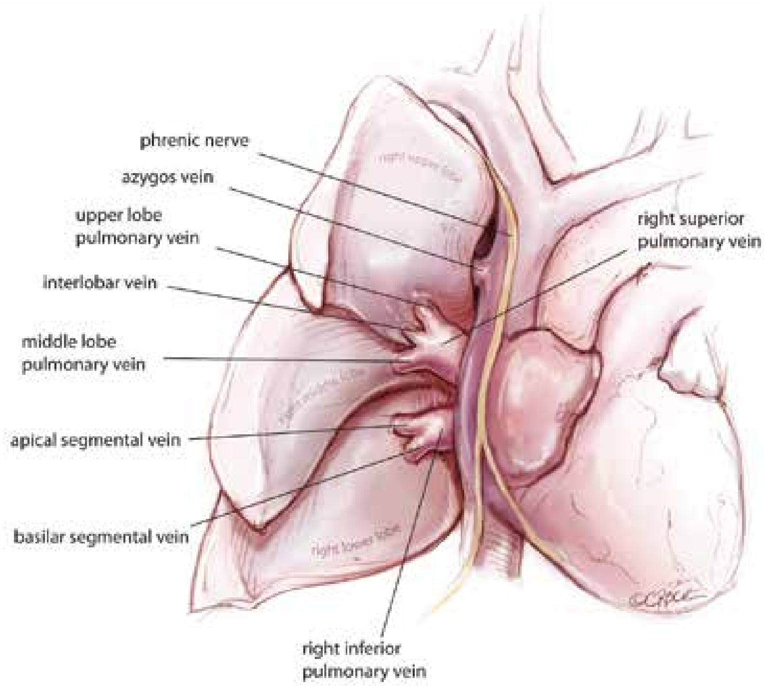

Figure 3 Segmental anatomy of the pulmonary veins viewed from the anterior hilum.

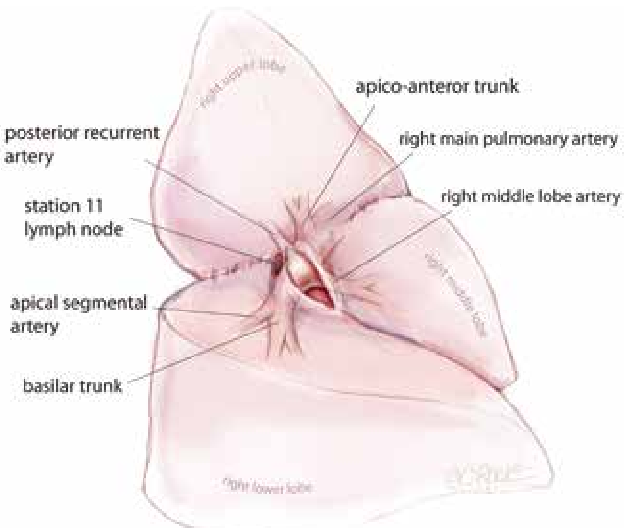

Figure 4 Pulmonary artery is revealed by separating the overlying pleura using blunt dissection.

and posterior margins of the artery. The apical lower branch of the PA is often exposed during this dissection (*Figure 4*).

For all lobectomy and segmentectomy procedures excepting middle lobectomy, the lung is then reflected anteriorly and the posterior pleural reflection is divided using sharp and blunt dissection. On the right, this process should clear lung tissue away from the angle between the bronchus intermedius and the upper lobe bronchus, exposing the posterior hilar lymph nodes in this position (*Figure 5*). One lymph node packet, the station 11 lymph node, sitting at the bronchial bifurcation between the right upper lobe and the bronchus intermedius is the 'landmark' lymph node to me, because just superficial to this, it indicates a safe passage from the interlobar fissure to the posterior hilum over the pulmonary artery. From the anterior port site, dissecting forceps are passed gently immediately superficial and posterior to this station 11 'landmark' lymph node, where it has been identified in the oblique fissure (*Figure 6*). When the lung is retracted anteriorly, the tips of the long artery forceps will emerge through the incised posterior pleural reflection, above the 'landmark' lymph node that is now viewed from the posterior hilum. This maneuver is the key step for any VATS lobectomy or segmentectomy via the posterior approach on the right side. Care should be taken during this maneuver not to disrupt this lymph node lying on the bronchial bifurcation. A sling is then passed behind the posterior fissure, which is divided with an endoscopic linear stapling device. The PA is now clearly seen and the distinction between the upper and lower lobes is established.

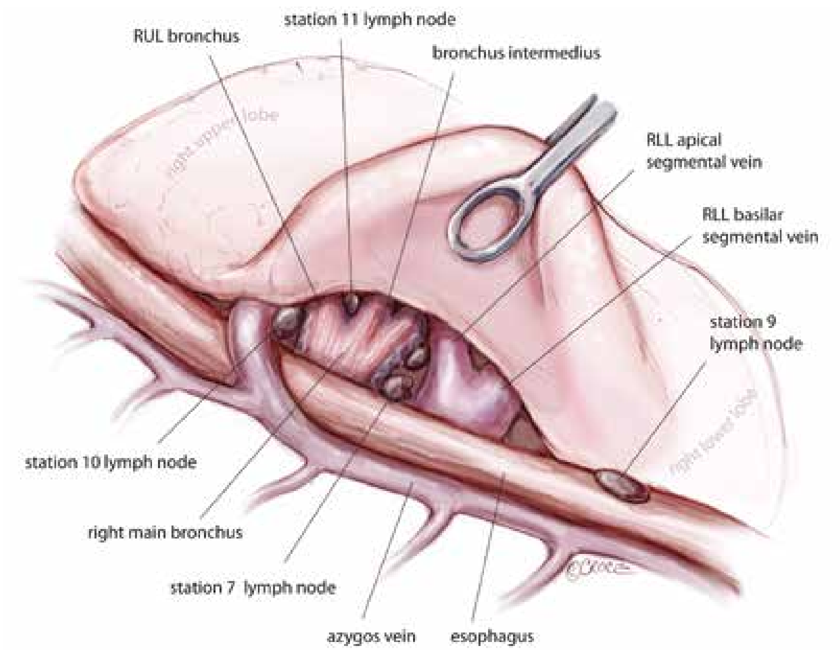

Figure 5 Viewed from the posterior hilum, the 'landmark' station 11 lymph node is exposed by clearing the lung tissue away from the bronchus intermedius and the upper lobe bronchus.

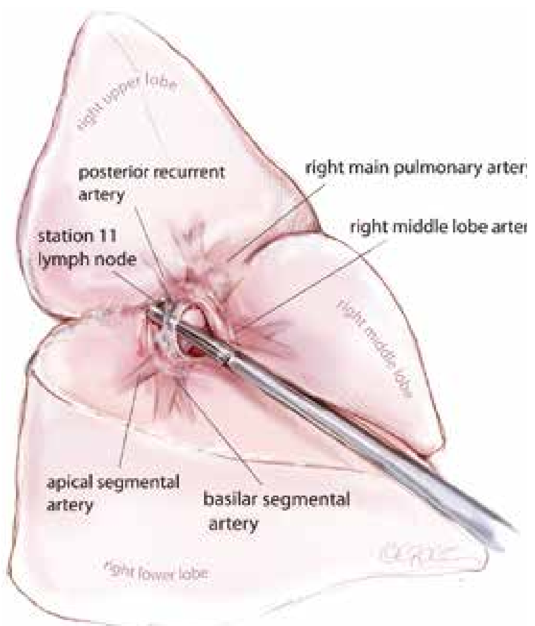

Figure 6 From the anterior port site, dissection forceps are passed gently immediately superficial and posterior to this station 11 'landmark' lymph node, where it has been identified in the oblique fissure. When the lung is retracted anteriorly, the tips of the forceps will emerge through the incised posterior pleural reflection, above the 'landmark' lymph node between the right upper lobe bronchus and the bronchus intermedius, as seen in the previous figure.

Dissection then proceeds according to the lobe or segment to be resected.

Right upper lobectomy

Having divided the posterior fissure, the posterior ascending segmental branch of the PA is often evident, and should be divided at this stage if appropriate. It is frequently small enough to clip. The upper lobe bronchus is then identified and dissected out. It is common to find a substantial bronchial artery running alongside the bronchus, which should be ligated with clips and divided. Note that clips are only used on the proximal end and the distal end is not clipped since clips in this position may interfere with subsequent stapling of the bronchus. The upper lobe is then retracted inferiorly and blunt dissection with mounted pledgets is used to free the cranial border of the upper lobe bronchus and define the apico-anterior trunk. The azygos vein is often closely related to the bronchus and can be pushed away using a gentle sweeping motion. Long artery forceps are passed around the upper lobe bronchus close to its origin in the plane between the bronchus and the associated node packet (*Figure 7*). It should be appreciated that the apico-anterior trunk lies immediately anterior to the bronchus, but sometimes separated by station 11 right

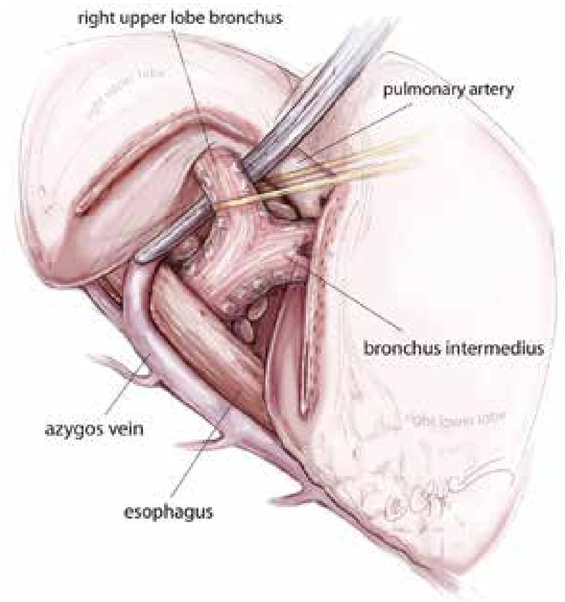

Figure 7 Long artery forceps are passed around the upper lobe bronchus close to its origin in the plane between the bronchus and the associated node packet.

upper lobe lymph nodes. The bronchus is transected at this level using an endoscopic linear stapling device. It is not necessary to inflate the lung to test that the correct bronchus is being divided, as the vision is invariably excellent via the posterior approach and the re-inflated lung may subsequently obscure the view for remainder of the resection.

Following division of the bronchus, the feeding vessels to the right upper lobe bronchus node packet are clipped and divided, allowing the nodes to be swept up into the operative specimen. Clasping the distal end of the transected bronchus with an endoscopic toothed grasper, the upper lobe can be reflected upwards. The posterior segmental artery is divided at this stage if not already dealt with and the apical and anterior segmental arteries or common stem artery are carefully cleaned, dissected out (*Figure 8*) and divided with an endoscopic stapler. Finally, the lung is retracted posteriorly facilitating dissection of the superior vein. This can be divided from either the posterior or anterior aspect as convenient, taking care in either case to identify clearly and preserve the middle lobe vein. The transverse fissure is then divided. The middle lobe artery is most easily identified and protected if the stapling device is first passed through the inferior port and fired from posterior to anterior. Division of the transverse fissure is

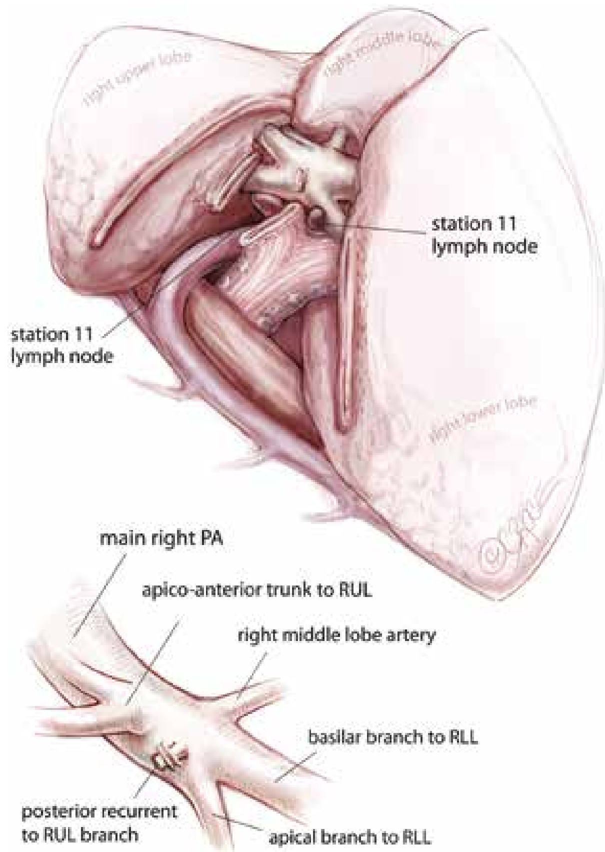

Figure 8 The posterior segmental artery is divided at this stage if not already dealt with and the apical and anterior segmental arteries or common stem artery are carefully cleaned, dissected out.

then completed, passing the stapling device through the anterior port. The inferior pulmonary ligament is divided to facilitate expansion of the right lower lobe.

Right lower lobectomy

Having identified the PA in the oblique fissure and divided the posterior oblique fissure, the pulmonary artery is then divided either in one or separately as a basal trunk artery and the apical segmental artery to the lower lobe. The space between the superior and inferior veins is developed and a long clamp is passed into this space emerging anterior to the PA in the oblique fissure. A sling is passed into this plane and the anterior oblique fissure is then divided. The lower lobe is mobilized by dividing the inferior pulmonary ligament. The inferior vein is dissected free from surrounding tissue and divided using an endoscopic linear stapling device. The bronchus is identified and the

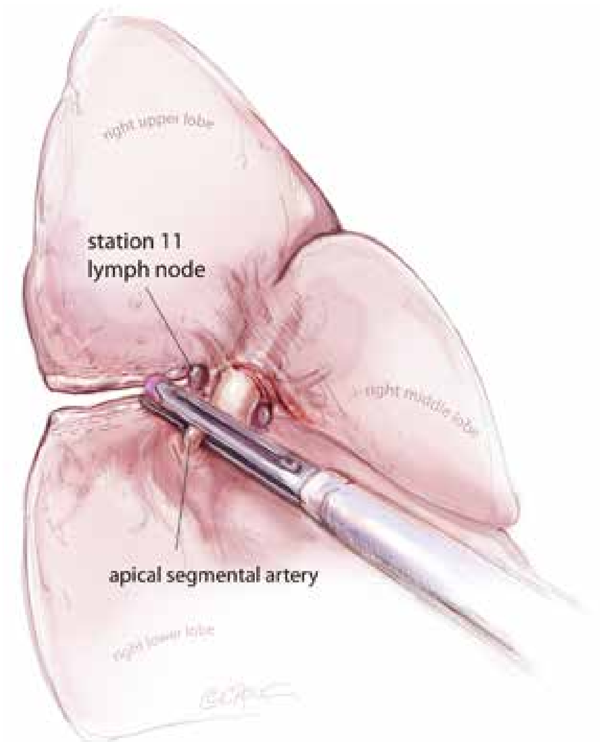

Figure 9 The apical segmental artery is divided using a vascular stapler.

bronchial vessels are clipped proximally. Lymph nodes are cleared from its medial and lateral margins. The lower lobe bronchus is divided through its apical and basal branches preserving airflow to the middle lobe. The middle lobe bronchus must be visualized prior to stapling.

Right middle lobectomy

The PA is identified and the anterior oblique fissure is divided as for right lower lobectomy. The vein, bronchus and arteries are then seen clearly, like three little 'soldiers' when the right upper lobe is retracted superiorly and are divided in sequence. The transverse fissure is divided as described for right upper lobectomy.

Left upper lobectomy

The PA is identified in the oblique fissure and the posterior aspect of the oblique fissure is divided in a similar way to the right side. The arterial branches to the left upper lobe are then divided sequentially. Division of the anterior aspect of the fissure is completed in similar manner to that on the right side. It is important to develop the space between the pulmonary veins and central to the fused anterior oblique fissure thoroughly. When passing a clamp through the utility incision and under the fused fissure, the surgeon will feel the lower lobe bronchus and should allow the clamp to pass superficially in order to preserve the airway to the lower lobe. Gentle blunt dissection is used to separate the superior pulmonary vein from the anterior surface of the bronchus. A long clamp is passed around the base of the bronchus, taking particular care not to damage the PA. Retraction of the PA using a mounted pledget may be helpful. A sling is passed around the bronchus and used to elevate it (crane maneuver) in relation to the pulmonary artery and create a space via which an endoscopic stapling device can be inserted to divide the bronchus. The superior vein is cleaned and divided. The inferior pulmonary ligament is divided up to the level of the inferior vein to facilitate expansion of the lower lobe.

Left lower lobectomy

As on the right side, having identified the PA and divided the posterior aspect of the oblique fissure, the arterial branches are identified. The anterior portion of the oblique fissure is divided as for left upper lobectomy and the arterial supply divided with an endostapler. The inferior pulmonary ligament is divided up to the level of the inferior pulmonary vein. The margins of the vein are clearly delineated and it is then divided. Bronchial vessels are clipped proximally and divided, and the lymph node chains are cleared off the medial and lateral aspects of the bronchus, which is divided at its base.

Segmentectomy-'three-directional' stapling technique

Apical segmentectomy of the lower lobe is a common procedure. In this article, I describe the technique of thoracoscopic apical segmentectomy using a 'three-directional' stapling technique. Having identified the PA in the oblique fissure and divided the posterior oblique fissure, the pulmonary artery is then prepared using blunt dissection by 'dragging' the lung tissue distally along the pulmonary artery until its bifurcation to apical and basal segmental branches is clearly seen. The apical segmental artery is divided using a vascular stapler (*Figure 9*). Once the apical artery is divided, the PA is pulled forward to reveal the bronchus intermedius posteriorly and its bifurcation to the lower lobe, i.e., apical and basilar segmental bronchi

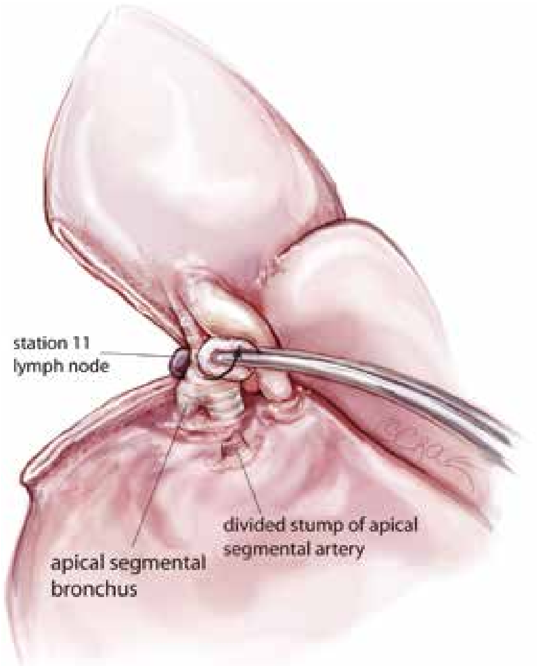

Figure 10 Once the apical artery is divided, the pulmonary artery is pulled forward to reveal the bronchus intermedius posteriorly and its bifurcation to the lower lobe, i.e., apical and basilar segmental bronchi.

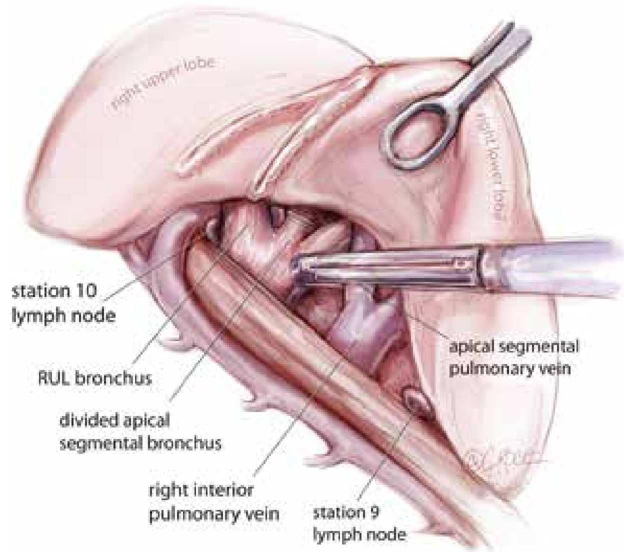

Figure 11 The apical segmental vein is divided using an endoscopic linear stapling device.

(*Figure 10*). The apical segmental bronchus is divided with a stapler, passed through the anterior access port. Lymph nodes are the cleared from the medial and lateral margins of the bronchus. The lower lobe is then retracted forward to exposure the posterior hilum. The lower lobe is further mobilized by dividing the inferior pulmonary ligament. The inferior vein is dissected free from surrounding tissue and the confluence of the apical and basilar segmental veins is developed by 'pushing' the lung tissue distally using a small pledget mounted on the tips of long dissecting forceps. The apical segmental vein is divided using an endoscopic linear stapling device (*Figure 11*).

Finally, the apical segment is separated from the basilar tri-segments using a 'three-directional' stapling technique. It is clear that each lobe is a three-dimensional structure or pyramidal in shape. By simply compressing the lung tissue and dividing it using a heavy stapling device in one plane, not only is it not possible to achieve an anatomical segmentectomy, but also the staples may not be able to hold the thick lung tissues together, resulting in prolonged air-leak. It is important to first orientate the segment to its anatomical position. The 'three-directional' stapling technique requires the first stapler coming from the anterior access incision towards the distal limit of the apical segmental bronchus, compressing the interlobar surface with the anterior surface of the lobe; the second stapler coming from the posterior direction towards the distal limit of the segmental bronchus, compressing the lateral and posterior surfaces of the lobe; and the third stapler dividing the lung parenchyma medial and parallel to the apical segmental bronchus, hence completing the segmentectomy in three directions (*Figure 12A*). The final apical segmentectomy specimen should be pyramidal in shape with individually divided segmental artery, bronchus and vein (*Figure 12B*). All hilar and segmental level nodes relevant to the resected segment are excised. At mediastinal level either extensive sampling or lymphadenectomy is preferred.

Postoperative care

A size 32 Fr apical drain is placed through the mid-axillary line port site and is usually removed on the first postoperative day subject to a satisfactory chest radiograph and aerostasis. Patients are typically nursed on the general thoracic ward after immediate extubation. Analgesia is provided using a patient-controlled analgesia pump and a local anaesthetic paravertebral catheter. Early mobilization is strongly encouraged with the availability of physiotherapy

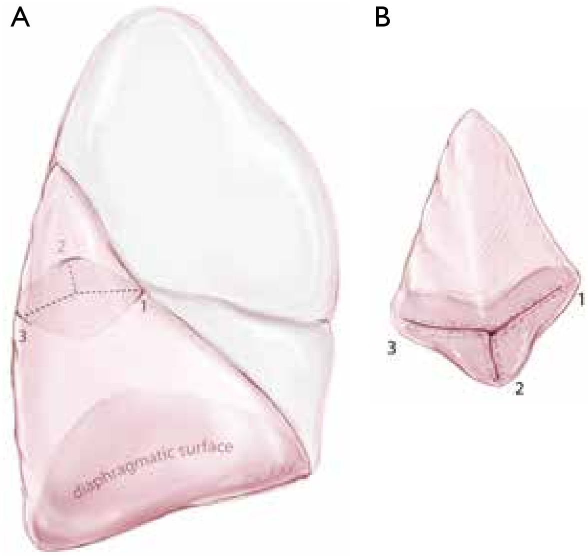

Figure 12 (A) The 'three-directional' stapling technique requires the first stapler coming from the anterior access incision towards the distal limit of the apical segmental bronchus, compressing the interlobar surface with the anterior surface of the lobe; the second stapler coming from the posterior direction towards the distal limit of the segmental bronchus, compressing the lateral and posterior surfaces of the lobe; and the third stapler dividing the lung parenchyma medial and parallel to the apical segmental bronchus, hence completing the segmentectomy in three directions; (B) the final apical segmentectomy specimen should be pyramidal in shape.

seven days per week, and discharge as early as postoperative day 2 or 3 is often possible.

Comments

The posterior approach is a safe, reliable and reproducible approach to VATS lobectomy and segmentectomy. VATS has been shown to compare favorably with open thoractomy in terms of immediate post-operative recovery and is considered to be oncologically equivalent. Our cross-sectional survey on 838 thoracic surgeons worldwide showed that 95% of surgeons who performed VATS agreed with the CALGB definition of 'true' VATS lobectomy; 92% of surgeons who did not perform VATS were prepared to learn this technique, but were hindered by limited resources, exposure and mentoring (5). Majority of thoracic surgeons believed advanced VATS techniques should be incorporated into thoracic surgical training and for more standardized workshops to be made available. A recent consensus from 50 major minimally invasive thoracic surgeons showed that increased use of VATS techniques for lobectomy and segmentectomy would be highly desirable (1).

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VATS segmentectomy utilizing the Copenhagen approach

René Horsleben Petersen, Henrik Jessen Hansen

Department of Cardiothoracic Surgery, Copenhagen University Hospital, Rigshospitalet, Denmark

Correspondence to: René Horsleben Petersen. Department of Cardio-thoracic Surgery, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark. Email: rene.petersen@rh.regionh.dk.

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Clinical vignette

The patient is a 68-year-old woman with a history of thoracoscopic (VATS) lobectomy of the right lower lobe in 2011 for T2aN0M0, stage Ib (4.9 cm) adenocarcinoma. She did not receive adjuvant chemotherapy and her comorbidities include hypertension and alcohol consumption. On follow-up computed tomography (CT) scans, a growing tumor central in the left upper lobe was discovered. Her pulmonary function tests demonstrated 69% of predicted FEV_1 and 59% of predicted DLCO. VATS left upper trisegmentectomy was scheduled. This article and the accompanying video (*Video 1*) will discuss the minimally invasive segmentectomy approach used in this case.

Surgical techniques

Preparation

The basic set-up used for a VATS segmentectomy is the same as previously described for VATS lobectomy (1,2). The patient is positioned on the side, with the table bending at the level of the xiphoid to allow the intercostal spaces to open. The surgeon and the assistant are positioned on the anterior (abdominal) side of the patient and with the surgeon cranially. All VATS segmentectomies are performed with a 10 mm, 30 degree angled HD video-thoracoscope. A double-lumen tube is used for deflation of the left lung.

Operation

A 4 cm anterior utility incision is made without any tissue retractor or rib spreading. The wound is protected by a plastic soft tissue retractor (Alexis Retractor, Applied Medical USA), which also improves exposure. This incision is later used for specimen retrieval and is positioned between the breast and the lower angel of the scapula in the fourth intercostal space, just anterior to the latissimus dorsi muscle. In case of a conversion to open procedure, this incision can be easily expanded to a 10 to 15 cm muscle sparring thoracotomy. Through this incision, the cavity is evaluated with the camera looking for unexpected pathology, adhesions, and the level of the diaphragm. A low anterior 1 cm camera-port is positioned at the level of the top of the diaphragm and anterior to the level of the hilum and the phrenic nerve. The third incision is 1.5 cm, positioned at the same level but more posteriorly and inferiorly from the scapula and anterior to the latissimus dorsi muscle. To palpate, free and prepare the structures, we used an array of peanut or sponge sticks and an electrocautery blade hook controlled with a normal surgical handhold. The tip of the hook can then be used to lift and divide the tissue. To present vessels and other structures to be divided, we use an elastic vessel loop made of rubber.

Localization of the tumor is confirmed by palpation. The pleura over the hilum is divided and the vein branches from the upper lobe segments are visualized. The plane between the artery and the upper lobe vein is opened, so the vein from the three upper segments can be exposed using a vessel loop. The branches are divided with a tan Tri-stapler (Covidien, USA) introduced from the posterior port. Next the superior branch of the pulmonary artery is divided in the same way and thereafter, a plane between the artery and the bronchus can be created. The bifurcation of the left upper and lower lobe bronchi is identified, and the left upper lobe bronchus is dissected to the next level of division to visualize the bronchus to the three upper segments. Following application of a sling, a purple Tri-stapler is subsequently introduced via the posterior port. The bronchi to the three upper segments are closed with the stapler and the left lung is inflated by the anesthesiologist. The borders of the segments are visualized and the level of division is confirmed, allowing subsequent division of the bronchus. Hilar lymph nodes are removed, followed by stapling with a purple or black Tri-stapler along the borders of the segments. The port protector is removed and the segment is removed in a protective bag.

Lymph node dissection is performed with an en-block removal of lymph nodes from station 5, 6, 7, 8. The remaining lung is inflated under water to ensure expansion and is then tested for air leak. Finally, one intercostal drain is placed through the anterior camera incision. After surgery, the patient was transferred to an intermediate ward and to the normal ward the day after.

Comments

Clinical results

The postoperative course of the patient was uneventful, with an in-hospital stay of four days. Final pathology revealed another primary lung cancer (adenocarcinoma 11 mm T1aN0M0, stage Ia). She was scheduled for follow up with CT scans for the next five years.

Advantages

The Copenhagen anterior approach for a VATS segmentectomy represents a standardized, effective approach to VATS lobectomy, with secure access to the mains vessels in the hilum. In case of conversion, the anterior utility incision can be expanded to a muscle sparring anterior thoracotomy within few minutes. The utility incision allows for bi-digital palpation of even small tumors deep in the lung parenchyma, making it easier to secure sufficient resection margin in segmentectomies.

Caveats

Since the approach is anterior, difficulties can occur during exposure of the posterior field in superior segmentectomies of the lower lobe. Occasionally, the camera is introduced through the posterior port in these cases. Like any other procedure, there is a learning curve. However for surgeons experienced in VATS lobectomy, this approach will allow shorter operative duration compared to transition from open to VATS lobectomy (3).

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Role of segmentectomy for pulmonary metastases

Mark F. Berry

Department of Surgery, Division of Thoracic Surgery, Duke University Medical Center, Durham, North Carolina, USA

Correspondence to: Mark F. Berry, MD. DUMC Box 3652, Department of Surgery, Duke University Medical Center, Durham, North Carolina, USA. Email: mark.berry@duke.edu.

Abstract: Pulmonary metastasectomy has not been proven by randomized trials to be more effective than non-operative management, but currently has a well-accepted role for certain primary cancers, in particular colorectal cancer and sarcoma. One of the principal tenets for pulmonary metastasectomy is that all lesions are resected. A major technical difference compared to surgical management of primary lung cancer is that management of metastatic disease frequently requires the resection of multiple and possibly bilateral lesions. In addition, surgeons and patients must often consider repeat surgery for management of metachronous lesions that develop some time after a previous resection, given the nature of metastatic cancer. Therefore, surgeons must ensure complete resection of lesions with negative margins but also must be cognizant of minimizing resection of functional lung tissue as much as possible, in order to ensure that both current and future lesions can be resected while leaving patients with adequate pulmonary function. Segmentectomy is generally infrequently utilized for pulmonary metastasectomy, but has a role for lesions for which a wedge resection is technically not possible but a lobectomy is not required. Segmentectomy can be an important tool in achieving the dual goals of complete resection and impacting pulmonary function as little as possible. Using minimally invasive techniques with thoracoscopy to perform segmentectomy is associated with less short-term morbidity than thoracotomy. Although the use of minimally invasive techniques limits manual palpation and therefore potential resection of small lesions not identified by pre-resection imaging, the current literature does not suggest that these procedures should be done via thoracotomy.

Keywords: Metastasectomy; neoplasm metastasis; pulmonary surgical procedures; thoracoscopy; thoracotomy

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Introduction

The lung is one of the most common sites where metastatic disease is found for many malignancies. Some lesions are discovered due to symptoms such as pneumonia, cough, hemoptysis or pain, but most are asymptomatic and are found on routine staging or surveillance imaging (1). A pulmonary metastasis is typically a well-circumscribed nodule, found in the periphery of the lung in two-thirds of cases (2). In contrast to screening for lung cancer, computed tomography (CT) scans performed on patients with a history of a previous cancer do not have a high false-positive rate (3). A new lesion that is larger than 1 cm very likely represents a malignant process if the clinical situation does not suggest infection.

Although many malignancies can metastasize to the lungs, the most common cancers for which pulmonary metastasectomy are considered and performed are epithelial cancers, sarcoma, melanoma and germ cell tumors. The epithelial malignancies for which pulmonary metastasectomy have been reported include gastrointestinal cancers, breast cancers, urothelial cancers, gynecological cancers, head and neck cancers, and thymic cancers. In current practice, pulmonary metastases are most commonly resected in patients with sarcoma and colorectal cancer (4).

Evidence supporting pulmonary metastasectomy

Randomized trials showing that pulmonary metastasectomy improves survival compared to non-resection management have not been performed (4). At present, pulmonary metastasectomy is offered to patients based on the observation that long-term survival can be seen after resection, while long-term survival with systemic therapy alone as treatment for patients with pulmonary metastases appears extremely unlikely (2). The data that supports pulmonary metastasectomy consists of registry data and non-controlled retrospective studies. These studies typically show good survival after pulmonary metastasectomy but have selection bias as an inherent limitation, in that the patients included in these studies by definition were considered potentially resectable and therefore likely had a limited number of metastases. These patients are therefore likely to have a better prognosis than other stage IV patients who have more widespread disease, and may have experienced prolonged survival even if pulmonary metastasectomy had not been performed (5,6).

Despite the lack of randomized data, many studies have documented reasonable survival after pulmonary metastasectomy. In an analysis from the International Registry of Lung Metastases which included 5,206 patients from 18 institutions in North America and Europe who underwent pulmonary metastasectomy from 1991 to 1995, complete resection was achieved in 4,572 (88%) patients (7). The actuarial survival for patients who underwent complete metastasectomy in this cohort was 36% at five years, 26% at ten years and 22% at 15 years. A single institution study of 490 patients who underwent complete metastasectomy at the European Institute of Oncology in Milan, Italy, for a wide distribution of primary cancers from 1998-2008 also showed a very reasonable actuarial five-year survival of 46% (8). Another multi-institution retrospective review of 378 patients who underwent pulmonary resection for colorectal cancer metastases with curative intent from 1998 to 2007, an era of modern chemotherapy, showed a 3-year overall survival of 78% (9). The 5-year survival in a series of 97 patients who underwent pulmonary resection for metastatic sarcoma was 50% (10).

Factors that are associated with improved survival after resection of pulmonary metastases have also been documented. In the analysis of the 5,206 patients in the International Registry of Lung Metastases, survival after pulmonary metastasectomy was best with smaller numbers of pulmonary metastases and longer intervals between diagnosis of the primary and the metastatic diseases (7). Completeness of resection, histology and disease-free interval greater than 36 months all predicted improved survival in the analysis of 490 patients from the European Institute of Oncology in Milan (8). In this cohort, prognosis was best for patients with germ cell tumors, followed by those with epithelial tumors, while patients with sarcoma and melanoma had the worst prognosis. In the analysis of 378 colorectal cancer patients, age younger than 65 years, female gender, a disease-free interval between primary and metastatic disease less than one year, and more than three metastases were all predictors of recurrence (9).

A randomized trial investigating colorectal metastasectomy is currently being performed (4). Until the results of that trial are reported, care will continue to be driven by the data from retrospective series. The decision to proceed with surgical resection of pulmonary metastases should be a multidisciplinary one, made jointly by the thoracic surgeon and the medical oncologist (1). Given that the benefits of resection in this setting have not been definitively established, avoiding both short-term and long-term morbidity for these patients who already have a poor prognosis is critical.

Criteria and goals for pulmonary metastasectomy

Several criteria establishing whether or not pulmonary metastasectomy is reasonable have been developed (1,2). First, the primary site of disease has to be either controlled or appear controllable. In addition, complete resection of pulmonary metastatic disease has to be feasible and anticipated to be tolerated by the patient. Finally, alternative therapies that are better than resection must not be available (2).

In order to achieve complete resection of pulmonary metastatic disease, surgeons often must plan for the resection of multiple and possibly bilateral lesions. Given that a new lesion that is larger than 1 cm on CT scan is very likely to represent a malignant process in a patient with a history of previous cancer if the clinical situation does not suggest infection, surgeons must plan to find and resect all suspicious lesions at the time of metastasectomy (3). The need to plan for the resection of multiple lesions, and the need to consider that a patient may require re-resection in the future if other metachronous lesions occur make the surgical management of metastatic lesions different from the surgical management of primary lung cancer. In addition, surgical management of primary lung cancer generally requires an anatomic resection for both staging purposes and to minimize the chance for local recurrence. In contrast, surgical management of a metastatic lesion only requires complete resection of each lesion with negative margins (11). When performing pulmonary metastasectomy, surgeons therefore must completely resect all lesions with negative margins while minimizing resection of functional lung tissue as much as possible, to ensure that both current and future lesions can be resected while leaving patients with adequate pulmonary function. Ultimately, the volume of disease, the location of the lesions, and the performance status of the patient guide the surgical approach (2).

Segmentectomy for pulmonary metastasectomy

Pulmonary metastasectomy must achieve resection of all lesions both identified on imaging before surgery and found intra-operatively, while preserving as much normal pulmonary parenchyma as possible (1). In contrast to primary lung cancer as described above, an anatomic pulmonary resection for metastatic disease does not improve survival compared to wedge resection (11). Because most pulmonary metastases are located in the lung periphery, resection most often requires wedge resection of the lung parenchyma. An anatomic resection is therefore indicated only when wedge resection would not achieve complete resection (2). More extensive surgical procedures such as lobectomy and pneumonectomy are sometimes technically necessary to allow complete resection of centrally located metastases. These more extensive resections may be appropriately indicated and offer some patients the best chance for long-term survival, but must be considered carefully as patients can subsequently develop metastases in the remaining lung, which could be unresectable depending on the patients' previous resections.

Segmentectomy should be the first resection option carefully considered for all lesions that cannot be removed via wedge resection. As discussed above, pulmonary metastasectomies must accomplish the dual goals of achieving complete resection while preserving as much functional lung tissue as possible. Patients that undergo attempted complete resection of metastatic disease have been shown to have a significant loss of lung function. In 117 patients who underwent a variety of resections, the mean loss at three months after resection of percent-predicted FEV1 and percent-predicted DLCO from preoperative values was 10.8% and 9.7% respectively (12). Factors that predicted worse lung function were post-resection chemotherapy and bilateral procedures. Segmentectomy is associated with significant preservation of pulmonary function compared with lobectomy, and should be considered and explored for all lesions that do not absolutely technically require a lobectomy due to their central location (13,14).

Minimizing the amount of lung resected during metastasectomy is also important for preserving adequate functional lung tissue, as this allows the patient to undergo additional future resections if they develop metachronous lesions for which repeat metastasectomy is indicated. In the International Registry of Lung Metastases report, 20% of 5,206 patients underwent repeat resections; 5% of patients underwent three or more procedures overall (7). In addition, minimizing the extent of resection also likely improves perioperative outcomes. In the International Registry of Lung Metastases report, the operative mortality was 0.6% for sublobar resections, 1.2% for lobectomies and bilobectomies and 3.6% for pneumonectomies (7). The lack of definitive evidence proving a survival benefit to resection and the patients' overall poor prognosis in general makes it even more critical to minimize its morbidity and subsequent impact on pulmonary function.

In general, pulmonary segmentectomies can be performed safely with acceptable morbidity and mortality. The 30-day mortality was 1.1% and the overall morbidity was 34.9% in one series of 785 anatomic segmentectomy patients, 41 of whom had a metastatic lesion resected (15). The major morbidity rate was 9.3%. Of 41 patients who had a segmentectomy for a metastatic lesion, 2 (4.9%) developed a locoregional recurrence. Resection of metastatic disease was the indication for surgery in 30 patients in another series of 77 segmentectomy patients (16). The mortality in this series was 2.6% (2 patients) and the morbidity was 32.5%. The most common complications were atrial arrhythmia (10 patients, 13%), pulmonary complications (9 patients, 12%) and prolonged air leak (7 patients, 9%). In these series, the performance of all common segmentectomies was reported including superior segmentectomy, basilar segmentectomy, lingulectomy and lingular-sparing upper lobectomy. In addition, segmental resections of the individual segments of the right upper and right middle lobe were also reported. *Figure 1* shows some examples of central pulmonary metastases that were resected via segmentectomy.

Anatomic segmentectomies are generally uncommonly used in the treatment of pulmonary metastases, accounting for between 3% and 23% of all resections in several relatively large series (7-9,17-19). *Table 1* summarizes the use of segmentectomy in these series. The use of segmentectomy appears to be increasing over time, which may reflect increasing recognition of the importance of preserving pulmonary parenchyma for this disease process. Surgeons should consider segmentectomy for all cases where wedge

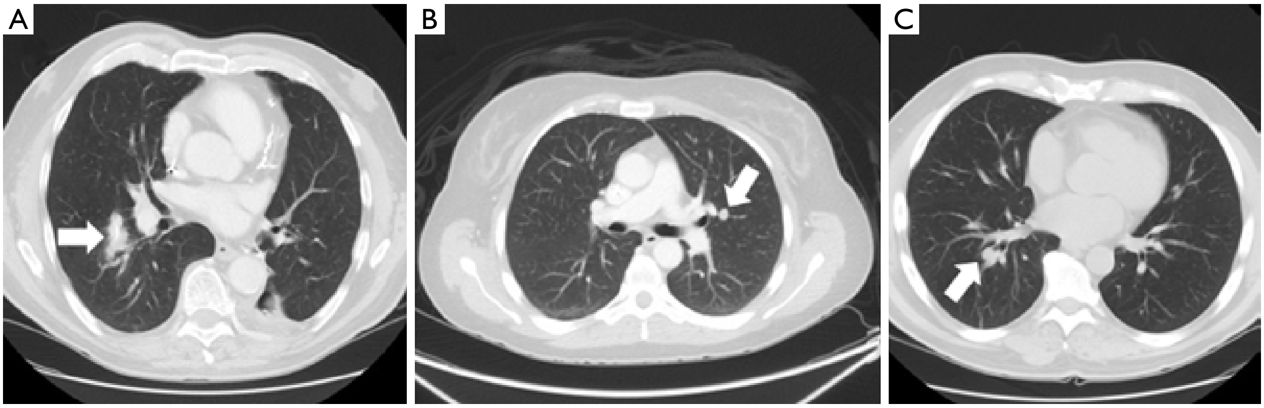

Figure 1 CT scan images of patients with pulmonary metastases that were resected via segmentectomy. (A) Colorectal metastasis (arrow) resected via right superior segmentectomy; (B) Colorectal metastasis (arrow) resected via lingular-sparing left upper lobectomy; (C) Head and neck squamous cell carcinoma metastasis (arrow) resected via right basilar segmentectomy. CT, computed tomography.

Table 1 Summary of segmentectomy use to accomplish resection in several large series of pulmonary metastasectomy

Study	Years of study	Metastatic disease source	Number of procedures	Number of segmentectomies [%]
Welter *et al*. (12)	2008-2010	Multiple	117	27 [23]
Casiraghi *et al*. (8)	1998-2008	Multiple	708	58 [12]
Onaitis *et al*. (9)	1998-2007	Colorectal cancer	378	25 [7]
Rena *et al*. (17)	1980-2000	Colorectal cancer	98	9 [9]
Pastorino *et al*. (7)	1991-1995	Multiple	5,206	449 [9]
Stewart *et al*. (18)	1969-1989	Multiple	69	2 [3]
Venn *et al*. (19)	1980-1987	Multiple	156	4 [3]

resection is not feasible. Surgeons or centers that do not perform segmentectomy should consider referral to a center that does, to ensure that patients receive optimal care when undergoing pulmonary metastasectomy.

Use of minimally invasive approach

An area that is somewhat controversial is whether a minimally invasive technique with video-assisted thoracoscopic surgery (VATS) is appropriate for the resection of pulmonary metastases. Because manual lung palpation is limited with VATS, the identification of pulmonary nodules by VATS relies heavily on the preoperative CT scan and on the ability to visualize lesions in the periphery of the lung. However, pre-resection imaging with CT scans often underestimates the number of pulmonary nodules present (1,20). Metastases that are not detected on CT scan but are found when the lung is explored are noted in 16-46% of patients (3,21-24). Thoracoscopic resection of all lesions seen on CT scan with subsequent open exploration has also revealed missed metastases in 29-56% of patients (25,26). Although improvements with CT scans over time may decrease the number of missed nodules, many surgeons feel that using a thoracotomy so that the lung parenchyma can be fully palpated is essential and a VATS approach without palpation is suboptimal (3). In fact, an investigation of approach for pulmonary metastasectomy in the European Society of Thoracic Surgery (ESTS) practice patterns showed that 65 percent of surgeons thought palpation was necessary for adequate metastasectomy (27).

However, the data supporting the need to perform manual lung palpation via thoracotomy rather than reliance on imaging to guide resection is considered to be weak (3). Although multiple well-designed non-randomized studies have consistently shown that nodules are missed without

Table 2 Results from segmentectomy series that included VATS

	Years of study	Number of patients	VATS approach	Mortality	Morbidity
Atkins *et al*. (16)	2000-2006	77	48	2.6% overall 0% VATS	VATS morbidity: - atrial arrhythmia 15% - pulmonary 10% - air leak 10%
Leshnower *et al*. (32)	2002-2009	41	15	4.8% overall 0% VATS	No morbidity reported after VATS approach
Schuchert *et al*. (15)	2002-2010	785	468	1.1% overall	Overall morbidity: - atrial arrhythmia 6.5% - respiratory failure 5.5% - pneumonia 4.5% - air leak 3.8%

VATS, video-assisted thoracoscopic surgery.

palpation, studies have not shown that missing and not resecting these tiny nodules impacts survival. Several studies have not shown that a thoracotomy approach to pulmonary metastasectomy improves survival compared to VATS, although these studies are all somewhat limited by small sample sizes (28-30). A recent review of current data, which was noted to be limited to non-randomized retrospective studies that did not fully adjust for potential confounding factors, found no difference in survival between thoracoscopic and thoracotomy approaches (31). Thoracoscopic resection of metastases was associated with improved short-term outcomes in two studies, including shorter hospital stays, shorter chest drainage duration and fewer perioperative complications (28,29). Therefore, although the use of minimally invasive techniques limits manual palpation and therefore potential resection of small lesions not identified by pre-resection imaging, an approach of relying on imaging to guide resection via VATS is considered reasonable if careful follow-up is planned so that repeat resection of newly discovered nodules can be performed (3).

A VATS approach should be considered if segmentectomy for a metastasis is planned. Using minimally invasive techniques with thoracoscopy to perform segmentectomy has less short-term morbidity than thoracotomy. VATS segmentectomy has been shown to be a safe procedure that is associated with fewer complications and a reduced hospital stay when compared with an open segmentectomy (16,32). The VATS approach can be used for all potential segmental resections (15,16). The rates of conversion from VATS to open segmentectomy have been reported as 0-6.4%, with the most common reasons for conversion cited as inadequate exposure, hilar fibrosis and bleeding (15,16). The 30-day mortality in a series of 785 segmentectomies, of which a VATS approach was used for 468 patients, was 1.1% (15). There were no peri-operative mortalities in two smaller series of VATS segmentectomies (16,32). *Table 2* summarizes several reports on the use of VATS to perform segmentectomies.

Conclusions

Pulmonary metastasectomy has a well-accepted role for certain primary cancers, in particular colorectal cancer and sarcoma, although this practice has not been proven by randomized trials to be more effective than non-operative management. However, patients have been observed to experience good long-term survival after resection of lung metastases, while long-term survival with systemic therapy alone as treatment for patients with pulmonary metastases is considered to be very unlikely. Because removal of all metastatic lesions has been consistently shown to be of great prognostic significance, surgeons must strive to remove as little lung tissue as possible while still achieving complete resection of each lesion. In this way, the patient will be able to tolerate resection of not only all synchronous disease but also possibly repeat resection if metachronous lesions develop. Segmentectomy has generally been infrequently utilized for pulmonary metastasectomy, but should be the first resection consideration if wedge resection technically cannot be performed for a lesion due to size or location. Avoiding lobectomy or even a more significant resection will allow a patient better preservation of pulmonary function, and likely allow them to tolerate resection of more lesions if necessary. Although the use of minimally invasive techniques limits manual palpation and therefore potential resection of small lesions not identified by pre-resection imaging, the current literature does not suggest that these procedures should be done via thoracotomy. Using VATS to perform segmentectomy is associated with less perioperative morbidity. However, careful follow-up surveillance imaging should be planned when manual palpation is not performed so that repeat resection of any new disease that appears can be considered.

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VATS segmentectomy for pulmonary metastasis

Kevin Phan[1], **Tristan D. Yan**[1,2]

[1]The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia; [2]Department of Cardiothoracic Surgery, Royal Prince Alfred Hospital, University of Sydney, Sydney, Australia

Correspondence to: Tristan D. Yan, MD, MS, PhD, FRACS, Professor of Cardiovascular and Thoracic Surgery, Macquarie University Hospital, Sydney, Australia; The Collaborative Research (CORE) Group, Macquarie University, 2 Technology Place, Sydney, Australia. Email: tristanyan@annalscts.com.

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Clinical vignette

We present a case of a 55-year-old man with solitary colorectal pulmonary metastasis (*Video 1*). He is an ex-smoker with near normal lung function, however positron emission tomography (PET) and computed tomography (CT) scans revealed a 2 cm glucose-avid metastasis, located in the lingular segment of the left lung. Informed consent was obtained for video-assisted thoracoscopic surgery (VATS) segmentectomy using the Edinburgh approach. The procedure provides anatomical resection and individual division of the segmental artery, bronchus and vein, as well as superior clearance of local-regional lymph nodes.

Surgical techniques

A 3 cm utility port incision is made in the seventh intercostal space in the anterior axillary line. A 1 cm posterior camera port is inserted in the auscultatory triangle to accommodate the camera. A third 1 cm access incision is made in the eighth intercostal space along the posterior axillary line.

The first step is to identify the pulmonary artery in the oblique fissure. In some patients the artery is immediately visible, but in the majority of cases, it is revealed by separating the overlying lung tissue using a kissing ‘Peanut’ technique. If the fissure is incomplete, a fissure-last approach should be considered.

The anterior aspect of the oblique fissure is divided by using a purple Covidien Tristapler. With the Edinburgh approach, the tip of the instrument is clearly visualized at all times. This will greatly improve the safety of the procedure. After dividing the fissure, which “opens like a book”, the lingular artery is now clearly exposed, which is then skeletonised and divided with a 45 mm Tristapler. The left upper lobe is retracted upwards to expose the station 11 lymph node packet, adherent to the lingular bronchus. The lingular bronchus is delineated both anteriorly and posteriorly using blunt dissection. A purple 45 Tristapler was then used to divide the lingular bronchus.

The left lung is retracted posteriorly to expose the anterior hilum, especially the confluence between the lingular and upper trisegmental veins. A blunt dissector can be used to separate these structures, followed by Tristapler division of the lingular vein. Finally, 3 purple Tristaplers were used to separate the lingular segment from the upper trisegment by passing the staplers through the anterior access incision. The specimen is carefully removed from the thoracic cavity in a retrieval bag to avoid contamination of the wounds with cancer cells.

Comments

VATS is now well established as an alternative to open thoracotomy for major resections of lung cancer and benign disease. Compared to open surgery, the minimally invasive approach has a number of benefits in the immediate post-operative period that include reduced pain, better lung function, shorter hospital stay, improved cosmesis and lower risk of developing chest infection (1). VATS lobectomy is equivalent to open surgery in terms of long-term outcomes, is less invasive and enables more patients to commence and complete postoperative chemotherapy if required. Furthermore, minimally invasive techniques are cost effective and better tolerated by our patients.

We have adopted the Edinburgh posterior approach to minimally invasive lung resection (VATS) as the surgical strategy of choice for all cases of peripheral lung cancer of 7 cm or less in diameter and for suitable benign disease. This criterion is decided according to the 'VATS Lobectomy Consensus Statement' by 50 minimally invasive thoracic surgeons worldwide (2). VATS techniques may also be used in patients with advanced disease such as moderate or central chest wall involvement and pneumonectomy for low bulk central involvement. However given the trend towards lung conservation strategies, pneumonectomy is now only considered for cases where bronchovascular reconstruction is not feasible.

In our experience, the main advantage of the Edinburgh approach is the excellent visualization of the posterior hilum, which facilitates dissection of the airways and branches of the major pulmonary artery. In the Edinburgh approach, the tips of the instruments come towards the operating surgeon and are therefore easily seen whilst in use, increasing the safety of dissection (3). More importantly, the lymph node packets are clearly seen, allowing thorough lymphadenectomy.

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Minimally invasive VATS left upper lobe apical trisegmentectomy

Harmik J. Soukiasian, Robert J. McKenna Jr

Division of Thoracic Surgery, Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, California, USA

Correspondence to: Robert J. McKenna Jr, MD. Third St, Suite # 240E, Los Angeles, California, USA. Email: Robert.mckenna@cshs.org.

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Clinical vignette

The patient is a 75-year-old female with a 40-pack-year smoking history. Low dose lung screening computed tomography (CT) scan found a 1-cm left upper lobe (LUL) mass. The patient denies any hemoptysis, weight loss, bone pain or neuro status changes. Her pulmonary function tests are not normal. Her pulmonary function tests demonstrated that the forced expiratory volume (FEV_1) was 58% of predicted FEV_1 and 80% of predicted diffusion lung capacity (DLCO). A lingular sparing LUL apical tri-segmentectomy was thus planned.

Surgical techniques

Preparation

The patient is intubated with a dual lumen endotracheal tube. The left lung is then isolated. The patient is positioned on a beanbag in the right lateral decubitus position, with the left side up. The break in the table is between the level of the nipples and the iliac crest.

Exposition

Four incisions are made.

1st incision (2 cm): inferiorly and medial, one space below mammary crease, generally in the 6th intercostal space and tunneled posteriorly. A finger is placed into the thoracic cavity and the costophrenic angle palpated.

2nd incision: mid axillary line, between 8th or 9th intercostal space. A 5-mm trocar is placed through the space to accommodate the 5-mm, 30-degree thoracoscope.

3rd incision (4-5 cm): utility incision is made in the intercostal space directly over the level of the superior pulmonary vein. This incision is 4 cm and is started on the anterior border of the latissimus muscle and extended anteriorly. A wound retractor is placed in this incision to keep the tissues from co-apting and causing a vacuum during the use of the suction device.

4th incision: four fingers below tip of the scapula, halfway to spine in the auscultatory triangle.

Operation

The thoracoscope is inserted and the hilum is exposed. The level 5 & 6 lymph nodes are dissected free. The lung is retracted laterally and posteriorly through the posterior and the anterior incisions. The Vagus and recurrent laryngeal nerve are identified and preserved. Dissection is carried out along the superior border of the superior pulmonary vein as far up onto the hilum as possible, generally until the descending aorta is visualized. This will help in freeing the superior aspect of the anterior trunk of the pulmonary artery. The superior pulmonary vein is inspected and care is taken to ensure that a common trunk is not present. The lingular vein is identified and preserved. The veins draining the superior segment are isolated. A stapler is passed from the 4th incision below the scapula and the veins transected.

The lung is now pulled inferiorly to help expose the anterior trunk of the pulmonary artery. Lymph nodes present on the LUL bronchus must be dissected free. This node dissection will in turn aid visualization of the anterior trunk and allow for safer dissection of the plane between the bronchus and the anterior trunk. The plane between the bronchus and the anterior trunk is established. A stapler is passed from the 4th incision below the scapula and the anterior trunk is transected. The second branch is often visible from this exposure and may be taken at the same time as the anterior trunk.

Through the posterior incision, the lung is now positioned superiorly and slightly anteriorly. There will often be a slight notch in the periphery that can aid in identifying where the fissure should be, between the apical trisegment and the lingula. The pulmonary artery is identified in the hilum/fissure. A stapler passed through incision 1 separates the lingula from the apical trisegment to the level of the hilum. Blunt dissection is used to create a tunnel between the artery and the rest of the fissure. The lung parenchyma is lifted away from the artery, exposing the tunnel created on top of the artery. A stapler is passed through incision 1 and the fissure is transected. This is repeated until the fissure is completely transected. The lingual and the posterior segment are rolled forward onto the stapler anvil which is held in place and not advanced. The lingular artery is identified and preserved. This in essence duplicates a division of the fissure between the lingual and the upper division from posterior to anterior.

The lung is then returned to its anatomic position and the lingula is retracted superiorly and anteriorly via the posterior port. The pulmonary artery is again identified and now dissected in the fissure to expose the upper lobe arterial branches. Then the lingular artery is identified and kept safe. The stapler is passed from incision 1 and the artery to the posterior segment is divided, taking care not to injure the lingular artery. Careful inspection is carried out to ensure all arterial branches to the apical trisegment have been transected. If any remain they may be transected either from incision 1 or 4, depending on which incision allows for the safest angle of approach.

The lung is now retracted anteriorly to help expose the bronchus. The bronchus is dissected towards the lung parenchyma until the carina between the upper division and the lingula is identified. A stapler passed from incision 1 is used to transect the upper division bronchus, while taking care to preserve the lingular bronchus.

Completion

Upon division of the segment, it will be placed in a large Cook brand lap sack and removed via the utility incision (#3 incision). Local anesthetic is used to accomplish intercostal nerve blocks from T2-T8. Chest tubes are placed. The incisions are then closed in three layers.

Comments

Clinical results

We evaluated the results of our institutional outcomes for VATS trisegmentectomy (1). A total of 73 VATS trisegmentectomies were performed between 1998 and 2010. The average age was 72 years old; 49 female, 24 male. Diagnoses for the trisegmentectomies included: primary lung cancer 91% (66/73), benign disease 4% (3/73) and metastatic disease 5% (4/73). Of the patients undergoing VATS trisegmentectomy for primary lung cancers, 68% (45/66) were for stage IA, 17% (11/66) were for stage IB, 15% (10/66) were for stage 2 and above. A total of 73 LUL trisegmentectomies were performed. The mean hospital stay for patients undergoing VATS trisegmentectomy was 3.8 days (SD =3.3) *vs*. 5.5 days (SD =7.9) for VATS LUL lobectomy $P=0.0736$ ($P>0.05$). There was no statistical difference in overall complication rates between the two groups. There was also no difference in survival between patients undergoing VATS trisegmentectomy and those undergoing LUL lobectomy for either stage IA lung cancer or stage IB lung cancer.

Advantages

We believe that segmentectomy can be performed by VATS with no more morbidity or mortality than that for VATS lobectomy (1,2). Additionally, LUL trisegmentectomy provides the same chance of survival as lobectomy for stage IA and IB tumors (1,3). Transecting parenchyma for the segmentectomy does not translate into a longer stay than post lobectomy (1,4). The lingula does not need to be resected for small apical lung cancers, as LUL trisegmentectomy provides the same survival as lobectomy for stage IA and IB tumors (1-5). Our experience supports the use of lingula-sparing trisegmentectomy in the treatment of IA and IB lung cancer.

Caveats

The biggest concern for a cancer operation is survival rates. In our series, the overall survival was the same for the segmentectomies and the lobectomies. That rate however, can be affected by many factors, including staging and comorbidities. Some studies have shown better survival with lobectomy, however the debate continues in regards to optimal approaches.

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Totally thoracoscopic left upper lobe tri-segmentectomy

Dominique Gossot

Thoracic Department, Institut Mutualiste Montsouris, Paris, France

Correspondence to: Dominique Gossot. Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, Paris, France. Email: dominique.gossot@imm.fr.

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With continued growing interest in sublobar resections from the international surgical community (1,2), mastering thoracoscopic segmentectomy is an important challenge for the surgeon. With respect to sublobar resections of the left upper lobe, it is now considered that for T1 tumors, a lingual-sparing upper lobectomy is oncologically equivalent to an upper lobectomy (3).

The main segmental resections involving the left upper lobe are: tri-segmentectomy (S1 + S2 + S3) (lingula-sparing lobectomy), apicoposterior segmentectomy (S1 + S2) and lingulectomy (S4 + S5). In this article, we will describe the technique of a full thoracoscopic approach and illustrate it with a video. Lymph node dissection is similar to lymphadenectomy for an upper lobectomy and hence will not be described here.

Clinical summary

The presenting case is a 66-year-old female patient who had an incidental finding of a nodule during follow-up of a severe chronic obstructive pulmonary bronchitis. The nodule was 1 cm in diameter and was located at the junction between the posterior and apical segments of the left upper lobe (*Figure 1*). PET-CT revealed an isolated tumor (SUVmax: 2.7). As the patient was fragile and had a FEV1 of 61% predicted, it was decided to perform a sublobar resection.

Anatomical landmarks

The landmarks are obtained from CT-scans with 3-dimensional reconstruction (*Figure 2*). The use of CT reconstruction can be helpful at the beginning of a thoracoscopic experience (4,5).

Bronchi

The segmental bronchi are concealed by arteries which must be divided first (*Figure 2A*). The upper lobe bronchus

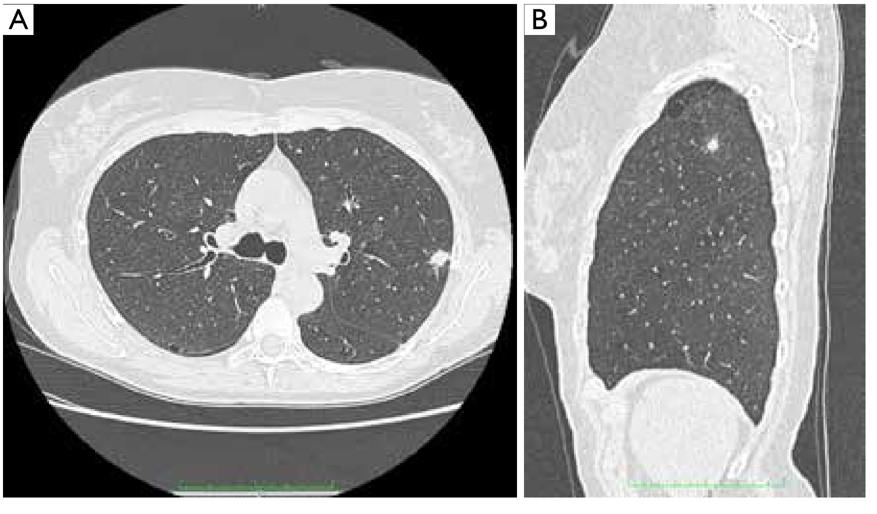

Figure 1 Preoperative CT-scan.

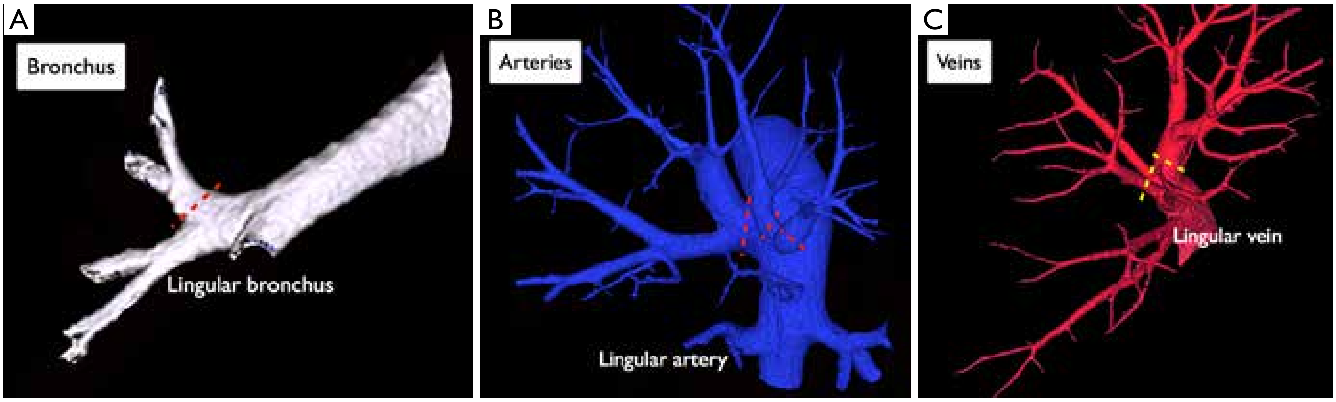

Figure 2 Anatomical landmarks. (A) Bronchi; (B) Arteries; (C) Veins. Dotted lines: level of division.

splits immediately into the lingular bronchus and a common stem which separates into an anterior bronchus and an apicoposterior bronchus. These segmental bronchi have short courses which can make their dissection and identification difficult.

Arteries

The truncus anterior, posterior and lingular arteries supply the left upper lobe (*Figure 2B*). The truncus anterior is often broad and short and supplies the apico-posterior and anterior segments. The posterior segmental arteries originate in the fissure and distribute themselves over the curve of the pulmonary artery. Their number varies from 1 to 5, but most often from 2 to 3. All but the lingular artery, must be divided.

Veins

The superior pulmonary vein usually has three major tributaries (*Figure 2C*). The superior branch drains the apicoposterior segments and frequently blocks access to the apicoposterior arteries. The middle branch drains the anterior segment and the lowermost branch drains the lingula. The latter must be preserved.

Technique

The procedure is performed under general anesthesia with split ventilation using a double-lumen endotracheal tube. Patients are positioned in the right lateral decubitus position. We use a deflectable scope housing a distal CCD (LTF, Olympus, Tokyo, Japan) connected to a high definition camera system (HDTV) (Exera II, Olympus, Tokyo, Japan). Only endoscopic instruments are used. These are inserted through 3 to 4 trocars, depending on whether an additional lymph node dissection is performed. Ports are inserted as indicated in *Figure 3*.

The procedure is similar to a left upper lobectomy, sparing the lingular vessels and the anterior portion of the fissure.

Step 1: division of the fissure and arteries

The lobes are separated to expose the middle portion of the fissure. The upper lobe is gently pulled forward, avoiding any undue traction which could injure the vessels. Dissection is conducted cephalad and all encountered posterior arteries are divided by turn. Traction helps exposing the first segmental artery whose dissection is usually easy. It is controlled by clipping, with a vessel sealing device or with a combination of both.

As the posterior segmental arteries are sequentially divided, the upper lobe unfolds and uncovers the posterior aspect of the truncus anterior which can be approached posteriorly. It is then also dissected from above and from the front, using various views thanks to the deflectable scope. Gentle blunt dissection is used to clear the origin of the trunk. If the trunk bifurcates into two large branches, these are dissected with caution and stapled independently.

An inferior branch of the truncus anterior is present in one-quarter of patients (*Figure 4*). It is usually impossible to predict whether this branch supplies the anterior segment or the lingula or both. When in doubt, it is advisable to preserve it.

Step 2: division of the segmental veins

The upper lobe is retracted posteriorly. The mediastinal

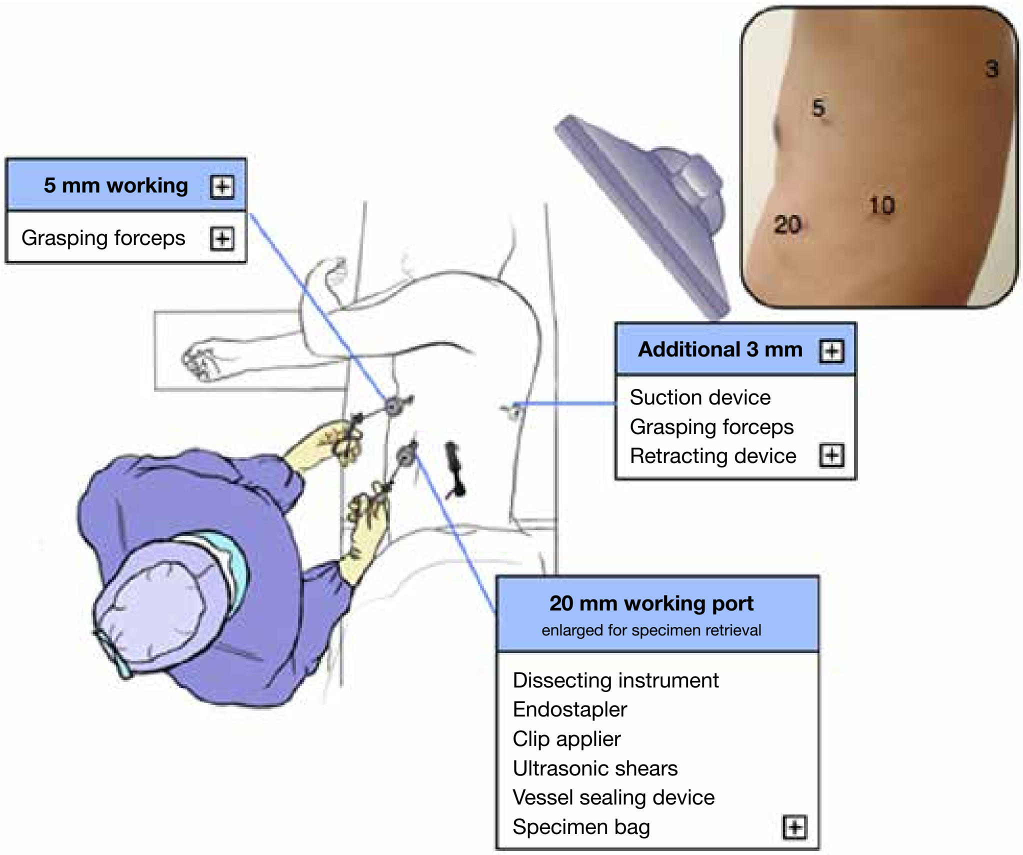

Figure 3 Ports for totally thoracoscopic left upper lobe tri-segmentectomy.

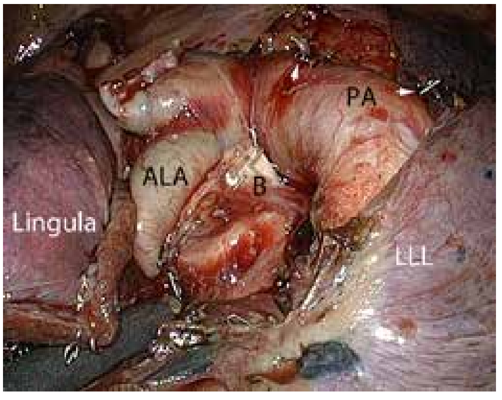

Figure 4 Accessory lingular artery arising from the truncus anterior. ALA, accessory lingular artery; PA, pulmonary artery; B, bronchial trunk; LLL, left lower lobe.

pleura is then incised posterior to the phrenic nerve. Dissection of the vein is achieved by a combination of blunt dissection and bipolar electrocautery. Only the two superior branches are divided using either a stapler, or clips or a vessel sealing device, depending on their diameter. The inferior tributary which drains the lingula is preserved (*Figure 5*).

Step 3: division of the bronchial trunk and parenchyma

Once the arteries and veins have been divided, traction on the parenchyma helps to expose the segmental bronchi. The origin of the lingular bronchus is visualized and the upper trunk—which separates into an anterior bronchus and an apico-posterior bronchus—is exposed, cleared using a blunt tip dissector and stapled as a stem (*Figure 6*).

The parenchyma must be stapled between the lingula and the upper division. A clamp is applied on the parenchyma, the lung is reventilated to identify the intersegmental plane and the parenchymal division is then performed using an endostapler loaded with thick-tissue staples.

The specimen is removed in the usual fashion and the inferior pulmonary ligament is divided.

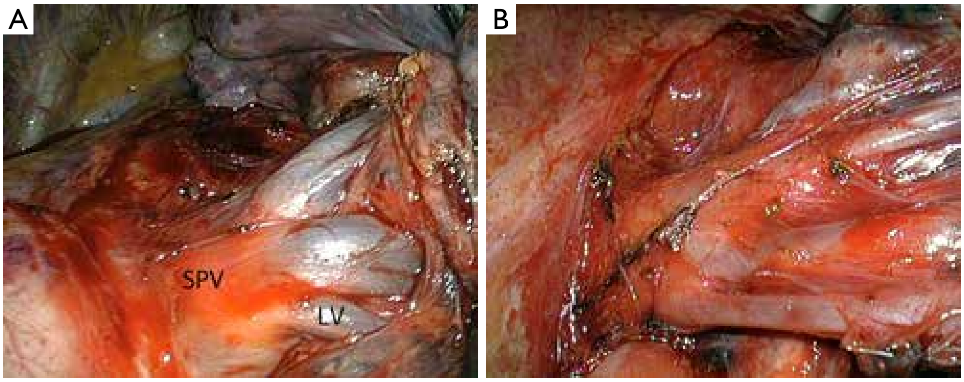

Figure 5 Exposure of the superior pulmonary vein. (A) Normal distribution; (B) Multiple branches. SPV, superior pulmonary vein; LV, lingular vein.

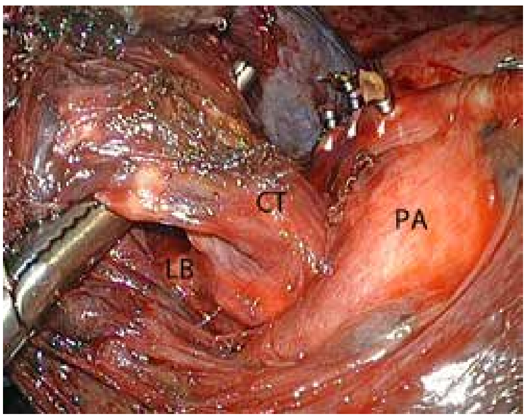

Figure 6 Exposure of the bronchus. CT, common bronchial trunk; LB, lingular bronchus; PA, pulmonary artery.

Comments

A left trisegmentectomy is similar in conduct to a right upper lobectomy. However, control of the truncus anterior may be more difficult on the left side because there are more anatomical variations and because the artery can be short.

Possible risks of the procedure are as follows:

- ❖ Inadvertent injury of the lingular vein when the distribution of the superior pulmonary vein comprises multiple small branches, as shown in *Figure 5B*;
- ❖ Twisting of the lingular segments when the anterior part of the fissure is loose. If in doubt, the lingula must be anchored to the lower lobe;
- ❖ Confusion between the anterior bronchus (B3) of the common trunk and the lingular bronchus;
- ❖ Ignorance of an accessory lingular artery that could be mistaken for a branch of the truncus anterior (*Figure 4*).

Some authors advocate against using stapling for division of the parenchyma because this can impair the expansion of the lingular segments (6). As shown in the video, this has not been an issue in our practice. Although stapling can slightly reduce the volume of the lingula, it has the major advantage of minimizing postoperative air leaks. In our series of 129 thoracoscopic segmentectomies, with stapling of the intersegmental plane, the mean postoperative stay was 4.9 days and only one patient had a prolonged air-leak. Miyasaka *et al*. failed to demonstrate a difference in postoperative complications and pulmonary function, between stapling of the intersegmental plane and division with electrocautery (7).

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Totally thoracoscopic pulmonary anatomic segmentectomies: technical considerations

Dominique Gossot, Rym Zaimi, Ludovic Fournel, Madalina Grigoroiu, Emmanuel Brian, Charles Neveu

Thoracic Department, Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France

Correspondence to: Dominique Gossot. Thoracic Department, IMM, 42 Bd Jourdan, F-75014 Paris, France. Email: dominique.gossot@imm.fr.

Background: While video-assisted thoracic surgery (VATS) lobectomies are being increasingly accepted, VATS segmentectomies are still considered as technically challenging. With the renewed interest for sublobar resection in the management of early stage lung carcinomas, the thoracoscopic approach may have a major role in a near future. We report our technique and results.

Patients and methods: Totally thoracoscopic anatomic segmentectomiy, i.e., using only endoscopic instrumentation and video-display without utility incision, was attempted on 117 patients (51 males and 66 females), aged 18 to 81 years (mean: 62 years). The indication was a clinical N0 non-small cell lung carcinoma in 69 cases, a solitary metastasis in 17 cases and a benign lesion in 31 cases. The following segmentectomies were performed: right apicosuperior [26] right superior [10], right basilar [18], lingula sparing left upper lobectomy [15], left apicosuperior [11], lingula [7], left superior [14], left basilar [13] and subsegmental resection [3]. Segmentectomy was associated with a radical lymphadenectomy in 69 cases.

Results: There were 5 conversions to thoracotomy. The mean operative time was 181±52 minutes, the mean intraoperative blood loss was 77±81 cc. There were 12 postoperative complications (11.7%). The median postoperative stay was 5.5±2.2 days. Out of the 69 patients operated on for a cN0 lung carcinoma, 6 were finally upstaged.

Conclusions: Totally thoracoscopic anatomic pulmonary segmentectomies are feasible and have a low complication rate.

Keyword: Segmentectomy; thoracoscopy; video-assisted thoracic surgery (VATS)

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Video-assisted thoracic surgery (VATS) and thoracoscopic major pulmonary resections are accepted as a valid alternative to open surgery as it is now evident that minimally invasive surgery is beneficial in terms of reduced postoperative pain, shorter hospital stay, shorter recovery and better compliance to adjuvant chemotherapy, without compromising oncological principles (1). However few series of video-assisted pulmonary segmentectomies have been published and totally endoscopic-so-called complete VATS-segmentectomies series are even more infrequently reported (2,3). Many different techniques of thoracoscopic major pulmonary resections have been described, depending on the use of an accessory mini-thoracotomy, endoscopic instrumentation, and, video display. In the totally endoscopic approach only endoscopic instruments and monitor visualization are used. This is the technique that will be described in this article (4). By totally endoscopic we mean: (I) 100% video display; (II) no access incision and (III) only use of trocars and endoscopic instruments (5) (*Figures 1,2*). The aim of this article is not to discuss the oncologic validity of segmentectomies for early stage lung carcinomas but to describe and discuss some technical aspects and the results of totally thoracoscopic anatomic segmentectomies (TTAS).

Patients and methods

From January 2008 to January 2013, TTAS was attempted in 117 patients (51 males and 66 females) ranging in age from

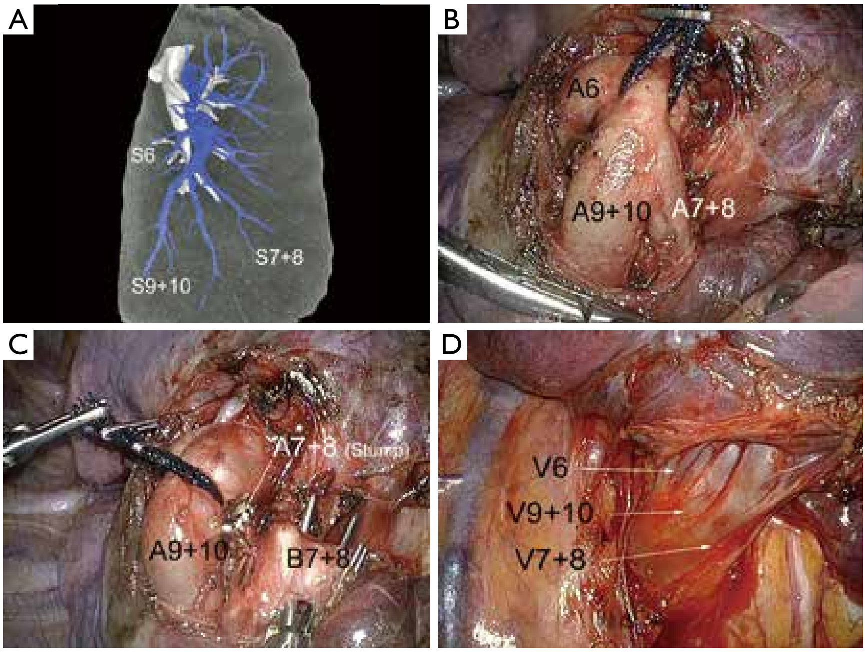

Figure 1 Main steps of a right anterior basilar subsegmenectomy of segments 7+8. A. Three-dimensional reconstruction of arteries and bronchi; B. a loop is passed around the main basilar arterial trunk and helps exposure of the arterial branches; C. after division of the artery to the anterior segments, backward traction of the loop helps exposing the bronchus to segments 7+8; D. segmental distribution of the branches of the right lower pulmonary vein. (A, artery; B, bronchus; V, vein; S, segment).

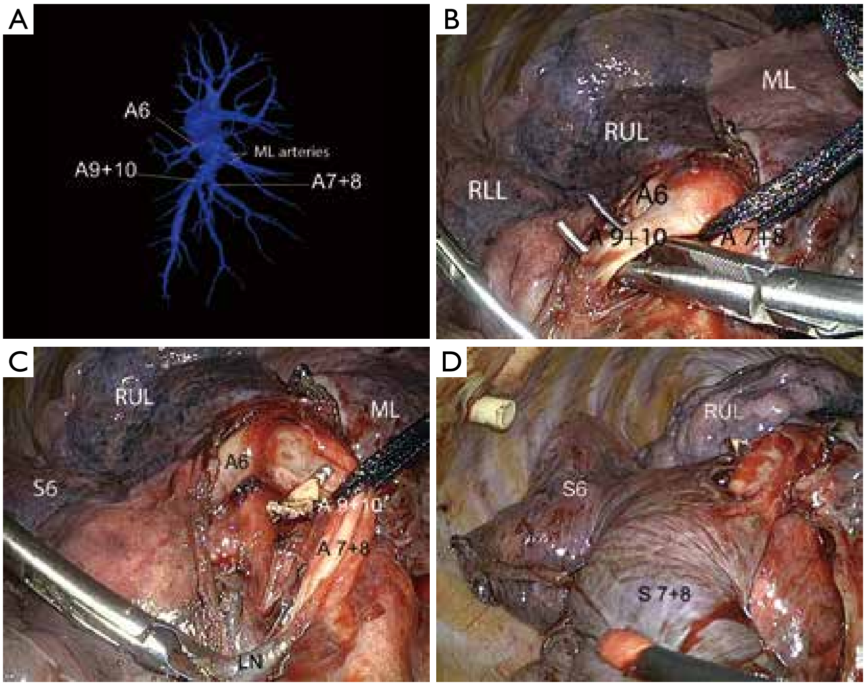

Figure 2 Main steps of a posterior subsegmenectomy of segments 9+10. A. Three-dimensional reconstruction of arteries; B. Dissection of the artery to the posterior segments; C. after division of the artery to the posterior segments, forward traction of the loop helps exposing the bronchus to segments 9+10; D. final aspect before reventilation after removal of the posterior segments. (RUL, Right upper lobe; ML, middle lobe; A, artery; B, bronchus; V, vein; S, segment).

Table 1 Resected segments (112 patients)

Right	N	Left	N
Apicoposterior (S1+2)	26	Upper division (S1+2+S3)	15
Superior (S6)	10	Apicoposterior (S1+2)	1
Basilar segments (S7-10)	18	Lingula (S4+5)	7
Posterior Basilar segments (S7-8)	1	Superior (S6)	14
Anterior Basilar segments (S9-10)	2	Basilar segments (S7-10)	13

18 to 81 years (mean: 62 years). The indication was either a benign lesion (31 patients), a solitary metastasis (17 patients), or a suspicion of clinical stage I non-small-cell lung carcinoma (NSCLC) (69 Patients). The reason for performing a segmentectomy for an NSCLC was an impaired lung function and/or a previous history of pulmonary resection, clinical stage IA in fragile patients or carcinoid tumor.

Patients' consent was routinely obtained. Intraoperative and postoperative data were recorded in a prospective manner into a database that was approved by our Institutional Review Board. The variables entered in the database were the following: need for conversion to thoracotomy, duration of the surgical procedure as noted on the operating room records, operative blood loss, intraoperative complications, number of collected lymph nodes and of dissected lymph node stations for patients operated on for NSCLC, duration of chest drainage, postoperative stay and postoperative complications. The types of segmentectomy are specified in *Table 1*.

Technical aspects

We have previously described our technique in detail (Gossot, 2010#53). In brief, the procedure was performed under general anesthesia with split ventilation using a double-lumen endotracheal tube. Patients were positioned in lateral decubitus as for a thoracotomy. The surgeon stood anterior or posterior to the patient, depending on the segments to be resected. He usually stood posterior to the patient for right sided resections and anteriorly for left sided ones. Two monitors were used and the thoracoscope was placed on a mechanical scope holder. In a fashion similar to our technique of totally endoscopic lobectomies, we used a deflectable thoracoscope housing a distal CCD (LTF, Olympus, Tokyo, Japan) (6) connected to a high definition camera system (HDTV) (Exera II, Olympus, Tokyo, Japan). Only specifically designed endoscopic instruments for VATS major resections were used. As a rule, trocars with a diameter ranging between 3 mm (micro-instruments) and 15 mm (endostapler and retrieval bag were utilized). For lung cancer patients, intersegmental lymph nodes, when present, were analyzed by frozen section to confirm the indication for segmentectomy. Larger vessels were divided with endostaplers while haemostasis of small caliber vessels was performed with clips, with a bipolar vessel sealing device (LigaSure™, Valleylab, Boulder, CO, USA) or with a combination of both methods. The root of the intersegmental veins was preserved and used as landmark for identification of the intersegmental plane. Demarcation between the resected and preserved segments was usually made possible by gentle reventilation and adequate application of a long 5-mm lung forceps whose position was adapted according to the inflation-deflation line. The intersegmental plane was divided by a combination of bipolar sealing device (for its peripheral and thin portion) and stapling (for its central and thick portion) using 4.8 mm staples (Endo-GIA II, Covidien Autosuture, Mansfield, MA). When the remaining segment was mobile and at risk of torsion, it was anchored to the adjacent lobe with a TA endostapler. An additional radical lymphadenectomy was performed for all patients operated on for a suspicion of lung carcinoma, according to a previously described technique (7). No utility incision was used. On completion of the pulmonary resection, the specimen was wrapped into an endobag and retrieved through one of the port sites that was enlarged to a length of 2 to 4 cm, depending on the specimen size. The use of a rib spreader was never required for specimen extraction. In most cases, only 1 chest tube was placed through one of the port site. Its removal was decided according to usual rules, i.e., no air leakage and output inferior to 200 cc per day.

Results

There were 5 conversions to thoracotomy (4.2%) for a fused fissure (2 cases) and for non-controllable hemorrhage (3

Table 2 Postoperative complications (112 patients)

None	100
Segmental ischemia requiring reoperation	2
Prolonged air leak (>5 days)	3
Pneumothorax requiring chest drainage	1
Sputum retention requiring bronchoscopy	2
Neurologic disorder	1
Pulmonary embolism	1
Pulmonary oedema	1
Arythmia	1

Table 3 Final pathological diagnosis (112 patients)

Primary malignant	69
Adenocarcinoma	33
Squamous cell carcinoma	3
Carcinoid tumor	9
Metastasis	17
Benign	31
Bronchectasia	3
Aspergillosis	2
Mucormycosis	1
Tuberculosis	1
Bronchial atresia	5
Bulla	1
Other benign conditions	6

cases). In 1 of these hemorrhagic complications, the planned right apicoposterior segmentectomy was finally converted into an upper lobectomy. All 5 patients had a simple postoperative course. In the 112 other patients who had a totally thoracoscopic procedure, there were 3 intraoperative complications, i.e., a partial disruption of the staple line during division of the intersegmental plane requiring endoscopic suturing. The postoperative course of these 3 patients was simple and they were discharged between postoperative day 4 and 5. Operative time ranged from 87 to 315 minutes (mean, 181±52 minutes). The estimated blood loss ranged from 0 cc (non-measurable) to 450 cc (mean, 77±81 cc). No patient needed blood transfusion. All but 12 patients had an uneventful postoperative course (90%). Complications are listed in *Table 2*. Out of the 12 complications, 10 were minor whereas 2 were major, i.e., requiring a reoperation. These 2 patients had an ischemia of the remaining lingula after a lingula sparing left upper lobectomy. They underwent a lingulectomy by thoracoscopy (1 patient) or by thoracotomy (1 patient), with a simple postoperative course. The drainage duration ranged from 1 to 7 days (mean, 3.3±1.9 days) and the hospital stay from 2 to 22 days (mean, 5.5±2.2 days). The final pathological results are listed in *Table 3*. For the 69 patients who were operated on for a suspicion of primary lung carcinoma and who had an additional lymphadenectomy, the mean number of removed hilar lymph nodes (station 10) ranged from 0 to 6 (mean, 3±2) and from station 11-12 ranged from 1 to 9 (mean, 3±2) was. The mean number of collected mediastinal lymph nodes was 21±7 and the mean number of dissected lymph node stations was 3.5±1. For patients operated on for lung cancer, the tumors were staged pathological N0 in all but 2 cases which were upstaged N1 and 4 cases which were upstaged N2.

Discussion

Anatomical landmarks

Segmentectomy is considered a challenging procedure if done by thoracotomy and even more so if it is performed thoracoscopically (2). Not only the anatomical relationships are difficult to grasp, especially for the young and less experienced surgeons, but the identification and division of the intersegmental plane is a concern. The issue is more relevant for upper segmentectomies. Not only the number of arteries arising from the pulmonary artery is variable but their distribution is sometimes difficult to appreciate because the vessels can usually not been dissected to a sufficient length. This is especially true for the ascending arteries to the right upper lobe. These arteries can supply only the posterior segment of the upper lobe or both the posterior and anterior segments. The study of preoperative computed tomography three-dimensional reconstruction helps assessing the number, size and direction of these arteries without doubt (8). Having the vascular pattern in mind helps the surgeon performing a safer dissection of the branches of the pulmonary artery, especially when the fissure is fused and/or when lymph nodes are present. In a series of 49 patients selected for VATS lobectomy, Fukuhara *et al.* found that preoperative three-dimensional computed pulmonary angiography was identifying the PA branches in 95% of the cases (9). In their series, only some small branches (less than 2 mm in diameter) were missed. In the beginning of our experience, most patients

Table 4 Technical data available for published series of VATS or totally thoracoscopic segmentectomies

First author	N	VATS/TT	Number of trocars	Utility incision (cm)	Optics	Op. Time* [min]	Op.Blood loss* [mL]	Division of intersegmental plane
Shiraishi 2004 (13)	34	TT	6	None	Rigid 30°	240±72	169±68	Ultrasonic shears
Okada (14)	102	VATS	2	4-8	NS	129 [60-275]	50 [10-350]	Electrocautery + fibrin sealant
Atkins (15)	48	VATS	1	4	NS	136±45	250±200	Stapling
Oizumi (16)	29	TT	4	None	Rigid 30°	216 [146-425]	100 [3-305]	Stapling
Schuchert (17)	104	VATS	3	4	Rigid 0°	136 [120-152]	171 [133-209]	Stapling
Watanabe (11)	41	VATS	2	4 (3.5-6)	NS	220 [100-306]	183 [30-770]	Electrocautery + Stapling + fibrin sealant
Shapiro (18)	31	VATS	2	NS	NS	NS	NS	Stapling
Leshnower (19)	15	VATS	3	NS	Rigid 30°	145±55	NS	Stapling
Yamashita (20)	90	TT	4	None	Rigid 30°	257±91	132±181	Stapling
This series	117	TT	4-5	None	Deflectable			Stapling

N, number; VATS, video-assisted thoracic surgery; TT, totally thoracoscopic; cm, centimeter; min, minutes; mL, milliliter; NS, Not stated; *, expressed as mean and range or mean ± standard deviation.

candidate to an upper segmentectomy had a multidetector row preoperative computed tomography (CT) angiography with three-dimensional volume-rendering reconstruction of arterial and venous anatomy. Nevertheless, CT reconstruction was not done for the lower segments since anatomical variations of the vascular supply to the lower lobes has less impact on the surgical technique and can be easily managed (8-10). As we felt more confident with the technique and the thoracoscopic vision of anatomical landmarks, the resort to preoperative CT reconstruction was progressively abandoned.

Intersegmental plane

Another difficulty faced during thoracoscopic segmentectomy is the identification and division of the intersegmental plane. When performed through a thoracotomy, this step is facilitated by the use of manual palpation which is not possible via thoracoscopy. Several methods have been described. The most common is the creation of a ventilated-deflated line by reventilating the operated lung once the segmental bronchus has been stapled. This technique has drawbacks: (I) reventilation obscures the vision and this is a much more troublesome problem than during thoracotomy; (II) the segments to be resected can be partly reventilated through the collateral canals, leading to an unclear demarcation line. Therefore some authors have suggested acting reverse, i.e., reventilating the whole lung once the segmental bronchus has been divided and then collapsing it, so that only the diseased segments remain inflated (11). Others have suggested using selected jet ventilation in the segmental bronchi to be divided (12). In emphysematous patients we have used a similar method by injecting air through the channel of a bronchofiberscope, after selective endoscopy of the segmental bronchus.

Once the intersegmental plane has been determined, the last issue is the choice of the division method. Some authors have used a combination of blunt dissection, electrocautery and application of fibrin sealant (12). When air leaks were observed, some surgeons applied mattress suture with pledgets (12). These methods have the advantage of sparing parenchyma, but comprise a risk of postoperative air leak. Actually, most authors use staplers (*Table 4*). Stapling is however not that easy. First, it may require using many cartridges, up to 5 in the series of Watanabe (11). Second, the limited opening of the endostaplers and the thickness of the parenchyma expose to disruption of the staples line, an adverse event that occurred twice in our series. The consequences were not serious but leaded to troublesome blood loss and required hand suturing.

Segmental ischemia

In our series, 2 patients had to be reoperated for an ischemia

Table 5 Results for published series of VATS or totally thoracoscopic segmentectomies

First author	N	VATS/TT	Conversion rate	Morbidity	Chest tube duration* [days]	Postoperative. stay* [days]
Shiraishi (13)	34	TT	0%	11.7%	4.5±3.2	12.7±3.6
Okada (14)	102	VATS	NS	9.8%	1	NS
Atkins (15)	48	VATS	0%	31.3%	3.5±4	4.3±3
Oizumi (16)	29	TT	0%	10%	1 [1-7]	NS
Schuchert (17)	104	VATS	NS	26%	NS	5
Watanabe (11)	41	VATS	0	10%	3 [1-9]	NS
Shapiro (18)	31	VATS	13%	26%	2 [1-33]	4 [1-98]
Leshnower (19)	15	VATS	0%	0%	2.8±1.3	3.5±1.4
Yamashita (20)	90	TT	4.8%	19%	4.8.±3.4	12.2±8.2
This series	117	TT	4.3%	11.7%	3.3±1.9	5.6±2.4

N, number; VATS, video-assisted thoracic surgery; TT, totally thoracoscopic; NS, Not stated; *, expressed as mean and range or mean ± standard deviation.

of the lingula after an upper division of the left upper lobe. In one case, it was unclear whether ischemia was related to the torsion of the remaining segment or to an injury of the lingular vein, while torsion was obvious in the second case. This complication has been reported by others (21).

Although the thoracoscopic approach offers a clear and magnified view, one of its limitations is the difficulty in obtaining a global vision of the operative field, especially as the lung is reinflated. Therefore, a wrong positioning of the remaining segment can be overlooked. In addition, securing the segment to the adjacent lobe by thoracoscopy is not that easy. When performed by thoracotomy, it is usually done by applying anchoring stiches on a partially reventilated parenchyma. This is almost impossible to perform by thoracoscopy due to the lack of space caused by reinflation of the lung. We have overcome this difficulty by applying 1 or 2 cartridges of staples, using an endostapler with no knife (Endo-TA, Covidien). Thorough examination of the remaining segment is required to avoid mispositioning. Should a reoperation be necessary, it can be performed by re-thoracoscopy (22), as occurred in one of our patient.

Lymph node dissection

Several works dealing with the issue of the validity of lymph node dissection during VATS lobectomy and segmentectomy have been recently published. Basing on a cohort of 14,473 patients, Whitson *et al*. have shown that survival was less after segmentectomy than after lobectomy, even for T1a tumors (23). This was confirmed by the work of Wolf *et al*. (23), but these authors demonstrated that survival was not statistically different between lobectomy and segmentectomy if a lymph node dissection was performed (24).Therefore, the quality of lymph node dissection during segmentectomy for lung cancer is most likely a crucial part of the procedure. Recently, Hattori *et al*. showed that the rate of positive lymph nodes was high for solid T1A tumors especially in case of high standardized uptake value (SUV_{max}). They advocate for a thorough intraoperative evaluation of lymph nodes to prevent locoregional recurrence (25). However, it seems that lobar and segmental lymph node clearance is a weak point of the thoracoscopic approach for sublobar resection. Boffa *et al*. have demonstrated that nodal upstaging form cN0 to pN2 was no statistically different between the open and thoracoscopic approach but that upstaging form cN0 to pN1 was significantly higher when the patient was operated on via thoracotomy (9.3% versus 6.7%) (26). This difference tended to be minimized with experience of the surgeon (26). A satisfactory clearance of stations 11 and 12 can be achieved with the use of patience, appropriate dissection and hemostatic tools and frozen section if any suspicion of nodal metastasis (24).

Tumor-free margins

In case of lung cancer, frozen section must also be used for examination of the margins after completion of segmentectomy. Indeed, local recurrence after limited resection is related not only to nodal involvement but also to the size of the lesion and to the width of the surgical margins (19).The majority of recurrences are seen when the ratio between the margin and the tumor size is less than (27). Accordingly, frozen section should be used if any doubt exists as to completeness of resection.

Conclusions

Although a totally endoscopic approach to anatomic segmentectomies can seem challenging and difficult, the operation time in our series was acceptable and the morbidity rate was low (*Table 5*). Combining the advantages of an endoscopic approach and an anatomic limited resection could be highly beneficial for those of the patients who fulfill the criteria of a sublobar resection. With the renewed interest for sublobar resection in the management of early stage lung carcinomas, the thoracoscopic approach may have a major role in a near future (28,29), provided the following criteria are fulfilled: (I) true anatomic resection with hilar division of bronchovascular elements; (II) adequate clearance of intersegmental lymph nodes and (III) tumor- free margins.

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Indication for VATS sublobar resections in early lung cancer

Antonio E. Martin-Ucar[1], Maria Delgado Roel[2]

[1]Department of Thoracic Surgery, Nottingham University Hospitals NHS Trust, Nottingham, UK; [2]Complejo Hospitalario Universitario A Coruna, La Coruna, Spain

Correspondence to: Mr Antonio E. Martin-Ucar, Consultant, Thoracic Surgeon. Department of Thoracic Surgery, Nottingham University Hospitals NHS Trust, City Campus, Hucknall Road, Nottingham NG5 1PB, UK. Email: lungsout@yahoo.com.

Abstract: When dealing with early non-small cell lung cancer (NSCLC) sublobar resections still remain part of the surgical armamentarium. In selected patients with lung cancer, the combination of the potential benefits of parenchyma sparing procedures to the limited trauma provided by Video Assisted Thoracic Surgery (VATS) techniques can become very appealing. Two main groups are included: non-anatomical (wedges) and anatomical (segmentectomies) excisions. We describe the techniques, results and potential indications of both of these techniques.

Keywords: Minimally invasive surgery; segmentectomy; wedge

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Introduction

At present, surgery remains the most used radical treatment for early stage non-small cell lung cancer (NSCLC) (1). Lobectomy has been traditionally considered the gold standard procedure for early NSCLC following the Lung Cancer Study Group (LCSG) randomized controlled trial (2). However, the attempt to increase resection rates led to the need to offer surgery to patients with higher surgical risks: the elderly, the breathless and the ones with multiple co-morbidities (3-5). To manage these potential surgical risks and the possible long-term impairment in quality of life and respiratory function, surgeons have applied sublobar techniques to the management of lung cancer. These can be divided very clearly into two groups: non-anatomical resections (wedge) and anatomical resections (segmentectomies). The difference is the attempt during segmentectomies to follow the oncological principles of a lobectomy by achieving anatomical division of segmental veins, arteries and bronchi as well as good parenchymal clearance.

Video Assisted Thoracic Surgery (VATS) is on the increase in the management of benign and malignant processes. Large experiences have convinced the surgical community not only of the safety and possibilities of VATS surgery in early lung cancer, but of the benefits when compared to open surgery in terms of postoperative pain, length of recovery, return to activities, immune response to surgery and oncological results (6-9). As with open surgery where there is a variety of surgical approaches described (posterolateral, anterior, muscle-sparing, hybrid thoracotomies), VATS can also be performed with different surgical accesses: posterior approach, anterior approach, 2-port approach and single-port access (10-13).

We aimed to explore the potential possibilities and current experiences of the combination of sublobar resections and VATS techniques for early NSCLC.

Non-anatomical sublobar resections (wedge)

Wedge resections involve the excision of a pulmonary lesion with clear parenchymal margins with no attempt to deal with the hilar lobar structures (arteries, veins or bronchi). Although traditionally has been considered as a compromise operation due to the results of the LCSG trial that reported increase local recurrence compared to lobectomy, the indications for wedge excisions may be on the increase (2). Invariably, it is necessary that the lesion is peripheral so it can be identified and "wedged out" safely with sufficient margins. Despite the theoretical limitations as a sound oncologic procedure, wedge resection has continuously been used in certain circumstances for patients with lung cancer (14,15).

Technique

Wedge resections can be performed via VATS using a

Video 1 Prompt identification and excision of a peripheral pulmonary nodule at the base of the left lower lobe.
Available online: http://www.asvide.com/articles/133

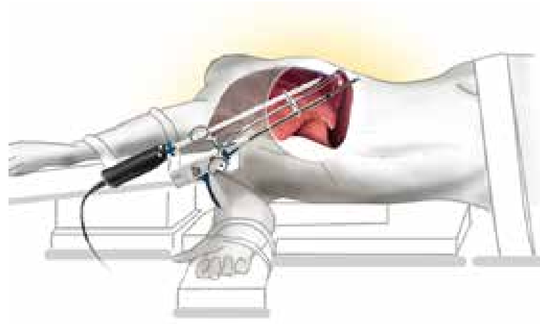

Figure 1 Diagram showing the position of the optics and instruments during VATS wedge excision of a pulmonary nodule.

number of incisions including the single-port approach (16). Ideally the lung should be collapsed as it facilitates location of pulmonary nodules and instrumentation, but it can potentially be performed in a ventilated lung in patients that can't tolerate single lung ventilation. There are different ways to identify the lesions including palpation with instruments or the tip of the finger, but also more complex techniques using technology such as placement of metal wires/coils (17,18), instillation of different contrasts (19-21) or use of intraoperative ultrasound techniques (22).

Once the nodule has been identified, surgical staplers are applied to excise and seal the pulmonary parenchyma with clear margins. A brief example of a diagnostic excision of a nodule in the left lower lobe via a single port incision is demonstrated in *Video 1* with the position of the incision and instruments is illustrated in *Figure 1*.

Results

There is very limited evidence available to assess the role of wedge resections in lung cancer. One randomized controlled trial by the LCSG reported a similar survival, but increased recurrence of cancer in patients undergoing sublobar compared to lobar resections (2). The surgical community accepted the results and acknowledged the effort of the trialists and, even accepting the trial limitations, considered lobectomy as the procedure of choice for early lung cancer thus reserving sublobar resections for specific cohorts of patients who might benefit of the preservation of the parenchyma or a quicker procedure.

The experiences reported in the use of VATS wedge resections when compared to lobectomy are consistent with traditional reports in the thoracotomy approach. Wolf *et al*. reported a retrospective comparative series of 154 sublobar resections (43% via VATS) and 84 lobectomies (10% via VATS) performed in patients with small early lung cancer. Patients who underwent lobectomy had a better survival and disease-free survival, but the sublobar group was significantly older and with worse respiratory reserve, highlighting the selection bias in this and every other study of its kind (23). Landreneau *et al*. reached similar conclusions in a multicenter study evaluating 102 wedge resections (60% by VATS) when compared to lobectomies (24).

One of the potential limitations of the use of VATS in deep-sited small lesions is the difficulty to locate them during surgery. The use of technologies has helped the identification of these nodules. Lee *et al*. were successful in 101 of 103 cases with small pulmonary nodules with the wire location techniques with an average operative time of 11 minutes (16). Molins *et al*. reported 50 out of 52 patients successfully underwent VATS excision of small nodules also identified by wires in the ambulatory setting (18). Similar success rates are reported by surgeons using different markers (methylene blue, radionuclides or contrast) (19-21). Finally, the use of intraoperative ultrasound has been reported by VATS, even in the single-port approach (25). Whatever the technology available, all these techniques seem to aid in identification of deep or small nodules during VATS surgery.

Indications

Based on the limited available evidence and the reported use of wedge resections in certain cohorts of patients with lung cancer we can identify possible indications for sublobar wedge resection in early NSCLC:

I. Cases in which preservation of parenchyma is

Video 2 Division of pulmonary artery, vein and segmental bronchus during anatomical left apical upper tri-segmentectomy. Available online: http://www.asvide.com/articles/134

mandatory. These include patients with very limited pulmonary reserve with COPD, significant pulmonary fibrosis that carry poor prognosis when lobectomy is performed, pulmonary hypertension and, more recently, in the management of metachronous or synchronous lung cancers;

II. Cases where preoperative histology could not be obtained or confirmed. Not only in very small pulmonary nodules unable to be biopsied percutaneously, but cases with history of distant malignancies where diagnosis metastasis/primary couldn't be made, or when radiological appearances are not very suggestive of cancer but patients request histological confirmation;

III. Diagnostic dilemmas in patients with underlying nodular lung disease (tuberculosis, sarcoid, rheumatoid) where one or more nodules are suspicious for malignancy during the course of their chronic disease in which a possible early NSCLC could be missed;

IV. Patients with severe comorbidities or very advanced age presenting with a peripheral nodule where a very short general anaesthesia period is preferred, where a wedge can be perform within few minutes, even with patients spontaneously ventilated.

Anatomical sublobar resections (segmentectomies)

Segmentectomies consist in the anatomical excision of one or more pulmonary segments. It is required to divide segmental branches of pulmonary artery, vein and bronchi related to the excised segments. The traditional technique of finding the segmental parenchymal plane by hand or electrocautery has now been substituted in many cases by the use of surgical staplers placed beyond the intersegmental plane with the potential benefit of reducing air leaks and parenchymal bleeding (26-28).

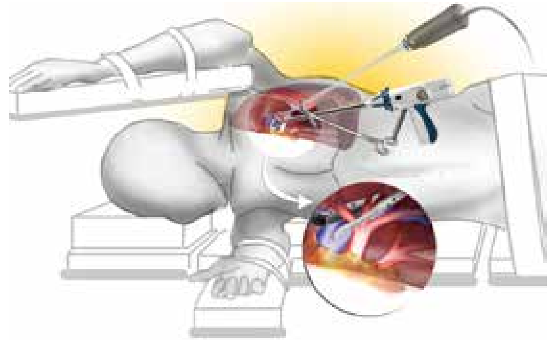

Figure 2 Diagram of a left apical upper tri-segmentectomy via single port VATS.

Segmentectomies for early lung cancer have been reported in the literature, and appear to be used more frequently (29,30). Surgeons have identified the potential role as an alternative to lobectomy in situations to increase operability (the elderly, patients with poor respiratory reserve, previous pulmonary resection) and resectability (multifocal ground-glass opacities, synchronous tumors, history of other solid malignancies where diagnosis of metastasis is a possibility), but also as the preferred option in small early stage NSCLC (31,32).

There is a limited but growing experience in the use of VATS segmentectomies, championed by experienced thoracoscopic surgeons but progressively being adopted by more units (33,34). The procedures can be performed via all the different VATS approaches including the Uniportal one (*Video 2*) and the instruments position is shown in *Figure 2*.

Technique

Segmentectomies can be divided into Typical (where parenchymal division involves 2 planes) or Atypical (more complex and technically demanding, when the segmental excision involves 3 planes). Examples of the former are excision of segments 6 on either side, lingulectomies, left apical upper tri-segmentectomies, left basal trisegmentectomies, right 7-10 segmentectomy. The rarer atypical segmentectomy examples are segmentectomy of 7-8 in the right, or 9-10 bilaterally.

With the patient on the lateral decubitus and forced hyperextension of the chest cavity to increase the intercostal

Table 1 Reports showing experiences in VATS segmentectomy for lung cancer

Author	Year	Operations	Number	Locoregional recurrence
Atkins	2007	Open segmentectomy; VATS segmentectomy	28; 48	8.3%; 7.7%
Saphiro	2009	VATS lobectomy; VATS segmentectomy	113; 31	3.6%; 3.5%
Yamashita	2011	VATS lobectomy; VATS segmentectomy	71; 38	5.6%; 7.1%
Soukiasian	2012	VATS lobectomy; VATS segmentectomy	266; 73	Ns (same survival)
Zhong	2012	VATS lobectomy; VATS segmentectomy	81; 39	4.9%; 5.1%
Zharo	2013	VATS lobectomy; VATS segmentectomy	138; 36	4.4%; 2.8%

space, a 4 cm incision is performed anterior to the latissimus dorsi edge at the level of 4^{th}-5^{th} intercostal space. The 30-degree thoracoscope is inserted to explore the pleural cavity. The thoracoscope is kept at the most posterior end of the wound allowing the insertion of 2, 3 or even more thoracoscopic instruments without interfering with them. Initially adhesions are divided with electrocautery and the left apical upper trisegmentectomy is performed. The Pulmonary Artery is identified and the initial branches are isolated and divided with an endo stapler. The segmental veins with preservation of the branches draining the lingula are then isolated and divided. Slightly more difficult is the identification of the segmental bronchus. Once this is isolated, we recommend that an inflation test is carried out prior to bronchial division as errors have been reported in VATS procedures. Once the bronchus has been divided, the parenchymal plane is identified by the inflation method prior to the excision. The specimen is removed with the help of a specimen bag in order to facilitate extraction and to minimize theoretical risk of wound seeding. A single intercostal drain is inserted after division of the inferior pulmonary ligament, lymph node excision and satisfactory lung re-expansion. Surgeons have employed other methods to identify the segmental plane: indocyanine green instillation or isolated inflation of the segments to be resected, all of them valid.

Results

The only randomized controlled trial including anatomical segmentectomies for lung cancer is the LCSG that, unfortunately, grouped segmentectomies together with wedge excisions. It concluded that survival after sublobar resections was equivalent to lobectomy but recurrence rates were much higher making a strong case for lobectomy to be considered the procedure of choice in early lung cancer. Unfortunately, the conclusions were impossible to extrapolate into a whole segmentectomy cohort due to the trial design (2).

Following this, few case-matched reports and several comparative series have indicated the value of anatomical segmentectomies to be similar to lobectomies in small size lung cancers, not only in the high-risk but also in the overall population (35-37). While survival or recurrence rates appear to be similar, there is evidence to demonstrate the lesser impact on pulmonary function after segmental resections.

If we apply the potential advantages seen in large experiences of surgeons performing VATS lobectomies compared with open lobectomies (less pain, early recovery, less complications and reduce immune response) the prospect of VATS anatomical segmentectomies might be very appealing (6-9). Several authors have described their experiences with a variety of VATS approaches from 4 to Single-port, and there are some comparative series between VATS and Open segmentectomy for lung cancer (38).

Overall, authors have not seen any significant differences in perioperative outcomes, survival or rates of recurrence between VATS segmentectomy and VATS lobectomy (*Table 1*) (39-43). The loco-regional recurrence rates vary between 2.8% and 7.7% in the different reports, similar to after VATS lobectomy by the same surgeons. One manuscript by Atkins *et al*. compared the outcomes between open and VATS segmentectomies performed in an experienced thoracoscopic unit, with perioperative results indicating that VATS techniques do not compromise outcomes (38).

Authors have not seen a significant reduction in the patients' hospital stay after VATS segmentectomy compared to VATS lobectomy, maybe as a consequence of longer lasting air leaks after segmentectomy due to the more extensive parenchymal trauma than after a fisureless VATS lobectomy (39-43). In the VATS experience we are yet to confirm the benefits on pulmonary function that segmentectomy seems to have over lobectomy in thoracotomy cohorts (44).

Indications

Based on the limited available evidence, and pending the results of modern studies underway (CALBG-140503 trial of segmentectomy *vs*. lobectomy for early lung cancer), the possible indications for VATS sublobar resections in NSCLC include:

I. Nodules in patients with a previous history of solid malignancies in cases where intraoperative frozen sections can not differentiate a primary lung cancer from a distant metastasis;
II. Multicentric ground glass opacities previously described as bronchoalveolar carcinoma;
III. Second primary in cases who have undergone pulmonary resection in the past;
IV. Surgery in patients deemed to have a high-risk for a lobectomy including respiratory diseases, extreme age;
V. An increasing number of segmentectomies are being used as procedure of choice in patients with peripheral early lung cancer of less than 2 cm.

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Techniques to define segmental anatomy during segmentectomy

Hiroyuki Oizumi, Hirohisa Kato, Makoto Endoh, Takashi Inoue, Hikaru Watarai, Mitsuaki Sadahiro

Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Correspondence to: Hiroyuki Oizumi. Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan.
Email: hohizumi@med.id.yamagata-u.ac.jp.

Abstract: Pulmonary segmentectomy is generally acknowledged to be more technically complex than lobectomy. Three-dimensional computed tomography (3D CT) angiography is useful for understanding the pulmonary arterial and venous branching, as well as planning the surgery to secure adequate surgical margins. Comprehension of the intersegmental and intrasegmental veins makes the parenchymal dissection easier. To visualize the segmental border, creation of an inflation-deflation line by using a method of inflating the affected segment has become the standard in small-sized lung cancer surgery. Various modifications to create the segmental demarcation line have been devised to accurately perform the segmentectomy procedure.

Keywords: Segmentectomy; thoracoscopy; video-assisted thoracic surgery (VATS); three-dimensional computed tomography (3D CT); slip knot; subsegmentectomy

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Introduction

In recent years, the diagnosis of small lung nodules and non-solid lung cancers has been increasing due to developments in computed tomography (CT) technology. It is reported that the prognosis of such malignancies is good even with a sublobar resection (1-3). It is reasonable to perform a less invasive resection of a smaller volume of lung tissue, and the simple procedure of wedge resections may be sufficient if tumors are located in the peripheral sub-pleural parenchyma. However, wedge resection is inadequate for most primary lung cancers and for nodules located deep in the lung. Segmentectomy is preferred in such cases to secure an adequate surgical margin (4). In open thoracotomy surgery, a tumor is dissected bluntly by maintaining a sufficient margin while directly palpating the tumor. However, in thoracoscopic surgery, in which a hand cannot be passed directly into the thoracic cavity, it is important to proceed with the operation with a clear anatomical understanding.

Anatomical segmentectomy

In a lobectomy, demarcation of the lobar anatomy is usually relatively straightforward. In contrast, segmentectomy is more complex. In particular, the recognition of the subsegmental fissures within the pulmonary parenchyma may be difficult, with unclear boundaries between adjacent segments. In addition, when the target disease is a malignant tumor, it is necessary to secure enough surgical margin. In a thoracotomy, the tumor is dissected bluntly from the adjacent segments by maintaining a sufficient margin while directly palpating the tumor, and involved blood vessels are also treated. During thoracoscopic surgery, in which a hand cannot be passed directly into the thoracic cavity, it is important to proceed with the operation with a clear anatomical understanding.

The lung segments extend to the peripheries with the bronchus as the base. There are ten segments in the right lung (upper lobe, three; middle lobe, two; lower lobe, five) and eight segments in the left lung (upper lobe, four; lower lobe, four). Each segment has a different morphology, size and blood vessel branch, which depend on its site, and there are many variations among patients (5-7). The left upper lobe is divided into the upper and lingular divisions, while the bilateral lower lobes are generally divided into the superior and basal segment that is combined with the remaining area. As lobation is occasionally observed between these segments, the anatomy is relatively simple and easily understood. Therefore, video-assisted thoracic surgery

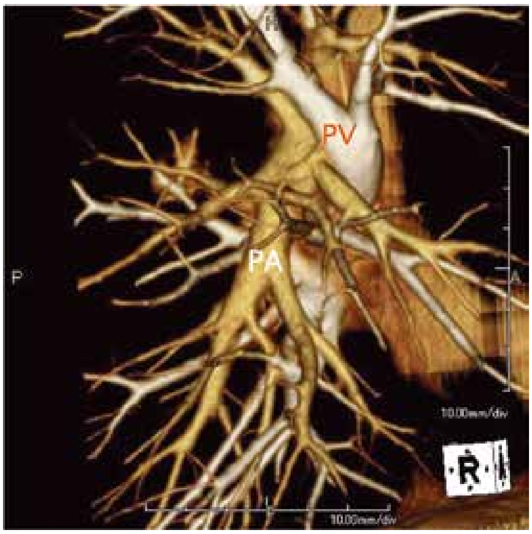

Figure 1 Three-dimensional computed tomography angiography. PA, pulmonary artery; PV, pulmonary vein.

(VATS) segmentectomy has often been performed along this plane (8,9). The problem lies with resections of other segments. It is important to plan and accurately perform the procedure (10-12). A variety of methods have been devised and used clinically, especially in thoracoscopic surgery, to solve the problem of the lack of tactile guidance (13-15).

With non-anatomical segmentectomy, the pulmonary parenchyma is roughly incised after treating the pulmonary artery and bronchus at the pulmonary hilum. However, it is not yet possible to cover resection of all segments with this method alone. The next branch of the segmental bronchus is called a subsegmental bronchus (16). Thoracoscopic resection of this subsegment has recently been performed (17). Thus, we describe herein the methods of understanding the dissection required for anatomical segmentectomy.

Understanding vascular structure

As the segmental artery is located at the pulmonary hilum in the superior segment of the lower lobe, identification and dissection are relatively easy. However, as arterial branches are embedded in the pulmonary parenchyma in some segments, it is sometimes necessary to preserve the proximal branch and divide the peripheral. Also, in many cases, more than one arterial branch is present even in a single segment. In such cases, it is useful to observe in detail and understand the morphology of the branch by employing contrast-enhanced CT, in order to carry out the surgery smoothly. A segmental artery normally accompanies the segmental bronchus. After completing division of the affected artery, the segmental bronchus can be easily traced as it is less flexible in the surrounding tissues.

With rapid advances in multi-detector CT (MDCT) in recent years, it has become possible to easily perform three-dimensional (3D) processing not only in a workstation but also on a personal computer (*Figure 1*). By using MDCT, we understand each patient's individual anatomy and can perform operations mainly by defining the course of arteries and veins (13-15). Usually, radiologists or technicians construct the 3D image using a workstation. The arteries and the veins are separately segmented and color-coded by CT value, and these volume-rendered images are then merged into the 3D-CT angiography. This image is ideal but it takes a long time to create. Thoracic surgeons know the basic anatomy of the lung, and therefore don't need complex images. When we use volume rendering methods, we prepare simple images that meet our needs in as little time as approximately seven minutes (http://www.youtube.com/watch?v=tSO58k9Lja8). By cutting out the area of interest, the image can be magnified, de-magnified or rotated during surgery (*Figure 2*). We previously reported that port-access thoracoscopic segmentectomy could be safely be performed in all segments using this approach, termed Segmentectomy Achieved by MDCT for Use in Respective Anatomical Interpretation (SAMURAI) (15). Since 2004, we have performed thoracoscopic segmentectomy in 160 patients including subsegmentectomy in 20 patients, and our completion rate is 98%. The surgical results for small lung cancer are still insufficient, with a mean follow-up period of only 3.5 years as yet. However, the 5-year survival rate is 100%, which is very favorable.

The venous branches within the segment become intersegmental veins as they converge, and return to the hilum. In segmentectomy, it is very important to understand these intersegmental and intra-segmental veins (*Figure 3*). The pulmonary parenchyma is dissected along the intersegmental vein, and intrasegmental vein thereby is identified. Division of the intrasegmental veins allows identification of the intersegmental border and facilitates the further parenchymal dissection (14,15). It is as if a clam can be opened when the adductor is cut.

Surgical margin

The SAMURAI method not only defines the running of

Figure 2 S1+2a (apical subsegment in left apical posterior segment) resection of the left upper lobe. (A) Three-dimensional computed tomography angiography with a marking of the tumor indicates two subsegmental arterial branches should be divided from the left apical posterior segmental artery. White arrow, first branch of the subsegment; Black arrow, second branch of the subsegment; (B) Operative view of the patient. The white arrow indicates the first arterial branch; (C) Operative view of the patient. The white arrow indicates the stump of the first arterial branch. The black arrow indicates the second arterial branch that was encircled in the deep parenchyma.

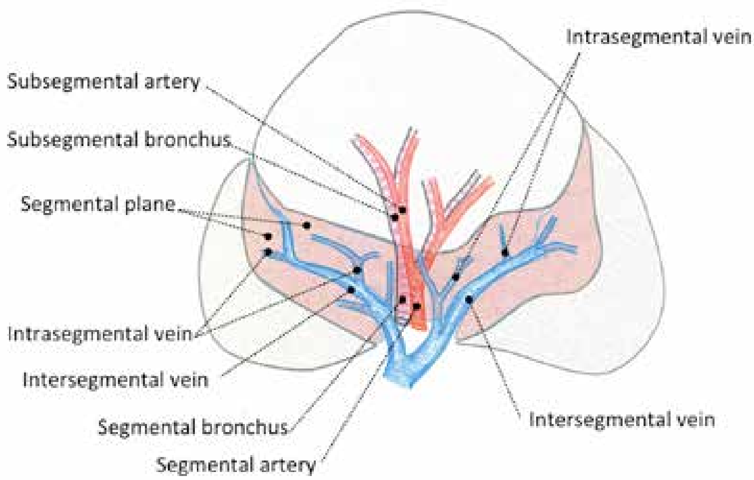

Figure 3 Schema of lung segmentectomy. The intersegmental plane is dissected preserving the intersegmental veins. Intrasegmental veins of the affected segment should be identified and divided.

blood vessels but also determines the extent of resection by virtually defining surgical margins. If it is difficult to preserve the margin in a single segment resection, we perform an extended resection of the parenchyma of adjacent segments.

Iwano and colleagues reported that radiologists propose the extent of resection to surgeons by superimposing a spherical safety margin on 3D images using a workstation for CT (18). While this method is ideal, preparing the images can be complex and time-consuming for surgeons. Although the SAMURAI method cannot create a perfect sphere in images, the surgeons themselves can evaluate resection margins intraoperatively using an appropriate scale in real time (15).

Identification of the intersegmental border

Inflation-deflation line

The basis of segmentectomy is to isolate and divide the bronchus and then dissect its peripheral pulmonary parenchyma. For conventional segmentectomy in open thoracotomy, division at the intersegmental border was generally performed by dissecting the bronchus in the affected lung and collapsing the lung on the peripheral side.

Figure 4 Inflation-deflation line created by slip knot method.

In lung cancer patients, the actual method involved securing a margin by directly palpating the tumor. Meanwhile, Tsubota reported a method of inflating the affected segment to be beneficial (19). Moreover, Okada and colleagues visualized the intersegmental plane by selectively inflating the segment using a jet ventilator and reported this approach to be effective in securing an operative field. Expansion of the affected segment allows not only visualization of intersegmental borders but also maintains the morphology and size of the resected lung in the same state as the actual systemic physiological state, thereby achieving more accurate evaluation of resection margins (11). Therefore, it is considered to be more advantageous oncologically and is becoming a standard method in Japan.

Thus, jet ventilation is useful as an inflation method for the affected segment in thoracoscopic surgery or small thoracotomy. However, this method requires equipment and another doctor to maneuver the bronchoscope. Some institutions experienced such difficulties and various modifications have been devised. Direct inflation into the bronchus using a butterfly needle from the operative field was reported to be useful (20). However, great care is essential as this approach can reportedly cause air embolism (21).

We were not able to effectively insert the bronchoscope into the smaller bronchi during resection at the subsegmental (third order) bronchial branches (16). Therefore, we attempted to block the bronchus by ligation with expansion of the affected segment, especially in segmentectomy of smaller bronchial calibers. We ligated a bronchus conventionally using a knot pusher after ventilation when the bronchus was narrow. However, this method cannot be performed quickly after inflation; therefore, the affected segment will be partly deflated. We found that the monofilament slip-knot, customized from the previously reported modified Roeder knot, was useful since it enabled the surgeon to ligate the bronchus during ventilation of the lung. The bronchus is closed by pulling the thread (http://www.youtube.com/watch?v=XH2jt7kL3mo), and was effective for creating the inflation—deflation line (*Figure 4*) (22). We believe that this method can be generalized because it doesn't need any special equipment and is applicable at any time.

Intersegmental veins

As described earlier, intersegmental pulmonary veins serve as important landmarks (15). The dissection of their branches, the intrasegmental pulmonary veins, facilitates intersegmental dissection. When it is difficult to reach the segmental artery and bronchus located in the deep areas of the pulmonary parenchyma, we can reach the target bronchus by dissecting the parenchyma along the intersegmental pulmonary vein. For example, in segmentectomy of S9+10 or S10 of the lower lobe, the bronchus is located in a very deep area far from the interlobar area. We have devised a posterior approach to dissecting the pulmonary parenchyma along the vein (V6) between the superior and the basal segment, initially, thereby reaching the bronchus posteriorly (http://www.youtube.com/watch?v=V2Rq92JB6vk) (23). Once the bronchus is reached, a line between the inflated and deflated areas is created using the aforementioned method. This facilitates dissection of S9 and S10, formerly classified as the most difficult segments, and reduces the operative time. As such, visualization of the line between the inflated and deflated areas and the intersegmental vein dissection are both important in performing intersegmental dissection.

Other techniques

There is a report describing a fluorescence method, wherein indocyanine green is injected into a blood vessel after treating the target segmental artery (24,25). It is based on the premise that the segmental bronchus is accompanied by the pulmonary artery. As the running vessels do not match in some cases, it is necessary to read CT images in detail to identify the pulmonary artery to ultimately be treated. A method of injecting dyes into the bronchus has also been reported (26). While this direct method is promising, it requires an additional procedure of injecting materials via bronchoscopy. Although both

Figure 5 A solid model of pulmonary arteries and veins of right upper and middle lobe molded from computed tomography data using three-dimensional (3D) printer.

methods require special instruments and procedures, we anticipate that there will be further reports describing their general use in the future.

Future simulation: virtual to real

Computer technology is rapidly advancing. We are now able to visualize the surfaces of pulmonary blood vessels, output the dendritic structure as an STL file, and create a 3-dimensional solid model using a 3D printer. After sterilization, this device can be hand held and observed during surgery (*Figure 5*). As 3D printer equipment and consumable supplies are expensive, there is an issue of cost in creating the model. While it still cannot be regarded as an item for actual use as compared with virtual technology, there is potential for this approach to become a useful tool if the manufacturing cost can be brought down in the future.

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Thoracoscopic superior segmentectomy

Jacob R. Moremen[1], Betty C. Tong[2], DuyKhanh P. Ceppa[1]

[1]Division of Cardiothoracic Surgery, Indiana University School of Medicine, Indianapolis, Indiana, USA; [2]Division of Cardiothoracic Surgery, Duke University, Durham, North Carolina, USA

Correspondence to: DuyKhanh P. Ceppa, MD. Division of Cardiothoracic Surgery, Department of Surgery, Indiana University School of Medicine, 545 Barnhill Drive, EH 215, Indianapolis, Indiana, USA. Email: dpceppa@iupui.edu.

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Clinical vignette

The patient is a 59-year-old formerly smoking male with a history of T2N0M0, stage I colon cancer. He underwent a left hemicolectomy five years prior to presentation and was referred for an enlarging 7 mm pulmonary nodule noted on surveillance imaging. His past medical history was significant for coronary artery disease and hypertension. Given the deep location of the pulmonary nodule and the patient's limited pulmonary function, we opted to perform a diagnostic and therapeutic superior segmentectomy.

Surgical technique

Preparation

All patients undergoing a pulmonary resection are evaluated pre-operatively with pulmonary function testing (spirometry and diffusion capacity). Upon arrival at the operating room and induction with general anesthesia via a dual lumen endotracheal tube, the patient is placed in a lateral decubitus position with the bed flexed just above the hip. The surgeon stands anterior to the patient and the assistant drives the thoracoscope while standing posteriorly to the patient.

Exposition

The patient is prepped and draped in a sterile fashion. We use a two-incision approach—the first incision is at the eighth interspace at the posterior axillary line and the second access incision is at the fifth interspace anteriorly. The access incision is approximately 3 cm in length.

Operation

The hemithorax is explored for evidence of pleural disease, effusions, or additional, unexpected pulmonary nodules. The presence of the lung nodule of interest is confirmed. The lung is retracted superolaterally as the inferior pulmonary ligament is incised, along with the pleura anterior and posterior to the hilum. With the lung retracted superolaterally, the inferior pulmonary vein is encountered first. The branch draining the superior segment is identified, circumferentially dissected out and ligated. More superolateral retraction reveals the lower lobe bronchus, and the segmental bronchus to the superior segment is identified. Once the superior segmental bronchus is circumferentially dissected out and transected, more superolateral retraction on the lung exposes the pulmonary artery. The pulmonary artery branch to the superior segment is circumferentially dissected out and ligated.

Upon division of the hilar structures, the fissure is completed and the parenchymal margin is divided. The parenchymal margin is occasionally identified by a segmental fissure. Otherwise, a test inflation may assist in delineating the parenchymal margin. The segment is removed from the hemithorax in a specimen bag. All structures are divided using a linear stapler with a vascular load for the vein and artery and a 3.5 to 4.5 mm load (or equivalent) for the bronchus and parenchyma.

Completion

Upon completion of the segmentectomy, a mediastinal lymph node dissection is performed. The vascular and bronchial stumps are inspected for hemostasis. A thoracostomy tube is introduced via the camera incision and the lung is reinflated under direct visualization. All ports and the camera are then removed. The anterior access incision is closed using absorbable suture to reapproximate the serratus fascia and skin.

Comments

Clinical results

Segmentectomy was originally popularized as a procedure for tuberculosis, bronchiectasis and other suppurative pulmonary processes. While still useful in this scenario, segmentectomy is now more commonly utilized in the treatment of early stage lung cancer in patients with limited pulmonary function and in the treatment of pulmonary metastasectomy. Although a technically more challenging operation than lobectomy, segmentectomy has been shown to have similar complication rates, local recurrence rates, and 5-year survival (1). The only randomized trial comparing sublobar pulmonary resection with lobectomy demonstrated a higher recurrence and cancer-related death rate in the sublobar resection cohort (2). However, this study did not distinguish between wedge resection and segmentectomy. The study also did not specifically assess the role of segmentectomy in smaller nodules and one third of the tumors were greater than 2 cm. A more recent series by Okada *et al*. reviewed the outcomes of segmentectomy versus lobectomy in over 500 patients with tumors less than 2 cm (3). They report that the 5-year survival in both cohorts were similar.

Advantages

A meta-analysis of 24 studies from 1990 to 2010 demonstrated the benefit of lobectomy over sublobectomy—but not over segmentectomy—in overall survival and cancer specific survival for patients with stage I NSCLC (4). This survival advantage was lost, however, in patients with stage IA tumors less than 2 cm. Current literature suggests that compared to lobectomy, segmentectomy has equivalent cancer-free survival and local control with its main advantage being preservation of lung parenchyma (5). Postoperative pulmonary function testing in patients undergoing lobectomy found a significantly decreased forced expiratory volume in one second (FEV1) at two and six months and reduced exercise capacity when compared to patients undergoing segmentectomy (6). Reduced morbidity, decreased hospital length of stay, and lower cost are additional advantages of thoracoscopic segmentectomy over segmentectomy by thoracotomy (5). Furthermore, when compared to wedge resection of small pulmonary nodules, segmentectomy has been associated with a better lymph node dissection and increased parenchymal margin (7).

Caveats

Despite its advantages, thoracoscopic segmentectomy is more technically challenging than lobectomy. Additionally, this technique should be reserved for small pulmonary lesions (≤2 cm) that can be fully resected with an adequate parenchymal margin by segmentectomy. Data from randomized trials investigating the role of segmentectomy versus lobectomy are currently under way.

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Single incision video-assisted thoracoscopic anatomic segmentectomy

Diego Gonzalez-Rivas[1,2]

[1]Department of Thoracic Surgery, Coruña University Hospital, Coruña, Spain; [2]Minimally Invasive Thoracic Surgery Unit (UCTMI), Coruña, Spain
Correspondence to: Diego Gonzalez-Rivas, MD, FECTS. Department of thoracic surgery, Coruña University Hospital, Xubias 84, 15006, Coruña, Spain. Email: diego.gonzalez.rivas@sergas.es.

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Introduction

Anatomic segmentectomy was first described in 1939 by Churchill and Belsey (1). Although segmentectomy is usually indicated for benign lesions or for metastasis when the goal is resecting the lesion while sparing parenchyma, anatomic segmentectomy has also been demonstrated to be effective in the resection of small lung cancers (2). Recently, due to the increasing incidence of small lung tumors, there has been renewed interest in the use of anatomic segmentectomy, especially for patients unable to tolerate lobectomy. Several recently published studies have shown that segmentectomy can be performed safely without compromising oncologic results (3,4). Video-assisted thoracoscopic surgery (VATS) is currently a better choice than thoracotomy for segmentectomy. Although most surgeons use three to four incisions, the surgery can also be performed using only one (5).

Surgical technique

Single-incision VATS segmentectomy follows the principles of major pulmonary resections by VATS: individual dissection of segmental veins, segmental arteries and the segmental bronchus, as well as complete mediastinal lymphadenectomy with a video-assisted thoracoscopic approach and no rib spreading.

The size of the incision is comparable to the utility incision commonly used in a double- or triple-port approach and is usually smaller than that for a lobectomy, approximately 3 cm long (6). The incision is usually made at the level of the 5th intercostal space to provide access to upper hilar structures and lymph node stations. Both the surgeon and assistant are positioned anteriorly to the patient in order to have the same thoracoscopic vision during all the steps of the procedure and be more coordinated with the movements. Instruments with a proximal and distal articulation are preferable as they reproduce the same experience as a conventional instrument but also allow the insertion and manipulation of three to four instruments simultaneously (Scanlan International, Inc., MN, United States).

Optimal exposure of the lung is crucial for facilitating the dissection of the segmental structures and to avoid instrument malposition. The 30° high-definition thoracoscope is usually placed in the posterior part of the incision and the instruments are placed below the camera. Bimanual instrumentation is crucial to achieve a successful segmental resection through a single port VATS. A single chest tube is placed at the end of the procedure through the same working incision.

In this video we show seven different anatomic segmentectomies performed through a single incision thoracoscopic approach, including: (I) Right upper lobe apico-posterior segmentectomy (S1-S2); (II) Right upper lobe apical segmentectomy (S1); (III) Left upper lobe trisegmentectomy (S1-S2-S3); (IV) Left lower lobe superior segmentectomy (S6); (V) Right lower lobe basilar segmentectomy (S7-S8-S9-S10); (VI) Anatomic lingulectomy using vascular clips (S4-S5); and (VII) Anatomic lingulectomy using endostaplers (S4-S5).

Right upper lobe apico-posterior segmentectomy (S1-S2)

Exposure of the vein is achieved by retracting the upper lobe posteriorly. The common apico-posterior segmental vein is dissected as distal as possible and divided with an endostapler.

The upper lobe is then retracted upward and forward in order to expose the apical artery which is dissected and divided using a stapler.

When the fissure is complete, the posterior ascending artery can be easily dissected and divided from the fissure. When the fissure is incomplete, a fissureless technique is performed in order to expose the posterior artery. The anterior portion of the intersegmental plane is divided using a stapler to expose the posterior ascending artery and the bronchus. A posterior segmental artery is then discovered. A vascular clip for proximal transection and ultrasonic energy device to do the distal division. Now the trifurcation of the upper lobe bronchus is exposed. The apical and posterior lobar bronchus are dissected separately and freed from its attachments to the upper lobe. A loop is passed around the two segmental branches and both bronchus are cut with an endostapler.

Finally, the parenchyma is divided by placing the stapler in the border between the apico-posterior and the anterior segment plane. The specimen is inserted into a protective bag and retrieved through the single incision.

Right upper lobe apical segmentectomy (S1)

The second video shows an apical segmentectomy of a 2.5 hilar tumor not possible to remove with a wedge resection. The first step is to identify the mediastinal trunk of the artery. Once the segmental vein for segment 1 is dissected we use a vascular stapler to divide it. We usually insert the staplers through the inferior part of the incision and the camera is normally placed above.

By using scissors we release the adherences of the anterior branch of the artery from the inferior portion of the tumor.

We divide the apical artery using vascular clips. The anterior portion of the intersegmental plane is divided by a 60 mm stapler. After identification of the branches for the anterior and posterior segment, we continue with the division of the parenchyma by placing the staplers above the stumps. In this particular case, the apical bronchus is divided through the intersegmental plane due to the benign nature of the tumor.

Left upper lobe trisegmentectomy (S1-S2-S3)

The third case shows a trisegmental resection of left upper lobe (also known as lingular-sparing lobectomy). The view of the apico-anterior arterial trunk is direct, and this branch is approached anteriorly, dissected and ligated by a stapler. The upper division of the pulmonary vein is dissected and divided [anterior, apical and posterior veins, preserving the lingular vein (LV)]. The trisegmental bronchus is easily visualized after ligation of the segmental vein and arteries, with care taken during this dissection to avoid injury of the lingular artery. After the bronchus is stapled, the posterior artery is usually visualized and is then divided by using vascular clips. The last step is to divide the parenchyma through the segmental plane by using staplers.

Left lower lobe superior segmentectomy (S6)

The resection of the superior segment (S6) of the lower lobe is straightforward as there are consistent anatomical landmarks. The conduct of segmentectomy will vary slightly depending on whether the fissure is complete or not. In this case, the fissure is complete so the superior segment artery is exposed through the fissure. The artery is easily divided by using an endostapler.

With a long lung grasper, the lower lobe was held and the pulmonary ligament was cut to find the segmental vein for dissection, followed by division by using a vascular stapler. We dissect and expose the superior segmental bronchus and it was stapled in the same way as mentioned for the vein. The last step is to divide the intersegmental plane and remove the segment using a protective bag.

Right lower lobe basilar segmentectomy (S7-S8-S9-S10)

Removal of four segments in the right lower lobe (S7-S8-S9-S10) while sparing the apical segment (S6) is called basal segmentectomy. These segments are usually removed together since they are dependent on a single bronchus.

After identification of the artery in the fissure, a stapler was placed above to better expose the artery. The anterior portion of the fissure is stapled, which allowed division of the basilar artery using a stapler.

The next step is dissection of the basilar segmental vein. The direct view provided by the single incision approach allows excellent visualization of the plane between the superior segmental vein and basilar vein. The basal vein was divided with a stapler. Once the inferior segmental vein has been divided, the lower lobe basilar segmental bronchus is exposed, dissected and divided from its inferior aspect to its bifurcation with the middle lobe bronchus on the right side or the upper lobe bronchus on the left side. Dissection of the bronchus with development of the plane between the bronchus and artery is performed with visualization of the artery. We recommend the removal of the interbronchial lymph nodes to better define the anatomy. The intersegmental plane is completed last. The lung is inflated to confirm an adequate ventilation of the superior segment of the lower lobe.

Anatomic lingulectomy using vascular clips (S4-S5)

The next video shows two different ways to perform an anatomic lingulectomy. In the first video we used vascular clips for vessels. The lingula is retracted laterally and posteriorly and the pleura overlying the LV is incised. In this particular case, the tumor was involving part of the lower lobe in the fissure, so the first step was to divide the anterior portion of the fissure from an anterior view.

The identification of the LV, lower lobe vein (LLV) and the artery indicates the location to place the stapler to divide the anterior portion of major fissure. The anvil of the stapler is placed between the LLV and LV, and above the upper part of the artery, and the parenchyma is retracted into the jaws of the stapler.

This maneuver facilitates the dissection of the LV. A ring forceps is then placed while holding the lingula for traction, exposing the small recurrent lingular artery which is then divided with clips. Once this small vessel is divided, the lingular bronchus is exposed. In this particular case there was no angle for the stapler, so the bronchus was transected using scissors and the stump was closed using a stapler at the end of the procedure. Subsequently the main lingular artery is exposed and divided by using vascular clips.

Finally the intersegmental plane is divided and the stump of the bronchus with is closed with an endostapler at the end of the procedure.

Anatomic lingulectomy using staplers (S4-S5)

The last segment of this video shows a non-edited lingulectomy using endostaplers. The fissure is complete so the lingular artery is easily exposed, dissected and divided in the fissure by using a vascular stapler. The LV is dissected and divided by using a 30 mm vascular stapler. Once the vein is divided, the lingular bronchus is exposed and transected using endostaplers. The last step is to divide the intersegmental plane.

Comments

Uniportal VATS segmentectomies are usually more difficult than lobectomies. From June 2010 to February 2014, we have performed 28 uniportal VATS anatomic segmentectomies. The mean surgical time was 89.5±3 minutes (range, 40-150 minutes). The mean number of nodal stations explored was 4.1±1 (range, 0-5) with a mean of 11.5±1.8 (range, 7-25) lymph node resections. The mean tumor size was 2.24±1 cm (range, 1-4 cm). The median chest tube duration was 2 days (range, 1-6 days) and the median length of stay was 2 days (range, 1-6 days).

None of these segmentectomy cases required conversion, which may be attributed to experience in uniportal lobectomy, including vascular dissection, the management of fissures, as well as experience in more complex cases (lobectomy after induction therapy, hilar calcification, and pneumonectomy) (7).

Comparing segmentectomies by thoracotomy with uniportal thoracoscopic segmentectomies, the latter was associated with a shorter length of stay and with equivalent morbidity and mortality (8).

The advantage of using the camera in coordination with the instruments is that the vision is directed to the target tissue, addressing the target lesion from a straight perspective and thus obtaining a similar angle of view as with open surgery. In standard three-ports VATS, the geometric configuration of a parallelogram generates interference with the optical source, creating a plane with a torsion angle not favorable on the flat two-dimensional vision of currently available monitors (9).

Another potential advantage of this approach could be a reduction in postoperative pain, although this has not yet been demonstrated. There could be several explanations for this issue: only one intercostal space is involved and avoiding the use of a trocar could minimize the risk of intercostal nerve injury. During instrumentation, force is applied only over the superior aspect of the inferior rib through the utility incision.

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Nonintubated thoracoscopic segmentectomy—left upper lobe trisegmentectomy

Ming-Hui Hung[1,2], Hsao-Hsun Hsu[3], Ya-Jung Cheng[1], Jin-Shing Chen[3,4]

[1]Department of Anesthesiology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; [2]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan; [3]Division of Thoracic Surgery, [4]Division of Experimental Surgery, Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

Correspondence to: Jin-Shing Chen, MD, PhD. Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, 7, Chung-Shan South Road, Taipei 10002, Taiwan. Email: chenjs@ntu.edu.tw.

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Introduction

Enhanced computed tomography screening protocols have recently identified increasing numbers of small lung tumors in patients with high surgical risks (1). Consequently there has been increasing interest in minimally invasive surgical approaches, including thoracoscopic approaches, parenchyma-sparing resection, and less invasive anesthesia for management of lung tumors (2). The role of thoracoscopic segmentectomy is therefore increasingly reevaluated, not only as a traditional parenchyma-sparing procedure in high-risk patients with compromised medical conditions but also in patients with non-small cell lung cancer less than 2.0 cm (1).

From 2009, we started a nonintubated thoracoscopic surgery program for patients who were reluctant or unsuitable to have a conventional intubated single lung ventilation during thoracic surgery (3). With a combination of target-controlled sedation and regional anesthesia—either by thoracic epidural anesthesia or intercostal nerve blocks with intrathoracic vagal blockade—the results of nonintubated thoracoscopic surgery are encouraging (2-5). In the current video, we demonstrate how a nonintubated technique was applied in thoracoscopic segmentectomy and mediastinal lymphadenectomy to treat a patient with early stage lung cancer (*Video 1*).

Clinical vignette

A 74-year-old man, who had undergone a total gastrectomy for gastric cancer in a different institution in 2003, was transferred to our hospital for management of an incidentally discovered left upper lobe lung nodule. Computed tomography-guided biopsy of the tumor revealed a primary pulmonary adenocarcinoma. Preoperative pulmonary function tests showed that he had a mild obstructive defect with forced expiratory volume in one second being 84.9% of predicted. Considering his age and reduced lung function, lingual-preserving left upper lobectomy (left upper lobe tri-segmentectomy) was planned instead of left upper lobectomy to preserve more lung parenchyma after surgery.

Surgical techniques

Preparation

After standard monitoring, the patient was induced with target-controlled infusion of propofol. The patient spontaneously breathed oxygen through a ventilation mask. Depth of sedation and respiratory rate were monitored by bispectral index and capnography, respectively. The patient was then placed in the right lateral decubitus position.

Exposition

Thoracoscopic segmentectomy was performed using a 3-port method. The operative lung was deflated gradually after creation of an iatrogenic pneumothorax.

Operation

Under thoracoscopic guidance, we first performed intercostal nerve blocks by infiltration of 0.5% bupivacaine from the third to the eighth intercostal nerve under the parietal pleura, 2 cm lateral to the sympathetic chain. Vagal block was also produced at the level of the aortopulmonary window to prevent triggering of cough reflex. After identifying the tumor site, incomplete interlobar fissures to the affected segment was divided. Hilar dissection was then performed to isolate and divide the apicoposterior segmental artery, upper division of left superior pulmonary vein and upper division of left upper bronchus with endoscopic stapling devices. The resected segment was removed in a protective bag through the utility port. Mediastinal lymph node dissection was then performed.

Completion

At the end of the surgery, the operated lung was manually ventilated through the mask to check air leakage. A 28 F chest tube was placed through the lowest incision.

Comments

Using regional anesthesia—either by thoracic epidural anesthesia or intercostal nerve blocks—with intrathoracic vagal blockade and target-controlled sedation, we had performed 51 cases of nonintubated thoracoscopic segmentectomies, including anterior and apicoposterior segmentectomy of right upper lobe, lingulectomy and apical trisegmentectomy of left upper lobe, and superior segmentectomy of the lower lobes of both sides.

Clinical results

There were 44 patients with primary or metastatic lung cancer and 7 patients with benign tumors. No patients required conversion to a thoracotomy or lobectomy. However, one patient required conversion to intubated one-lung ventilation because of vigorous mediastinal and diaphragmatic movement. The mean duration of postoperative chest tube drainage and mean hospital stay were 2.2 and 4.8 days, respectively. Operative complication was only developed in one patient who had an air-leak for more than five days after surgery. No death or major complications occurred.

Advantages

The reasons to use nonintubated technique for thoracoscopic surgery are mainly to avoid adverse effects associated with general anesthesia and endotracheal intubation for single-lung ventilation. In our cohort, nonintubated patients reported less postoperative nausea and vomiting, early recovery of oral intake and clear consciousness, and better postoperative analgesia in comparison with intubated patients (2-4). In high-risk patients, such as the elderly, this technique also has fewer overall complication rates, compared to intubated general anesthesia (5).

Caveats

Although nonintubated thoracoscopic anatomical segmentectomy was feasible and safe in our cohort (2), further investigations are still necessary to clarify its efficacy and true benefits in different groups of patients, such as medically compromised patients or those with early stage lung cancer. For readers who hope to use this technique, we suggest a cooperative and well-communicating thoracic surgical team, including the thoracic surgeon and anesthesiologist.. Patients should be carefully selected in the early learning phase. Obese patients often use significant abdominal effort during respiration, associated with vigorous diaphragmatic movement after iatrogenic pneumothorax, which makes invasive hilar dissection difficult. Although intrathoracic vagal blockade may be effective to attenuate a cough reflex, surgeons are still reminded to retract the lung and manipulate the hilum gently. In cases of dissection of subcarinal lymph nodes, the contralateral main bronchus can be occasionally irritated, which might induce transient coughing. Oxygenation is usually satisfactory after supplemental oxygen during spontaneous one-lung breathing but mild to moderate hypercapnia may occur because of carbon dioxide rebreathing. Although the incidence of conversion to intubated general anesthesia or thoracotomy is low, a conversion protocol in cases of failed nonintubated method should be prepared in advance.

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Analysis of feasibility and safety of complete video-assisted thoracoscopic resection of anatomic pulmonary segments under non-intubated anesthesia

Zhihua Guo[1,2*], Wenlong Shao[1,2*], Weiqiang Yin[1,2*], Hanzhang Chen[1,2], Xin Zhang[1,2], Qinglong Dong[3], Lixia Liang[3], Wei Wang[1,2], Guilin Peng[1,2], Jianxing He[1,2]

[1]Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; [2]Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China; [3]Department of Anesthesiology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China

*These authors contributed equally in this study.

Correspondence to: Jianxing He, MD, PhD, FACS. Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, No. 151, Yanjiang Rd, Guangzhou 510120, China. Email: drjianxing.he@gmail.com.

Objective: To explore the feasibility and safety of complete video-assisted thoracoscopic surgery (C-VATS) under non-intubated anesthesia for the resection of anatomic pulmonary segments in the treatment of early lung cancer (T1N0M0), benign lung diseases and lung metastases.

Methods: The clinical data of patients undergoing resection of anatomic pulmonary segments using C-VATS under non-intubated anesthesia in the First Affiliated Hospital of Guangzhou Medical University from July 2011 to November 2013 were retrospectively analyzed to evaluate the feasibility and safety of this technique.

Results: The procedures were successfully completed in 15 patients, including four men and eleven women. The average age was 47 [21-74] years. There were ten patients with adenocarcinoma, one with pulmonary metastases, and four with benign lung lesions. The resected sites included: right upper apical segment, two; right lower dorsal segment, one; right lower basal segment, two; left upper lingular segment, three; left upper apical segment, one; left upper anterior apical segment, two; left upper posterior segment, one; left lower basal segment, one; left upper posterior and apical segments, one; and left upper anterior and apical segments plus wedge resection of the posterior segment, one. One case had intraoperative bleeding, which was controlled with thoracoscopic operation and no blood transfusion was required. No thoracotomy or perioperative death was noted. Two patients had postoperative bleeding without the need for blood transfusions, and were cured and discharged. The pathologic stage for all patients with primary lung cancer was IA. After 4-19 months of follow-up, no tumor recurrence and metastasis was found. The overall mean operative length was 166 minutes (range 65-285 minutes), mean blood loss 75 mL (range 5-1,450 mL), mean postoperative chest drainage 294 mL (range 0-1,165 mL), mean chest drainage time 2 days (range 0-5 days), and mean postoperative hospital stay 5 days (range 3-8 days).

Conclusions: Complete video-assisted throacoscopic segmentectomy under anesthesia without endotracheal intubation is a safe and feasible technique that can be used to treat a selected group of IA patients with primary lung cancer, lung metastases and benign diseases.

Keywords: Video-assisted thoracoscopic surgery (VATS); segmentectomy; lung cancer

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Introduction

Lung cancer is the most common cancer worldwide, accounting for about 15% of cancer cases around the world, and 28% of cancer deaths (1). Lung cancer is also associated with the highest morbidity and mortality among all malignant conditions in China (2). Surgical resection by thoracotomy or thoracoscopy is the preferred treatment for early-stage non-small cell lung cancer (3). Since the early 1990s, video-assisted thoracoscopic surgery (VATS) has been rapidly developed and widely applied in the world, involving almost all areas of general thoracic surgery. Compared with thoracotomy, VATS enables a smaller incision without removing or stretching the ribs open, sparing respiratory muscles from injures and thus minimizing the loss of lung function. Moreover, with a smaller incision, patients will suffer less pain postoperatively and expectorate more easily, reducing the incidence of postoperative pulmonary infection and complications as well (4). Thoracoscopic lobectomy is a representative application of thoracoscopic surgical techniques in thoracic surgery.

With the development and extensive application of imaging techniques such as high-resolution computed tomography (HRCT) and low-dose spiral computed tomography (CT), the detection rate of small lung nodule of unknown nature has been increasing. Lung resection is considered to be applicable for early lung cancer (T1N0M0), small metastases and localized benign lesions (such as bronchiectasis and tuberculosis) (5-8). Compared with lobectomy, segment resection better preserves lung functions while removing small nodules (9). With the intensified aging population, some patients are often complicated with cardiovascular diseases that make them unable to tolerate lobectomy, and therefore segmental resection has also been considered for the treatment of patients with primary lung cancer and poor cardiopulmonary function (3).

For now, general anesthesia with one-lung intubated ventilation is the standard anesthesia in thoracic surgery. Intubated anesthesia is, however, often associated with postoperative throat discomfort, including primarily irritating cough, and throat pain in some patients. On the other hand, non-intubated anesthesia can reduce general anesthesia-related complications, and many investigators have therefore begun to explore its application in general thoracic surgery. Dong *et al.* reported that thoracoscopic wedge resection under non-intubated anesthesia was feasible and safe (10). Chen *et al.* reported the safety and feasibility of thoracoscopic resection under non-intubated anesthesia (lobectomy, lung resection and wedge resection) in 285 patients (11). Hung *et al.* reported segmental resection under non-intubated anesthesia in 21 patients, finding that the technique preserved maximum normal lung tissue while reducing the loss of lung functions, and general anesthesia-related adverse reactions (12). This study summarizes 15 patients undergoing C-VATS resection of anatomic pulmonary segments under non-intubated anesthesia in our department.

Subjects and methods

Clinical data

Patients undergoing C-VATS resection of anatomic pulmonary segments from July 2011 to November 2013 were enrolled. All patients received pre-operative chest high-resolution thin-slice enhanced CT scans and pulmonary function tests. For those suspected of lung cancer, additional upper abdomen CT, head MRI, whole body bone scintigraphy or whole body PCT examination was needed to exclude distant metastases. Patients were eligible when they had an ASA grade of I-II, BMI <25 and no evident airway secretions or contraindications for epidural puncture in preoperative anesthesia assessment (11). All operations were performed by the same group of thoracic surgeons and anesthesiologist team. The primary outcome measures included the operative time, intraoperative blood loss, hospital stay, chest drainage, chest tube duration, and type of lung resection.

Indications for segmental resection

The indications for segmental resection included: (I) a lung mass close to the hilum in which wedge resection is not possible; (II) history of lung lobe resection, leading to the consideration of an additional primary lesion; (III) past history of other malignancies and lung solitary tumors, for which differentiation with primary lung cancer is not possible via intraoperative frozen sections; (IV) multiple pulmonary ground-glass shadows, for which atypical adenomatous hyperplasia (AAH), adenocarcinoma *in situ* (AIS) or minimally invasive adenocarcinoma (MIA) may be suspected; (V) a complication with any cardiopulmonary disease that makes lobectomy intolerable; and (VI) peripheral early lung cancer ≤2 cm in diameter.

Surgical methods

Administration of anesthesia: with established intravenous rehydration, an epidural catheter is inserted in the thoracic T6-7 space. In the supine position, 2 mL of 2% lidocaine is injected through the epidural catheter. If signs of spinal anesthesia are not present in five minutes, fractionated injection of 12 mL 0.375% ropivacaine is administered. Before surgery, the anesthesia level should reach between T2 and T10. Propofol and remifentanil are infused for sedation and analgesia during surgery, with the BIS values maintained between 40 and 60. During surgery, masked and nasopharyngeal airway assisted ventilation is given with an inhaled oxygen concentration FiO_2 of 0.33. Monitors are mounted on both sides along the patient's head, which generally lies on the opposite side to the operating site, with the hilum and waist padded to further widen the intercostal space. The operator stands in front of the patient, the first assistant on the patient's back side, and the second assistant handles the thoracoscope. The first port is generally made in the 7th or 8th intercostal space at the anterior axillary as the observation port. It should be noted that, in case that the diaphragm is too high or unclear on the X-ray images, this port should be positioned at a higher intercostal space to avoid injuring the abdominal organs. The second port is usually in the 7th intercostal space at the posterior axillary line and the third port close to the lesion, which form a triangle on the chest wall. All of them are treated with soft incision protectors to serve as the surgical operation channels. All video-assisted thoracic operations are performed using Stryker 1288 HD 3-Chip Camera/1288 with a three-chip HD camera system and specially designed endoscopic instruments in our department. After insertion of the thoracoscope from the first port, full chest exploration is conducted to determine whether there is evidence that the lesion is unresectable, such as pleural metastasis or other sign of metastases. Local vagus nerve block is achieved with 2 mL of 2% lidocaine under thoracoscopic guidance in the chest cavity, followed by spray of appropriate amount of the same concentration on the surface to reduce coughing that may induced by pulling of the lung tissue, ensuring a steady operation environment.

The thoracoscopic lung resection is done following the basic principle for lobectomy, in the order of arteries, bronchi, veins, and lung parenchyma in general. For resection of upper segments in the left upper lung, the veins are treated first because the superior branch of the superior pulmonary vein is anterior to, and blocks part of, its anterior branch, and thereby it should be first transected. The use of staplers and vascular clips is at the discretion of the operator depending on the vessel sizes during the surgery. According to the experience of the surgeons in our department, the use of hemolok and titanium clips should be avoided when clamping blood vessels. That is mainly because their application may affect the appropriate operation of other equipment such as stapler. (For example, a clip being caught in the stapler may prevent it from being successfully triggered.). Although in the event that vessels are well exposed, a stapler can be used to directly close or ligate and cut them off, there are still many factors that may affect those operations to such an extent that vessels are excessively pulled and injured when the stapler passes through them. In such cases, the tip of a linear stapler can be guided through the stapler guiding catheter to safely pass the posterior part of a vessel to successfully cut it off. The same method can be used to cut off bronchi, with satisfactory results. After the vessels and bronchi at the lesion segment are resected, the lung segment is in an atelectasis state. The anesthesiologist is instructed to maintain low volume low pressure ventilation to help determine the intersegmental plane. In addition, when the veins around the segment and in the surrounding segments to be preserved are well exposed, they can also be used to help identify the intersegmental plane. Mediastinal lymph node assessment is an essential component in thoracoscopic segmental resection for non-small cell lung cancer. Systemic lymph node dissection is performed following the segmental resection. Frozen sections of the segmental bronchus stumps and lymph nodes are sent for pathological tests. When positive intersegmental or interlobular metastases are present, switch to lobular resection is always preferred as long as the patient's physical conditions allow. If there is so little residual tissue following the resection that the high mobility makes lung torsion likely, Gossot *et al.* suggests connecting with the adjacent lobes via TA to reduce the postoperative complication (10). During surgery, if SpO_2 drops to below 90%, mask assisted ventilation is needed to improve oxygenation. If blood gas analysis shows an arterial carbon dioxide partial pressure of ≥80 mmHg, the operation needs to be suspended followed by mask-assisted gas exchange. If the ventilation does not improve in this way, endotracheal intubation is required (9). Chest tube drainage is routinely used after the surgery. When there is no leakage and thoracic fluid volume is less than 200 mL per day, removal of the drainage can be considered.

Specific methods of segmental resection

(I) Resection of right upper posterior apical segments: the

Table 1 Basic characteristics of patients

Characteristics	Number of patients (n=15)	Percentage
Median age (years)	47 [21-74]	
Gender		
Male	4	27
Female	11	73
Smoking history		
No smoking history	15	100

Table 2 Postoperative pathology

Pathological type	Number of patients (n=15)	Percentage
Primary bronchogenic carcinoma		
Adenocarcinoma	10	66.7
Metastasis		
Lung metastasis of breast cancer	1	6.7
Benign disease		
Pulmonary sclerosing hemangioma	1	6.7
Bulla	1	6.7
Proliferation of fibrous connective tissue	1	6.7
Arteriovenous fistula	1	6.7

apical and posterior segments can be treated separately, but they are usually removed at the same time. The posterior ascending aorta anterior to the upper lobular bronchus is treated before the bronchi. The upper lobe is pulled forward to expose the posterior mediastinum. The pleura of the upper lobe bronchus close to the mediastinum are opened using coagulation hook, "peanut" gauze or a combination of both. A 45-mm endoscopic stapler is used to open the posterior part of the oblique fissure to help expose the ascending aorta, and the artery is transected. With combined use of the cautery hook, right-angle clamp and ultrasonic scalpel, the surrounding soft tissue is separated until the apical segmental bronchus is fully exposed. The apical artery is located posterior to it. A cutting stapler is used to close the bronchus while the posterior arteries are properly protected. After transection of the segmental bronchus, the apical artery is revealed. The upper lung lobe is pulled backwards to expose the apical vein anterior to the hilum, which is then closed and cut. When eventually cutting the lung parenchyma, the anesthetist is instructed to maintain low-pressure ventilation so that the boundary line between ventilated and non-ventilated areas can be followed as the cutting line.

(II) Resection of the upper segment in the right lower lung: with combined use of the coagulation hook and ultrasonic scalpel, the pleura around the hilum in the right lower lung are divided and the oblique fissure opened using a stapler. The pulmonary arteries are gradually exposed. After the upper segmental artery is divided and cut, the posterior bronchus is revealed, separated, stapled and cut. The inferior pulmonary ligament is transected through to the inferior pulmonary vein. Gauze is used to expose the superior segmental vein upwards from the inferior pulmonary vein, and the former is then cut with a vascular clamp or stapler.

(III) Resection of the basal segment in the right lower lung: the anterior part of the oblique fissure is opened to expose the basal segment artery, which is transected and closed. The segmental bronchus is separated from the deep structure of the artery. The anesthesiologist is instructed to help identify if the basal segment bronchus is closed off by ventilation. The inferior pulmonary ligament is transected through to the inferior pulmonary vein. With the inferior lobe is pulled up, the surrounding tissue of the inferior pulmonary vein is divided using the cautery hook and peanut gauze. The basal segment vein is exposed and transected.

(IV) Lingular segment of the left upper lung: the lingular artery is separated and transected to reveal the upper lobular bronchus and lingular segmental bronchus. The latter is clamped, and low ventilation is used to identify its closure before transaction. The superior pulmonary vein is separated until its lowermost branch is exposed. If the lingular segmental vein can be located, it is transected before the intersegmental pulmonary tissue is handled. Otherwise, the lingular segmental vein can be treated until the lingular segmental tissue is fully separated.

Results

The procedures were successfully completed in 15 patients, including four men and eleven women. The average age was 47 [21-74] years. The patient characteristics are listed in *Table 1*. Pathological examination showed ten patients with adenocarcinoma, one with pulmonary metastases, and four with benign lung lesions (*Table 2*).

Segmental resections were successful in all patients without switching to thoracotomy or lobectomy. The

Table 3 Thoracoscopic resection of lung segments

Sites	Number
Left	
S4 + S5	3
S1 + S3 + PS2	1
S1	1
S2	1
S7 + S8 + S9 + S10	1
S1 + S3	2
S1 + S2	1
Total	10
Right	
S1	2
S6	1
S7 + S8 + S9 + S10	2
Total	5

Note: S1, apical; S2, posterior; S3, anterior; S4 + S5, lingular; S6, superior; S7, medial basal; S8, anterior basal; S9, external basal; S10, posterior basal.

Table 4 Intra- and post-operative conditions of lung resection surgery

Characteristics	Value/number of patients
Mean operation length (min)	166 [65-285]
Mean intraoperative blood loss (mL)	75 [5-1,450]
Mean drainage volume, mL	294 [0-1,165]
Mean drainage days	2 [0-5]
Mean postoperative stay (days)	5 [3-8]
Perioperative complications	
Postoperative bleeding, n (%)	2 (13.4)

resected sites included: right upper apical segment, two; right lower dorsal segment, one; right lower basal segment, two; left upper lingular segment, three; left upper apical segment, one; left upper anterior apical segment, two; left upper posterior segment, one; left lower basal segment, one; left upper posterior and apical segments, one; and left upper anterior and apical segments plus wedge resection of the posterior segment, one. Resected lung segments are shown in *Table 3*.

One case had intraoperative bleeding of 1,450 mL, which was controlled with thoracoscopic operation and no blood transfusion was required. There were no perioperative deaths. Two patients of postoperative bleeding were controlled with hemostatic medicine without the need for blood transfusions, and no other serious complications occurred. All patients were cured and discharged. The overall mean operative length was 166 minutes (range 65-285 minutes), mean blood loss 75 mL (range 5-1,450 mL), mean postoperative chest drainage 294 mL (range 0-1,165 mL), mean chest drainage time 2 days (range 0-5 days), and mean postoperative hospital stay 5 days (range 3-8 days) (*Table 4*).

Of the ten patients with primary lung cancer, nine received mediastinal lymph node dissection or systemic lymph node sampling, and the pathological staging showed stage IA for them; one patient who did not receive the above procedure had micro invasive adenocarcinoma in the left lung. After 4-19 months of follow-up for the patients, no tumor recurrence and metastasis was found.

Discussion

Whether segmental resection can achieve comparable effects to lobectomy for the treatment of early stage lung cancer is still controversial. Previous studies have shown that for early lung cancer, particularly when the tumor diameter is ≤2 cm, segmental resection can yield comparable long-term survival as with lobectomy (13,14). However, evidence in this regard comes mainly from retrospective case comparisons and meta-analyses, and the role of segmental resection in NSCLC needs to be further confirmed by large international multi-center randomized controlled clinical studies (CALGB 140503 in the United States and JCOG0802/WJOG4607L in Japan).

Complete thoracoscopic segmental resectionis a complex and technically demanding procedure, requiring the surgeon to be extremely familiar with the anatomic structures of every segmental vessel and bronchus. One of the major technical difficulties is confirmation of the plane between segments. Most investigators traditionally suggest low-pressure ventilation after occlusion or transection of segmental bronchi, so that the plane can be determined by differentiating between the collapsed and expanded interface. The purpose of the ventilation is to avoid the influence on endoscopic vision and operation by excessive expansion of lung tissue. According to our experience, a long-handled tong may be used to clamp the plane after low-pressure ventilation, as it provides two main advantages: (I) in view of the traffic between the lung segments, adjacent lung segments can be expanded with ventilation, blurring the lung segment boundary;

(II) a stapler only provides a limited opening angle that is likely to injury the lung parenchyma when coming across the thicker portion of it, leading to the need of manual stitches and bleeding control after the resection, which will increase the length of operation. The use of this recommended instrument can provide local compression, making it easier for a stapler to pass the lung segment boundary. Some investigators on the other hand suggest the use of selective lung ventilation in patients with COPD, in which the target segment is expanded through bronchoscopy and separated from other collapsed lung segments, reducing the impact of endoscopic vision by lung expansion (15). Segmental veins can also be helpful in identifying the intersegmental plane, and separation along pulmonary veins and loose connective tissue in the lung segments usually does not damage large bronchi and pulmonary arterial branches. Some lesions are located between segments, and when reliable surgical margins are not secured, resection of the adjacent segments can be considered.

Compared with traditional surgery under general anesthesia, epidural analgesia reduces intubation-related complications and facilitates early mobility of patients (10,11,16). It also reduces the dose of intraoperative anesthesia drugs, which will help restore the breathing and digestive functions. Four to six hours after non-intubation segmental resection, the patients could start eating, drinking, and get out of bed. Chest X-ray scans could be performed on the same the day after surgery. If imaging tests suggest good lung recruitment and no air leaks, and 24-h chest drainage is less than 200 mL, the drainage can be removed. With non-intubated anesthesia, coughing induced by postoperative throat discomfort is significantly reduced. Coughing may worsen wound pain, which in turn suppresses the cough reflex, making pulmonary secretions difficult to discharge after surgery, and indirectly leading to alveolar hypoventilation due to rapid and shallow breathing; some patients may even experience atelectasis or lung infection after surgery. Therefore, non-intubation endoscopic resection of lung segments may reduce the incidence of pulmonary complications, maximize protection of lung function and reduce postoperative pain, shorten chest tube duration, shorten the length of hospital stay, and allow faster recovery to preoperative mobility.

Non-intubated anesthesia combined with C-VATS lung resection surgery should be one of the most minimally invasive lung cancer surgery at present. With non-intubation anesthesia, the biggest challenge for surgeons is the remarkable mediastinal motion, which requires full cooperation among the surgeon, anesthetists and assistants. Mediastinal movement occurs when the ipsilateral intrathoracic pressure was significantly higher than that of the contralateral side in open pneumothorax, resulting in mediastinal shift to the contralateral area that further limits expansion of the contralateral lung. During inhalation and exhalation, the unbalanced pleural pressure on both sides experiences cyclical changes so that the contralateral mediastinum moves toward the contralateral side during inhalation and the opposite side during exhalation. In non-intubation segmental resection, the patient's spontaneous breathing has to be retained in order to achieve atelectasis of the operative side and good ventilation of the contralateral lung, so that both the oxygen supply and a favorable operating field can be secured. With collapsed ipsilateral lung after thoracotomy, some patients will have obvious mediastinal swing, which will affect the surgeon's surgical operation, particularly when dealing with blood vessels in which excessive traction may lead to bleeding. To mitigate the impact of the mediastinal swing during surgery, anesthesiologists can increase the amount of opioids based on the operation, reduce the breathing frequency or the respiratory tidal volume, thereby reducing the amplitude of the swing. At the same time, appropriate ventilation can be given based on the results of blood gas analysis to avoid serious hypercapnia, so as to maintain the body's acid-base balance.

Based on the fifteen patients undergoing non-intubated anesthesia combined with C-VATS lung resection in our department, the technique is feasible and safe with the help of skilled anesthetists with experience in thoracoscopic lobectomy and non-intubated anesthesia. So far, there has been no shift to thoracotomy and lobectomy. Although there was one case of bleeding, it was well controlled endoscopically without the need of blood transfusion. As for the two cases of postoperative bleeding, no blood transfusions were needed and no other complications were observed. The incidence of perioperative complication was 13.4%. The mean operative time was 166 minutes, mean intraoperative blood loss 75 mL, mean postoperative chest drainage two days, and mean postoperative hospital stay five days. The operative time and the number of days in hospital are comparable to those reported with VATS under general anesthesia, while intraoperative blood loss, chest drainage time and perioperative complications were better than the latter (*Table 5*).

In summary, complete video-assisted thoracoscopic surgery (C-VATS) under non-intubated anesthesia for

Table 5 Thoracoscopic segmental resection (17-29)

Lead author	Year of publication	Number of cases	Operation time (min)	Intraoperative blood loss (mL)	Chest tube drainage (days)	Postoperative hospital stay (days)	Perioperative complications (%)
Tracheal intubation, VATS segmentectomy							
Shiraishi	2004	34	240±72	169±168	4.5±3.2	–	11.8
Atkins	2007	48	136±45	250±200	3.5±4.0	–	25.8
Watanabe	2009	41	220±56	183±195	3.0±2.0	–	31.3
Shapiro	2009	31	–	–	2 [1-33]	4 [1-98]	26.0
Schuchert	2009	104	136 [120-152]	171 [133-209]	–	5	6.9
Oizumi	2009	30	216 [146-425]	100 [3-305]	1 [1-7]	–	0
Leshnower	2010	15	145±55	–	2.8±1.3	–	11.6
Gossot	2011	50	188±54	91±82	3.3±1.0	–	19.0
Moroga	2011	20 a	303±103	182±291	4.6±3.4	–	20.0
Moroga	2011	63 b	241±82	118±127	5.1±3.8	–	34.5
Dylewski	2012	35	146 [82-229]	50 [20-100]	–	2 [1-15]	33.9
Yamashita	2012	90	257±91	132±181	4.8±3.4	–	34.6
Pu	2012	20	155 [120-235]	50 [10-600]	3 [1-6]	6 [3-9]	25.0
Lin	2012	20	133 [90-240]	85 [50-200]	3.2 [2-7]	6.7 [4-11]	0
Nonintubated VATS segmentectomy							
Present study		15	166 [65-285]	75 [5-1,450]	2 [0-5]	5 [3-8]	13.4

a, with SNB; b, without SNB; SNB, sentinel node biopsy.

the resection of anatomic pulmonary segments in the treatment of early lung cancer (T1N0M0), benign lung diseases and lung metastases is safe and feasible, and can reduce postoperative pain, improve the appearance with small incisions, shorten chest drainage duration and postoperative hospital stay, provide maximum protection of lung functions, and reduce complications after general anesthesia. However, it requires that the surgeon has extensive experience in thoracoscopic lung resection in good cooperation with anesthesia doctors. Due to the short follow-up period, the long-term efficacy needs to be further confirmed. The long-term effect of non-intubated thoracoscopic anatomic segmental resection needs to be further studied and identified in a larger-scale study.

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How to set up a VATS lobectomy program

Joel Dunning[1], William S. Walker[2]

[1]Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK; [2]Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK

Correspondence to: Joel Dunning, MD, PhD, FRCS. Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK. Tel: +447801548122; Fax: +441642815761. Email: joeldunning@doctors.org.uk.

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Introduction

Video-assisted thoracic surgery (VATS) lobectomy was first performed in Italy in1991 (1). It was first performed in our Unit in Edinburgh in 1992 (2). Although it was slow to be adopted initially, due to many factors, acceptance has risen rapidly and its use has doubled to 13% of all lobectomies in the UK in 2011 (3). In that time, many publications have highlighted the benefits of VATS lobectomy (4-8), including a shorter hospital stay, earlier chest tube removal, reduced complication rates and equivalent cancer free survival, with a 2008 systematic review demonstrating all these benefits in 3,114 VATS lobectomy patients compared to 3,256 open thoracotomy patients. Other studies have demonstrated a significantly higher administration of chemotherapy after VATS lobectomy compared to the open procedure (9,10). We need a line here to explain this comment Thus the benefits of VATS lobectomy are well reported and there is enthusiasm for its adoption. In this article, we attempt to provide a framework for the successful implementation of a VATS lobectomy program. This article represents a joint perspective of the Royal Infirmary of Edinburgh, where VATS lobectomies were first performed in the UK and from James Cook University Hospital where the VATS lobectomy program was set up according to lessons learnt from the Royal Infirmary, Edinburgh.

Surgical technique training

Ferguson *et al*. reported that, compared to the established surgeon, if carefully supervised, the first 50 cases by the trainee will be slower, but just as safe in terms of survival, blood loss and complications (11). Other authors have pointed to a learning curve over their first 50 cases at their own institution, demonstrating reduced times and sometimes reduced blood loss and morbidity after this period (12,13). Our experience suggests that if the operating surgeon is able to spend a significant training period with a surgeon experienced in VATS surgery, then this greatly enhances their confidence when starting in their own practice. This also increases the likelihood that they will persist with a VATS lobectomy program. In addition, we recommend a period of training, whilst commencing a VATS lobectomy program in one's own institution with frequent re-visits to the original training institution, as inevitably there will be questions and difficulties which may be addressed by maintaining these links.

Team approach

We recommend reading an outstanding article published in the Harvard Business Review (14). This is a study of 16 hospitals, which implemented a minimally invasive cardiac surgical procedure. They studied 660 operations and examined human factors that determined successful implementation of the program and also factors that caused failure. This article details features of a successful team. It acknowledges that learning new procedures is a complex and time consuming exercise.

Initial procedure

Prior to assembling the surgical team, you must ensure that the hospital administration and operating theatres will be able to provide the resources and permission for the new procedure. In our own institution, this involved an application to the new procedures committee, but this may be the responsibility of an appropriate ethics committee elsewhere. These committees oversee the implementation of all new procedures. Administration is appraised of the financial case for the procedure and costs for the initial and ongoing scenarios are outlined as best as possible. Delays may occur between organizing the surgical team and ultimate approval from administration to perform the first procedure. It is important to maintain team confidence and morale during this period. In general terms, familiarity with surgical equipment, e.g., staplers, should be present and the temptation to use new or unfamiliar instruments when commencing a VATS lobectomy program should be avoided.

The Harvard Business School report suggests that creating the right team is the key to successful implementation of a new procedure. This report cites 3 key factors in the creation of a successful team: (I) Successful teams are designed for learning; (II) Their leaders framed the challenge in such a way that team members were highly motivated to learn; (III) The leaders' behavior created an environment of psychological safety that fostered communication and innovation.

The team should have the hallmarks of successful co-operation including harmonious co-employment, discipline, general problem solving approach, keenness to learn together and general rapport. Substituting team members after initial training should be avoided if possible. The Harvard report found that teams, which changed regularly adopted the new procedure much more slowly than teams which remained the same. Our initial team consisted of 2 identified anesthetists, an operating department assistant, 2 scrub nurses, a surgeon's assistant, and 3 members of the ward staff in addition to the surgeon.

Training the surgical team

We commence training by taking the team together to the experienced unit to see 2 cases being performed. In order to promote team interaction, the team arrives together and stays overnight prior to the day's observation of the VATS lobectomies. The night before the operation, we will discuss the Harvard Business school paper in addition to hearing talks and watching videos about the surgical procedure. The idea is to get the team to spend time together talking about the operation and fostering the idea that everyone's contribution is important.

The concept of bringing all staff together promotes harmony and a sense of equality with all contributions and interactions regarded as important. Firstly, patient positioning on the operating table, specific one-lung ventilation and pain management in VATS lobectomy is important. Secondly, ward staff, by observing the rapid mobilization of post-operative VATS lobectomy patients will be motivated to aspire to similar outcomes in their own unit. Thirdly, maintaining correspondence and communication with colleagues at the training institution is very important when questions arise at any stage. The staff will also have realistic expectations regarding the time that the procedures take and will observe the equipment in use.

Setting the correct tone as a team leader is vital to the success of the team. Repeated analysis of successful team working shows that all members of the team look to the leader for cues as to how they need to behave. Harvard Business School recommend: (I) Be accessible, make sure your team is encouraged to make suggestions and to flag potential problems and take them seriously; (II) Ask for input and proactively ask your team members what they think or what they thought could be improved; (III) Serve as a fallibility model. If the surgeon in charge occasionally in the debriefing says 'Well I shouldn't really have done it like that' or 'I wish I had done that bit differently', this encourages an atmosphere of open disclosure, in which team members will be comfortable to flag problems or raise issues that they are having.

The first case

We advocate trying to reduce the time between the team's first training event and the first case. Secondly, we advocate, if possible, inviting the senior surgeon from the training unit to our unit for the first case. If a scrub nurse is also able to come down then this is also very useful. This creates a positive atmosphere in the unit and a great desire to make sure things go well and professionally for the visiting surgeon. It also allows you to fully implement the procedure the way you have been taught. Issues like getting full flexion of the table, the correct analgesia and the correct equipment available does seem easier if you are asking for all these new changes 'for the visiting surgeon' rather than as a departure from what you normally do.

For this first day assisted and possibly for your first day solo, we would also advocate a comprehensive debrief, preferably in a relaxed environment. These debriefs will further allow the team to make suggestions, but are also an important conclusion to the weeks of preparation. One recommendation for new procedures is often the prior setting of parameters for conversion. Agree with your team in advance the parameters with which you are going to convert the case to a thoracotomy. A reasonable parameter may be if you have not divided a pulmonary vessel by 1.5-2 hours. This will ensure that you will not get tunnel vision and struggle with difficult cases in the early phase, and the operative time will remain fairly uniform in all your cases. Converting the patient to the way you would have done the case the week before is preferable to the patient and staff undergoing a prolonged operation, which may also lead to further time-related problems, e.g., subsequent list cancellation.

The postoperative care of the VATS lobectomy patient deserves special attention. If the VATS lobectomy patient is treated like an open lobectomy patient then it is likely they will be discharged on the same day as an open lobectomy patient. Therefore, it is important to educate ward staff with respect to early mobilization. Avoiding catheters, unnecessary cannulae and wall suction all promote early mobilization. Air leaks may be managed with ambulatory bags instead of standard chest drain bottles, and even discharge home with the ambulatory bags will encourage early mobilization. Early discharge is potentially possible with measurable reduction in the length of hospital stay.

Public relations exercises and specific information public information briefs require special attention and are best performed in close consultation with appropriate hospital media departments and administration.

We recommend the following advice. Firstly, do not invite the media to follow your first case. This is very stressful for you and your staff and if things go wrong then you have no control over what they may report. Secondly, keep meticulous notes and begin a quality assurance program, which is mandatory for all new surgical procedures. Report and discuss any unexpected morbidity and mortality resulting from the relatively new procedure. Thirdly, develop an appropriate database specific to VATS lobectomy. This will obviously entail important factors, e.g., transfusion requirements, pain score, length of stay, chemotherapy compliance and survival compared to open lobectomy.

After an appropriate period of performing VATS lobectomy with good results, presentation of data to interested parties, e.g., respiratory physicians, medical oncologist, general practioners and paramedical staff may enhance overall knowledge and awareness for this procedure.

Conclusions

VATS lobectomy programs require special training for the surgical team and embarking on this program at the hospital level brings many challenges. This article outlines some guidelines for the surgeon wishing to commence a program for VATS lobectomy. Along with this article, many educational references and aids exist to assist with program set-up. Further information or clarification may be sought by contacting the corresponding author.

Acknowledgements

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Video-assisted thoracoscopic lobectomy: The Edinburgh posterior approach

Jennifer M. J. Richards, Joel Dunning, Jonathan Oparka, Fiona M. Carnochan, William S. Walker

Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK

Correspondence to: William S. Walker, MD. 51 Little France Crescent , Old Dalkeith Road, EH164SA Edinburgg. Tel/Fax: +44 131 5361000. Email: william.walker@luht.scot.nhs.uk.

Editor's Key Points

1. The main advantages of the Edinburgh posterior approach include: (I) easy access to posterior hilum including the bronchial branches and the pulmonary arteries; (II) lymph nodes are better seen and c) tips of the instruments are coming towards the camera, which provides safer dissection
2. In contrast to the anterior approach, the main differences in techniques of the posterior approach include: (I) the surgeons stand posterior to the patient; (II) utility incision is made at the 6th or 7th intercostal space anterior to latissimus dorsi muscle, instead of the 4th intercostal space; (III) camera port is made through the auscultatory triangle, instead of lower anterior incision; (IV) thorascoscopy is 0º rather than 30º; and (V) the order of dissection is from posterior to anterior, by opening up the fissure first to identify and isolate pulmonary arterial branches.

--A.H.

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Introduction

Video-assisted thoracoscopic surgery (VATS) is now well established as an alternative to open thoracotomy for major pulmonary resections of bronchogenic carcinoma and benign disease (1,2). Compared to open surgery, the minimally invasive approach has a number of benefits in the immediate post-operative period that include reduced pain, better pulmonary function, shorter hospital stay, improved cosmesis and lower risk of developing pneumonia (3-7). VATS lobectomy is equivalent to open surgery in terms of oncological outcomes, is less immunomodulatory and enables more patients to commence and complete adjuvant chemotherapeutic regimens (7-10). Furthermore, minimally invasive techniques are cost effective and at least equivalent to open techniques in terms of long-term survival (11-13).

Whilst the anterior approach is preferred by many surgeons, the main advantages of the posterior approach in our experience is the excellent view that is obtained of the posterior hilum which facilitates dissection of the bronchi and branches of the pulmonary artery. In addition, the mediastinal node packets are clearly seen, allowing thorough lymphadenectomy. Importantly, in the posterior approach the tips of the instruments come towards the camera and are therefore easily seen whilst in use increasing the safety of dissection.

More than 800 VATS major pulmonary resections have been performed in our centre over the last 20 years and we here describe our method for fissure-based VATS lobectomy using a posterior approach.

Pre-operative assessment

Selection criteria

We have adopted VATS resecetion as the surgical strategy of choice for all cases of peripheral carcinoma of 5 cm or less in diameter and for suitable benign disease. Lobectomy and anatomic segmentectomy are standard procedures. It is possible to utilise VATS techniques in patients with more advanced disease such as moderate chest wall or pericardial involvement and, rarely, for pneumonectomy in patients with low bulk hilar involvement. However with the trend towards lung conservation strategies, we now reserve pneumonectomy for rare individuals in whom broncho-vascular reconstruction is not feasible.

Fitness for surgery

Baseline pulmonary function is assessed using a combination of spirometry and CO transfer factors for all patients. In addition, all patients undergo exercise testing. Cardiological assessment is carried out as relevant to the individual patient. Echo assessment of pulmonary (PA) pressure is undertaken in patients at risk of pulmonary hypertension (PAP>45 mmHg). Few patients are declined surgery on the basis of poor pulmonary function data. This serves as guidance for post-operative surveillance and respiratory management but our experience supports the view that even patients with a significantly reduced pulmonary function (>2 S.D. below normal) still fare well with a VATS approach.

Staging

In addition to a contrast-enhanced computed tomography scan of the head, chest, abdomen and pelvis, positron emission tomography-CT (PET-CT) with ^{18}F-fluordeoxyglucose (^{18}F-FDG) is performed in all patients with bronchogenic carcinoma under consideration for resection.

We have previously demonstrated that even in patients with no radiographic features of mediastinal lymph node spread, there is a 5% false negative rate for detection of lymph node metastases when compared to the gold standard of mediastinoscopy and lymph node biopsy (14). We therefore perform mediastinoscopy with sampling of ipsilateral stations 2 and 4, contralateral station 4 and the subcarinal (station 7) groups (consistent with current European Society of Thoracic Surgeons guidelines) in all patients being considered for VATS lobectomy for malignant disease in whom the procedure is not otherwise contraindicated.

In patients considered suitable for lobectomy, the VATS approach is attempted in all patients meeting size and stage criteria. The only absolute contraindications are those patients in whom the pleural cavity is obliterated on radiological grounds or who clearly have very proximal disease requiring a pneumonectomy. The requirement for sleeve lobectomy is a significant relative contraindication but not absolute. The conversion rate in our series is <7%.

Operative techniques

Anaesthesia and positioning

Following induction of anaesthesia, the patient is positioned in the lateral decubitus position. The hands are placed unsupported in the “prayer” position in front of the face and the operating table is manipulated to extend the thorax laterally opening up the intercostal spaces.

As soon as the double lumen endotracheal tube is confirmed to be in the correct position, whilst the patient is still in the anaesthetic room, ventilation is switched to the contralateral lung to optimise deflation of the lung that is to be operated upon. Suction is occasionally used if the lung does not deflate readily. The respiratory rate can be increased to 20 breaths/min or more in order to reduce the tidal volume and hence the degree of mediastinal excursion due to ventilation. This provides a more stable operating field. We rarely use central lines or urinary catheters but always use an arterial line and large bore venous cannulae.

Intercostal nerve blocks are used for perioperative analgesia in preference to epidural anaesthesia. Unless the parietal pleura has been disrupted, a local anaesthetic paravertebral catheter is placed at the end of the operation and remains in place for 48 hours. In addition, a patient-controlled morphine pump is supplied to the patient for post-operative analgesia.

The positioning of the surgical, anaesthetic and nursing teams and the equipment is illustrated in *Figure 1*. The surgeon and their assistant stand at the patient’s back with the screen directly across the table and the scrub nurse obliquely opposite. We utilise two additional large (55 inch) wall-mounted high definition screens. One is positioned opposite the scrub nurse and provides an operative view, which also allows anaesthetic staff, circulating nurses, students and observers to follow the progress of the operation. The other is positioned opposite the surgeon and provides large-scale high-definition radiology images, which the surgeon can view continuously in order to inform intra-operative decision-making.

Incisions

Three access ports are used and port position is standard

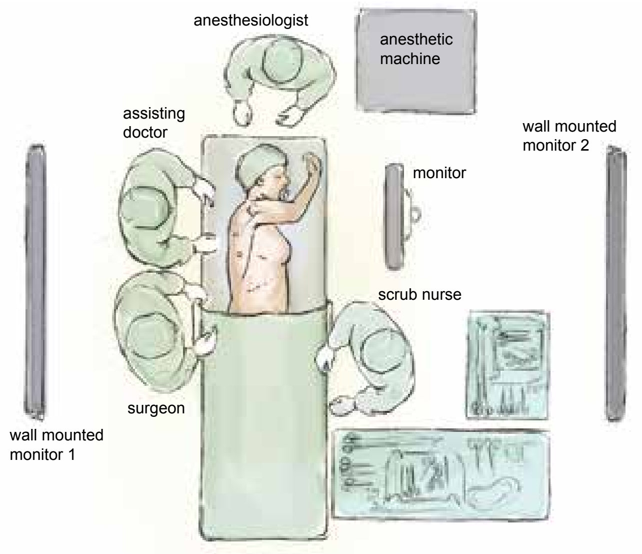

Figure 1 Schematic drawing of the surgical, anaesthetic and nursing teams and the equipment layout.

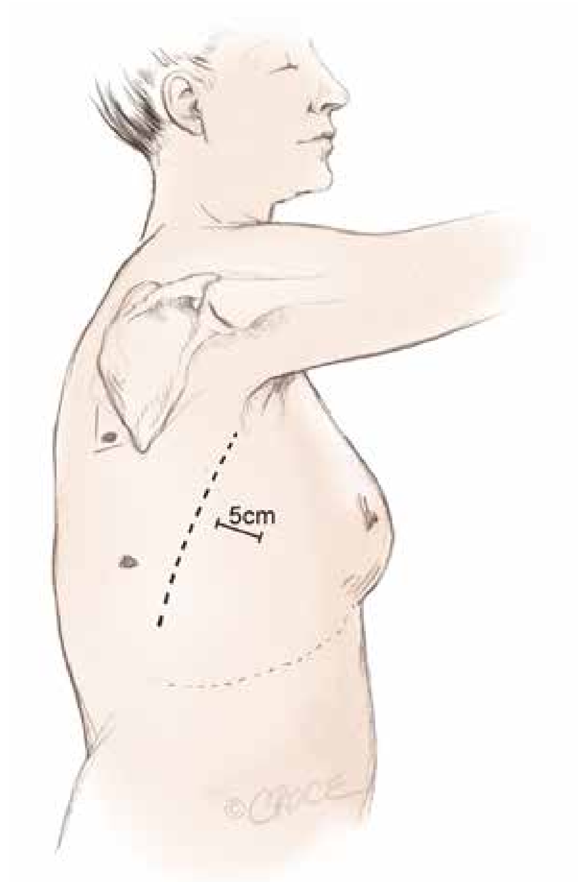

Figure 2 Incisions and port positions in relation to anatomical surface landmarks for the posterior approach, including a 5 cm utility incision anterior to the latissimus dorsi muscle.

irrespective of the lobe to be removed (*Figure 2*). A 5 cm utility port site incision is made in the sixth or seventh intercostal space (whichever is the larger) just in front of the anterior border of the latissimus dorsi muscle. The camera is temporarily introduced through this port to facilitate safe creation of a 1.5 cm incision posteriorly in the auscultatory triangle at the point nearest to the upper end of the oblique fissure. A port is inserted to accommodate the camera, which is positioned in this posterior port for the remainder of the procedure. A further 2 cm port is created in the midaxillary line level with the upper third of the anterior utility port. The anterior and posterior ports lie at opposite ends of the oblique fissure.

Instruments

We prefer a zero degree 10 mm high definition video thoracoscope as this provides a single axis view allowing easy correction of orientation. A combination of endoscopic and standard open surgical instruments is used. Lung retraction and manipulation are performed using ring-type sponge-holding forceps. Long artery forceps (30 cm) with or without mounted pledgets are employed for blunt dissection. These are particularly useful for exposing the PA at the base of the oblique fissure, cleaning structures and clearing node groups. A range of curved forceps and an endodissector are used gently as probes to create a passage between the lung parenchyma and major hilar structures. A right-angled dissector or long curved artery forceps is used to dissect out and pass slings around pulmonary arteries and veins. Endoscopic clips are used to ligate small vessels whilst large vessels and lung parenchyma are divided using endoscopic stapling devices to ensure haemostasis and aerostasis. We have found both endoscopic shears and specific VATS Metzenbaum type scissors to be helpful. The latter have the advantage of curved blade ends which reduce the risk of vascular injury.

Technique

A video-imaged thoracoscopic assessment is performed to confirm the location of the lesion, establish resectability and exclude unanticipated disease findings that might preclude resection. *Video 1* is an edited video clip, which demonstrates several key points of VATS lobectomy via the

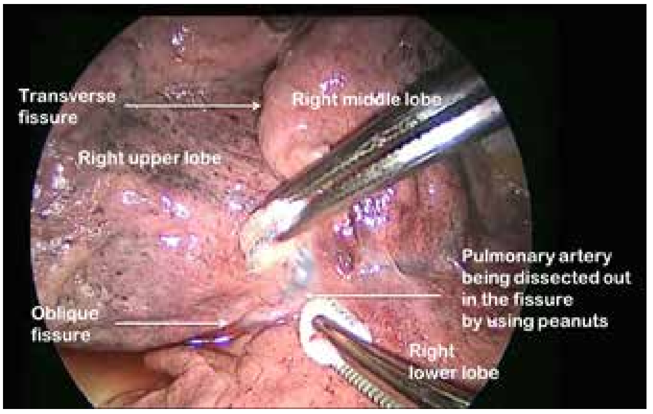

Figure 3 Pledget dissection of pulmonary artery in the oblique fissure on the right side.

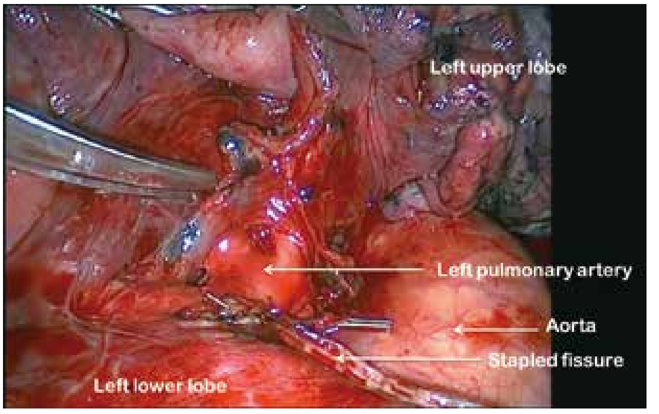

Figure 4 Left pulmonary artery exposed in oblique fissure.

Edinburgh Posterior approach.

The first step is to identify the PA within the central section of the oblique fissure. In some patients the PA is immediately visible, but in the majority of cases, the PA is revealed by separating the overlying pleura using blunt dissection with mounted pledgets (*Figure 3*). If the fissure does not open easily or is fused, an alternative approach utilising a fissure-last dissection as described below should be considered. Once the PA has been identified, the sheath of the artery is grasped with a fine vascular clamp or long artery forceps and an endoscopic dissector is used to enter the sheath defining the anterior and posterior margins of the artery. The apical lower branch of the PA is often exposed during this dissection.

For all lobectomy procedures excepting middle lobectomy, the lung is then reflected anteriorly and the posterior pleural reflection is divided using sharp and blunt dissection. On the right this process should clear lung tissue away from the angle between the bronchus intermedius and the upper lobe bronchus exposing the lymph nodes in this position. On the left, the lung is swept away from hilum exposing the pulmonary artery (*Figure 4*). From the anterior port site, long artery forceps are then passed gently immediately posterior to the PA where it has been identified in the oblique fissure and central to the fused posterior fissure emerging through the incised posterior pleural reflection. On the right side care should be taken during this manoeuvre not to disrupt the lymph nodes lying along the bronchus intermedius. A sling is passed behind the posterior fissure, which is divided with an endoscopic linear stapling device. The PA is now clearly seen on the right side (*Figure 5*) and the distinction between the upper and lower lobes is established. Dissection then proceeds according to the lobe to be resected.

During division of the truncal pulmonary veins we place a central vascular clamp on the vein so that the vein will be secure and unable to retract away in the event of a mishap with the vascular endostaple.

All resected specimens are removed from the thoracic cavity in a retrieval bag to avoid contamination of the wounds with malignant cells.

Right upper lobectomy

Having divided the posterior fissure, the posterior ascending segmental branch of the PA is often evident and if it is should be divided at this stage. It is frequently small enough to clip. The upper lobe bronchus is then identified and dissected out. It is common to find a substantial bronchial artery running alongside the bronchus which should be ligated with clips and divided. Note that clips are only used on the proximal end and the distal end is not clipped since clips in this position may interfere with subsequent stapling of the bronchus.

The upper lobe is then retracted inferiorly and blunt dissection with mounted pledgets is used to free the cranial border of the upper lobe bronchus and define the apico-anterior trunk. The azygos vein is often closely related to the bronchus and can be pushed away using a gentle sweeping motion. A long artery forceps or vascular clamp is passed around the upper lobe bronchus close to its origin in the plane between the bronchus and the associated node packet (*Figure 6*). It should be appreciated that the apico-anterior trunk lies immediately anterior to the bronchus.

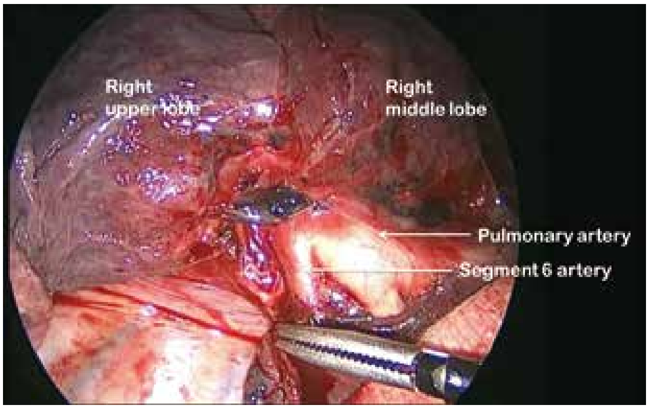

Figure 5 Right pulmonary artery exposed in oblique fissure.

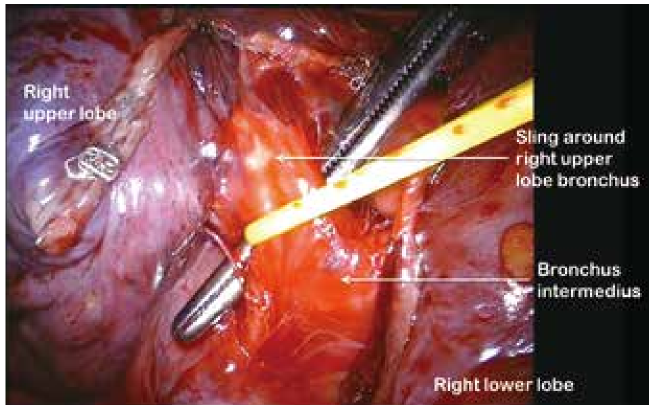

Figure 6 Right upper lobe bronchus ready to be stapled.

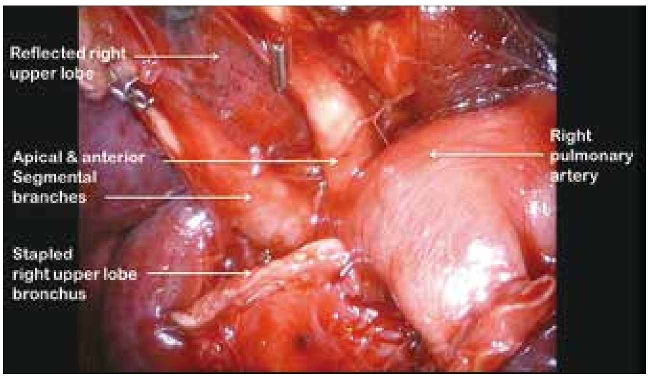

Figure 7 View of apical and anterior segmental arteries after dividing the right upper lobe bronchus and reflecting right upper lobe superiorly.

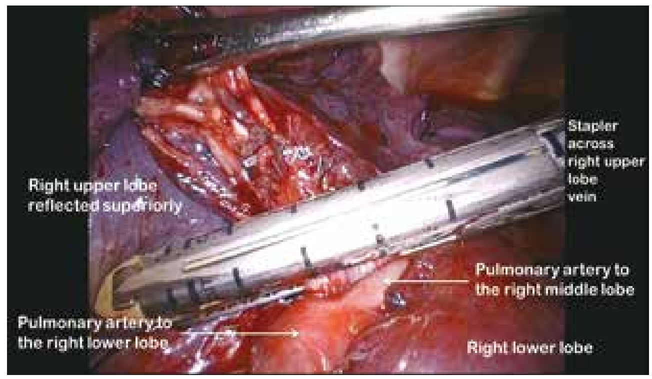

Figure 8 Right upper lobe vein divided using a stapler.

The bronchus is transected at this level using an endoscopic linear stapling device. We do not find it necessary to inflate the lung to test that the correct bronchus is being divided as the vision is invariably excellent and the reinflated lung may then obscure the view for remainder of the resection. Following division of the bronchus the feeding vessels to the right upper lobe bronchus node packet are clipped and divided allowing the nodes to be swept up into the operative specimen.

Clasping the distal end of the transected bronchus with an endoscopic toothed grasper, the upper lobe can be reflected upwards. The posterior segmental artery is divided at this stage if not already dealt with and the apical and anterior segmental arteries or common stem artery are carefully cleaned, dissected out (*Figure 7*) and divided with an endoscopic stapler. Finally, the lung is retracted posteriorly facilitating dissection of the superior vein. This can be divided from either the posterior (*Figure 8*) or anterior aspect as convenient, taking care, in either case, to identify clearly and preserve the middle lobe vein. The transverse fissure is then divided. The middle lobe artery is most easily identified and protected if the stapling device is first passed through the inferior port and fired from posterior to anterior. Division of the transverse fissure is then completed passing the stapling device through the anterior port. The inferior pulmonary ligament is divided to facilitate expansion of the right lower lobe.

Right lower lobectomy

Having identified the PA in the oblique fissure and divided the posterior oblique fissure, the pulmonary artery is then divided either in one or separately as a basal trunk artery and the apical segmental artery to the lower lobe. The space

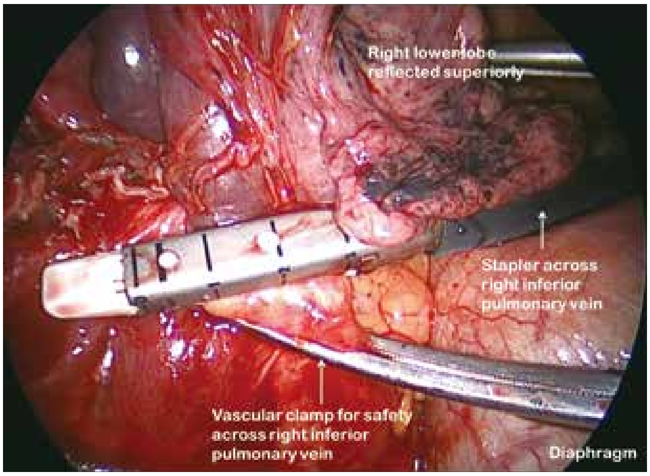

Figure 9 Right inferior vein divided with proximal vascular clamp.

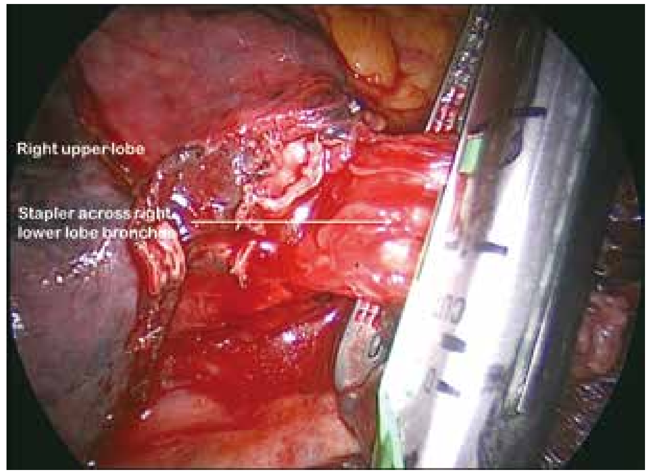

Figure 10 Division of right lower lobe bronchus across apical lower and basal trunk origins.

between the superior and inferior veins is developed and a long clamp is passed into this space emerging anterior to the PA in the oblique fissure. A sling is passed into this plane and the anterior oblique fissure is then divided. The lower lobe is mobilised by dividing the inferior pulmonary ligament. The inferior vein (*Figure 9*) is dissected free from surrounding tissue and divided using an endoscopic linear stapling device. The bronchus is identified and the bronchial vessels are clipped proximally. Lymph nodes are cleared from its medial and lateral margins. The lower lobe bronchus (*Figure 10*) is divided through its apical and basal branches preserving airflow to the middle lobe. The middle lobe bronchus must be visualised prior to stapling.

Right middle lobectomy

The PA is identified and the anterior oblique fissure is divided as for right lower lobectomy. The vein, bronchus and arteries are then seen clearly and are divided in sequence. The transverse fissure is divided as described for right upper lobectomy.

Left upper lobectomy

The PA is identified in the oblique fissure and the posterior aspect of the oblique fissure (*Figure 4*) is divided in a similar way to the right side. The arterial branches to the left upper lobe are then divided sequentially. Division of the anterior aspect of the fissure is completed in similar manner to that on the right side. It is important to develop the space between the pulmonary veins and central to the fused anterior oblique fissure thoroughly. When passing a clamp through the utility incision and under the fused fissure, the surgeon will feel the lower lobe bronchus and should allow the clamp to pass superficial to that so preserving the airway to the lower lobe. Gentle blunt dissection is used to separate the superior pulmonary vein from the anterior surface of the bronchus. A long clamp is passed around the base of the bronchus taking particular care not to damage the PA. Retraction of the PA using a mounted pledget may be helpful. A sling is passed around the bronchus and used to elevate it (crane manoeuvre) in relation to the pulmonary artery and create a space via which an endoscopic stapling device can be inserted to divide the bronchus (*Figure 11*). The superior vein is cleaned and divided. The inferior pulmonary ligament is divided up to the level of the inferior vein to facilitate expansion of the lower lobe.

Left lower lobectomy

As on the right side, having identified the PA and divided the posterior aspect of the oblique fissure, the arterial branches are identified (*Figure 12*). The anterior portion of the oblique fissure is divided as for left upper lobectomy and the arterial supply divided with an endostapler. The inferior pulmonary ligament is divided up to the level of the inferior pulmonary vein. The margins of the vein are clearly delineated and it is then divided. Bronchial vessels are clipped proximally and divided and the lymph node

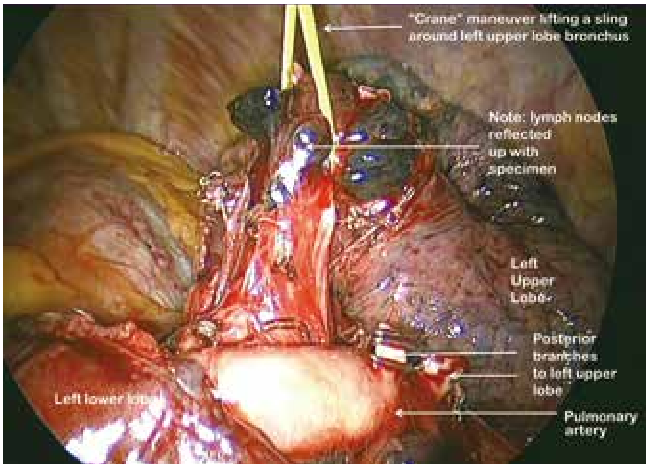

Figure 11 Use of "Crane" manoeuvre to elevate left upper lobe bronchus.

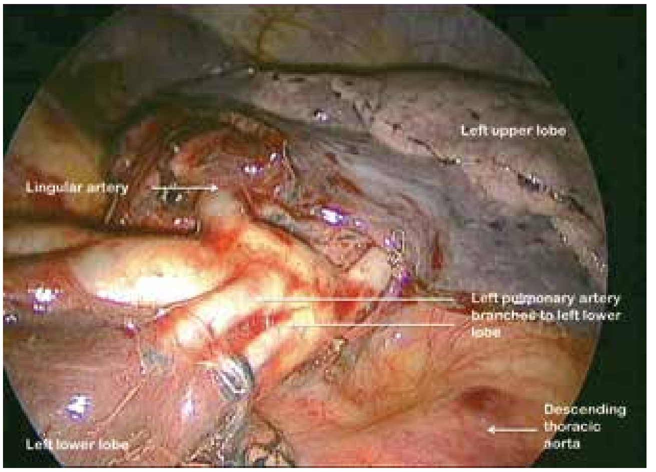

Figure 12 Left pulmonary artery branches to left lower lobe fully displayed.

chains are cleared off the medial and lateral aspects of the bronchus, which is divided at its base.

Strategies for dealing with challenging fissures

In some patients only a partial fissure is evident between the upper and lower lobes whilst in others the upper and lower lobes are completely fused. In such patients, the above techniques may have to be modified. *Table 1* demonstrates a grading system for fissure quality (15).

It should be noted that there are important differences between the right and left oblique fissure. Fissural depth on the right is often not consistent so that while the fissure may be very thick in its upper part, the PA may be relatively easy to identify lower down where the basal trunk vessel is near the lung surface. In this situation the arterial sheath can be entered as described and the lung overlying the vessel divided retrogradely exposing the artery more centrally. On the left the PA can lie very posteriorly so that for upper lobectomy, the artery can be accessed simply by displacing the lung anteriorly.

We have developed two strategies for managing challenging fissures (Grade III/IV) in which the pulmonary artery is not accessible.

The first option is to reflect the lung anteriorly and divide the pleural reflection on the posterior aspect of the hilum. This allows the PA to be readily identified on the left and identified in the angle between the bronchus intermedius and upper lobe bronchus on the right. A clamp is then carefully placed adjacent to the PA and the fissure is draped over it tenting it up and thus identifying the point in the fissure that needs to be divided in order to let the clamp pass through. A sling is then passed through this space allowing the posterior part of the oblique fissure to be divided. The operation then proceeds as previously described.

The second alternative is to take a "fissure last" approach (*Video 1*). Beginning at the posterior pleural reflection, the artery, bronchus and vein are identified and divided first, with the fissure divided once these structures have been dealt with. This is a straightforward strategy for lower lobectomy as all the structures can be accessed by division of the pulmonary ligament and then serial division of the vein, bronchus and artery. It is not our first choice of approach, as we prefer to control the artery first if at all possible and to have optimum exposure of the bronchi in order to facilitate node management.

As a generalisation, in the very rare situation where the fissure is refractory to dissection we prefer the first strategy as it allows a standard dissection thereafter. When that seems technically awkward a fissure last approach is used. Sometimes, a hybrid approach based on the opportunities presenting as the procedure develops may be appropriate.

Lymph node management

All hilar level nodes relevant to the resected lobe are excised. At mediastinal level either extensive sampling or lymphadenectomy is preferred. We have utilised two strategies for lymphadenectomy either routine

Table 1 The Royal Infirmary Anatomical Classification of the Pulmonary Fissures

Grade I: The PA is readily visualised without dissection
Grade II: The PA is revealed following minimal dissection
Grade III: A shallow fissural cleft whereby a large amount of dissection is required to identify the PA.
Grade IV: There is no discernable fissural cleft at all on initial inspection

operative lymphadenectomy or prior mediastinoscopic lymphadenectomy, which typically accesses stations 2, 4, 7 with subsequent operative excision of the remaining mediastinal stations (*Video 1*). In our experience, prior video-mediastinoscopic adenectomy can result in significant tethering of the station 10 nodes and hilar fibrosis if there is any delay in proceeding to the VATS resection. As we prefer to await formal pathological analysis of the mediastinoscopic samples for staging purposes rather than rely on frozen section this induces a delay of several days in our management sequence and has made the VAMLA approach less attractive. We are currently examining our data and from this it is our evolving opinion that routine mediastinoscopy is probably sufficient to exclude station 2 and 4 disease but not for station 7. Thus preperative mediastinoscopy followed by routine formal adenectomy of station 7 and other node groups excluding stations 2 and 4 in this setting will likely be our future strategy.

Post-operative care

A size 32 Fr apical drain is placed through the mid-axillary line port site and is usually removed on the first post-operative day subject to a satisfactory chest radiograph and aerostasis. Patients are observed on a high dependency unit overnight and are typically nursed on the general thoracic ward thereafter. Analgesia is provided using a morphine patient controlled analgesia pump and a local anaesthetic paravertebral catheter placed under vision prior to port site closure. Early mobilisation is strongly encouraged with the availability of physiotherapy seven days per week, and discharge as early as post-operative day 3 is often possible.

Comments

We have presented a safe, reliable and reproducible approach to VATS lobectomy. VATS lobectomy has been shown to compare favourably with open thoractomy in terms of immediate post-operative recovery and is considered to be oncologically equivalent. We believe that the increasing use of minimally invasive techniques for lobectomy and other major pulmonary resections would be highly desirable.

Acknowledgments

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Video-assisted thoracoscopic pneumonectomy: The Edinburgh posterior approach

Jonathan Oparka, Tristan D. Yan, Jennifer M.J. Richards, William S. Walker

Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK

Correspondence to: William S. Walker, MD. 51 Little France Crescent, Old Dalkeith Road, EH164SA Edinburgh, UK.

Email: william.walker@luht.scot.nhs.uk.

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Introduction

Twenty years of experience in Video-assisted thoracoscopic lung surgery (VATS), have led to the development of innovative techniques to rival open thoracotomy for major lung resections (1,2). Acceptability of the technique relates to benefits including; reduced length of hospital stay, decreased blood loss, decreased pain, improved cosmesis, earlier return to normal activities and improved tolerance of chemotherapy (3-6). Whilst the technique was initially limited to pulmonary lobectomy, centers are now routinely performing VATS pneumonectomy. Whilst it remains unclear as to whether the technique affects survival, VATS pneumonectomy provides a safe alternative to open resection, which confers many of the benefits outlined above (7,8). An additional plus, is that patients are not subject to postoperative air leaks, which are one of the major complications of VATS lobectomy, often resulting in prolonged hospital stays and increased morbidity and mortality (9,10).

The technique of VATS pneumonectomy described here is that which is currently employed in the unit of cardiothoracic surgery at the Royal Infirmary of Edinburgh.

Clinical summary

A 70-year-old lady presented with an incidental finding of a left upper lobe lesion on plain chest X-ray, during investigation of probable chronic obstructive pulmonary disease. Past medical history included a right upper lobe, small cell lung cancer in 2002, successfully treated with chemo/radiotherapy. Co-morbidities were emphysema, a transient ischemic attack and at the time of surgery the patient had a SVC stent in-situ for SVC obstruction.

PET CT imaging revealed a 50 mm AP × 30 mm TR, T2bN0M0 lesion in the left upper lobe which may be adherent to the aorta and pulmonary artery (*Figures 1*, *2*). Bronchoscopy demonstrated an intraluminal lesion obstructing the left upper lobe bronchus orifice and CT guided biopsy returned a diagnosis of Non-Small Cell Lung Cancer.

Lung function was assessed via formal spirometry with a FEV1 of 1.85 (105% predicted), a FVC of 2.6 (112% predicted) and an FEV1/FVC ratio of 72% (*Video 1*).

Pre-operative assessment

Pneumonectomy is associated with high morbidity and mortality (11). Patient selection is therefore paramount and pre-operative assessment is perhaps the most crucial stage of the process. Operator experience is also a key factor and individuals unfamiliar with VATS techniques should not attempt VATS pneumonectomy.

Whilst lung conservation is a primary aim of surgery, anatomical considerations often preclude suitability for lobar and sub-lobar resections. In patients where broncho-vascular reconstruction is not viable, VATS pneumonectomy is the procedure of choice in our unit for individuals in whom there is low bulk hilar involvement.

Pre-operative assessment, anaesthesia and positioning is the same as for VATS lobectomy as described by Richards *et al.*, with the key points summarized here (12). Pulmonary function is assessed via a combination of spirometry and CO_2 transfers in all surgical candidates. Whilst providing an estimate of predicted lung function following resection,

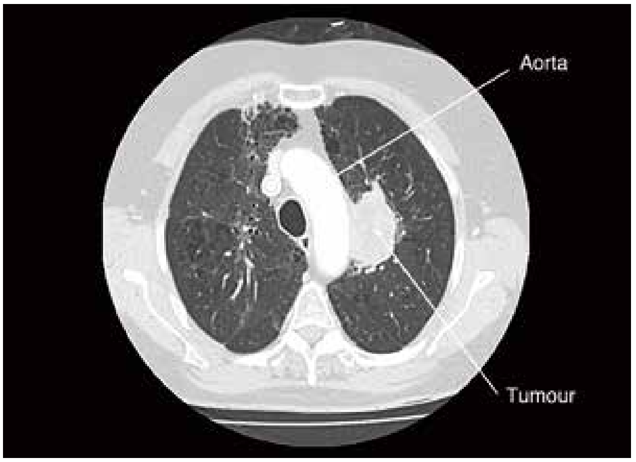

Figure 1 Relationship between the tumour and aorta.

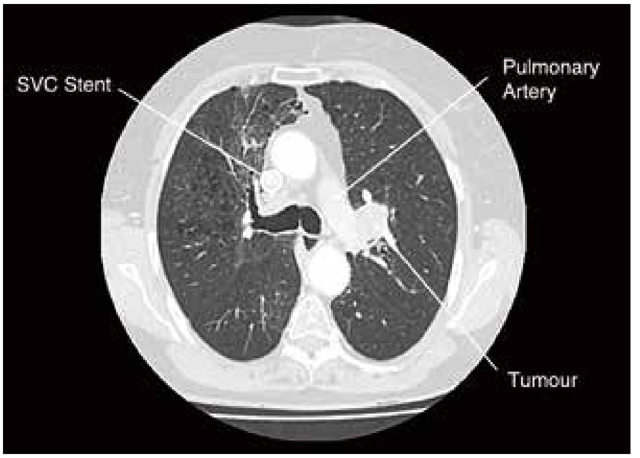

Figure 2 Relationship between the tumour and pulmonary artery.

this also gives a useful baseline value for post-operative comparison and predicts tolerance to double-lumen intubation. In individuals in whom there is a theoretical risk of pulmonary hypertension, Echo assessment of pulmonary artery pressure is undertaken prior to surgery. Further assessment is performed depending on existing co-morbidities.

As part of the staging process, all surgical candidates undergo positron emission tomography-CT (PET-CT) with 18F-fluordeoxyglucose (18F-FDG) subsequent to routine imaging. Regardless of the outcome however, we currently perform mediastinoscopy on all patients due to a 5% false negative rate for detection of lymph node metastases with PET-CT (13). The sampling of lymph node stations is performed in accordance with current guidelines from the European Society of Thoracic Surgeons.

Anaesthesia and positioning

The patient is placed in the lateral decubitus position with the arms extended to 90º and the elbows flexed to 90º. To protect the intercostal neurovascular bundles the table is "broken" or flexed to maximise the intercostal spaces.

General anaesthesia is induced and intubation is achieved via a double lumen endotracheal tube, which allows independent ventilation of either lung. This permits the lung on the operative side to be deflated whist ventilation is maintained to the contralateral lung. Intercostal nerve blocks are utilized for peri-operative analgesia rather than of epidural analgesia to avoid the risk of phrenic nerve involvement and hypotension.

Technique

Three VATS ports are created to facilitate optimal views of the posterior hilum and placement of instruments (*Figure 3*). For VATS pneumonectomy it is necessary to use a slightly extended utility port to permit extraction of the entire lung. A 5-6 cm incision (which can be extended later if necessary) is made in the 7th intercostal space adjacent to the anterior border of latissimus dorsi. A zero degree 10 mm high definition video thoracoscope is temporarily placed through this port to allow safe completion of the anterior and posterior port sites. The posterior incision (approx. 1.5 cm) is made in the auscultatory triangle at the point nearest to the upper end of the oblique fissure. A final 2 cm incision is made in the mid axilliary line in a horizontal plane corresponding to the upper third of the utility port.

The first step in the procedure is to confirm resectabilty and identify invasion of the chest wall, pleurae and hilar structures including the aorta, pulmonary artery and bronchus. The posterior approach allows excellent visualization of the posterior hilum and the structures mentioned above. It is also beneficial in assessing the hilar lymph nodes adjacent to the bronchus.

Dissection is commenced in the posterior hilum with a combination of blunt and sharp incision of the mediastinal pleura, overlying the descending aorta. Any adherent vessels are identified, clipped and cut. At this stage in the procedure care must be taken to avoid inadvertent injury to the vagus, phrenic and recurrent laryngeal nerves. It

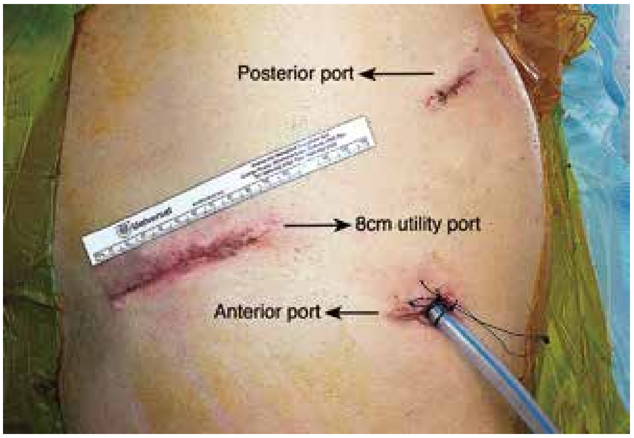

Figure 3 Port placement.

may however be necessary to deliberately sacrifice these depending on tumour spread. The pleura is reflected with a blunt instrument and a Roberts is passed anteriorly to the main bronchus taking care not to injure the pulmonary artery which lies directly anterior. A vascular sling is passed into the jaws of the Roberts which permits gentle retraction. During this manoeuvre, better visualization of hilar lymph nodes, (5&7 demonstrated in the video here) is enabled. Excision of these lymph node packets at this stage will facilitate exposure of the sub-carinal region and the proximal bronchus, and frozen section can be requested if deemed necessary.

Attention is now turned to the inferior and anterior hilum, with the inferior pulmonary ligament divided first. This allows exposure of the inferior and superior pulmonary veins and the pulmonary artery sequentially. When exposure is adequate blunt dissection is used to skeletonize the pulmonary veins.

At this stage consideration is given to the order of division of the hilar structures. Experience tells us that the order of division does not affect outcome and therefore safety should be a priority during this part of the operation.

In the case presented here the superior pulmonary vein was divided using a tan 45 mm tri-stapler passed through the posterior port. Leaving the inferior pulmonary vein at this stage can prevent vascular engorgement, which may hinder progress. Attention was then turned to the bronchus. The key manoeuvre here is to apply gentle retraction to the vascular sling permitting adequate exposure of the bronchus at the hilum. This will allow the bronchus to be taken as close to the carina as possible. Ensuring this is achieved will reduce the risk of broncho-pleural fistula post-operatively. This is accomplished with a purple 45 mm tri-stapler passed through the anterior port. Division of the bronchus allows direct visualization of the pulmonary artery, which is taken with a tan 45 mm tri-stapler. The final vessel remaining is the inferior pulmonary vein. This is taken with a tan 45 mm tri-stapler passed through the anterior port.

Following division of the hilar structures the specimen is retrieved through the utility port. A plastic bag is passed through the utility incision to prevent contamination and tumour seeding in the wound. A paravertebral catheter is placed adjacent to the sympathetic chain through which local anaesthetic can be administered. Finally, a 32F chest drain is placed through the anterior port prior to closure of the port sites. Final pathology revealed a T4N1M0 carcinosarcoma which involved the vagus nerve.

Post-operative management

All patients undergo a routine post-operative chest X-ray whilst in the recovery room. A naso-gastric tube is tube is passed whilst the patient is still sedated. The patient is kept nil by mouth with a fluid restriction of 1.5 L. These measures help to prevent aspiration and development of post-pneumonectomy pulmonary oedema. Analgesia, antibiotics and anti-coagulation are administered routinely in accordance with local guidelines.

Comments

Current debate exists as to whether thoracoscopic pulmonary resections are more effectively performed via an anterior or posterior approach. Based on experience from over 800 VATS major lung resections the preference of the authors is the posterior approach. This technique permits superior views of the posterior hilum, which is crucial during pneumonectomy when dissecting and dividing the main bronchus and major pulmonary vessels. As reported by Richards *et al.*, this approach also enhances the view of the mediastinal node packets which facilitates lymphadenectomy (13). Additionally, the positioning of the camera in the posterior approach allows direct visualization of the instrument tips which is essential for safe dissection.

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Video-assisted thoracoscopic lobectomy using a standardized three-port anterior approach - The Copenhagen experience

Henrik J. Hansen, René H. Petersen

Department of Cardiothoracic Surgery 2.15.2, Rigshospitalet, Copenhagen University Hospital, Denmark

Correspondence to: Henrik J. Hansen, MD. Department of Cardiothoracic Surgery 2.15.2, Rigshospitalet, DK 2100 Copenhagen O, Denmark. Tel: +45 3545 2906; Fax: +45 3545 2182. Email: henrik.jessen@rh.regionh.dk.

Editor's Key Points

1. In experienced hands, VATS lobectomy could be performed in majority of cases [70-80%] without compromising the completeness of resection and offering less morbidity while maintaining less than 1% 30-day mortality rate.
2. A standardized 3 port anterior approach is consistently used and structures are divided from anterior to posterior as they come across.
3. Patients with Tuberculosis, previous surgery, or chemo-radiotherapy are still considered as candidates for VATS approach.
4. Vascular control at hilum is relatively easier in anterior approach
5. Simulation and teaching is easier as surgeon and assistant stand on the same side

--A.H.

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Introduction

Video-Assisted Thoracoscopic Surgery (VATS) lobectomy is now well established and performed all around the world. Formerly there was much debate about the feasibility of the technique in cancer surgery and proper lymph node handling. Although there is a lack of proper randomized studies, it is now generally accepted that the outcome of a VATS procedure is at least not inferior to a resection via a traditional thoracotomy. Several papers have concluded that there is no significant difference in survival rates and that there might even be a better outcome by VATS (1-3).

A VATS lobectomy and even more a VATS anatomical segmentectomy is a challenging and technically demanding procedure to perform; and yet there is still no consensus about the basic principles in the technique. Different techniques have been described including the simultaneously stapled lobectomy (4), a VATS assisted operation with some rib spreading (5) and a true VATS lobectomy defined by no rib spreading along with anatomical hilar dissection and only monitor based vision rather than looking through the utility incision. The procedure is performed with up to 5 incisions and is even reported with a uniportal approach (6). Different lobe specific approaches have been reported (7) and a wide variation in instruments and camera positions is seen.

At our institution we have a large experience with about 1,000 cases performed by a standardised three-port anterior approach with sequential division of the hilar structures, proper lymph node handling, no rib spreading and vision relying on the monitor only. This allows us to perform VATS lobectomies in the majority of the cases even if there are significant difficulties (8). We find that our standardized three-port anterior approach facilitates the VATS lobectomy, and it is our experience from visiting surgeons that our technique can easily be adapted by many surgeons, especially those who are used to an open anterior approach.

The major advantages of the standardized anterior approach are:

- ❖ The mini-thoracotomy is placed directly over the hilum and the major pulmonary vessels. Easy to

clamp the major vessels in case of major bleeding
- ❖ No need of changing the surgeons' position or the place of the incision if a conversion is required
- ❖ The first structures to be transected are the major vessels
- ❖ The same approach to all lobes makes it easy to reproduce and learn
- ❖ The lung tissue only pushed backwards gently with peanuts and never grasped with forceps and therefore not torn apart
- ❖ Easy to teach as the surgeon and the assisting surgeon stand on the same side and use the same monitor. They do not work opposite to each other and therefore maybe against one and another. This facilitates a fluid learning process

Indications for VATS lobectomy

VATS lobectomy is commonly performed for selected peripherally located T1 or T2 tumours and usually reserved for patient where complications are not expected. We think that the advantages of a minimally invasive approach would also benefit cases that are more advanced and therefore the question in our daily clinically practice is: Are there any contraindications to perform the planned lobectomy as a VATS procedure?

At present we find the following contraindications:
- ❖ T3 or T4 tumours.
- ❖ Tumours larger than 6 cm.
- ❖ Tumours visible in the bronchus by bronchoscopy within 2 cm of the origin of the lobe to be resected and where a possible Sleeve resection might be needed.
- ❖ Centrally placed tumours in the hilum and adherent to vessels.

This means that patients with former Tuberculosis, previous cardiothoracic surgery and patients who have received preoperative chemo-radiotherapy are still considered as candidates for a VATS lobectomy. All our patients have a preoperative examination with lung function testing, PET/CT, bronchoscopy and EBUS/mediastinoscopy for preoperative staging (unless it is a peripheral placed T1 tumour on PET). With growing experience, we perform VATS lobectomy in the majority of the cases at our institution, even if they do present with co-morbidity. In the last few years, between 70% and 80% of all cancer lobectomies in our institution were performed by VATS and we now perform well over 200

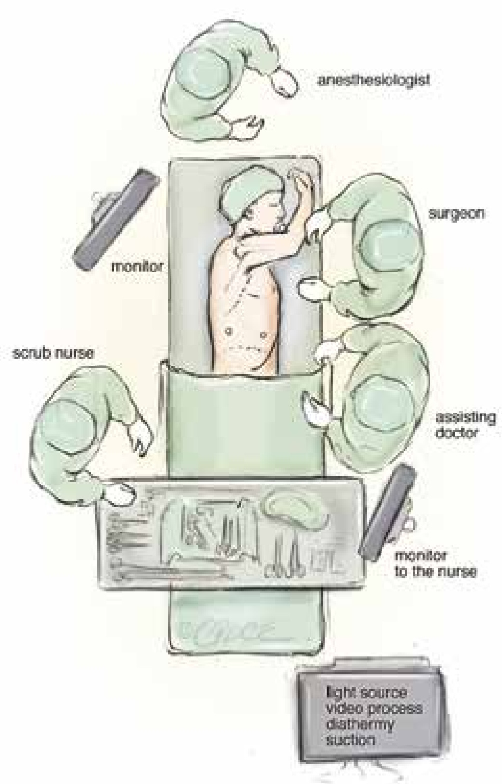

Figure 1 Operating room set-up for the anterior approach of video-assisted thoracoscopic lobectomy.

VATS lobectomies and quite a few anatomical VATS segmentectomies each year (17 in 2011) with a very low conversion rate (2% in 2011).

Operating room set-up and basic surgical principles

A standard set-up is with one monitor placed on each side of the table in front of the surgeons and the scrub nurse (*Figure 1*). Other screens in the room allow other persons in the theatre to follow the surgery. We have two dedicated VATS theatres designed by the author together with Olympus Inc at our clinic and these theatres are only used for thoracic procedures. The basic principle is that the theatre is symmetrical so it is suitable for both right and left sided procedures. The light setting is a dynamic and colored lighting that enhances the surgical ergonometry.

All VATS lobectomies are performed with a 10 mm, 30 degree angled HD video-thoracoscope. The 30-degree angulation allows a superior view within the chest cavity. In a 10 mm camera, the power of the light source is stronger than the light source in the existing 5 mm cameras, and is

Figure 2 Three incisions made for the anterior approach forming a triangular configuration, with the utility incision at the apex of the triangle, measuring 5 cm in length.

not easily flooded by even a minor bleeding.

The surgeon and the assistant are positioned on the anterior (abdominal) side of the patient and with the surgeon cranially. The scrub nurse is opposite to the assistant and follows the operation on a separate screen and still positioned face to face with the surgeon (*Figure 1*). Initially, a 5 cm anterior utility incision is made without any tissue retractor or rib spreading. The wound is protected by a plastic soft tissue retractor kept in place by a ring in the chest cavity and one outside the skin (Alexis Retractor, Applied Medical USA). This incision is later used for specimen retrieval, and is positioned between the breast and the lower angel of the scapula in the fourth intercostal space just anterior to the latissimus dorsi muscle (*Figure 2*). In case of a conversion to open procedure, this incision can be easily expanded to a 10 to 15 cm muscle sparring thoracotomy within a few minutes.

The cavity is evaluated with the camera through this incision looking for unexpected pathology, adhesions, and the level of the diaphragm. A low anterior 1 cm camera-port is positioned at the level of the top of the diaphragm and anterior to the level of the hilum and the phrenic nerve. The final 1.5 cm incision is positioned at the same level but more posterior in a straight line down from the scapula and anterior to the latissimus dorsi muscle. This results in a triangle with two approximately 10 cm limbs and the camera positioned at the apex, with a working channel on each side, which makes the procedure more easy and natural to the surgeon (*Figure 2*). The camera is in the lower anterior corner of the chest cavity with a good overview and it is usually not necessary to change camera port at any point of the procedure.

To palpate, free and prepare the structures, we use an array of a peanut or a sponge stick, an electrocautery blade hook controlled with a normal surgical handhold. The tip of the hook can be used to lift and divide the tissue. To present vessels and other structures to be divided we use an elastic vessel loop made of rubber, as slings of other materials present a risk of tearing, especially the fragile arteries to upper lobes. We do not place clamps on the vessels before stapling but two vessel clamps are ready on the table in case of an emergency bleeding and furthermore a set up for open surgery is present in the theatre.

The vessels, the fissures and the bronchus are divided sequentially, with appropriate endostaplers. For the vessels and thin parenchyma we use a tan Tri-stapler (Covidien, USA) and for poorly defined fissures and the bronchus, we transect with a purple Tri-stapler. Any specimen with suspicion of malignancy is removed with an endobag

Energy-based devices can also be used and we have some experience with an electro-thermal bipolar tissue sealing system (Ligasure, Valleylab Inc., USA) and find it useful to transect minor pulmonary arteries up to the size of 3-4 mm and they are very useful for lymph adenectomy where it facilitates an “en bloc” dissection.

Due to a high percentage of patients with prolonged air-leakage in our early experience, we have changed our strategy to a “fissure non-touch technique”. This means no dissection or use of electrocautery in the fissure. Instead the fissure is stapled with the visceral pleura intact as a seal above the parenchyma, giving a more tight closure within the stapling line, and no scars in the tissue next to the clips. To facilitate this, the fissure stapling is performed quite late in the procedure after the majority of the hilar structures are divided.

At the end, one intercostal drain is placed in through the camera incision. After surgery, the patient is transferred to an intermediate ward and next day to the normal ward. The patients are mobilised on the day of surgery and lung physiotherapy is provided for training. The tube is removed

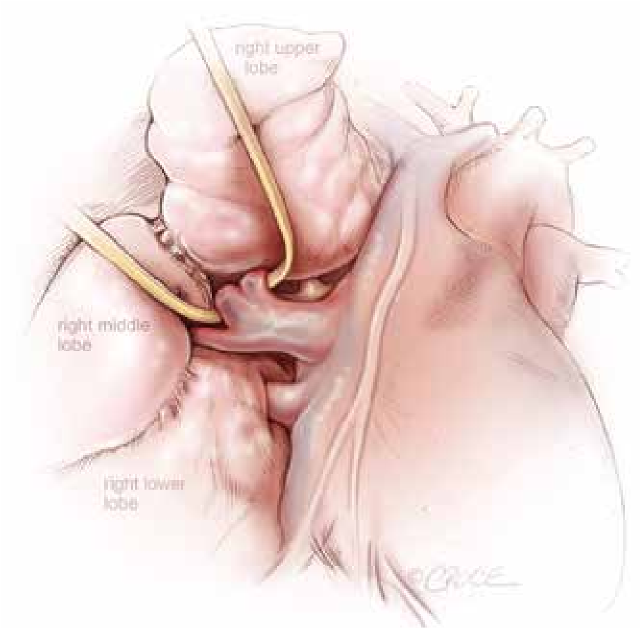

Figure 3 VATS right upper lobectomy: right superior pulmonary vein from right upper lobe is encircled by a vascular loop, while the pulmonary venous drainage from the right middle lobe is clearly seen.

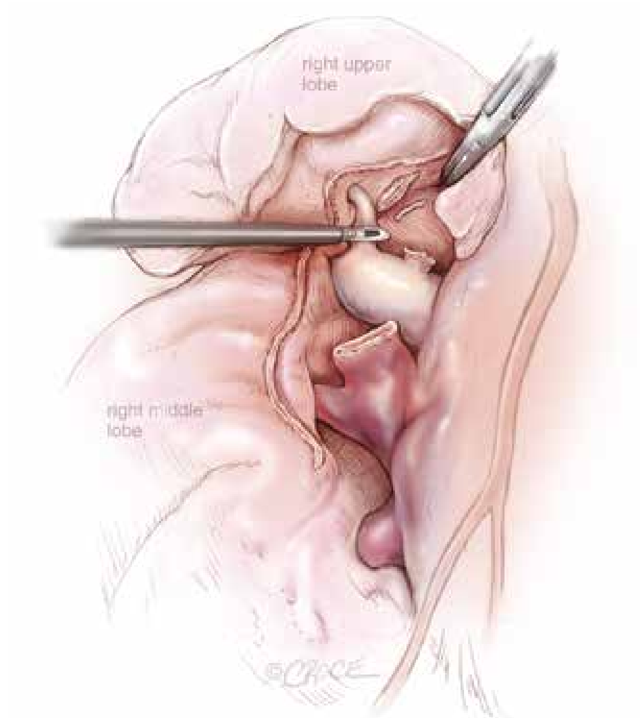

Figure 4 VATS right upper lobectomy: after division of right upper lobe pulmonary vein and truncus anterior, posterior ascending segmental artery to the right upper lobe is being divided by a Ligasure.

when there is no air-leakage and less than 500 cc of fluid in 24 hours. Patients are usually discharged one day after tube removal and seen ten days later in the outpatient clinic.

Operative techniques

After inspection of the cavity and confirmation of the indication for lobectomy, the structures are divided as you encounter them during the operation from anterior to posterior.

Right upper lobectomy

First the pleura over the anterior hilum and along the azygos vein are divided and next a thoracoscopic DeBakey forceps, introduced through the posterior port, is passed behind the superior pulmonary vein after clear identification of the middle lobe vein. The superior pulmonary vein is then encircled with a vessel loop and enough space to introduce a stapler around the vessel is created (*Figure 3*). The endovascular stapler is introduced through the posterior port and the thin blade is passed behind the superior pulmonary vein, which is then divided after removal of the vessel loop.

When the pulmonary vein is divided, the pulmonary artery and the truncus anterior are visualized and the superior trunk is transected in the same way as the vein. The pulmonary artery can then be visualized down to the branches to the middle lobe and the minor fissure is divided with endostaplers (*Figure 4*). The central landmark is the posterior border of the artery just above the middle lobe and below the divided vein to the upper lobe. After the transection of the fissure past the artery, the middle lobe drops down and exposes the posterior part of the artery and the remaining arterial branches to the upper lobe , which are then transected (*Figure 4*). Next the bronchus and the posterior part of the fissure is divided one by one. The bronchus is transected with a purple endostapler (in large-size patients a black Tristapler might be needed) and the device is closed and opened a few times to crunch the bronchus before firing to make the closure tighter. The lobe is then placed in an endobag and removed via the utility incision.

Right middle lobectomy

The anterior part of the pleura over and between the veins

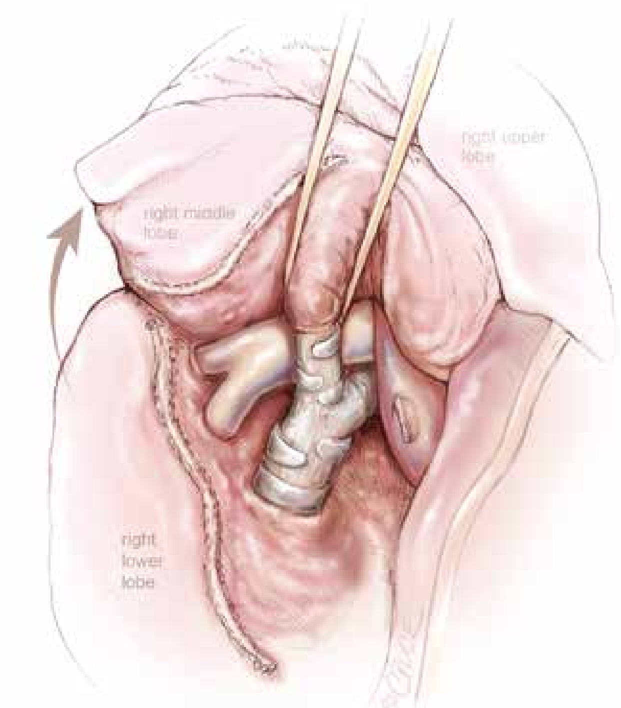

Figure 5 VATS right middle lobectomy: bronchus of the right middle lobe is presented through the oblique fissure after division of the right middle lobe vein.

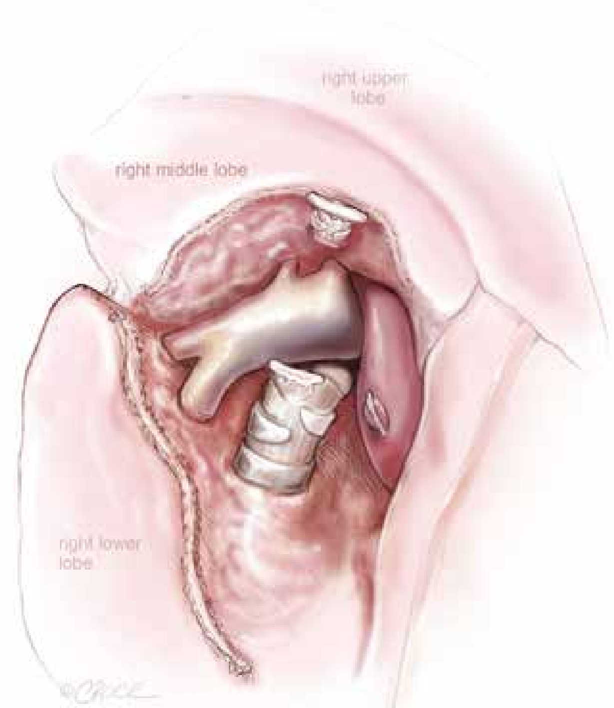

Figure 6 VATS right middle lobectomy: after the division of the right middle lobe vein and bronchus, pulmonary artery branches to the right middle lobe and lower lobe is exposed.

is divided with the hook to expose and allow division of the middle lobe vein. Next, the middle lobe bronchus is exposed by blunt dissection in the hilum but sometimes the anterior part of the major fissure need to be transected. The bronchus is presented with a vessel loop and the stapler is introduced from the posterior incision (*Figure 5*). There will now be a good view of the artery and branches to the middle lobe are exposed (*Figure 6*), encircled and transected. The fissures are then completed beginning with stapling of the central part next to the artery via the posterior port.

Left upper lobectomy

The pleura over the hilum is divided and the artery and both veins are identified. The plane between the artery and the upper lobe vein is opened so the vein is exposed by a vessel loop coming from the anterior utility incision and it can then be transected with the stapler introduced from the posterior port. Next the superior branch of the pulmonary artery is divided in the same way and thereafter a plane between the artery and the bronchus can be created. The bifurcation of the left upper and lower lobe bronchi is identified, and the left upper lobe bronchus is transected from the posterior port by a purple Tristapler. The lobe is pushed posterior and the remaining branches on the pulmonary artery including the lingular artery are exposed and transected by stapler or a mixture of clips and energy based devices. The fissure is finally transected with endostaplers via the posterior port (*Figure 7*).

Lower lobectomies

The lower lobe is retracted superiorly and the inferior pulmonary ligament is divided. This exposes the inferior pulmonary vein which can be encircled with a rubber loop and transected with the stapler from the utility incision. Next in the sequence is the artery where the pleura above are opened to allow the artery to be dissected in the sheath (*Figure 8*). The artery is lifted away from the parenchyma with a vascular sling and divided. In some cases, the superior segment of the right lower lobe artery needs to be divided separately, when it arises high up. The anterior part of the

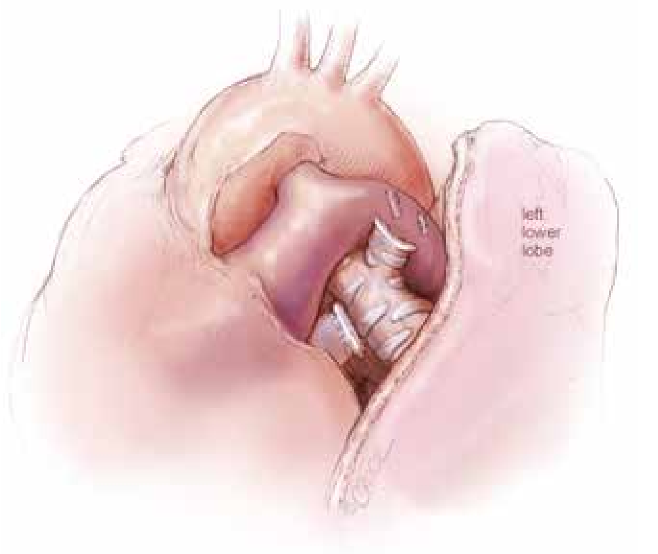

Figure 7 VATS left upper lobectomy: left upper lobe bronchial and vascular stumps are visualized, after left upper lobectomy and en bloc removal of Station 5 and Station 6 lymph nodes.

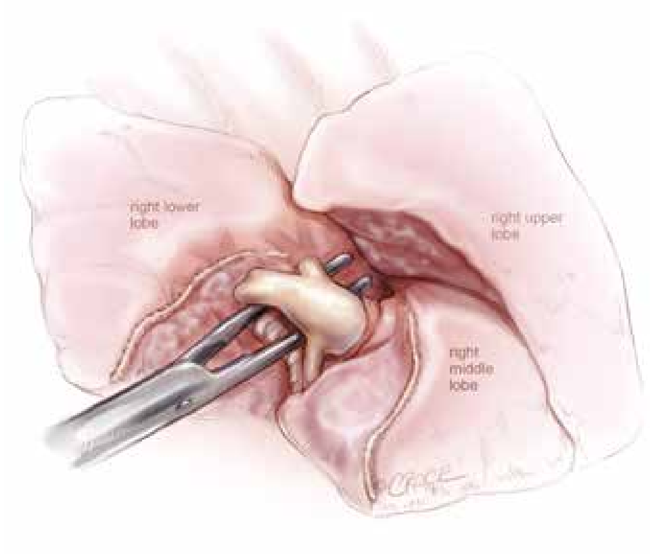

Figure 8 VATS right lower lobectomy: pulmonary artery to right lower lobe, including superior segmental artery is isolated, after dividing the oblique fissure anteriorly.

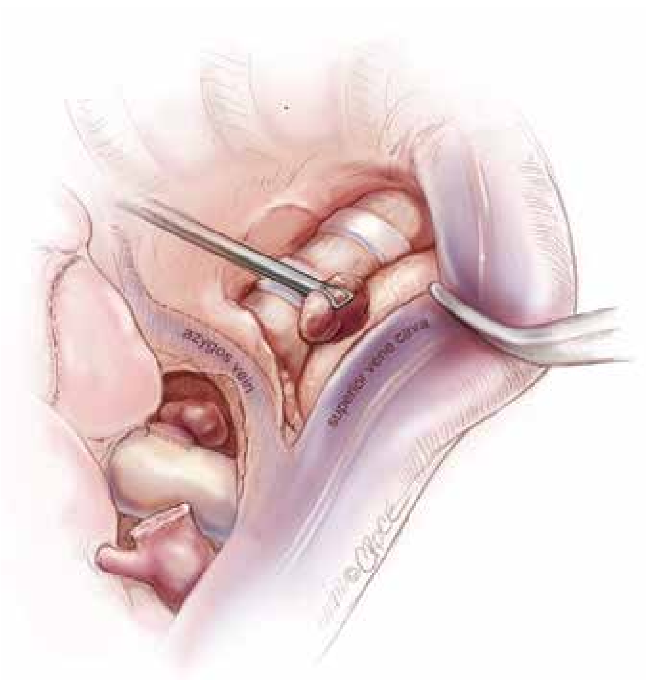

Figure 9 VATS lymph node dissection: superior mediastinal lymph node dissection on the right side.

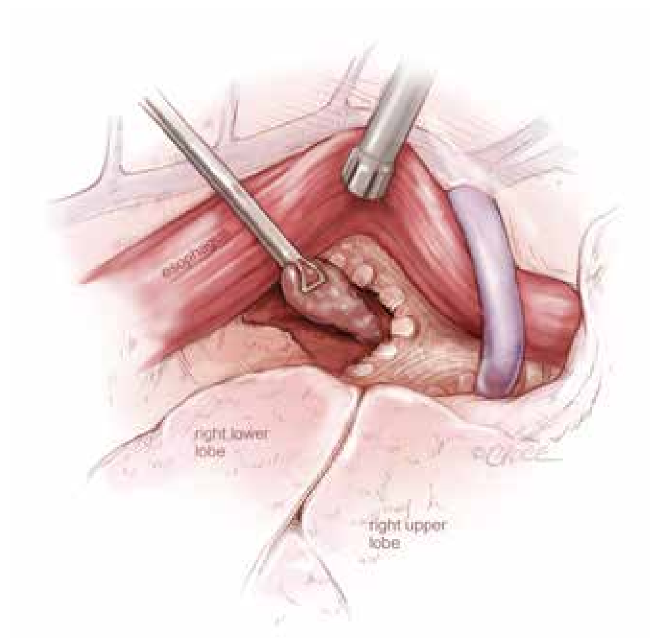

Figure 10 VATS lymph node dissection: subcarinal lymph node dissection from the right side, by retracting the esophagus posteriorly and the lung anteriorly to expose the membranous trachea and the subcarinal region.

fissure is divided before or after the artery and the bronchus and the posterior fissure can be transected step by step.

One should be sure of the position of the middle lobe bronchus on the right side and when in doubt, the stapler should be closed at the site of the planned firing and the lung is then inflated to demonstrate airflow in the middle lobe.

Lymph node dissection

In our opinion it is doubtful whether a complete mediastinal lymph node dissection has a therapeutic benefit, or if the lymph node sampling only relates to stage identification. In all our cases we do a systematic lymph node dissection using the electro-thermal system (Ligasure) or electrocautery with removal of lymph nodes from at least 3 stations of N2 nodes according to the IASLC/Mountain classification.

In right-sided procedures, the nodes removed are from station 2R and 4R en-bloc. First, the pleura is opened above and under the azygos vein. The dissection begins at the tracheobronchial angle and progresses upwards under the azygos vein. After cleaning of the inferior part of the fatty tissue of the superior mediastinum the fatty tissue including the nodes is gripped from above and the dissection continues on so the level 2 nodes are included and the whole tissue packet is removed in one piece (*Figure 9*).

To approach the subcarinal nodes the inferior ligament is divided and the pleura on the posterior limit of the lung is opened up to the azygos vein. The remaining lung is pushed anteriorly and the camera is angled so it looks along the oesophagus and the station 7 is exposed and removed so that the carinal bifurcation and the opposite bronchus are clean (*Figure 10*).

On the left side nodes are removed en-bloc from station 5 and 6 (as seen on *Figure* 7 between the aorta and the main pulmonary artery), station 7 is removed like on the right side. In lower lobe resections nodes from station 8 and 9 on the affected site are removed as well. Station 10 nodes are in upper lobe resections removed as part of the procedure to expose other structures.

Comments

We have a VATS lobectomy program that deals with the majority of our institution's pulmonary resections. All operations are performed with a standardized three-port anterior approach independent of the procedure and the part of the lung to be addressed. There is a low conversion rate with a very low mortality (in the last few years <1% 30-day mortality) and a low morbidity.

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A video-atlas of video-assisted thoracoscopic lobectomy using a standardized three-port anterior approach

Henrik J. Hansen, René H. Petersen

Department of Cardiothoracic Surgery 2.15.2, Rigshospitalet, Copenhagen University Hospital, Denmark

Correspondence to: Henrik J. Hansen, MD. Department of Cardiothoracic Surgery 2.15.2, Rigshospitalet, DK 2100 Copenhagen O, Denmark. Tel: +45 3545 2906; Fax: +45 3545 2182. Email: henrik.jessen@rh.regionh.dk.

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In this issue of the Annals of Cardiothoracic Surgery, we would like to demonstrate how we perform video-assisted thorascopic lobectomies via a standardized three-port anterior approach, a surgical strategy that is routinely performed at the Rigshospitalet in Copenhagen. Four video clips are included in this Masters of Cardiothoracic Surgery section.

The first video clip demonstrates patient positioning and incisions made for the anterior approach (*Video 1*). *Video 2* highlights several special aspects in a right upper VATS lobectomy, including control of the pulmonary vein, sequential divisions of the arterial branches, anterior fissure and right upper lobe bronchus and mediastinal lymph node dissection (*Video 2*). The second surgical case describes the techniques for a left upper VATS lobectomy (*Video 3*) following the similar basic principles as illustrated in the previous video clip. Finally, a case of left lower VATS lobectomy is demonstrated (*Video 4*). It is our hope to provide viewers with a video-atlas of our techniques in a step-by-step manner. The major advantages of the standardized anterior approach include: (I) the surgeon and the mini-thoracotomy are placed directly over the hilum and the major pulmonary vessels, which facilitates the clamping of major vessels in case of major bleeding; (II) no need of changing the surgeons' position or the place of the incision, if a conversion is required; (III) the first structures to be transected are the major vessels; (IV) the same approach to all lobes makes it easy to reproduce and learn; (V) the lung tissue only pushed backwards gently with peanuts and never grasped with forceps and therefore not torn apart; and (VI) easy to teach as the surgeon and the assisting surgeon stand on the same side and use the same monitor. This facilitates a fluid learning process.

We have a VATS lobectomy program that deals with the majority of our institution's pulmonary resections. All operations are performed with a standardized three-port anterior approach independent of the procedure and the lobe being operated on.

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Techniques of VATS lobectomy

John D. Mitchell

General Thoracic Surgery, Division of Cardiothoracic Surgery, University of Colorado School of Medicine, Aurora, Colorado, USA

Correspondence to: John D. Mitchell, M.D. Division of Cardiothoracic Surgery, University of Colorado School of Medicine, 12631 E. 17th Avenue, C-310, Aurora, Colorado 80045, USA. Email: John.Mitchell@ucdenver.edu.

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Introduction

Despite the objections of some zealots, there is clearly more than one way to successfully complete a video-assisted thoracoscopic or "VATS" lobectomy, and further refinements to the technique are added yearly. Most thoracic surgeons would define VATS lobectomy as one in which the dissection is completed with reliance on a video image, without the use of a retractor to spread the ribs and increase the width of the intercostal spaces. The actual number, location and aggregate length of the involved incisions are largely a matter of surgeon preference. Further, the actual methods used-fissure dissection compared with a "fissure-less" approach; Use of sharp, blunt or cautery techniques-is also at the discretion of the surgeon, as long as the basic tenet of individual dissection and ligation of the lobar structures is observed.

Operative technique

Preoperative assessment

Early stage (stages I and II) lung cancer is the most common indication for thoracoscopic lobectomy, although increasingly these techniques are applied in the setting of locally advanced disease following induction therapy. Benign tumors and focal areas of bronchiectasis are also usually amenable to a minimally invasive approach. The indications and contraindications to VATS lobectomy are covered in detail in another chapter in this monograph.

The preoperative assessment of patients considered for VATS lobectomy is routine, and is tailored to the indications for surgery. Preoperative imaging studies, including the use of computed tomography (CT) and positron emission tomography (PET), are helpful to confirm the planned extent of resection and the suitability of a VATS approach. Adequate pulmonary reserve is assessed through the use of pulmonary function testing, with occasional use of perfusion scanning and exercise testing when appropriate. Testing for occult cardiac disease is performed when indicated. In general, the preoperative assessment of a prospective patient is similar to any individual considered for pulmonary resection.

Anesthesia and preoperative bronchoscopy

The anesthetic technique for VATS lobectomy is similar to other cases of pulmonary resection. A means for lung isolation, either with the use of a double lumen endotracheal tube or bronchial blocker, is routine. Placement of a thoracic epidural catheter for postoperative pain control, while common in open thoracotomy cases, is usually not needed following thoracoscopic resection and is routinely omitted. It is often helpful to place intercostal blocks using 0.25% bupivacaine at the end of the procedure to aid immediate postoperative analgesia.

Surgeons are well advised to perform bronchoscopy prior to the procedure, to assess the targeted lobar orifice for abnormalities or any variations in anatomy which could have a significant impact on successful completion of the case. For example, encroachment of tumor on the planned line of bronchial resection could lead to abandonment of the minimally invasive approach.

Incisions and general dissection techniques

The vast majority of thoracoscopic lobectomy techniques employ either two, three, or four incisions, with three perhaps the most common. In all approaches, the camera port (5 to 10 mm) is typically placed low in the chest—7th or 8th intercostal space—and either in the mid or anterior axillary line. A "utility" or "access" incision (3 to 6 cm) is usually placed in the anterior axillary line, over the anterior hilum (about 5th intercostal space) in the cases of upper lobectomy, and an interspace or two lower (adjacent to the major fissure) for middle and lower lobectomies. Third and fourth incisions, commonly 10 mm in size, are placed either through the auscultory triangle, high in the mid-axillary line, or low in the chest in the posterior axillary line. In all cases, no rib spreading is used at any of the incision sites. A soft tissue retractor, either a weitlaner or a commercially available device, is often used at the utility incision. Care must be used at all the incisions to avoid excessive "torqueing" of the rigid instruments on the adjacent ribs and intercostal bundles to avoid postoperative neuralgia.

The surgical procedure is facilitated by roughly aligning the view of the camera with the general direction of the dissection. This is most easily achieved with cameras designed to provide an angled view, either at 30 or 45 degrees from the long axis of the scope. This also allows the surgeon to "see around" the hilum with the camera in a trocar site low in the chest. It is important for the surgeon to remember that occasionally a better view may be available by placing the camera in the access or posterior incision; Flexibility with the operative technique in this fashion can often dramatically lessen the difficulty of the procedure.

Dissection of the hilar structures may be accomplished either using a largely blunt, sharp or cautery-based technique. A thorough knowledge of the hilar anatomy greatly enhances the safety of all of these techniques. Vital structures such as the phrenic nerve or recurrent laryngeal nerve should be identified early and preserved. While all of these techniques are useful, each has obvious drawbacks. It is likely that a combination of approaches probably produces the best results.

Pulmonary vessels and bronchi within the hilum are ligated with endoscopic staplers, although a "TA" type stapler may be used for the bronchus at the surgeon's discretion. It is important to introduce the stapler into the chest such that, once around the vessel or bronchus, it exits into "free space" and is not encumbered by other structures. This will avoid injury to other tissues, and assure a secure closure of the target. Bronchial arteries may be cauterized or clipped, or stapled in rare cases involving long standing pulmonary infection. Fissures are typically stapled unless complete, in which case cautery may be used. It is recommended that specimen removal is achieved with the use of a specimen bag, to minimize contact with the soft tissues at the access incision site. Use of this technique has reduced the incidence of "port-site" recurrence which plagued early attempts at thoracoscopic resection.

In cases of malignancy, nodal dissection may be performed either before or after completion of the pulmonary resection. Initial dissection often facilitates the subsequent lobectomy by increasing the mobility of the specimen at the hilar level. Further, identification of significant N2 disease, previously unrecognized, would allow for termination of the procedure prior to resection to allow for induction therapy. Alternatively, access to the various nodal stations is often improved after the pulmonary resection, thus enhancing the completeness of the dissection. Removal of the hilar and lobar nodes is performed during the ligation of the various hilar structures.

Recently, reports of minimally invasive lobectomies utilizing a single port, or "uniport" approach, have been published. This fascinating technique, still in evolution, is described in a separate submission to this monograph.

Right upper lobectomy (RUL)

The most common technique for "fissure-less" right upper lobectomy utilizes an "anterior to posterior" approach, wherein the dissection progresses from the anterior structures in the hilum to the more posterior structures, dividing the involved fissures last. This technique is felt to minimize complications of air leak which may be associated with significant dissection within an incomplete fissure.

The branches of the superior pulmonary vein pertaining to the RUL are dissected free, and divided with a vascular stapler. In most cases, the stapler is best introduced through the posterior trocar site, or through the camera port. The pleura is incised around the top of the hilum, extending posteriorly to the bronchus intermedius. This allows dissection of the truncus anterior branch of the pulmonary artery, which is divided in a similar fashion. Great care must be taken to avoid excessive retraction of the lobe posteriorly during this maneuver, which may result in arterial injury. It is a good practice to minimize traction on pulmonary vessels during staple ligation, leading to a more secure vascular closure.

Division of the truncus anterior branch will allow improved retraction of the lobe posteriorly, exposing the right upper lobe bronchus and the posterior ascending branch of the pulmonary artery. Either may ligated first, allowing improved exposure for the second structure. Dissection along the ongoing pulmonary artery will allow identification of the middle lobe branches, as well as the branch to the superior segment of the lower lobe. Occasionally, a separate arterial branch may be identified to the anterior RUL segment. Access to the structures to be divided may be enhanced be initiating division of the minor fissure anteriorly; Alternatively, one may divide the RUL bronchus from a posterior approach.

Finally, one completes the major and minor fissures pertaining to the upper lobe with a stapler. As the RUL becomes more mobile, the surgeon must be careful not to prevent twisting or torsion of the lobe at this step, which may lead to inaccurate completion of the fissures.

If the major fissure is complete or nearly so, it is certainly permissible to dissect and expose the artery within the fissure. Doing so will likely aid in completion of the minor fissure, facilitate identification of the superior segmental pulmonary artery, and may improve exposure to the posterior ascending branch of the pulmonary artery for ligation. However, the surgeon should avoid routine dissection within the fissure for a RUL, as is commonly taught in open surgical techniques. Avoidance of air leak is important to maximize the benefits of a thoracoscopic approach, producing shorter chest tube duration and hospital stay.

Left upper lobectomy (LUL)

The location and number of incisions is analogous to those used in right upper lobectomy. An anterior to posterior, or fissure-less approach, is used. Retracting the lung posteriorly and caudally, the pleura overlying the anterior, superior, and posterior hilum is excised. The superior pulmonary vein is dissected free and ligated with a vascular endoscopic stapler. The surgeon must be assured that a separate inferior vein is present and not included in the stapler, as it is not uncommon on the left side for the two pulmonary veins to join prior to entry into the pericardium. The first branches of the pulmonary artery are then dissected free, a maneuver facilitated by removal of adjacent lymph nodes. Again, the surgeon must take care to avoid excessive traction on the LUL, which may lead to arterial injury as the surgeon attempts to expose these initial branches. Introduction of the vascular stapler for these branches is usually through the access incision or the camera port; the anterior location of these incisions allows the stapler anvil to slip around the branch into free space, with minimal torque on the vessel itself.

At this point, only the pulmonary artery branches to the posterior segment and the lingula remain. Exposing these branches is often helped by division of the LUL bronchus. After division of the superior vein, the surgeon has ready access to the crotch between the upper and lower lobe bronchi. Dissection in this area, along with separation of the pulmonary artery from the LUL bronchus as the former wraps around the bronchus superiorly, allows safe isolation of the LUL bronchus. Introduction of an appropriate endoscopic stapler from the anterior camera port will allow safe passage of the stapler between the bronchus and the pulmonary artery into the free space superior to the hilum. After bronchial division, it is fairly straightforward to identify and ligate the remaining pulmonary artery branches to the LUL. The fissure is then completed with a stapler. Occasionally, analogous to the RUL technique, it is advantageous to initiate fissure division prior to this point, to allow better exposure to the deeper hilar vessels.

Right middle lobectomy (RML)

A completely "fissure-less" technique for RML resection is not possible, due to the location of the lobe between the upper and middle lobes. However, as the dissection proceeds in a caudal to cranial direction, the minor fissure is divided last. Despite this, the RML is perhaps the easiest lobe to using thoracoscopic techniques. For this resection, it is helpful to employ an auscultory triangle port to allow passage of the endoscopic stapler, as noted below.

The RML vein is isolated and divided, with the vascular stapler introduced via the posterior (if present) or camera port. Minimal dissection within the major fissure usually yields the pulmonary artery, and the portion of the major fissure between the middle and lower lobes may be completed either with a stapler or the cautery if nearly complete. The surgeon must be careful to identify and preserve a small pulmonary artery branch, invariably present, arising in the medial major fissure to the medial basilar segments of the right lower lobe.

Completion of the fissure allows access to the RML bronchus. The bronchus is freed by developing the plane between the pulmonary artery in the fissure and the bronchus, following the artery more proximally as it wraps around the bronchus superiorly. More anteriorly, the bronchus is separated from the pulmonary venous branches to the RUL, and the bronchus is encircled and then ligated with an endoscopic stapler introduced via the posterior port.

With the bronchus divided, the lobe is retracted cephalad, and one or two pulmonary artery branches are exposed to the RML. Just superior to this, the vein to the posterior segment of the RUL is seen. The arterial branches are isolated and divided either individually or occasionally with the same vascular stapler. If a posterior port is used at this point, it is important that it not be located too caudal, which will make the safe passage of the stapler more difficult. After arterial division, the minor fissure is completed, separating the middle from the upper lobe.

Lower lobectomy (RLL, LLL)

In the case of either right or left lower lobectomy, the operation starts with division of the inferior pulmonary ligament, followed by isolation and ligation of the inferior pulmonary vein. The surgeon should attempt to visualize and include the branch to the superior segment, which in some cases may arise low or even separate from the basilar vein branch. In addition, the left side identification of a separate superior vein is prudent, as mentioned previously. Pleural division posteriorly to the area of the upper lobe and anteriorly to the major fissure facilitates this portion of the case.

At this point, as the dissection proceeds cephalad into the subcarinal space, the surgeon makes a choice about the fissure. If complete or nearly so, the fissure may be completed first, allowing access to isolate and divide the pulmonary artery branches to the lower lobe. On the right, the posterior ascending branch to the RUL must be visualized and preserved, while on the left the lingular artery must be identified. After arterial division, only the bronchus remains, which is dissected free of adjacent nodal material for isolation and ligation using either an endoscopic or TA stapler. The bronchial stump should be short, but on the left care must be taken not to incorporate the bronchial side of a migrated double lumen endotracheal tube in the staple line.

If the fissure is incomplete, one may dissect down through the fissure, identify the pulmonary artery, and proceed as above. However, a better approach is to complete a "fissure-less" dissection in a caudal to cranial fashion, developing the fissure last. To do so, after vein ligation, the surgeon proceeds with the dissection into the lower subcarinal space. Anteriorly, the wall of the lower lobe bronchus is followed into the fissure. On the right, the RML bronchus is identified and kept cephalad to the line of dissection. On the left, a similar approach is used to the identified upper lobe bronchus. If the pulmonary artery is seen at this point, this greatly facilitates dissection between the two structures. A similar dissection technique is utilized posteriorly. On the left, the pulmonary artery is simple to identify posteriorly, enabling dissection between bronchus and artery. On the right, dissection posteriorly proceeds just cephalad to the identified superior segmental bronchus. Working from both anterior and posterior directions, some blunt dissection may be needed to complete bronchial isolation. Partial division of the fissure at this point of the case may greatly enhance visualization. When the lower lobe bronchus is encircled, it is divided with an endoscopic stapler. This then allows isolation and ligation of the pulmonary artery to the lower lobe. Again, care must be taken with respect to the lingular artery and the posterior ascending branch on the right. Finally, the remaining major fissure is completed.

Closure and perioperative management

Following placement of a single chest tube and assurance of hemostasis, chest closure is routine. Absorbable suture is used for the muscle layers and soft tissues external to the chest wall, with no intercostal sutures placed. The skin is closed with absorbable subcuticular suture.

Postoperative management is also routine, but should incorporate a paradigm shift from management strategies used for open lobectomy. As mentioned earlier, some of the advantages in minimally invasive surgery are lost if care plans based on a several day hospital stay after thoracotomy are used. Early mobilization and ambulation, combined with aggressive chest tube management, will result in earlier discharge from hospital, faster recovery and better patient satisfaction.

Outcomes and conclusions

The safety and efficacy of thoracoscopic lobectomy have been demonstrated in several large studies, comparable to open lobectomy (1-3). VATS lobectomy has been shown to be associated with less morbidity (4-7), at least equivalent mortality (4,8,9), shorter hospital stays (4-8), improved functional outcomes (10-12), and less costs (13-15) compared with an open approach. Perhaps most important, minimally invasive lobectomy is oncologically equivalent (1,4,8,9,16,17), at a minimum, to lobectomy through open thoracotomy. A direct comparison with open lobectomy remains lacking, though, and the concept of a prospective randomized trial comparing the open and VATS approaches has been considered repeatedly. However, the recognized advantages of a thoracoscopic approach among dedicated thoracic surgeons have likely eroded any clinical equipoise needed for such a trial. Indeed, these advantages are not lost on practicing thoracic surgeons. Approximately 50% of lobectomies registered in the Society of Thoracic Surgeons General Thoracic Database are completed via a thoracoscopic approach (18), and the percentage continues to increase.

Current frontiers in thoracoscopic surgery now include chest wall resection and reconstruction, muscle flap transposition, sleeve resection, and the use of uniportal techniques. In the years ahead, we may expect advances in these areas, along with further refinement of established techniques in thoracoscopic surgery.

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Video-atlas of thoracoscopic formal lung resections emulating traditional open techniques

Todd L. Demmy

Department of Thoracic Surgery *Roswell Park Cancer Institute*, Elm and Carlton Streets, Buffalo, NY 14263, USA

Correspondence to: Todd L. Demmy, MD, Chair. Department of Thoracic Surgery, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA. Tel: (716) 845-5873; Fax: (716) 845-7692. Email: todd.demmy@roswellpark.org.

Editor's Key Points

1. VATS lobectomy can be safely performed using the same patient positioning and sequence of steps as for open thoracotomy
2. Choose endoscopic instruments that you are familiar and comfortable with
3. Adequate retraction and maximum exposure can be obtained by interchanging the placement of the thoracoscope and other instruments between the 2 ports and the additional access incision

--K.D.

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Thoracoscopic lobectomy began 20 years ago as a natural extension from performing less complex VATS operations. During this evolution, the traditional open lobectomy steps have been modified in some centers to accommodate the limitations in available technology, most notably resulting from the constraints in exposure, vantage point, and retraction. As an example, one such modification is to divide the interlobar fissure rather than the bronchus last.

These modified techniques are quite powerful but require training to become accustomed to the different views of the hilar structures. These variations in the standard thoracotomy approach often reflect individual practices and don't always build on aggregated surgeons' experiences, and also may be difficult to use when faced with complex and aberrant anatomy.

Given the rising popularity of less invasive surgery, technology has been developed to emulate or even surpass the exposure and retraction options used in traditional open techniques. Specifically, high-definition thoracoscopic cameras with deflectable optics provide excellent exposures. Angled, low profile (5 mm shaft) retractors and other instruments can be used simultaneously through single small incisions to set up the traction and counter-traction forces that uniformly enable safe dissection techniques.

This set of videos demonstrates methods that viewers can use to translate their open operative experiences to a successful minimally invasive practice. Even if the viewer has adopted a different preferred approach, many of the demonstrated techniques (like opening incomplete fissures) will come in handy in the presence of bulky tumors or aberrant vascular anatomy.

Table 1 lists the videos and some of the specific maneuvers of interest. The *appendix* provides a timed narrative to help locate specific points in the procedure. The viewer is encouraged to view all the videos as some basic elements are emphasized in only 1-2 of the compilations. Furthermore, it may be useful to view some portions of the videos repetitively concentrating first on the live action and then later on the side bar animation. The animation provides important information on which ports are used for the camera vantage point and or tool manipulations. Since the tools are constrained by the

Table 1 Highlighted maneuvers in each thoracoscopic lobectomy demonstrated in the video clips

Video	Highlighted Maneuvers
Left Upper Lobectomy (*Video 1*)	• Methods for deep nodule wedge • Division of superior vein and anterior artery • Optimal retractor usage for vascular exposure • Division of the anterior and posterior major interlobar fissure • Division of lingula and remaining artery branches • Division of the bronchus last
Complex Left Lower Lobectomy (*Video 2*)	• Control of vascular adhesions and diffuse oozing • Opening the fissure to safely divide continuation artery without sacrificing distal origin of lingular artery • Dissection of central tumor from esophagus. • Opening of pericardium to divide inferior vein • Division of bronchus last
Right Upper Lobectomy (*Video 3*)	• Division of the upper lobe portion of the superior vein and truncal artery • Division of the minor fissure • Division of the posterior major interlobar fissure • Exposure of the continuation pulmonary artery to safely divide the ascending posterior artery • Division of the bronchus last
Right Middle Lobectomy (*Video 4*)	• Division of the vein then bronchus to expose the middle lobe arteries • Division of the fissure last
Right Lower Lobectomy (*Video 5*)	• Division of the anterior and posterior major interlobar fissure • Division of the pulmonary artery and vein with optimal stapler angles • Low profile diaphragm retraction to optimize exposure of the inferior pulmonary ligament • Division of the bronchus last

ports, full lung mobilization (by dividing adhesions) is essential to move anatomic structures into the proper orientation for viewing and dissection. Retraction techniques (that are often not visible in the video frame) are the hardest elements to teach and the movies attempt to emphasize these using the sidebar animations.

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Disclosures: The author declares no conflict of interest.

Appendix 1 Narration of operative steps presented in the video clips

Time Stamp	Left Upper Lobectomy Narration (Video 1)
00 min 19 sec	This overhead view shows the initial port planning for thoracoscopic left upper lobectomy including the flexible camera port
00 min 27 sec	A needle defines the optimal position in line with the fissure but as anterior as possible
00 min 43 sec	Now the same finder needle finds the optimal wide anterior interspace that is useful for dissecting the critical structures of the superior hilum
00 min 54 sec	Here a 4 cm incision has been made and you can see how the two low profile retractors provide the necessary traction and counter traction enabling the passage of a 5 mm dissection tool to divide adhesions
01 min 09 sec	It is important to mobilize adhesions and now you can see the spiculated undiagnosed mass in the left upper lobe
01 min 19 sec	For tumor margins that are only palpable, marking with ink provides visual cues for deep wedge resections
01 min 24 sec	Also deep wedge resections are facilitated by lung compression clamps as demonstrated here
01 min 39 sec	An extra thick stapler load device divides this bulky tissue with less risk of bleeding or lung fracture
02 min 04 sec	Additional compressions are shown here and then the stapler is brought in and applied rapidly after removing the lung compression to allow passage of the stapler without injury by the anvil
02 min 19 sec	Another advantage of this wedge resection is that there is less tissue remaining to manipulate during the later lobectomy dissection
02 min 27 sec	As the tissue thins a standard stapler load is used
02 min 36 sec	Now the specimen is placed into an extraction sac and pulled out through the anterior access port
02 min 43 sec	While waiting for the pathologic diagnosis it is useful to perform intercostal nerve block at this point or even earlier for its preemptive effect
03 min 04 sec	Now viewing toward the working port one retractor depresses the diaphragm while a cautery instrument placed in the same port divides the inferior pulmonary ligament to give mobility to the lung for later re-expansion
03 min 25 sec	Viewing from the medial working port provides better exposure of the anterior and superior hilum
03 min 32 sec	Again you can appreciate this enhanced view
03 min 39 sec	Multiple retractors are placed through the former camera port to provide optimal retraction and counter-traction and to tense the pleura to make it easier to divide
03 min 51 sec	Generally one retractor is placed on the anterior upper lobe and another near the apex to provide this excellent exposure
04 min 04 sec	The superior vein with its lingular branch is demonstrated nicely here
04 min 28 sec	The retractors are manipulated to improve exposure and even a portion of the inferior vein can be visualized
04 min 37 sec	By using a blunt curved clamp it is possible to create a tunnel posterior to the superior vein
04 min 45 sec	It is safer to dissect closer to the heart where the vein anatomy is more predictable with fewer branch vessels
04 min 58 sec	For both right and left sided lobectomies it is useful to perform some posterior dissection early as it tends to improve mobility of the hilum
05 min 09 sec	Here retractors through the access and working ports and the Ligasure™ from the working port open the posterior pleura to expose the ongoing pulmonary artery nicely
05 min 26 sec	Now with the diagnosis confirmed, a lobectomy is indicated

Appendix 1 *(continued)*

Appendix 1 (continued)	
Time Stamp	Left Upper Lobectomy Narration (Video 1)
05 min 30 sec	A retractor swap is made so that the lung is grasped through the access incision and the curved tip stapler is passed through the former camera port while viewing through the working port to divide the upper lobe vein
06 min 03 sec	Now the retraction is moved back to the inferior port
06 min 33 sec	Blunt dissection now exposes the anterior segmental artery as well as to clean some of the posterior pleura not divided from the posterior view
06 min 50 sec	Here the third retractor safely grasps the distal cut portion of the superior vein to provide additional upward exposure to improve the view of the segmental artery
07 min 10 sec	A blunt tip clamp surrounds this vessel and another retraction swap is made
07 min 26 sec	A stapler is again passed through the former camera port to divide the segmental branch
07 min 53 sec	One can see the bronchus inferior to it
07 min 59 sec	Now it is useful to divide the rest of the arterial branches and this can be done by using a traditional camera vantage point by providing traction and counter-traction and rotation of the fissure to yield optimal visualization
08 min 11 sec	Here are the two working port instruments to provide this traction and counter-traction and optimize the visualization of this incomplete fissure
08 min 28 sec	As this is done one can use a third dissection tool via this anterior working port
08 min 45 sec	Now the arterial anatomy becomes clearer
08 min 57 sec	These small fibers can be thinned out by using a small clamp or, in this case, blunt dissection exposes the vessel nicely
09 min 09 sec	Now with retractors applied posteriorly to pull the lung medially the blunt tip clamp exits the space created by the earlier posterior dissection
09 min 20 sec	This tunnel is maintained with a silicone loop
09 min 26 sec	By retracting this loop through the access incision and replacing the stapler through the working port the posterior fissure is divided
09 min 35 sec	Alternatively a stapler with a catheter leader connected can pass through this tunnel as well
09 min 43 sec	The long incomplete anterior fissure is easy to divide and greatly improves the lung mobility and hilar exposure
09 min 56 sec	Access incision retraction and a retractor from the working port beside the stapler make it easier to take multiple safe divisions of that fissure and the artery visible and protected
10 min 18 sec	As this is done, it is easy to move the lung and hilum more efficiently
10 min 26 sec	Completing this anterior fissure will be demonstrated momentarily
10 min 35 sec	With one retractor on each lobe providing opposing retracting forces the residual tissue covering the bronchus is exposed
10 min 54 sec	Now by pulling the lung anteriorly the basilar artery branch to the lower lobe and the lingular branches to the upper lobe are being exposed
11 min 32 sec	Now a catheter leader can be placed between these 5 mm retractors and brought out through the access incision
11 min 54 sec	This leader catheter’s flange will be sufficient to grasp the tip of a standard round tip stapler
12 min 02 sec	However cutting it and applying it to the curved tip stapler allows it to pass through the tunnel with less resistance
12 min 13 sec	This is also useful when the flange is one the wrong end of the passage plane

Appendix 1 *(continued)*

Appendix 1 (continued)

Time Stamp	Left Upper Lobectomy Narration (Video 1)
12 min 24 sec	Here you can see completion of the remaining anterior fissure, which allows excellent exposure of the artery for further maneuvers
12 min 34 sec	Note how important the lower lobe retractor is to put the artery into perfect orientation for dissection
12 min 49 sec	Now a large right angle clamp is passed about the bronchus to completely create the space behind and the three lingular branches
13 min 03 sec	A retraction swap is again performed
13 min 15 sec	One inferior retractor remains to provide exposure while the curved tip stapler slides through the newly created tunnel
13 min 43 sec	There remains one additional posterior arterial branch
13 min 54 sec	Using the same lung retraction method as before pulling inferiorly on the lower lobe and cephalad on the upper lobe through the access incision the stapler passes through the anterior working port to divide this remaining branch
14 min 16 sec	Excessive upper lobe retraction can create an injury to these small vessels
14 min 26 sec	The branch is being inspected for hematoma or any other sign of injury
14 min 40 sec	A Diamond Flex Retractor can pull tissue up and away to allow cleaning of the bronchus
14 min 49 sec	And then through the same port the thick load stapler is passed to divide the bronchus
15 min 08 sec	The bronchus continuation to the lower lobe is clearly visible
15 min 16 sec	A test inflation is demonstrated here insures that the bronchus to the lower lobe is has not been impinged
15 min 21 sec	Alternatively one can view through a pediatric bronchoscope while doing this maneuver
15 min 28 sec	Using cooperating instruments the specimen is placed into the extraction sac
15 min 38 sec	Then to avoid rib injury it is useful to create a lead point through the sac and provide some additional force bluntly from inside to coax the specimen through the 4 cm access incision
16 min 05 sec	Cooperating instruments and low profile lymph node graspers as shown here dissect the lymph node packet for the AP window region as well as the lymph nodes in the level 10 L and level 8 positions
16 min 21 sec	Fibrin glue can be applied to any area of concern for later bleeding
16 min 32 sec	Viewing from the anterior working port it is useful to position the chest tube through the former camera port
16 min 42 sec	Viewing the stump under water while 20 cm of pressure is applied to the airway and then pulling back insures pneumostasis and reinflation of the remaining lung

Appendix 2

Time Stamp	Complex Left Lower Lobectomy Narration (Video 2)
00 min 13 sec	Here you can see the working port incision
00 min 18 sec	The left lower lobe is severely adherent to the posterior chest wall with signs of pleural fluid and active inflammation
00 min 32 sec	The Ligasure™ is used to separate the adhesions between the left lower lobe and diaphragm as well as the posterior chest wall
00 min 42 sec	Generally areas of movement such as the diaphragm and aorta have less adherent planes to dissect the overlying tissues away
00 min 52 sec	Close to the chronic inflammation you can see the oozing from all of these surfaces that will be controlled later by energy devices

Appendix 2 *(continued)*

Appendix 2 (continued)	
Time Stamp	Complex Left Lower Lobectomy Narration (Video 2)
01 min 00 sec	Here the plane between the aorta and the lower lobe is being created bluntly
01 min 10 sec	The Aquamantys™ bipolar tissue linking device is delivered through the access incision and does a nice job controlling the diffuse oozing typically for these cases
01 min 28 sec	It is evident that the inflammation extends into the inferior pulmonary ligament
01 min 34 sec	Both the Ligasure™ and the retractor are placed through the working port
01 min 39 sec	One tool depresses the diaphragm and the other tool divides the inferior pulmonary ligament extending up to the thickened pleura adjoining the aorta
01 min 47 sec	This area is also inflamed and hemostatic agents can be placed to promote clotting
01 min 56 sec	Attention is given to interlobar fissure for dissection to continue without wasting time
02 min 03 sec	Here a Heart-port™ grasper is used to tent the pleura while standard cautery opens the inflamed tissues to expose the pulmonary artery
02 min 19 sec	Better views of the pulmonary artery result from completely opening fissures
02 min 25 sec	Here the landing zone is created with a peanut dissector at the junction of the interlobar fissure and the medial hilum
02 min 38 sec	The pulmonary artery is shown there and a straight blunt clamp tunnels beneath the fissure posteriorly to terminate in the landing zone
02 min 56 sec	This allows passage of loop to help hold open the tract and then a curved tip stapler hugs the back of this dissection pathway to complete the anterior portion of the interlobar fissure
03 min 10 sec	Notice how two retractors both from the anterior working port provide traction and counter traction
03 min 16 sec	Once done it is now useful to complete the posterior fissure
03 min 31 sec	Again looking posteriorly between the aorta and the hilum the exit zone is identified and cleaned bluntly
03 min 41 sec	Then by using a slightly curved blunt clamp through the access incision and gently spreading in the direction of the landing zone it is possible to open the posterior fissure to expose the arterial anatomy safely
04 min 13 sec	Although not always necessary, loops such as this help to define the tunnel, particularly when using a standard round tip stapler
04 min 31 sec	Two retractors from the anterior working ports provide traction and counter traction and a peanut blunt tip retractor further defines the arterial anatomy
04 min 51 sec	A blunt instrument gently separates it away from lymphatic tissue
04 min 56 sec	A surgical stapler or a 5 mm energy sealing device can then be passed between the two retractor instruments through the same anterior working hole
05 min 04 sec	Here you can see the curved tip stapler device dividing the remaining posterior fissure to expose the superior segmental artery
05 min 13 sec	Notice that this artery arises from the continuation pulmonary artery proximal to the lingular artery
05 min 20 sec	Again using the same maneuver, it is divided with a curved tip stapler to preserve the continuation pulmonary artery down to the origin of the lingular artery
05 min 43 sec	The base of the artery branches are then dissected bluntly from the surrounding inflamed tissue
05 min 54 sec	Here a large right angled clamp is shown in accelerated speed demonstrating how multiple small spreads with no more force than the weight of the instrument will help it open that tunnel beneath the vessel
06 min 08 sec	Then using the supplied silicone extension of the curved tip stapler, the anvil is guided through safely to allow division of this artery, while preserving flow to the lingular segment
06 min 38 sec	A curved tip extension does not require removal before firing the stapler
06 min 49 sec	Pulsatile flow into the lingular artery is verified after the oblique firing of this vascular stapler
Appendix 2 *(continued)*	

Appendix 2 (continued)

Time Stamp	Complex Left Lower Lobectomy Narration (Video 2)
06 min 56 sec	Now the lung is transferred to a ring retractor passed through the access incision to allow separation of the inflamed thickened tissues
07 min 10 sec	If there is any question of aberrant venous drainage, vascular staplers can be used to divide these tissues
07 min 19 sec	This central lower lobe tumor was adherent to the esophagus
07 min 24 sec	You can see muscle fibers being thinned out and dissected off of the tumor
07 min 43 sec	This is a useful Diamond Flex retractor initially developed for laparoscopic liver retraction
07 min 49 sec	Even larger specimens like this can be controlled with a single instrument provided the dissection has been performed to the point that the diamond flex retractor can be passed around the hilum
08 min 02 sec	This 5 mm retractor also allows other instruments such as the stapler to pass beside it
08 min 08 sec	Here you can see the bulky tumor anatomy and its adherence to the esophagus and pericardium that keeps the inferior pulmonary vein within it from being divided at this point
08 min 21 sec	Lymph nodes, such as the level 8 station are shown
08 min 27 sec	To open the pericardium, it is grasped at an area where the heart can be seen moving beneath it. Here you can see pericardial fluid egressing and with an endoscopic scissors passed through the access incision further opening into the pericardium is created to allow safe visualization of the inferior pulmonary vein
08 min 56 sec	In this case it would have been very difficult to divide this vascular structure without entering the pericardium
09 min 09 sec	Further dissection of the pericardium off of the vein circumferentially is performed
09 min 14 sec	Here a large right angle clamp can be passed safely around the pulmonary vein and its insertion into the left atrium
09 min 36 sec	This right angle clamp can deliver a catheter to help guide the curved tip stapler through a tight passage such as demonstrated here
09 min 47 sec	One advantage of the curved tip anvil extension is that it no longer requires using the whole open flange of such a leader catheter
10 min 04 sec	The tubing can simply be cut, in this case it is 14 French red rubber tubing
10 min 11 sec	The catheter can be stretched onto the tip, just like the leader that comes with this product except it has the advantage of being much longer
10 min 42 sec	Since this stapler is going across thicker atrial tissue, notice that we are using the longer length purple load tri-staple cartridge
11 min 02 sec	In this view you can see the tumor and its effect on tissues immediately above the stapler
11 min 22 sec	Now the remaining pericardium and inflamed tissues around the bronchus are divided with an energy device
11 min 30 sec	The surgeon can help feel for the bronchus within this structure using the suction catheter
11 min 34 sec	Here you can see a lymph node grasper removing an 11 L lymph node. Additional lymphatics are divided with the Ligasure™ as the main-stem bronchus is being dissected
11 min 58 sec	The same Diamond Flex retractor provides downward force to lengthen the bronchus so that a black tri-staple load cartridge can be positioned and closed
12 min 12 sec	Green or black load staplers are useful for thick tissue like the bronchus
12 min 20 sec	Here the Diamond Flex retractor remains in and provides a convenient way to provide base stabilization of the triangular opening into the extraction sac
12 min 30 sec	Large specimens such as this are manipulated into the extraction sac using cooperating instruments one through the access incision and one sharing the anterior working port
12 min 45 sec	The site of the tumor is inspected and here you can see the application of fibrin glue sealant to the area of previous oozing and placement of a chest tube

Appendix 3	
Time Stamp	Right Upper Lobectomy Narration (Video 3)
00 min 10 sec	This view shows the thoracoscopic appearance of the right upper and middle lobe
00 min 24 sec	Adhesions are divided using the Ligasuretm
00 min 35 sec	A right angle clamp dissects the posterior pleura posterior to the right upper lobe bronchus
00 min 41 sec	Multiple graspers through a single port provide traction and counter traction for optimal viewing
00 min 51 sec	Now attention is giving to the interlobar fissure which is nearly complete in this patient except for the posterior fissure
01 min 00 sec	A thoracoscopic DeBakey forceps is used to lift the pleura and incise it
01 min 07 sec	Later this will be useful to complete division of the minor fissure
01 min 24 sec	This view shows the phrenic nerve and the superior hilum but by viewing from the anterior port there is a much better view of the middle lobe and upper hilum
01 min 36 sec	The middle lobe and upper lobe branch of the superior pulmonary vein is shown in this view
01 min 43 sec	With two retractors holding the lung in optimal orientation a large blunt clamp separates the vein to the upper lobe
02 min 04 sec	To aid passage of the stapler, an elastic retractor is placed as an optional step
02 min 10 sec	An important aspect of this technique is swapping retraction from the inferior port to the access incision to allow passage of the stapler
02 min 20 sec	The inferior port retraction is switched to the access incision to hold the upper lobe and the vein in the proper orientation
02 min 34 sec	The stapler coming from the inferior port is passed around the vein branch to the upper lobe
02 min 41 sec	Notice how the stapler has to be articulated and then rotated to allow the anvil to follow the correct course around the vein
02 min 51 sec	This orientation allows entry behind the vein and now rotation of the stapler allows the anvil to pop out behind and divide the vein
03 min 00 sec	This gains exposure for the continuation pulmonary artery and the apical trunk artery
03 min 18 sec	Still viewing from the anterior port, the pleura and the lymph node packet from the superior truncal artery are dissected
03 min 29 sec	Once the artery is properly dissected the same exchange of instruments is performed with graspers switching from below to the access incision
03 min 38 sec	Full articulation almost always provides an excellent angle for passing the stapler using the rotational move to allow the anvil to hug the back of the vessel
03 min 55 sec	The minor fissure is partially divided with a stapler from outside in
03 min 59 sec	Applying the stapler at the level of the chest wall adds to safety
04 min 08 sec	Now you can see a blunt clamp dissecting just lateral to the continuation pulmonary artery
04 min 22 sec	A large blunt right angle clamp manipulated through the access incision traverses all the way through to exit within the fissure where the pleura was dissected earlier
04 min 40 sec	To facilitate passage of the stapler and completion of the minor fissure a red rubber catheter can hold open the track
04 min 56 sec	The catheter tip needs to be sutured to another red rubber catheter which will then act as a leader for the stapler anvil

Appendix 3 *(continued)*

Appendix 3 (continued)	
Time Stamp	Right Upper Lobectomy Narration (Video 3)
05 min 12 sec	Once partially through as a leader the anvil is delivered by pushing tissue over top of the red rubber
05 min 21 sec	To ease passage of subsequent reloads for long incomplete fissures the leader can remain attached provided the stapler is not fired all the way to the tip
05 min 46 sec	In this case firing the stapler was aborted to further investigate the pulmonary vein drainage that appeared aberrant in this view
05 min 52 sec	By opening the posterior fissure the venous drainage to the upper lobe can be selectively dissected thereby exposing the ascending posterior pulmonary artery branch
06 min 19 sec	This is dissected with a large blunt clamp through the access incision while providing both traction and counter traction through the single anterior working port
06 min 53 sec	The stapler through the access incision is well aligned to divide structures that lie within the incomplete fissure using a 2.5 mm load
07 min 02 sec	Once the venous anatomy has been confirmed, it is then possible to repeat the earlier steps to complete the minor fissure
07 min 20 sec	Here the Snowden-Pencer Diamond Flex loop retractor is used to snare the upper lobe to define the remaining bronchus
07 min 30 sec	The Ligasure™ is used to clean the remaining tissue
07 min 39 sec	And then through the same port that the retractor holds the lobe, it is possible to pass a 4.8 mm green load stapler to complete the division of the upper lobe bronchus
07 min 53 sec	After division of the bronchus the upper lobe is removed using a specimen extraction sac as seen on the other videos

Appendix 4	
Time Stamp	Right Middle Lobectomy Narration (Video 4)
00 min 12 sec	The working port is created anteriorly in line with the interlobar fissure
00 min 18 sec	Then using a 4 cm access incision similar to that used for upper lobectomies a third interspace opening is created
00 min 29 sec	Here two retractors show manipulation of the upper and middle lobe
00 min 36 sec	This is viewed better by inserting retractors in the former camera port to show the tumor in the right middle lobe as indicated here
00 min 46 sec	These two retractors hold both the upper and middle lobe to put the superior vein on stretch so that the pleura can be resected bluntly off of it
00 min 55 sec	Here you can see two branch veins to the middle lobe coming into view during the dissection
01 min 09 sec	After creating a passage behind these two branch veins it is then necessary to pass the stapler from the former camera port to which the retractors are currently residing
01 min 19 sec	This requires transferring the retraction to a clamp through the access incision
01 min 31 sec	Then the curved tip vascular stapler hooks behind both of these veins to allow the easier passage of the stapler anvil through the tunnel
02 min 03 sec	With retractors back through the former camera incision the upper lobe is stretched to put tension on the middle lobe bronchus shown here to facilitate peanut sponge dissection
Appendix 4 *(continued)*	

Appendix 4 (continued)	
Time Stamp	Right Middle Lobectomy Narration (Video 4)
02 min 19 sec	Cautery is used to complete part of the interlobar fissure by incising the pleura
02 min 27 sec	Here a ring clamp extracts the lymph node next to the bronchus to improve the exposure
02 min 38 sec	As in this case, removing lymphatic tissues frequently improves visualization
02 min 56 sec	Now with a clear view of the bronchus a large blunt clamp can be placed safely around it
03 min 05 sec	Depending on the anatomy any of the working incisions can be used to pass the stapler
03 min 09 sec	In this case, the access incision had adequate angle to divide the bronchus
03 min 27 sec	This now improves exposure of the remaining vasculature the two branches of the middle lobe artery
03 min 33 sec	Some of the incomplete fissure is divided to ease passage of the stapler
03 min 40 sec	Again the retraction swap is being performed and you can see that the tunnel behind these branch arteries is somewhat long and serpentine
03 min 54 sec	A leader is useful to help guide the stapler through this passage
03 min 59 sec	Alternatively each branch could be divided individually
04 min 09 sec	The silicone leader is incorporated into the tip of the stapler thus being able to guide the stapler anvil without needing to dilate the tunnel excessively
04 min 39 sec	Putting the tissue on proper stretch allows passage of the stapler easily and then this enables division of the two branch pulmonary arteries
05 min 00 sec	While it would be possible to divide the minor fissure through this view, one can get a better view of the anatomy back through the original camera port
05 min 13 sec	Here one can see the interlobar boundary - the lobe is now positioned to facilitate dividing the fissure
05 min 22 sec	Because this tumor extends toward the upper lobe additional lung can be taken in continuity with the middle lobe to provide a better margin
05 min 32 sec	The stapler is passed through the anterior working port
05 min 44 sec	The lobe is viewed from this position then flipped over and viewed again from underneath being careful to keep the residual bronchus above the stapler
05 min 57 sec	Then an additional stapler fire completes the dissection
06 min 04 sec	As usual a specimen extraction sac is inserted and then the specimen is placed into it and removed through the access incision
06 min 13 sec	An intercostal nerve block is performed for most of the interspaces
06 min 20 sec	The right paratracheal space is inspected and dissected for the lymph nodes as well as the subcarinal space as shown
06 min 28 sec	Finally while viewing through the anterior working port the chest tube is inserted
06 min 32 sec	Under water it is possible to pass the scope to view the bronchial stump while ventilating with 20 cm of water pressure

Appendix 5

Time Stamp	Right Lower Lobectomy Narration (Video 5)
00 min 10 sec	This view shows the entry into the right chest exposing upper, middle, and lower lobes
00 min 16 sec	The working port should be as medial as possible and optimally in-line with the major fissure
00 min 21 sec	A 4 cm access incision is made over the continuation pulmonary artery because this is the area of most delicate dissection
00 min 31 sec	Now with two retractors through the anterior working port and instruments passed through the access incision, the pleura over the interlobar artery is opened
00 min 46 sec	This shows the anterior surface of the pulmonary artery
00 min 50 sec	To enable the posterior pleural dissection, the grasper pulls the superior segment of the lower lobe and posterior segment of the right upper lobe towards the sternum
00 min 58 sec	This makes it easy to open the posterior pleura starting at the right upper lobe bronchus and continuing inferiorly
01 min 05 sec	This also makes it easier to divide the posterior fissure later
01 min 21 sec	Once the pulmonary artery has been identified, it is then safe to bluntly dissect immediately posterior to it aiming toward the interlobar fissure termination that was just explored from the posterior view
01 min 47 sec	With the lung being pulled anteromedially the blunt clamp exits in the correct spot inferior to the right upper lobe bronchus
01 min 52 sec	This allows passage of a vessel loop to hold open the tract
02 min 04 sec	With the stapler introduced in the anterior working port and instruments passed through the access incision to retract the lung it is possible to pass the anvil of the stapler through this tunnel
02 min 32 sec	With the posterior fissure divided, it is then possible to explore this area by further retracting the lower lobe inferiorly, a blunt clamp is introduced into the access incision to create a posterior plane to the continuation pulmonary artery
02 min 55 sec	The basal segment artery branch is seen beside the bronchus
02 min 58 sec	A curved Harkin clamp is used to complete the posterior dissection
03 min 18 sec	The cautery is passed through the access incision to divide tissue behind the artery and then a loop provides additional exposure so that the stapler can be passed behind it safely
03 min 38 sec	The stapler is articulated inferiorly after passage through the anterior working port
03 min 48 sec	Rotation guides the stapler anvil behind the artery
03 min 56 sec	The loop is removed and the stapler is closed
04 min 08 sec	A small amount of additional fissure posteriorly is divided with the stapler as well
04 min 24 sec	This leaves only the bronchus and the inferior pulmonary vein
04 min 28 sec	To expose the inferior pulmonary vein the lower lobe is passed with retractors from the anterior working port to a ring clamp that is passed through the access incision
04 min 39 sec	Then the anterior working port retractor depresses the diaphragm to give good exposure to the inferior pulmonary ligament
04 min 46 sec	Through the same port that the retractor is passed a long spatula tip cautery divides the inferior ligament
04 min 53 sec	Additional posterior pleural attachments are mobilized between the bronchus intermedius and the vein
05 min 01 sec	Then a large right angle clamp is passed through the access incision and two retractors through the anterior working port provide optimal exposure
05 min 35 sec	The lung retraction is passed to the instrument through the access incision so that the stapler can be brought in through the anterior working port angulated downward and rotated behind the posterior vessel

Appendix 5 *(continued)*

Appendix 5 (continued)	
Time Stamp	Right Lower Lobectomy Narration (Video 5)
05 min 57 sec	Then the stapler is articulated so it can be pushed toward the left atrium
06 min 12 sec	Although the same retraction can be done with two instruments through the anterior working port, a single loop retractor for large lobes or large tumors is useful to provide exposure to clean the remaining tissue on the bronchus
06 min 35 sec	Here you can see that the bronchus to the middle lobe branches somewhat distally and therefore it is important to perform enough distal airway dissection so that the middle lobe bronchus is not impinged
06 min 56 sec	Now the stapler is passed through the same port through which the loop retractor currently retracts the lung and it is closed temporarily to test inflate the middle lobe
07 min 16 sec	Next the same loop retractor provides basal stabilization of the bag that was introduced into the access incision
07 min 23 sec	Then using cooperating instruments, one through the same port that the loop retractor resides and an angled instrument through the access incision the specimen is advanced into the sac
07 min 36 sec	This view shows the importance of selecting a lead point through the access incision so that the remainder of lobe can follow
07 min 44 sec	Gentle pushing from inside also is useful
07 min 56 sec	With the lobe removed, it is easy to dissect off the nodes in the level 8 position as well as continue this superiorly to remove nodes in the subcarinal space
08 min 04 sec	This is done using a ring clamp through the access incision
08 min 16 sec	An intercostal nerve block can be performed at any time during the case using a long needle
08 min 24 sec	Then the chest is filled with water and the camera port is used to place a chest tube
08 min 36 sec	While viewing through the anterior working port under water it is possible to inspect the bronchus with 20 cm of water pressure
08 min 43 sec	While withdrawing the camera lung inflation is confirmed

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Video-assisted thoracoscopic pulmonary resections - The Melbourne experience

Gavin M. Wright[1,2,3]

[1]Director of Surgical Oncology, St Vincent's Hospital, Melbourne, Australia; [2]Clinical Associate Professor, University of Melbourne Department of Surgery, St Vincent's Hospital, Melbourne, Australia; [3]Thoracic Surgical Lead, Division of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

Correspondence to: Gavin M. Wright, MD. 5th Floor, 55 Victoria Parade, Fitzroy VIC 3065, Australia. Tel: +61-3-9419 2477; Fax: +61-3-9417 1694. Email: gavin.wright@svhm.org.au.

Background: Despite its privileged economic and educational place in the world, Melbourne was relatively slow to embrace video-assisted thoracic surgery (VATS) for lobectomy. The initial driver of this was Professor C Peter Clarke at the Austin Hospital at the beginning of the new millennium. His legacy was carried on by his apprentice, but at St Vincent's Hospital. After a period of slow development, it became the procedure of choice from 2005, and began to filter sporadically to other hospitals from 2010.

Methods: This paper details the historical development, techniques and results of 343 VATS pulmonary resections (including lobectomies, sub-lobar anatomical resections, sleeve resections, bi-lobectomies and pneumonectomies).

Results: In-hospital and 30-day mortality was 2.0% and 5-year survival for all stages of NSCLC was 70%. Over 36% of patients were stage II-III using the new 7th revision TNM staging system. The conversion to thoracotomy rate was 4.7%. The estimated learning curve for this experience VATS lobectomy appears to be in the range of 15-20 cases. In this series, the same lymph node dissection or sampling was attempted and usually achieved as would have occurred at thoracotomy.

Conclusions: The results confirm the findings of other large case series that the benefits of a minimally invasive approach are achieved without compromising the long-term survival.

Keywords: Video-assisted thoracic surgery; pulmonary resection; lung cancer; Melbourne experience

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Introduction

Prologue - history of VATS lobectomy in melbourne: The austin years

Advanced thoracoscopic techniques were introduced to Melbourne, ostensibly by Professor C. Peter Clarke and his specialist Thoracic Surgical Unit at the Austin Hospital, in the early 1990s. Even at this time, there appeared to be no inclination, suggestion or prediction that a full lobectomy and node dissection by video-assisted thoracic surgery (VATS) would ever be considered. Although progressive in thoracoscopic techniques generally (e.g., oesophagectomy, sympathectomy, complex wedge resection), Melbourne was quite late in uptake of VATS Lobectomy by the standards of other centres around the world. At this time in the US, Kirby and colleagues in Cleveland, Dallas and Pittsburgh were working through that country's initial experience (1). Simultaneously in Taiwan, Liu and his colleagues at Chang Gung Memorial Hospital began performing VATS Lobectomy without the benefit of vascular staplers (2). McKenna also began his now enormous experience around this time (3), as did Walker in Edinburgh (4).

After 1999, Clarke instructed his senior registrar to perform exploratory thoracoscopy on every case of peripheral NSCLC as he was searching for the perfect case for a "VATS lobectomy". Eventually a 72 year-old female ex-smoker with a left lower lobe peripheral adenocarcinoma was identified with a wide-open complete fissure. After offering the advice that the registrar should make use of a “large-ish” incision from the outset (rather than extending a small incision at the end of the case to retrieve the specimen), he left the room to finish some dictating. By the time Clarke returned, the struggling registrar had dissected and tied the artery and divided the vein with an endoscopic stapler via a 5 cm anterior incision and two VATS ports. At this point, Clarke drily remarked that he had intended for the registrar to perform a normal thoracotomy incision, just without rib-spreading! Using the stapler normally used for bullectomy, the left lower lobe bronchus was divided after checking that the upper lobe still inflated. Retrieval of the lung was not too difficult being only a 2 cm tumour. The patient went home on day 5 without complication. On review two weeks later the patient was highly mobile, and grateful that she had been able to return to her ballroom dancing almost straight away. Despite this success, it was to be many years before VATS Lobectomy became a common operation at any hospital in Melbourne.

St Vincent’s Hospital - The learning curve

After completion of the fellowship at Austin Hospital, the author’s appointment at St Vincent’s Hospital commenced in 2001. This move coincided with the retirement of Professor Clarke, effectively ending the Austin Hospital VATS Lobectomy programme for the next 10 years. From 2001-2005, using the selection process inherited from Clarke, 13 VATS lobectomies were attempted at St Vincent’s Hospital. One had to be converted due to bleeding from the left superior segmental pulmonary artery branch of the left lower lobe. Another required an unexpected limited chest wall resection, but was still completed without rib-spreading. As a result of continuing Clarke’s selection policy all but one case was a lower lobectomy. The results were encouraging. The median post-operative stay was six days - one day less than our thoracotomies - with a single outlier of 43 days and no operative mortality. All, except perhaps one case (a carcinoid), were for malignant indications.

The single case of upper lobectomy was late in 2004. A young male patient required a metastasectomy for a small sarcoma metastasis deep in his right upper lobe. The plan had been to perform a hand-assisted thoracoscopic wedge resection (5), but after palpation, it was a little too deep. He had an unusually well formed horizontal fissure at exploration; therefore an attempt was made at VATS right upper lobectomy. At this time the author had become acquainted with the techniques of Rice, D’Amico and McKenna through various conferences and publications. Dividing structures from anterior to posterior, this was successful. It was time to widen the indications for this surgery.

Thoracic surgery sub-specialization at St Vincent’s

Thoracic workload increased markedly at St Vincent’s Hospital from 2000-2005. Following the recruitment of a VATS lobectomy-trained thoracic surgeon from Memorial Hospital in New York in 2005, it was possible to expand the VATS lobectomy program exponentially at both the public and private campuses of St Vincent’s hospital. The technique became a very reproducible procedure, with only selected cases receiving thoracotomy, rather than the reverse. Being at a major referral centre for sarcoma and colorectal carcinoma, as well as having cross-appointment with Peter MacCallum Cancer Centre, there was a significant metastasectomy referral practice, which meant every type of sub-lobar anatomical resection had to be added to the VATS lobectomy repertoire. The rate of VATS lobectomy subsequently increased from three or four to an average of 50 per year, and an in-house wet lab course was designed for surgeons to transition from open to VATS lobectomy. The methods and results of over a decade of VATS lobectomy development in Melbourne are detailed in this paper.

Methods

Patient selection

All patients with a tumour of short axis diameter <5 cm were considered eligible for exploratory thoracoscopy and trial dissection, unless they had clear invasion of mediastinal structures or required sleeve resection. From 2008, sleeve resection of the bronchus was no longer considered a contra-indication in the absence of malignant fixed hilar nodes. Revision surgery, hilar node involvement and adhesions that could result in lengthy or bloody dissections were considered a high risk for conversion.

Surgical technique

Patient positioning: The patient is placed into the appropriate lateral position with the exception that both legs are bent at the knee and the hip pulled posteriorly and the shoulder pushed anteriorly. A table break at the waist is used to widen the intercostal spaces and flatten the hip out of the operative field. This manoeuvre is especially useful in females, as the hip can impede movement of the camera head on the telescope. Standard preparation and draping is then performed as for a thoracotomy.

Port placement: Usually the first port is placed in the 7th interspace, mid axillary line, for exploratory thoracoscopy. For the posterior port, the surface marking is the 8th interspace, just posterior to the posterior axillary line. However, the thoracoscopic view is generally used to determine a location vertically above the free edge of the collapsed lower lobe. These ports are moved posteriorly 1-2 cm for the left-sided approach due to the presence of the left ventricle.

The location of the utility incision should always be determined by thoracoscopy, unless adhesions preclude this manoeuvre. From the mid to anterior axilla region, a long needle is used to localize the interspace that allows a perpendicular drop directly to the superior pulmonary vein. This interspace is optimal for upper and middle lobectomies, and the interspace below is optimal for lower lobectomies. If the interspace does not quite line up with the vein, the more cephalad interspace is chosen. In practice, this is usually the 4th interspace and the incision extends 4-5 cm from mid to anterior axillary lines, between the free edges of latissmus dorsi and pectoralis major.

A standard 10-12 mm port is used for the thoracoscope. An XS or XXS Alexis retractor (Applied Medical) is used to protect the posterior 20-25 mm port. A small rigid Alexis retractor is used to retract and protect the utility incision in the axilla. The large chest wall muscles do not have to be divided extensively as the Alexis retractor stretches up the defect atraumatically and provides a good working incision. Internally, the intercostal muscles can be divided more widely with diathermy to allow passive rib spreading and facilitate specimen removal.

Order of dissection: For upper and middle lobes, the appropriate pulmonary vein tributary is dissected and divided initially with an endoscopic vascular stapler. The truncus artery is divided next for upper lobectomy, or the middle lobe artery for a middle lobectomy. Division of the bronchus or the remaining pulmonary artery branches is performed depending on their accessibility and the completeness of the fissure. The fissure is divided last with an endoscopic stapler to prevent air leak.

Throughout the procedure, hilar and mediastinal lymph nodes are dissected and removed to aid the skeletonization of the hilar structures. This is best done prior to division of the next structure. Any unsampled or undissected lymph nodes stations are cleared after removal of the lobe in an EndoCatch™ (Covidien®) specimen retrieval bag.

Larger tumours may necessitate extension of the utility incision, or at least further division internally of the intercostal muscles to allow greater rib space separation.

Closure: A 28 French intercostal catheter is placed through the thoracoscope port site and secured with heavy silk. A figure of eight absorbable suture is adequate for the deep tissues of the posterior port. The utility incision is closed in layers starting with serratus anterior then latissmus dorsi. No attempt is made to close the intercostal muscles or re-approximate the ribs. Skin is then re-apposed with an absorbable subcuticular suture.

Statistical analysis

A retrospective analysis of prospectively collected dataset was performed. Perioperative morbidity and mortality results were tabulated and overall survival was calculated using the Kaplan Meier method.

Results

Between 2001 and 2012, 343 major pulmonary resections were undertaken by VATS. This included 257 lobectomies, 63 segmentectomies or segment-sparing lobectomies, 13 pneumonectomies, 6 bilobectomies, 4 sleeve resections. Patient ages ranged from 15-91 years with a median age of 67 years. For NSCLC, the median age was 70. Of the malignant pathologies, 236 cases were for NSCLC, 63 for metastasectomy, 22 for carcinoid, five for SCLC, and one case was for lymphoma. Benign diagnoses were found in 16 and included mycobacterial abscess, sequestration, bronchiolitis obliterans with obstructive pneumonia, bronchiectasis, amyloid, aspergilloma, bullitis, hamartoma and sarcoid.

For NSCLC, tumours ranged from 4 mm to 10 cm in diameter (including lepidic component), with a median of 25 mm. Using the 7th revision of the TNM system, the stage spread showed more than half of patients as stage IA or IB (*Table 1*). The median post-operative length of stay was 6 days (range, 2-48 days). There were 16 conversions (4.7%) for extensive adhesions, failure to progress, severe intra-operative haemorrhage or need for complex resection or reconstruction of a mediastinal or hilar structure.

Complications requiring prolonged admission, re-admission, re-operation or admission to ICU are listed in

Table 1 Stage spread of VATS Lobectomy NSCLC cases using the 7th Revision of the TNM system

Stage	n	%
1a	83	35
1b	67	29
2a	20	8.5
2b	24	10
3a	33	14
3b/4	9	3.5
TOTAL	236	100

Table 2 List of adverse events resulting in prolonged admission, re-admission, re-operation or admission to intensive care unit (Grade 3 Complications)

Adverse event*	n	%
Prolonged air leak	19	5.5
Pneumonia	18	5.2
Bleed from PA	7	2.0
Empyema	5	1.5
Re-op for bleeding	4	1.2
Sputum retention	3	0.9
SVT	3	0.9
NSTEMI	3	0.9
Bronchopleural fistula	2	0.6
Chyle leak	2	0.6
PA division	2	0.6
RML bronchus division	2	0.6
CVA	2	0.6
Acute tubular necrosis	2	0.6
Urinary retention	1	0.3
Bleed from left atrium	1	0.3
Bleed from Aortic branch	1	0.3
Urinary tract infection	1	0.3
Aspiration	1	0.3
Pulmonary hypertension	1	0.3
Delirium	1	0.3
ARDS	1	0.3

*Some patients had several complications so the number of adverse events exceeds the number of patients with adverse events. PA, pulmonary artery; SV, supraventricular tachyarrhythmia; NSTEMI, non-ST elevation myocardial infarction; RML, right middle lobe; CVA, cerebrovascular accident; ARDS, adult respiratory distress syndrome

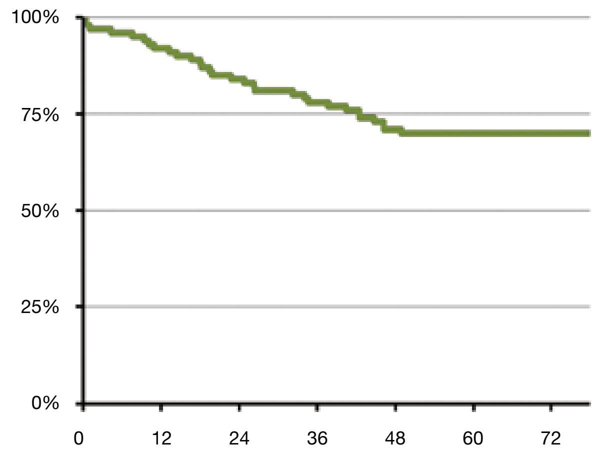

Figure 1 Cumulative survival after VATS lobectomy for non-small cell lung cancer (all stages).

Table 2. Those occurring at a rate of more than 1% were prolonged air leak (19, 5.5%), pneumonia (18, 5.2%), intra-operative bleed from pulmonary artery branch (7, 2.0%) and re-operation for haemorrhage (4, 1.2%). The 30-day mortality rate and in-hospital mortality rate were both 2.0%.

Overall survival for the whole cohort was 73% at 5 years, and for NSCLC, the overall survival was 70% (*Figure 1*).

Discussion

Despite being a relatively late adopter, by the standards of the major international VATS lobectomy centres, St Vincent's Hospital in Melbourne rapidly transitioned to a VATS Lobectomy-predominant practice including complex sub-lobar and reconstructive techniques. This trend has now spread to other centres in Melbourne. This has happened despite the reticence of the majority of thoracic surgery centres in Australia (and around the World) to develop the technique. The Surveillance, Epidemiology, and End-Results Medicare Database showed that between 1995 and 2002, the rate of VATS Lobectomy only increased from 1% to 9% (6). From then to 2007, using the more specialty-specific Society of Thoracic Surgeons Database, the rate of VATS lobectomy was still only 20%. One possible cause for this low rate is the difficulty in introducing these techniques in busy open-heart surgery units. Thoracic surgery tends to be relegated to filling empty lists, and few surgeons have the time to conduct research or up-skill and retrain in new thoracic techniques. This will perhaps be solved by a new generation of surgeons that are used to laparoscopic and thoracoscopic techniques as routine procedures. In our experience of training future thoracic surgeons, the enhanced visualization at VATS lobectomy offers advantages in teaching the anatomy and dissection for both open and thoracoscopic approaches.

The learning curve at St Vincent's Hospital lasted for about five years, partly due to a reluctance to break with the traditional approach to lobectomy, namely dissecting the artery from the fissure. In terms of case numbers, our learning curve was estimated to be between 15 and 20 cases. This is consistent with a recent robotic VATS lobectomy publication that determined that the learning curve amounted to 18 cases based on operative time and conversion rate (7). A previous publication estimated the learning curve for VATS lobectomy was 25 cases (8).

The St Vincent's Hospital results have been continually self-audited and longer-term survival monitored to ensure that at least as good results are being achieved as with open surgery prior to 2005. This is a pre-requisite for introducing a new variation of a technique. Despite the oft-quoted potential bleeding difficulties, which we indeed encountered, we believe that our results now justify this significant change in our practice.

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VATS anatomic lung resections—the European experience

Sofina Begum[1], **Henrik Jessen Hansen**[2], **Kostas Papagiannopoulos**[1]

[1]St. James's University Hospital, Leeds, UK; [2]Rigshospitalet, University of Copenhagen, Denmark

Correspondence to: Mr. Kostas Papagiannopoulos, MMED, THORAX, MD. Consultant Thoracic Surgeon, St. James's University Hospital, Department of Thoracic Surgery, Level 3, Bexley Wing, Beckett Street, LS9 7TF, Leeds, UK. Email: kpapagiannopoulos@yahoo.com.

Abstract: Video-assisted thoracoscopic surgery (VATS) has undergone significant evolution over several decades. Although endoscopic instruments continued to improve, it was not until 1992 that the first VATS lobectomy for lung cancer was performed. Despite significant seeding of such procedure in several thoracic units globally, the uptake was slow and frustrating. Many surgeons considered it complex and unsafe being skeptic about its oncological validity. The last decade has witnessed significant change of practice in many thoracic units with a new generation of VATS thoracic surgeons. Additionally the technique has been refined, standardized and proved its validity and superiority in lung cancer treatment.

Keywords: Lung cancer; neoplasms of the lung; video-assisted thoracoscopic surgery (VATS)

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Introduction

The advent of thoracoscopic surgery began over a hundred years ago when Dr. Jacobaeus, whilst working as a professor in internal medicine in Sweden, reported his initial experience using a thoracoscope in the diagnosis and treatment of pleural effusions (1). The majority of patients undergoing thoracoscopy at that time had tuberculosis. The development of medical anti-tuberculous medication made the use of thoracoscopy obsolete.

The discovery of fibre-optic light transmission and refinement of instruments led to a rejuvenation of the use of thoracoscopic surgery. In 1978 Miller *et al*. reported their experience using diagnostic thoracoscopy in previously undiagnosed thoracic disease (2). Alternative diagnostic modalities, available at the time, had failed to provide a diagnosis in every case. In a case series of 11 patients, thoracoscopy facilitated diagnosis in all without morbidity or mortality (2).

Traditional thoracoscope

The original thoracoscope consisted of a hollow tube with a small light bulb over the tip of the scope with a rheostat to control intensity. This resulted in a very limited and often poor view. The only person able to visualise the operative field was the operator. Available instruments were very limited.

Modern scopes

The use of video-assisted imaging systems revolutionised the function of thoracoscopy. In 1952, Fourestier, Gladu, and Valmiere developed a new imaging system which utilised a quartz rod to transmit an intense light beam distally along a telescope. The modern addition of computer chip television cameras further advanced the use of thoracoscopic surgery as it provided a means to project a magnified view of the operative field on to a monitor, freeing both the operating surgeon's hands, hence facilitating performance of complex procedures.

Further development of 30° and 45° angled viewing scopes has enabled better visualisation of the pleural cavity. Thus far surgeons have had to choose in advance which thoracoscope to use. This restricted their view of the surgical field and intra operative changes of thoracoscope were required to acquire a different viewing angle.

However, a thoracoscope with a variable viewing angle has now been developed. It allows the operator to adjust the viewing angle between 0° and 120° as required during the

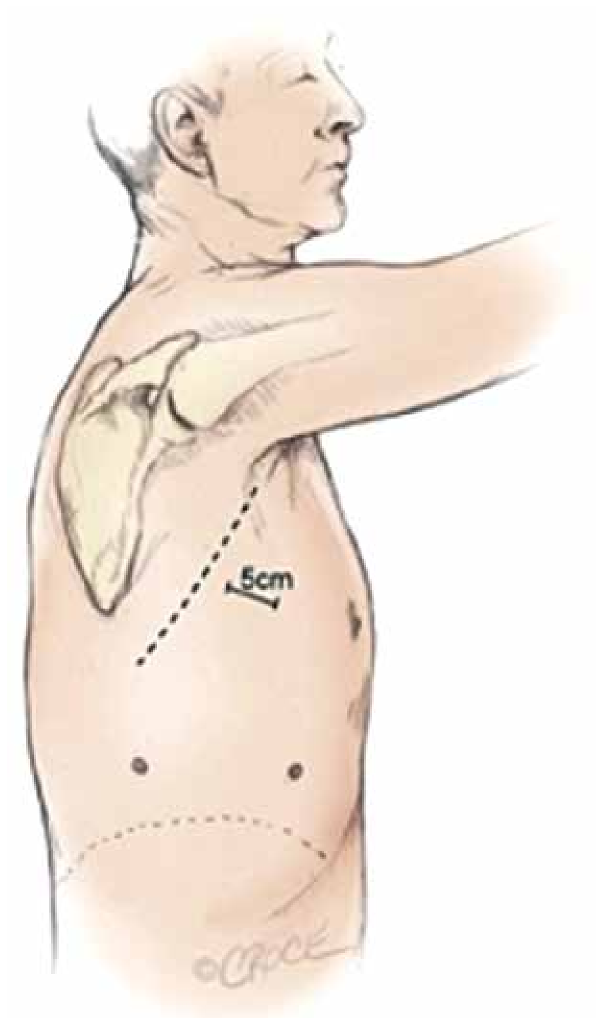

Figure 1 The three incisions made for the anterior approach forming a triangular configuration (8).

procedure.

Most authors recommend a 30 degree rigid telescope, a light source and cable, a camera and an image processor in order to perform video-assisted thoracoscopic surgery (VATS) (3,4). Recording facilities and a slave monitor are not essential but an added bonus. Appropriate theatre suites have now been developed. The thoracoscopes used can range in diameter from 3 to 10 mm, depending on the type of procedure being performed. The light source and cable used should also be appropriate for use in VATS. It is recommend that the light source used be an inert gas (e.g., Xenon) mediated "cold light" at 300 W or above. This is higher than that used in other file of minimally invasive surgery as blood in the operating field can absorb up to 50% of the light (5). The use of thinner fibre-optic cables resulted in improved transmission of light.

The invention of thoracoscopic instruments and modification of staplers to allow navigation around pulmonary vessels has led to a rapid increase in VATS procedures. Initially the instruments used in VATS were the same as those used in laparoscopic surgery. However, the increasing use of the VATS approach in thoracic surgery led to the development of tailor made instruments.

The technique

There is no single standardised operative technique in performing a VATS lobectomy. Current popular techniques use a utility incision and 0-3 ports. The original VATS lobectomies were performed using en-masse stapling of hilar structures (6). This approach however, is not recommended in support of individual isolation and ligation of hilar elements, as in open surgery due to oncological principles. VATS anatomical lobectomy for lung cancer was first described in 1992 (3).

Anterior approach

The anterior approach described by Hansen *et al.* utilises a 3 port technique (7). Both the surgeon and assistant stand on the anterior (abdominal) side of the patient with the surgeon positioned cranially. The approach uses a 10 mm 30° thoracoscope. In contrast to other published anterior approaches the utility incision is made first. It is placed directly over the hilum and the major pulmonary vessels between the breast and the inferior angle of the scapula in the fourth intercostal space anteriorly to the latissimus dorsi muscle (*Figure 1*).

The approach gives good access to the major vessels in case of major bleeding. Following inspection of the pleural cavity a low anterior 1 cm camera-port is positioned at the level of the top of the diaphragm and anterior to the level of the hilum and the phrenic nerve. Then a further 1.5 cm incision is positioned at the same level but more posterior in a straight line down from the scapula tip and anterior to the latissimus dorsi muscle. The sequence of dissection is the same for all lobes making it an easier technique to teach as both surgeon and assistant are positioned at the same side of the operating table. The first structures to be transected are the major vessels. To prevent air leaks there is minimal handling or dissection of the fissure. This is stapled with the visceral pleura remaining intact as a seal above the lung

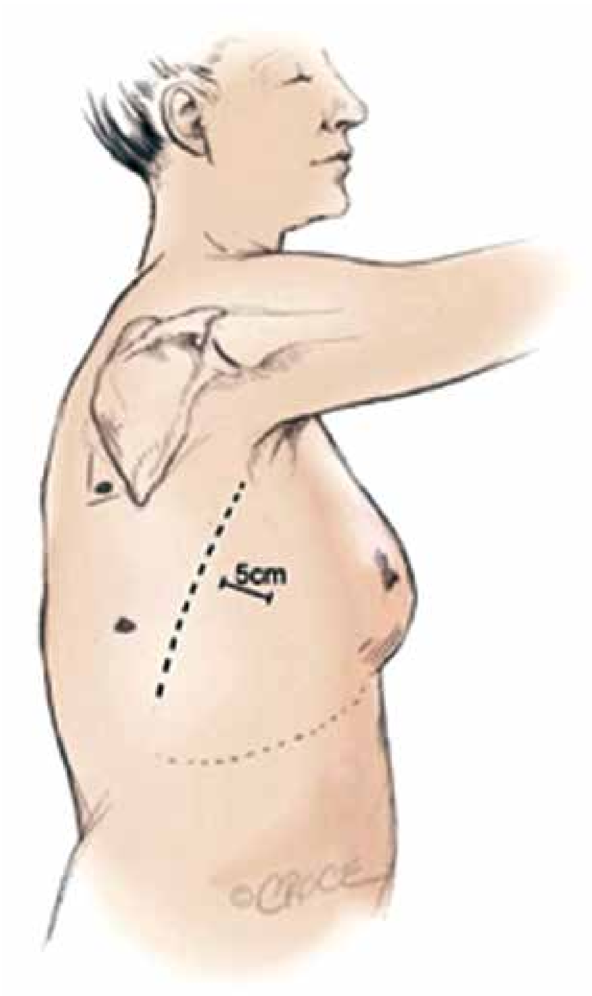

Figure 2 The incisions and port positions in relation to anatomical surface landmarks for the posterior approach (13).

parenchyma. To facilitate a "no touch technique" the fissure stapling is performed quite late after the majority of the hilar structures have been taken care off.

Most surgeons use an anterior approach. This was popularised by the results published by McKenna Jr *et al.* (9). The group published a series of 1,100 cases. Their approach utilised 3 sometimes 4 ports. In this series the reported mortality was 0.8% and conversion to a thoracotomy occurred in 2.5% of cases.

Onaitis *et al.* published a large series on a two port VATS technique (10). Their series reported 500 cases with a surgical conversion rate of 1.6%, an operative and peri operative (30-day) mortality of 0% and 1%, respectively and a median hospital stay of three days.

The first published results on major pulmonary resections performed by a uniportal approach were published by Gonzalez *et al.* (11).

Posterior approach

The use of the posterior approach in performing a VATS lobectomy was first published by Walker *et al.* (12). The surgeon is positioned posteriorly to the patient (13). The utility incision is made in the 6th or 7th intercostal space anterior to latissimus dorsi muscle (*Figure 2*). The camera port is delivered in the auscultatory triangle and the approach utilizes a 0° thoracoscope rather than a 30°. The order of dissection is from posterior to anterior; the oblique fissure is developed first in order to identify and isolate pulmonary arterial branches.

The proposed benefit of the posterior approach is that it provides excellent visualization of the posterior aspet of the hilum facilitating dissection of the bronchi and branches of the pulmonary artery. The sequence of dissection in the posterior approach varies according to the lobe being removed. Furthermore in the posterior approach the tips of the instruments come towards the camera and are therefore easily seen.

Walker *et al.* published their initial experience having performed 158 cases via this approach (14). Their results showed a combined, inpatient and 30-day outpatient mortality of 1.8% with a conversion to open thoracotomy rate of 11.3%.

The evidence

Mortality and morbidity: open lobectomy

Two recently published large studies suggest that the mortality from open lobectomy is 1-2% with a morbidity of 32-37%.

The ACOSOG Z0030 is a prospective, multi-centre study involving 766 patients who underwent open lobectomy for early-stage non-small cell lung cancer (NSCLC), (T1N0 through T2N1) (15). The authors reported a mortality rate of 1% and an overall complication rate of 37%. However, these results reflect outcomes achieved in expert centres, with carefully selected patients.

Boffa *et al.* analysed data pertaining patients undergoing lobectomy for NSCLC from the Society of Thoracic Surgeons, database (16). This involved analysis of data on 6,042 patients operated on from 1999 to 2006. The reported mortality rate was 2% and the overall morbidity was 32%. This study included a very heterogeneous patient population and is likely to represent current clinical care and are strikingly similar to the results of the ACOSOG Z0030 trial.

Mortality and morbidity: video-assisted thoracoscopic lobectomy

There are several studies reporting the peri operative outcomes following VATS lobectomy (9,10,17-19). The Cancer and Leukemia Group B 39802 trial was published in 2007 by Swanson *et al.* (17). This prospective, multicentre study was designed to assess the peri operative outcomes of 127 patients undergoing VATS lobectomy for early NSCLC. Peri operative mortality was 2.7%. Conversely, the peri operative morbidity rate was only 7.4%. However, this was a small group of highly selected patients.

In the largest series published to date McKenna *et al.* reported a 0.8% mortality rate with a morbidity rate of 15.3% (20). A systematic review conducted by Whitson *et al.* included 39 studies with 3,256 thoracotomy and 3,114 VATS patients. The authors found that VATS lobectomy was associated with a lower morbidity rate, a shorter chest tube duration and shorter length of hospital stay (21).

Data from several prospective and large retrospective studies also confirm that VATS lobectomy compares favourably with open lobectomy (10,14,20,22-26). The use of VATS reduces morbidity rates to 7.7-24.1% and mortality to 0.8-2.5%. The reported lower morbidity rates included shorter duration of air leak, lower incidence of post operative pneumonia and arrhythmias.

Safety

The initial concerns regarding the intra operative safety of VATS lobectomy have not born fruition. Flores *et al.* reported only 13 major intra operative complications having operated on 633 patients over 8 years (27).

Another similar series of 410 patients reported only three major intra operative complications requiring emergent conversion (28).

Pain and quality of life

Demmy *et al.* compared VATS *vs.* open lobectomy in patients with unfavourable risk factors (29). The authors reported that despite case matching VATS yielded shorter hospital stay (5.3±3.7 versus 12.2±11.1 days, P=0.02), shorter chest tube durations (4.0±2.8 versus 8.3±8.9 days, P=0.06), and earlier return to full preoperative activities (2.2±1.0 versus 3.6±1.0 months, P<0.01). The authors also noted that pain was noticeably better in the VATS group (none or mild, 63% versus 6%; severe, 6% versus 63%; P<0.01) at 3 weeks follow up.

Long *et al.* conducted a prospective randomised trial comparing quality of life after VATS *vs.* open lobectomy for clinically early stage NSCLC (30). They found that a month after operation both dyspnoea and pain score were significantly lower in the VATS group (10.9±7.4 *vs.* 17.4±9.6, P=0.047; 13.7±9.5 *vs.* 23.0±12.2, P=0.028).

A further prospective, non-randomized study involving 145 patients carried out by Andreetti *et al.* compared postoperative pain after a VATS lobectomy to a mini-thoracotomy approach (31). They found that the differences in pain scores were significant at 1, 12, 24 and 48 h postoperatively (6.24 *vs.* 8.74, 5.16 *vs.* 7.66, 4.19 *vs.* 6.89 and 2.23 *vs.* 5.33; P=0.000).

Furthermore, mean forced expiratory volume in 1 second and 6 minutes' walk test values were better in the VATS group both at 48 h and 1 month following surgery.

Such observations were confirmed by Nagahiro *et al.* Their results showed faster and improved recovery rates of FVC, FEV1 and vital capacity with VATS lobectomy when compared with open lobectomy (32) at one and two weeks following surgery.

Oncological validity

Lymph node dissection is an essential part of any lung resection for lung cancer. Inadequate lymph node dissection results in inappropriate staging.

Both the National Comprehensive Cancer Network and The European Society of Thoracic Surgeons (ESTS) have developed comprehensive guidelines regarding adequate mediastinal lymphadenectomies (33).

There was though initial scepticism concerning the adequacy of lymph nodal dissection with VATS.

Studies so far though, have demonstrated comparable adequacy and operative mortality and morbidity with lymph node dissection when comparing VATS to open lobectomy (34).

A recent retrospective review of 770 patients with cN0-pN2 non-small lung cancer (VATS =450, open =320) by Watanabe *et al.* (35) looked at the total number of lymph nodes, nodal stations, mediastinal nodes and stations sampled during systematic lymph node dissection by VATS *vs.* open lobectomy. They observed no differences in any of these four categories. These findings are further supported by the ACSOG Z0030 trial (n=752, VATS =66, open =686) were a similar number of LN and LN stations were assessed (36) regardless of technique employed.

Competition with systemic/adjuvant therapy

Petersen *et al.* conducted a study of patients who underwent anatomic resection (37). They specifically looked at whether a thoracoscopic lobectomy was associated with a higher rate of completion of adjuvant chemotherapy when compared to open lobectomy. They reviewed 100 consecutive patients with NSCLC who underwent lobectomy and received adjuvant chemotherapy. They analysed the time to initiation of chemotherapy, percentage of planned regimen received, number of delayed or reduced chemotherapy doses, toxicity grade, length of hospitalization, chest tube duration, 30-day mortality, and major complications. There were 43 patients in the thoracotomy group and 57 in the VATS group. All patients received a complete resection and there were no conversions. Patients who underwent thoracoscopic lobectomy had fewer delayed (18% versus 58%, P<0.001) and reduced (26% versus 49%, P=0.02) chemotherapy doses. A total of 61% of patients who underwent thoracoscopic resection received 75% or more of their planned adjuvant regimen without delayed or reduced doses compared to 40% in the open group (P=0.03).

The immune response

There have been four studies that have looked at the acute-phase reactants and cellular immune responses in patients who received VATS *vs.* open lobectomies. All four studies show that VATS lobectomy resulted in a lesser degree of inflammatory response (lower interleukin and C-reactive protein levels), reduced postoperative reduction in CD4 and natural killer cells, and reduced impairment of cellular cytotoxicity than open lobectomy (38-42). These results could explain the superiority of VATS lobectomy in morbidity and mortality in comparison with open lobectomy. It remains to be seen whether this difference in biological response translates to a superior long-term outcome.

Cost effectiveness

A study by Swanson *et al.* compared hospital costs and peri operative outcomes for VATS and open lobectomy procedures in the United States in 3,961 patients (43). Of these 2,907 underwent a lobectomy via open approach and 1,054 via a VATS approach. Hospital costs were higher for open versus VATS at $21,016 and $20,316 respectively (P=0.027).

These findings concur with the findings of Casali *et al.* They compared the costs of VATS and open lobectomy in 346 (93 VATS lobectomy, 253 thoracotomy) patients operated on between January 2004 and December 2006. The authors reported that the overall cost for a VATS lobectomy was €(8,023±565) compared to the cost of an open lobectomy at €(8,178±167) (P=0.0002). They found that although theatre costs for a VATS lobectomy were higher [€(2,533±230) versus €(1,280±54) for an open lobectomy (P=0.00001)] critical care and LOS were lower in the VATS group resulting in a net saving when performing a VATS lobectomy.

European trends

It is difficult to record the exact number of VATS cases being performed across Europe. However, the ESTS collated data from 235 units across Europe. The database has 56,656 recorded procedures with clinical information on more than 43,330 lung resections. Data analysis demonstrated that the number of VATS procedures dramatically increased from 10.7% between 2007-2009 to 18.8% between 2010-2012. Furthermore the VATS lobectomy rate increased from 2.7% to 11.3% between these two periods.

There is though a large variation in VATS practice across Europe. Several reasons might prevent units from embracing VATS surgery. These include, but are not limited to, overall Centre experience in VATS surgery, cost implications and initial capitol investment in instrumentation, cultural approach and trust to VATS surgery, theatre capacity and cancer target breaches and perceived complexity of the procedure.

Denmark has the highest VATS resection rate across Europe with 55% of lobectomies being performed via a VATS approach across the country in 2011. These cases are split between four specialist units performing between 100 and 325 lung cancer surgeries per annum.

The group in Copenhagen has the largest experience in Europe with more than 1,500 cases performed and 80% of procedures being carried out via VATS. Their experience is evidenced in literature (7,8,13-15).

Despite the fact that the first VATS lobectomy was performed in Italy in October 1991 by Roviaro, the uptake of procedure has been relatively slow in Italy. Between then and December 2012 a total of 1,366 VATS lobectomies have been carried out in Italy. Twelve centers performed over 30 cases and only three centers performed over 100 cases.

In Norway and Sweden several VATS lobectomy programs have started but as yet no one single unit has performed over 100 cases. Similarly Germany, in recent survey of 39 respondents revealed a VATS resection rate of 10%, with all performed via the anterior approach. Two units have performed over 400 cases and seven over 100 cases.

There are 13 units in Austria of which 10 have established VATS lobectomy programs; 3 of these centers have performed over 100 cases (Spring 2013). In the majority of these centers VATS is performed by few surgeons. A total of 1,000 cases have been performed nationally with the VATS resection rate approaching 50% in active centers.

In Switzerland there are 9 public thoracic surgery centers and an unknown number of private centers. Only 2 of the public centers have done over 100 cases as most VATS lobectomy programs started in 2009 or later.

Of the 46 centers surveyed in Spain, 3 did not do VATS lobes, and 22 answered positively. Over 2,000 cases have been performed in total. These procedures were done either via a single port or 3 port approach. The first published results on major pulmonary resections performed by a uniportal approach come from Dr. Boffa *et al.* from Corunia, Spain (16).

In the Netherlands major centralization of thoracic surgery services and VATS programs began in 2006. One unit has performed over 500 cases and according to the Dutch lung cancer registry VATS lobectomies superseded open in 2012.

The data collated by the Society of Cardiothoracic Surgeons of Great Britain and Ireland shows that VATS resection rate has increased from 2% in 1993 to 14% in 2011. Data from the subsequent years is not yet published.

Conclusions

There is now enough body of evidence to suggest that VATS lobectomies offer a better outcome to cancer patients than open lobectomies. Selection remains the single most important factor to replicate results of studies. We are unlikely to be able to ethically justify a prospective, randomized comparison between open and VATS lobectomy.

This leaves us reliant on the best available current evidence. The current review confirms that VATS lobectomy is a superior procedure associated with lower peri operative morbidity and mortality than open lobectomy. It offers equivalent oncological results, is cost effective, and allows quicker return to social activitie.

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Training in video-assisted thoracoscopic lobectomy

Jennifer M. J. Richards[1], Joel Dunning[2], William S. Walker[1]

[1]Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK; [2]Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK

Corresponding to: Joel Dunning, MD, PhD, FRCS. Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK. Tel: +447801548122; Fax: +441642815761. Email: joeldunning@doctors.org.uk.

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Introduction

Video-assisted thoracoscopic surgery (VATS) is a minimally invasive alternative to open thoracotomy for major pulmonary resection and has been shown to have a number of benefits. VATS lobectomy is a safe and cost-effective treatment option (1,2). Compared to open thoracotomy, VATS lobectomy is associated with a reduction in post-operative pain, lower incidence of pneumonia and a shorter hospital stay, whilst maintaining equivalent oncological outcomes and long-term survival (3-9).

However, despite the perceived benefits of VATS lobectomy, the majority of lobectomies are still performed as open procedures with relatively few centres offering VATS. This may be because the VATS approach is considered to be technically demanding with the potential for catastrophic haemorrhage in the hands of an inexperienced surgeon. Furthermore, the difficulty in arranging training in VATS lobectomy has meant that the technique has been disseminated slowly.

We believe that senior trainees and consultants with ample experience of open lobectomy can be trained to perform VATS lobectomy by an experienced VATS surgeon without affecting patient outcomes. We here report the experience of a senior cardiothoracic surgical trainee undertaking a one-year fellowship with intensive exposure to VATS lobectomy under the supervision of a highly experienced consultant in a high-volume thoracic surgical unit.

Methods

A prospectively collected database of all patients undergoing VATS lobectomy in a single institution during a one-year period was reviewed. The database holds the demographic and baseline clinical characteristics of patients operated upon as well as intra-operative details and information regarding post-operative recovery and clinical outcome.

The supervising consultant has 20 years of experience of VATS lobectomy and has performed in excess of 800 major VATS resections. At the start of the fellowship the trainee had undertaken 55 open lobectomies and 75 minor VATS procedures (including lung biopsy and wedge resection) during six years of cardiothoracic surgical training, but had no previous experience of VATS lobectomy. The patients were listed for surgery according to clinical priority using our standard processes with no modification of case selection for the trainee.

Surgical technique

Our VATS lobectomy technique has been described in detail and aims to replicate the dissection used for open lobectomy whilst taking advantage of the benefits of smaller incisions. An entirely thoracoscopic approach was used for all patients. In brief, with the patient in the lateral decubitus position and the lung to be operated upon deflated, three port sites were created: a 5 cm utility incision anteriorly in the sixth or seventh intercostal space, a further 2 cm instrument port level with this in the mid-axillary line and a 2 cm camera port in the auscultatory triangle. A fissure-based posterior approach was used to access the hilum and dissect out the lobar pulmonary artery branches, pulmonary vein tributaries and bronchus, each of which were divided using an endoscopic linear stapling device. A comprehensive lymphadenectomy was performed complementing pre-operative mediastinoscopy. An intercostal drain was placed

Table 1 Patient characteristics

	Group 1	Group 2	Total
Age (mean, range, years)	67 (52-87)	69 (47-86)	68 (47-87)
Female (%)	19 (63%)	15 (52%)	34 (58%)
Benign disease (%)	1 (3%)	1 (3%)	2 (3%)

There were no differences in patient characteristics between the two groups (P=NS)

Table 2 Clinical and operative outcomes

	Group 1 (n=30)	Group 2 (n=29)	Total (n=59)
Primary procedure			
- Right upper	8 (27%)	11 (38%)	19 (32%)
- Right middle	3 (10%)	4 (14%)	7 (12%)
- Right lower	2 (7%)	3 (10%)	5 (8%)
- Left upper	8 (27%)	3 (10%)	11 (19%)
- Left lower	5 (17%)	1 (3%)	6 (10%)
- Segmentectomy	4 (13%)	7 (24%)	11 (19%)
Additional wedge resections	1 (3%)	2 (7%)	3 (5%)
Conversion to open thoracotomy	1 (3%)	1 (3%)	2 (3%)
Operation time (mean±SEM, min)	190±6	186±7	188±5
Blood loss (mean±SEM, mL)	142±27	87±9	115±15
Hospital stay (median, range, days)	6 (3-40)	4 (3-26)	5.5 (3-40)
30 day mortality	1 (3%)	1 (3%)	2 (3%)
Air leak >7 days	5 (17%)	2 (7%)	7 (12%)

There were no differences in operative or clinical outcomes between the two groups (P=NS)

and typically removed after 24 hours if the chest radiograph and aerostasis were satisfactory. A local anaesthetic paravertebral catheter was used alongside a patient controlled morphine pump for analgesia, and patients benefited from daily physiotherapy.

Data analysis

Only the 59 procedures performed by the trainee were analysed. For the purpose of analysis, the series was divided into two groups where group 1 included the first 30 cases and group 2 consisted of the last 29 cases performed by the trainee. These two groups were compared to see whether there were any differences in operative and clinical outcomes.

Unpaired two-tailed Student t-test and Fischer's exact (GraphPad Prism, GraphPad Software, USA) were used where appropriate. Two-sided $P<0.05$ was regarded as statistically significant.

Results

The trainee performed 59 of the 69 (86%) VATS lobectomy procedures undertaken during the study period. There were no differences in the patient characteristics between the two groups (*Table 1*). A similar range of operations was performed in both time periods (*Table 2*). There was no difference between the two groups in terms of the mortality rate or hospital stay. There was no significant difference in the rate of conversion to open thoracotomy or airleak persisting for more than 7 days. No patient required re-operation.

There was a gradual reduction in operating time with increasing experience (*Figure 1*) but this did not reach statistical significance. There was also a small reduction in operative blood loss (*Figure 2*) which was neither clinically

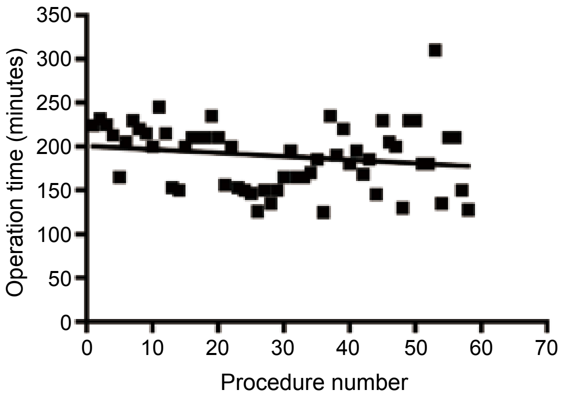

Figure 1 Operation time with increasing procedural experience.

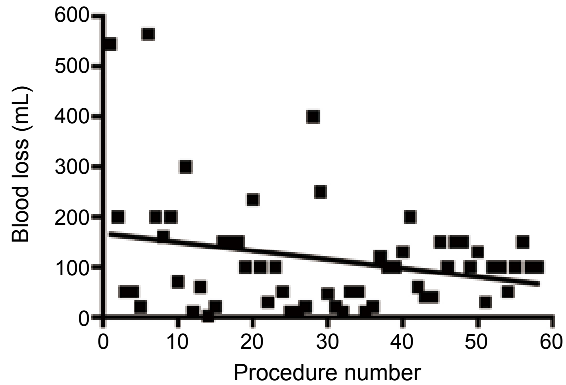

Figure 2 Blood loss with increasing procedural experience.

nor statistically significant.

Discussion

Video-assisted thoracoscopic lobectomy has a number of potential benefits when compared to open thoracotomy but is only practiced in a few thoracic surgical centres (1-7). VATS lobectomy is regarded as a technically complex procedure. Difficulty in obtaining training in such techniques may be part of the reason why VATS lobectomy is not employed more widely. We have previously shown that the performance of a consultant who was self taught in VATS lobectomy improved rapidly over the first 46 cases he performed, and continued to improve more slowly over the remaining 184 cases in the series (10). In this paper we report on the learning curve of a senior cardiothoracic surgical trainee learning VATS lobectomy under the supervision of the same, now highly experienced, consultant. Before undertaking this fellowship the trainee had previously performed 55 open but no VATS lobectomies. Interestingly, when supervised by the experienced consultant, the learning curve was almost eliminated when measured in terms of operating time and blood loss.

The operation time reported here for the trainee is similar to that reported in contemporary series for surgeons learning VATS lobectomy, and is approximately 20-30 min longer than for experienced VATS lobectomy surgeons (10,11). It is worth noting that direct comparison of operation times with those reported in historical series is confounded by the current practice of comprehensive lymphadenectomy which was not always undertaken for cases performed during earlier time periods and which adds 30-45 minutes onto the overall operating time. However, it would seem wise when scheduling cases to anticipate a slightly longer operation time if a trainee is performing the procedure. The operative blood loss for the trainee in this series also compares favourably to that reported in other series (10,11).

Importantly, clinical outcomes including persistent airleak, hospital stay and mortality were similar to those reported in other series and did not exhibit a learning curve effect. This supports the findings of two previous papers showing that VATS lobectomy can be taught safely to both trainees and consultants (11,12).

It would seem appropriate for VATS training opportunities to be reserved for those who are likely to benefit most from them such as recently appointed consultants and senior trainees with sufficient experience of open major pulmonary resection. In other specialties, laparoscopic simulators have been shown to attenuate the learning curve for a number of procedures as well as for basic laparoscopic skills such as dissection and suturing (13-16).

Development of generic laparoscopic skills using simulators prior to starting a VATS fellowship may be advantageous, allowing trainees to capitalise on the learning opportunities presented to them. Indeed a placement in another speciality, such as general surgery in which laparoscopic procedures such as cholecystectomy and appendicectomy are better established and more widely practiced, may also be beneficial in terms of building initial laparoscopic experience prior to a VATS fellowship.

In order for more patients to benefit from the VATS approach, the issues surrounding training in VATS lobectomy require to be addressed. We believe that intensive exposure to VATS lobectomy in a high-volume centre is advantageous to training. It may, therefore, be appropriate for national training programmes to be established with fellowships in designated high-volume centres. When aiming to disseminate VATS lobectomy to other centres it is important to remember that it is not just the surgeon that requires training. Opportunities should be created for theatre nursing staff and procurement teams to visit established VATS centres to observe the theatre arrangements and receive advice regarding the recommended equipment.

In conclusion, the data presented here demonstrate that a senior cardiothoracic surgical trainee can be trained in VATS lobectomy without impacting adversely on clinical outcomes. If VATS lobectomy is to become more widely practiced, consideration should be given to the provision of VATS fellowships and the availability of adjuncts to training.

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Teaching video-assisted thoracic surgery (VATS) lobectomy

Philip W. Carrott Jr[1], David R. Jones[2]

[1]Department of Surgery, University of Michigan, Ann Arbor MI, USA; [2]Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York NY, USA

Correspondence to: David R. Jones, MD, Professor of Surgery, Chief, Thoracic Surgery. Department of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, Box 49, New York, NY 10065, USA. Email: jonesd2@mskcc.org.

Abstract: Video-assisted thoracic surgery (VATS) lobectomy has become the standard of care for early stage lung cancer throughout the world. Teaching this complex procedure requires adequate case volume, adequate instrumentation, a committed operating room team and baseline experience with open lobectomy. We outline what key maneuvers and steps are required to teach and learn VATS lobectomy. This is most easily performed as part of a thoracic surgery training program, but with adequate commitment and proctoring, there is no reason experienced open surgeons cannot become proficient VATS surgeons. We provide videos showing the key portions of a subcarinal lymph node dissection, posterior hilar dissection of the right upper lobe, fissureless right middle lobectomy, and fissureless left lower lobectomy. These videos highlight what we feel are important principals in VATS lobectomy, i.e., N2 and N1 lymph node dissection, fissureless techniques, and progressive responsibility of the learner. Current literature in simulation of VATS lobectomy is also outlined as this will be the future of teaching in VATS lobectomy.

Keywords: video-assisted thoracic surgery (VATS) lobectomy; teaching; simulation

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Introduction

Video-assisted thoracic surgery (VATS) lobectomy has rapidly become the standard of care for early-stage lung cancer treatment throughout North America and increasingly in the world. A VATS lobectomy is defined as the use of a 3-6 cm access incision without rib-spreading, one to three additional 1 cm ports, and the use of a thoracoscope to visualize the dissection and subsequent lobectomy. Compared to an open thoracotomy and lobectomy, a VATS lobectomy has equivalent oncologic results, less post-operative pain, shorter hospitalization, earlier return to activities of daily living, earlier administration of adjuvant therapies, and is less expensive (1,2). Despite these advantages there are several barriers to the adoption of more advanced VATS procedures including lobectomy. These include a lack of formal education and training, cost, lack of access to technology (particularly in non-North American or Western European countries), and a continued lack of education about the oncologic merits of the procedure relative to an open thoracotomy.

A recent survey of thoracic surgery residents reveals that 58% believe they are proficient in performing a VATS lobectomy at the completion of their residency program. Those individuals who were dedicated thoracic surgeons were much more likely (86%) to be comfortable performing a VATS lobectomy relative to those individuals with a mixed practice (28%) (3). Collectively, this suggests that there needs to more emphasis on introducing, teaching, and monitoring progression of the VATS lobectomy procedure to our trainees as well as those surgeons who are interested in incorporating the procedure into their existing practice.

There is an increasing literature on how advanced technologic procedures should be introduced into surgical practice (4-6). It is now well established that there is distinct learning curve for learning how to safely and proficiently perform a VATS lobectomy (4-9). The actual technical aspects of the procedure including number of incisions and methodologies to dissect and divide bronchovascular structures will vary amongst surgeons and are also dependent on the tumor stage and biology. For these reasons, the purpose of this review is to highlight important aspects of teaching and learning VATS lobectomy with an emphasis on programmatic requirements, patient selection, and strategies to facilitate the learning process, including simulation. We will also discuss some basic technical considerations that apply to all VATS lobectomy procedures.

Programmatic and individual requirements

McKenna describes several important pre-requisites relative to beginning a VATS lobectomy program (9). One the most important points is that the entire operating room team (nurses, scrub technicians, first assistants) need to be familiar with open procedures before attempting VATS lobectomies. In addition, there should be an adequate volume of lobectomies (>25/year) in the practice. The surgeon who is performing VATS lobectomy procedures should have done a relative large number of smaller VATS procedures (i.e., wedge resection, lymph node biopsies, etc.). In addition, the surgeon should have observed several "live" VATS lobectomies and, if at all possible, assisted in the operations. There is no substitute (i.e., simulation, workshop, or video) for actual experience when one is adopting a new surgical technique. Frequently, this requires more than one observation or active participation. In addition, the best approach is for the scrub and circulating nurses to have also observed a live case or two so they can also become familiar with the basics of the procedure. These individual and programmatic pre-requisites apply to both new thoracic surgery residents and more experienced surgeons who are adopting this technology to their practices.

An additional pre-requisite that is rarely mentioned is the need for the appropriate VATS instrumentation, endostaplers, and the necessary instruments should conversion to an open procedure be indicated. Failure to have the appropriate VATS instruments, thoracoscopes and monitors can result in inadvertent intraoperative injuries, prolong the case, increase conversion rates, and demoralize surgeon and team morale and interest in the procedure. We routinely use a 45° thoracoscope while others prefer a 30° or flexible tipped camera (10). These angled scopes offer the most versatility in providing alternate angles to view the anterior and posterior hilum without switching camera port access sites. Use of dissecting two-point scissors, needle holders, long Harken or Semb clamps, DeBakey clamps and axial handle forceps are all basic and required instruments to facilitate performing a VATS lobectomy.

The last pre-requisite is for the surgeon and the other team members to understand their responsibilities should the case require conversion from VATS to open procedure. It is extraordinarily rare to require conversion emergently as most complications, including major bleeding, can be managed with elective or urgent conversion maneuvers.

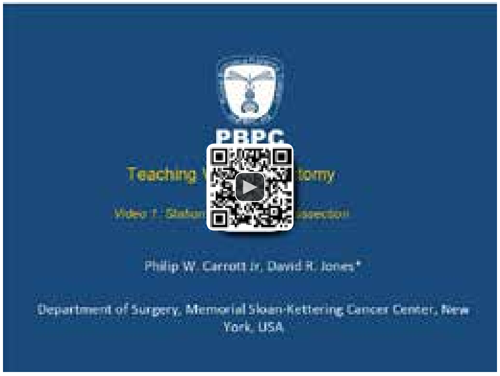
Intraoperative teaching

Incisions and surgeon positions

Once the patient is positioned, attention is given to selection of the appropriate locations of the incisions. We use a 5 mm thoracoscope and therefore place a small trocar in the 7th or 8th intercostal space (ICS) in the middle to posterior axillary line to guide subsequent incision placement. A 4 cm access incision is then made anteriorly in the 4th ICS for upper and middle lobectomies and in the 5th ICS for lower lobectomies. This incision needs to be quite anterior. A third 1 cm incision is then made depending on surgeon preference.

If the teaching surgeon is going to stand posteriorly at the patient's back, then it is easier to teach, guide, and first assist if the third incision is placed posterior to the camera port. If the teaching surgeon is going to stand anteriorly on the same side as the learner, then the third 1 cm incision is best placed anterior to the camera port. We prefer to have the teaching surgeon stand posteriorly and the learner stands anteriorly. We typically do not place trocars in these third incisions and thus only need a 5 mm trocar for the entire procedure. Additional ports are placed at the discretion of the surgeon. All ports should be separated by 6-8 cm in order to avoid unnecessary fencing of intrathoracic instruments. In teaching VATS lobectomy, as with other cases, there is a progression of responsibility for the case.

It is important to remember that an open lobectomy is typically performed via a posterior approach while a VATS lobectomy is almost always an anterior approach. Thus, a VATS lobectomy offers a "different view" for many surgeons. A final caveat is that if a two- or three-incision VATS lobe strategy is used, then the operating surgeon will need to operate more exclusively through the anterior access incision and therefore will most certainly need the



Video 1 Station 7 Lymph node dissection. We prefer to start our procedure with this posterior hilar dissection and removing N2 nodes during the initial dissection. The sub-carinal lymph nodes are removed as a packet whenever possible.
Available online: http://www.asvide.com/articles/135

Video 2 Posterior dissection RUL Bronch and PA. The bronchus and first pulmonary artery branch are dissected and divided from the posterior approach. This may be necessary for large anterior tumors that prevent anterior visualization.
Available online: http://www.asvide.com/articles/136

full armamentarium of VATS instrumentation.

The correct placement of the access incision and ancillary ports is one of the most critical aspects of performing a VATS lobectomy proficiently. One also needs to consider the patient's body habitus, a history of prior intra-thoracic procedures, and other considerations (i.e., breast implants, pacemakers, etc.).

Lymph node dissection

We perform the mediastinal nodal dissection first when performing a VATS lobectomy. Routine nodal dissection for right-sided tumors includes stations 2R, 4R, 7, and 10R. For left sided tumors we dissect stations 5, 7, and 10 L and station 6 if we observe a node in that region. Teaching the learner to dissect all the nodal tissue while avoiding bronchopulmonary structures as well as the superior vena cava (SVC), esophagus, and vagus, phrenic, and recurrent laryngeal nerves, is terrific first step in the learning process. This exposes the learner to much of the anatomy from an anterior approach as well as the various lung positioning and retraction maneuvers to facilitate the nodal dissection. While not routine, there are maneuvers that can be done to facilitate the N2 nodal dissection for the novice VATS lobe surgeon. For instance, division of the azygous vein at the junction of the SVC facilitates the dissection of 2R and 4R nodal stations.

We routinely begin our nodal dissection by retracting the lung anteriorly to completely dissect of station 7 (*Video 1*) and the posterior station 10L nodes. When indicated for more anteriorly located right upper lobe tumors or tumors near the minor fissure, it is also possible to begin to isolate and divide lobar bronchovascular structures from this posterior approach, as outlined in *Video 2*. In these cases the right upper lobe bronchus is isolated and divided first followed by the truncus arterial branch next, with the remainder of the segmental pulmonary arterial vessels and lobar veins taken from a continued posterior approach or from an anterior approach.

Teaching the N1 nodal dissection can be challenging for both the instructor and the learner. Notwithstanding the oncologic benefit, it is imperative that all N1 nodes be removed in order to facilitate the accurate identification of the lobar bronchi and perhaps more importantly the segmental branches of the pulmonary artery. We prefer a combination of blunt (metal suction device) and sharp dissection with either scissors or low-dose cautery to remove these nodes. The primary difficulty the learner has when performing a N1 dissection is the loss of haptic perception. Intraoperative teaching of this aspect of the procedure is best done by (I) having the correct VATS instrumentation; (II) explaining normal and common variant anatomy; and (III) moving anterior to posterior in the nodal dissection. Analysis of the STS database for upstaging of pulmonary malignancies following either VATS or open lobectomy found that significantly fewer N1 nodes were obtained following VATS lobectomy, indicating that VATS surgeons need to be more complete in sending N1 nodal tissue (11). The routine dissection and removal of the N1 lymph nodes

Video 3 Anterior approach to the RML. Right middle lobectomy is performed in a "Fissureless" technique, taking the hilar vessels and bronchus first, then the fissures to perform the lobectomy.
Available online: http://www.asvide.com/articles/137

Video 4 Fissureless LLL. The key steps of a fissureless left lower lobectomy are shown. Smaller portions of the dissection are shown to keep the video short.
Available online: http://www.asvide.com/articles/138

Table 1 Incremental steps of a VATS right upper lobectomy (RUL)

(I)	Correct placement of the access incision, thoracoscope and additional ports;
(I)	Inspection and retraction of lung;
(I)	Dissection of 7, 4R, 2R and 10R nodal stations;
(II)	Incision of posterior mediastinal pleura to expose the right mainstem and upper lobe bronchi;
(III)	Dissection of the sump node at the junction of the RUL bronchus and proximal bronchus intermedius;
(IV)	Incision of the anterior mediastinal pleura and isolation and division of the superior pulmonary vein;
(V)	Isolation and division of the truncus anterior and posterior ascending pulmonary arteries;
(VI)	Removal of peribronchial nodal tissue followed by isolation and division of the RUL bronchus;
(VII)	Division of the lung parenchyma;
(VIII)	Placement of the RUL specimen into an endocatch bag followed by removal from the pleural cavity;
(IX)	Apposition of the RML to the RLL to prevent a RML torsion syndrome (if indicated).

makes subsequent isolation and division of the segmental pulmonary arteries with the endostapler much more expeditious and safer.

Fissureless VATS lobectomy

The majority of VATS lobectomies do not require identification of the pulmonary artery in the fissure and thus division of the parenchyma is commonly the last step of the procedure. This fissureless approach is best taught during open thoracotomies for lobectomies. We perform a fissureless VATS lobectomy in the majority of cases. As shown in *Video 3* (a VATS middle lobectomy) and *Video 4* (a VATS left lower lobectomy) a fissureless approach is simple, straightforward and in my opinion is less likely to result in injury to segmental pulmonary arterial branches. On occasion partial division of a fissure may facilitate the dissection and when appropriate should be performed. In addition, an experienced VATS surgeon will occasionally need to dissect vascular structures in the fissure to safely remove centrally-located or large tumors. These types of operations are not, however, appropriate beginning cases for the novice VATS lobectomy surgeon.

In general, when teaching a fissureless approach the pulmonary vein is isolated and divided first. This is a relatively simple maneuver most of the time and one that an intermediate learner can do within 10-15 minutes. Once complete it offers exposure to the lobar bronchus (lower and middle lobectomies) and pulmonary arterial segmental vessels. Each successive division opens up the dissection of the next structure, until the fissures are the only remaining attachments. We find that dissection and confirmation with various instruments that mimic the angles of the stapling devices are helpful in orienting subsequent endostapler application. We utilize the VATS curved and straight DeBakey clamps to approximate the angles one must have for the endostaplers.

Case progression

When teaching any new surgical technique there needs to be a progression toward independence for all steps of the procedure. In general, one can divide the steps in a VATS lobectomy into discrete, defined maneuvers (see *Table 1* example). The learner and the instructor can both track progress, operative times per maneuver, and technical results and then make necessary adjustments on this data.

Simulation and VATS lobectomy

Advanced minimally-invasive procedures such as a VATS lobectomy require a specialized surgical skill set. Surgical simulation may be able to facilitate a more rapid and safe introduction into surgical practice without exposing the patient to unnecessary risk. There are a number of relevant issues regarding simulation in thoracic surgery including identification of an appropriate and realistic model (computer-based, animal, or tissue block) and validation of the model (12-15). As outlined by Tong *et al*. the utility of a task-based simulator depends on its fidelity and validity. Fidelity, also known as face validity, refers to how real the simulator experience feels to the student. Content validity evaluates whether the steps performed in the simulator are accurate to what is done in the actual procedure. Construct validity evaluates the ability of the simulator to discriminate between learners at different levels of experience (14).

Groups at the University of North Carolina at Chapel Hill and New York University have developed a porcine-block and a virtual reality trainer VATS lobectomy model, respectively (13,15). The porcine lung block model has been shown to have a high fidelity and is perhaps the best studied and most validated model for teaching VATS lobectomy (14,15). The porcine block left lung model is not anatomically identical to human anatomy, but the tissue and advanced dissection techniques are reproducible and are detailed in an evaluation by senior surgeons (15). Additional groups have developed simulators for open surgery as well, which could be easily transitioned to VATS (16).

The virtual trainer has advantages in ease of set-up and fidelity to human anatomic variants as well as the ability to improve the model as technology improves. The upfront costs are estimated to be $25,000-35,000 for required infrastructure and will need further development. The virtual reality trainer can score the movements of the surgeon, allowing users to track their progress and set benchmarks for resident progress (13). Validation studies of the porcine block model were performed by Tong *et al*. and showed that in 31 residents with varying experience with VATS lobectomy that this model discriminated well between novice, intermediate, and experienced VATS lobectomy surgeons (14).

In all likelihood, the use of both platforms will be advantageous at different points in thoracic surgery training and in learning the VAS lobectomy procedure. The virtual reality platform can be used as often as one likes, and would be a good starting point for novice VATS lobectomy surgeons. The porcine model can then be used once surgeons gain some operative experience and will facilitate the development of fine dissection skills and gain a "feel" for tissue strength with sharp and blunt dissection of hilar vessels. In the United States, thoracic surgery education and training is transitioning to shorter, integrated programs which will certainly need simulation to adequately prepare surgeons with a reduced time in training. Unfortunately, there is still no universally identified simulation model and exposure opportunities are varied and limited to individual institutions. A more uniform and accessible simulation strategy for teaching and learning the skills required to perform a VATS lobectomy is needed.

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Learning curve associated with VATS lobectomy

René H. Petersen, Henrik J. Hansen

Department of Cardiothoracic Surgery, Rigshospitalet, Copenhagen University Hospital, Denmark

Correspondence to: René H. Petersen, MD. Department of Cardiothoracic Surgery 2.15.2, Rigshospitalet, DK 2100 Copenhagen O, Denmark. Tel: +4535450525; Fax: +4535452182. Email: rene.petersen@rh.regionh.dk.

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Introduction

The first VATS lobectomy was performed in 1991 (1). Since then the implementation of VATS lobectomy has been rather slow. Data from the STS database shows a 32% rate of VATS lobectomies in 2006 (2). But it is only the best academic units that report to the STS database. This percentage is hence probably not representative for all the thoracic units in the USA. The implementation in Europe has been even slower than in the USA. But in the past years interest is rising, and in a recent report from The Society for Cardiothoracic Surgery in Great Britain and Ireland, the percentage of lobectomies performed by VATS has increased from 7% to 14 % in just one year (2010). The slow adoption despite the obvious advantages is considered by many to be due to a demanding learning curve. The procedure is considered technically demanding and has the risk of uncontrollable bleeding.

The introduction of VATS lobectomies in the surgical community was performed by self taught surgeons experienced in open surgery. The approaches varied from anterior, inferior to posterior, using 2-5 ports (3-6). These surgeons were pioneers and in case of intraoperative difficulties, conversion was their only option. The conversion rate was in many cases rather high (6). In *Figure 1*, the conversion rate and number of VATS lobectomies in Copenhagen between 1999 and 2011 is illustrated. The conversion rate declines with experience and number of cases per year. In the centres of the pioneers, the next generation learned the technique under guided supervision. The conditions for those surgeons' learning curves were better due to the possibility of learning under supervision by an experienced VATS surgeon and a better possibility for selecting cases suitable for a training surgeon. Furthermore the surgical outcome was very satisfactory with low conversion and complication rates (7,8).

Since the introduction of VATS lobectomy in 1991, there has been a substantial improvement in the image quality. The introduction of firstly the digital thoracoscopes and later high definition (HD), has made precise dissection close to major vessels possible. Furthermore, several companies have designed curved instruments tailored to VATS surgery and a continuous improvement in these instruments have made it easier to perform and learn the technique. The quality of staplers has also improved significantly resulting in less air leak and fewer bronchial leaks.

The length of the learning curve

The length of the learning curve has been suggested to consist of 50 VATS lobectomies (9). But several factors influence the length of the learning curve. As mentioned previously there is a difference in the learning curve between the surgeon who takes up the procedure from scratch and the surgeon who is taught in a centre with experienced VATS surgeons to supervise. The size of the centre and the potential number of VATS lobectomies to be performed influence the length of the learning curve. Once you begin with a new technique it is an advantage to perform many operations within a short time frame. If there is only a potential to perform 1 or 2 operations a month, it will take a long time to complete a learning curve. It will be like starting all over every time. Furthermore a high case load adds the potential of selecting cases for training.

The experience of the surgeon in training is important. Understanding the anatomy of the lung and experience with the many anatomical variations makes the learning curve shorter. Experience with other VATS procedures such as wedge resections, pleural biopsies and cyst resections is an

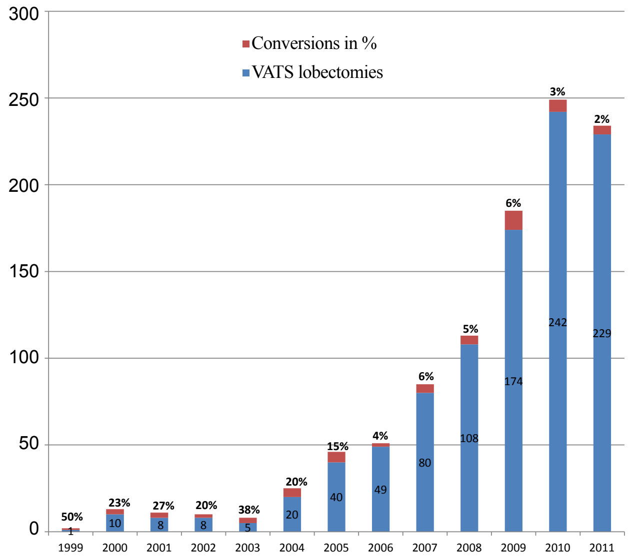

Figure 1 Number of VATS lobectomies performed in Copenhagen 1999 to 2011 and conversions in %.

advantage with respect to port placement and working in a monitor based setting.

It is an ongoing discussion about how the coming generations are going to learn to do VATS lobectomies. Once most lobectomies are performed by VATS, the lobectomies scheduled for thoracotomy may well be the difficult procedures only such as bronchial and vascular sleeves and chest wall resections. To teach such cases of open surgery to inexperienced surgeons can be demanding. One solution could be to let the inexperienced open surgeon do part of the operation. In our experience, we have had success in teaching VATS lobectomies to trainees with limited open experience given sufficient supervision and selecting the cases carefully. Finally, there are individual differences and some surgeons have more talent for the procedure and learn more quickly than others.

Simulators

The introduction of simulators of VATS lobectomy is supposed to make the learning curve of VATS lobectomies shorter. Simple simulators with an animal model, usually a porcine heart-lung tissue block filled with ketchup in a box, can simulate real surgery very well. This is a model used to train US thoracic surgery residents in VATS techniques (10). Other models used in formal VATS courses include VATS procedures on anaesthetized pigs. Although these models are effective at procedural teaching, they are limited by the cost and single use of animal tissue and the need for a thoracic surgeon to instruct. Virtual reality simulators have become an increasing popular modality for surgical education within recent years. In a recent randomised controlled trial of training with a virtual simulator developed for laparoscopy, the performance level of novices was increased to that of intermediately experienced laparoscopists and operation time was halved (11). The idea of letting residents practice with the simulator before doing surgery with improvement of cognitive and procedural skills can potentially lead to better patient safety. A recently developed virtual reality simulator uses a model for a right upper lobe lobectomy by VATS. Various anatomic variations and anomalies are randomized and loaded to present a unique surgical experience for each operation. The software is designed to identify common errors in procedural flow, including tears in pulmonary parenchyma that would result in air leaks, inappropriate ligation of vessels or bronchus to close to the pulmonary hilar origin, ligation of the vessels to the middle lobe or inferior lobe, and failure to ligate vessels to the right upper lobe. The model includes lymph node dissection (12). Virtual reality simulators will most likely play a significant role in the future training in VATS surgery. There seems to be many benefits. The amount of training is unlimited. The cost for each procedure is small, once the investment in the simulator is made. Performance scoring can be used for validation and credentialing. When introduced to surgery on patients, the surgeon is familiar with the tools and the steps of the procedure, which should enhance patient safety. We expect the learning curve in VATS lobectomy to be shorter once virtual reality simulators are introduced in the training programs.

Recommendations for a VATS lobectomy program

Before embarking on a VATS lobectomy program it is important to consider the local organisation. We believe it is important to have the potential to perform at least 25 VATS lobectomies a year. Furthermore each surgeon should have the potential to perform at least 25 VATS lobectomies a year. So given a limited number of potential VATS lobectomies, a limited number of surgeons should perform the operations. Especially in the beginning when introducing VATS lobectomy in a clinic, it is recommended to keep the VATS lobectomies on "a few hands" in order to complete learning curves for the first generation of VATS

Tabel 1 Recommendations for the introduction of a VATS lobectomy program

Perform open lobectomy by an anterior thoracotomy
Perform >100 minor VATS procedures
Attend formal courses in VATS lobectomy
Visit clinic with experience in VATS lobectomy
Training on simulators
Chose one approach
Consider volume/clinic/surgeon
Select patients
Stepwise introduction to surgical procedures
Prospective data collection

surgeons within a reasonable time. Then depending on the size of the clinic, the next generation of VATS surgeons can be trained in a supervised setting.

We have a set of recommendations for a surgeon embarking on a VATS lobectomy program (*Table 1*). Many different approaches to VATS lobectomy have been presented. We believe it is of utmost importance to choose one approach, and stick to it. If an anterior approach is chosen and the surgeon is used to perform a posterolateral thoracotomy, it is recommended to shift to anterior thoracotomy for a while, in order to become familiar with the hilar structures from an anterior approach. Performing more than a 100 minor VATS procedures like pleural biopsies, cyst resections and wedge resections is an advantage as the surgeon will get familiar with the port placement and working with the VATS tools in a monitor based setting. Furthermore it is highly recommended to take VATS courses and visit clinics with experience in VATS lobectomy, to observe the procedure or alternatively a fellowship in a clinic with a high volume in VATS lobectomy. Once these preparations are made, introduction can be performed in a stepwise manner. The first cases can be performed with an anterior thoracotomy, but without the use of a rib retractor. Conversion can be made very quickly and safely. Once more experience is gained, the incision can be minimized. Furthermore the procedure of the lobectomy itself can be introduced in a stepwise manner. Dividing the pulmonary ligament first, and then dissecting the vein and later turn to dissecting the arteries. Selecting the lobes is important in the beginning. Lower lobes are usually easier than upper lobes as there are fewer vessels to dissect. Small peripheral tumours are easier than central and larger tumours as the access to the hilar structures is easier. If there is suspicion of lymphatic spread, VATS lobectomies should not be attempted in the early phase of a learning curve. Previous thoracic surgery, tuberculosis or other inflammatory diseases known to give adhesions can be a difficult task for an inexperienced VATS surgeon. Incomplete fissures can be managed with a fissureless lobectomy, but there is a considerable learning curve to that technique as well. When dissecting, we recommend dissecting thoroughly in order to have a complete overview of the anatomy before dividing the vessels and bronchus, minimizing the risk of failure. Furthermore it is recommended to collect data for a prospective database to ensure quality control.

We hope that in the near future every patient with early stage lung cancer, suitable for a VATS lobectomy will be offered the procedure.

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Current costs of video-assisted thoracic surgery (VATS) lobectomy

Tunc Lacin, Scott Swanson

Department of Thoracic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Correspondence to: Tunc Lacin, MD. Department of Thoracic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA. Email: tlacin@partners.org or tunclacin@gmail.com.

Abstract: Video-assisted thoracoscopic lobectomy has many benefits over open surgery such as smaller incisions, less pain, less blood loss, faster postoperative recovery, shortened hospital stay, similar or superior survival rates. In contrast video-assisted thoracic surgery (VATS) has higher equipment costs, increased operating room times, at least initially, and a learning curve for the team. However when an experienced surgeon performs the surgery, significant hospital savings combined with better outcomes are achieved by video-assisted thoracoscopic lobectomy.

Keywords: Video-assisted thoracic surgery (VATS); lobectomy; costs; quality of life

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Background

Video-assisted thoracic surgery (VATS) has been used more and more in daily practice for diagnosis and treatment of lung diseases especially non-small cell lung carcinoma in the last decade (1,2). Despite the growing enthusiasm for VATS resections, this minimally invasive technique has had slow adoption due to concerns regarding oncologic principles, costs, possible complications, time spent on learning curve and lack of surgeon training (3). Potential benefits of VATS for lung resections are listed in the literature as smaller incisions, less pain, less blood loss, less respiratory compromise, shortened hospital lengths of stay and at least similar survival rates (3,4). VATS lobectomy is oncologically the same surgical procedure as a lobectomy through a thoracotomy; both use anatomic resection, individual hilar ligation, and lymph node sampling or dissection (4). Several reports indicate that the number of dissected lymph nodes is similar between VATS lobectomy and thoracotomy (5,6), although other reports question this assertion. Five year survival rates are comparable and in at least several meta-analyses better (7,8). The greatest advantage of a VATS lobectomy may be an improvement in perioperative quality of life (4). According to Demmy and colleagues' data, more patients who underwent thoracotomy required skilled nursing facilities after surgery (9) compared with a VATS approach. Several series have demonstrated that early postoperative pain is significantly less with VATS lobectomy (4,10). Patient who undergo VATS have a quicker recovery and have more strength to tolerate chemotherapy. As a result, theoretically, survival benefit will be higher if chemotherapy is started immediately after surgery (4). Postoperative pulmonary function also appears to be better after VATS than after a thoracotomy. In a nonrandomized comparison of patients who had a lobectomy by a thoracotomy or VATS, postoperative PaO_2, O_2 saturation, peak flow rates, forced expiratory volume in 1 second and forced vital capacity on both postoperative days 7 and 14 were better for the patients who had undergone the VATS procedure (11). The VATS patients have less impairment of pulmonary function and a better 6-min walk test than thoracotomy patients (12).

Recent data supporting advantages of VATS lobectomy

Several single institution series and a recent Society of Thoracic Surgeons (STS) database have demonstrated that compared with open thoracotomy, video-assisted thoracoscopic lobectomy may be associated with fewer postooperative complications (13). In the study of Paul *et al*. 73.8% of patients who underwent video-assisted

Table 1 The analysis of costs, surgery time and length of stay in open versus VATS lobectomy (3)

Procedure dependent variant	Lobectomy		P value
	Adjusted outcome	Standard deviation	
Hospital costs (dollars)			0.027
Open	$21,016.04	$5,645.14	
VATS	$20,316.19	$5,457.15	
Surgery time (hours)			0.000
Open	3.75	0.47	
VATS	4.09	0.52	
Length of stay (days)			0.000
Open	7.83	2.05	
VATS	6.15	1.61	

thoracoscopic lobectomy had no complications, where as 65.3% of patients underwent lobectomy via thoracotomy had no complications. Compared with open lobectomy, video-assisted thoracoscopic lobectomy was associated with a lower incidence of arrhythmias, reintubation, blood transfusion as well as a shorter hospital stay and chest tube duration (13). In addition to these early functional advantages, video-assisted thoacoscopic lobectomy has been shown to have comparable long-term outcomes (14,15). The peri-operative advantages as well as the short and long-term outcomes reported have assuaged the concerns of the safety and efficacy aspects of video-assisted resections for the thoracic oncology patient population. However the drawbacks to VATS include higher equipment costs, longer operative room times and steeper learning curves for surgeons and operating room personnel (3).

Economic comparison of VATS versus open lobectomy

In a recent study our group compared hospital costs and perioperative outcomes for video-assisted thoracoscopic surgery and open lobectomy procedures in the United States using the Premier Prospective Database (Premier Inc, Charlotte, NC) (3). The study included the time period from the third quarter of 2007 through 2008. A total of 3,961 patients (open n=2,907, VATS n=1,054) were included in this evaluation. Length of stay was 7.83 days versus 6.15 days for open versus VATS. Surgery duration was shorter for open procedures at 3.75 versus 4.09 hours for VATS (*Table 1*) (3). The risk of adverse events was significantly lower in the VATS group (P=0.019) (3). Although statistically not significant, pneumonia occurred more frequently in the open group (9.1%) versus VATS (8.1%). Arrhythmias, other cardiac events and bleeding were found to be significantly more prevalent in the open group than in the VATS group. The frequency of patients with prolonged lengths of stay (>14 days) was higher in the open group than in the VATS group. Hospital costs were higher for open versus VATS; $21,016 versus $20,316 (P=0.027). Given that there is both a reduction in adverse events and a 1.68 day reduction in length of stay with VATS, one might expect the difference in cost between open and VATS to be greater than $700. Therefore, we looked at surgeon experience to determine if this played a role in cost. We examined surgeon experience with VATS over the 6 months prior to each operation and found a significant association between surgeon experience and cost. Average costs ranged from $22,050 for low volume surgeons to $18,133 for high volume surgeons. For open lobectomies, cost differences by surgeon experience were not significant and both levels were estimated at $21,000. These data suggest that economic impact is magnified as the surgeon's experience increases.

In another recent retrospective study the relationship between volume and outcome in VATS surgery was evaluated (16). This relationship was striking for cost and utilization outcomes and VATS lobectomy as compared to VATS wedge resection. Outcomes following VATS surgery seems to be strongly associated with experience (16). This report showed that the reduction in cost and resource utilization increases significantly with greater experience and is most marked for VATS lobectomy for lung cancer. Moreover, thoracic surgeons have better VATS outcomes than non-thoracic surgeons and greater experience with open procedures does not correlate with better VATS outcomes. These findings reinforce the need for surgeons to focus on their VATS technique to achieve the best outcomes.

Another report on cost of VATS lobectomies revealed that the total hospital costs in the VATS group were lower than for those in the open lobectomy group ($5,391 *vs.* $5,593) (17). The reasons for the higher total hospital costs for open lobectomy were explained as longer hospital stays, longer chest tube duration and the need for more medications to control pain. Pulmonary complications, including respiratory dysfunction, pneumonia, atelectasis, empyema and prolonged air leak were less common with

VATS approach in this series. A subset of patients in this group were compared according to the surgeon's experience (early learning period *vs.* experienced learning period). Because of the decreased operation duration during the experienced learning period, the cost of anesthesia was significantly lower for these patients compared with those during the early period (17).

As the cost of surgical disposables play an important role in the total cost of VATS lobectomy, differences in the cost of resection of different lobes are also recorded (17,18). Casali and Walker demonstrated that upper lobectomy is more expensive than other types of lobectomy and that the difference in cost is mainly due to different need for the number of stapler cartridges (18). Cho demonstrated that the cost of surgical materials for resection of a lower lobe was lower than that for resection of the an upper lobe. The cost was $1,630 *vs.* $1,981 for right side and $1,655 *vs.* $1,908 for left side. When the total hospital costs were evaluated between the VATS lobectomy and open lobectomy groups for the five different lobes, VATS lobectomy for the left lower lobe was much more cost-effective than open lobectomy, although the difference was not statistically significant (17).

Using robotic technology to perform pulmonary surgery is of great current interest to the thoracic surgical community (19). Robotic lobectomies have been performed on a limited basis, with the advocates suggesting that the visualization and dissection are superior compared with a VATS approach. Robotic technology does have a certain appeal. The arms have a wrist-like movement and the magnification and depth of field of the robotic camera are superior to the standard VATS camera. However, it is not clear that these are significant advantages compared with VATS in the realm of cancer surgery. Compared with a VATS approach, the robotic incisions are the same size, the stapling instruments are the same, and the removal of the specimen is the same. The safety of VATS dissection of the vascular structures is excellent, with minimal reported problems after more than 17 years of experience. The completeness of lymph node dissection is complete with VATS and is not better with the robot, at least to date. Also, the surgical time and cost are significantly less for VATS (20). Robotic lobectomy has higher associated costs than VATS, primarily attributed to increased costs of the first hospital day, but it is less costly than thoracotomy approach for lobectomy (21). The average cost of VATS is substantially less than thoracotomy primarily because of a decreased length of stay. The cost of robotic assistance for VATS is still less than thoracotomy, but greater than VATS alone (21).

Conclusions

Minimally invasive techniques, such as VATS and robotics, are becoming the preferred approach in many surgical disciplines. Lobectomy performed by the VATS approach as compared with an open technique results in shorter length of stay, fewer adverse events and less overall cost. Patients who undergo VATS are discharged without home assistance and have low opiate requirements. Where there may be concern over the cost of the thoracoscopic equipment required for VATS, the significant hospital savings combined with better outcomes, particularly when an experienced surgeon performs the surgery, clearly favor the VATS approach over a thoracotomy. As the demand for health care resources increases, we must pay more attention to cost. Data, to date, shows a significant cost savings when a VATS approach is used compared to a thoracotomy for resection of lung cancer while enhancing short term outcomes and likely comparable or improved long term survival.

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VATS lobectomy lymph node management

Gavin M. Wright[1,2,3]

[1]Director of Surgical Oncology, St Vincent's Hospital, Melbourne, Australia; [2]Clinical Associate Professor, University of Melbourne Department of Surgery, St Vincent's Hospital, Melbourne, Australia; [3]Thoracic Surgical Lead, Division of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

Correspondence to: Gavin M. Wright, MD. 5th Floor, 55 Victoria Parade, Fitzroy VIC 3065, Australia. Tel: +61-3-94192477; Fax: +61-3-94171694. Email: gavin.wright@svhm.org.au.

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Introduction

Despite 20 years of development and published reports of thousands of cases (1), major pulmonary resections by video-assisted thoracic surgery (VATS) techniques have only recently experienced the uptake which was observed previously in other fields of minimally invasive surgery. One of the commonly stated reasons was the inability to perform an adequate complete mediastinal lymph node dissection, thus rendering the technique oncologically inadequate. On one occasion, I witnessed a prominent thoracic surgeon state this as "fact" during a major international lung cancer conference. Even before definitive evidence to the contrary became available, I felt this was a preposterous stance on several levels.

Firstly, population-based studies have shown that the adequacy of lymph node sampling, let alone complete mediastinal lymph node dissection, is extremely variable, and generally variably performed in open lobectomy cases (2,3). Secondly, this stance assumed that a surgeon who was capable of carefully dissecting out the unforgiving pulmonary artery, finding and dividing all of the correct broncho-vascular structures for the diseased lobe, and completing a difficult fissure, was somehow incapable of removing well defined anatomic areas of lymph node-bearing fat. Thirdly, albeit more recently, it has been shown in the American College of Surgeons Oncology Group (ACOSOG) Z0030 study, that if a single node at each lymph node station is negative on frozen section (or previous mediastinoscopy), then a complete node dissection is not required for an oncologically optimal lung cancer procedure (4).

Lymph node management at VATS lobectomy is therefore no different than it should be at lobectomy by thoracotomy. The first part of this perspective will therefore deal with the definitions of lymph node management and the evidence-based indications for sampling or complete mediastinal lymph node dissection regardless of surgical access. The remainder will deal with the practicalities of the VATS approach.

Definitions

Nodal Map in this perspective refers to the lymph node stations as charted by Rusch *et al.* for the International Association for the Study of Lung Cancer's 7th edition TNM staging system (5).

Complete mediastinal lymph node dissection (CMLND) is also known by various names such as systematic lymph node dissection, complete or radical mediastinal lymphadenectomy, and extended mediastinal lymph node dissection. There is no consensus on the ultimate radicality of these procedures as it can include bilateral or N3 level node dissection for some surgeons. I define this as a similar dissection as was demanded in the ACOSOG Z0030 trial protocol (4), with the exception that I do not routinely dissect station 2 L, and only dissect station 4 L if there is an intra-operative finding of a microscopically involved station 5 or 7 node.

Systematic node sampling (SNS) refers to either taking a single node at each numbered station as in the control arm of ACOSOG Z0030, or 2 nodes from each field or station with at least 3 fields dissected always including station 7 (European Society of Thoracic Surgeons recommendation) (6).

More minimal forms of sampling are characterized a random biopsy or by the surgeon's impression that particular nodes may be involved (the chance node), or use

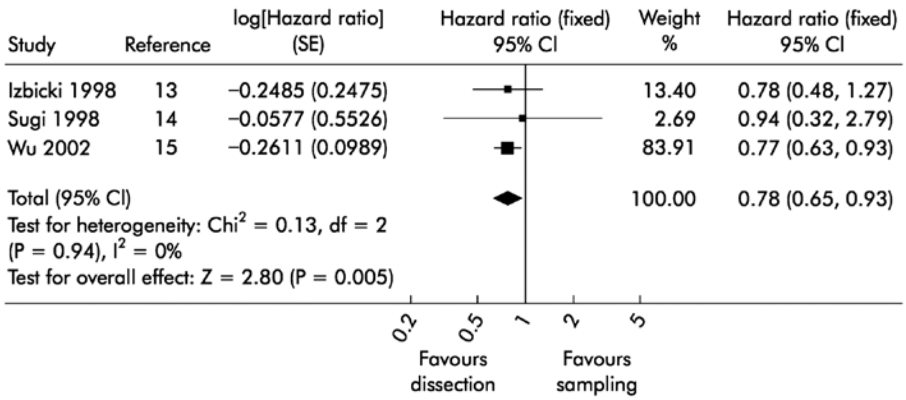

Figure 1 Forest plot from Wright *et al.*'s 2006 meta-analysis (8) of randomized controlled trials of systematic node sampling versus complete mediastinal lymph node dissection.

of sentinel node identification by Geiger counter and frozen section (the decision node) (7). Throughout this perspective I will be defining SNS as specified in the ACOSOG Z0030 trial protocol.

Indication for complete mediastinal lymph node dissection

CMLND has been the subject of controversy ever since lobectomies were accepted as standard therapy for non-small cell lung cancer (NSCLC). In 2006, a systematic review and meta analysis was published which suggested a moderate survival benefit for complete mediastinal lymph node dissection (*Figure 1*) (8). The hazard ratio was 0.78, which is similar to the benefit of adjuvant chemotherapy in Stage II-IIIA NSCLC. The ACOSOG Z0030 trial accrued over 1,100 patients from 1999-2004 and included patients from USA, Canada and my own institution in Melbourne, Australia (4). Patients in this trial had SNS, then frozen section analysis. If they were found to be node-negative for the mediastinal and hilar nodes, they were randomized to CMLND or no further lymph node treatment. This trial showed no survival benefit of CMLND after SNS in highly selected early stage NSCLC (*Figure 2*).

In light of this partially contradictory evidence, re-analysis of all CMLND randomized trials now highlighted the differences of this trial and Sugi's trial of small peripheral stage I adenocarcinoma (9) compared to the higher stage and more histologically diverse trials of Wu and Izbicki (10,11). The upshot of the evidence is now that CMLND remains standard of care for stage II-IIIA NSCLC (or unstaged NSCLC), but is not necessary for pathologically proven Stage I NSCLC (by pre-operative or intra-operative sampling by SNS).

Thoracic surgeons, regardless of whether performing VATS or thoracotomy, have to decide on their own protocol for lymph node management in the light of the above evidence and the realities of surgical practice. In my opinion, the cost and time wasted for SNS and frozen section analysis has outweighed the small additional time it takes for a complete mediastinal lymph node dissection. Given that the ACOSOG Z30 trial showed no clinically important difference in morbidity and the same survival, I routinely perform CMLND to ensure I get optimal staging (for adjuvant chemotherapy decisions) and any possible therapeutic advantage (in unexpected N1 or N2 disease).

VATS lobectomy lymph node management

Cheng *et al.* (12) and several other groups (13-16) have shown that the lymph node yield is similar by VATS or thoracotomy. In particular, in a prospective trial setting, a sub-analysis of the abovementioned ACOSOG Z0030 study showed no difference between VATS and thoracotomy for node dissection (15), and the only long term survival evidence showed no difference between a VATS approach and a thoracotomy approach (17). The difference between VATS and thoracotomy management therefore lies only in the tips and techniques required to obtain the appropriate sampling or complete dissection.

The approaches to VATS lobectomy itself vary; therefore I must set the scene for this overall perspective. Our routine VATS lobectomy consists of two standard thoracoscopic port sites, usually in the 7th and 8th interspaces, and a utility

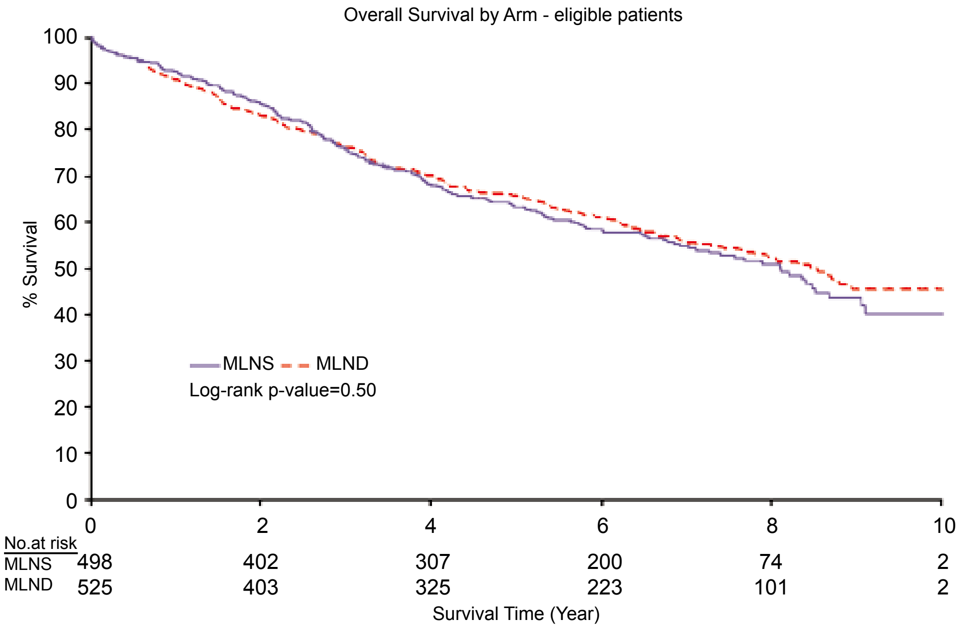

Figure 2 Cumulative survival curve from the ACOSOG Z0030 trial (4). This trial found no additional benefit of complete mediastinal lymph node dissection in patients who had undergone systematic node sampling and found to be N0 on frozen section.

incision (non-rib-spreading mini-thoracotomy incision) varying from 3-8 cm depending on the size of the tumour. The hilum is usually dissected from anterior to posterior (upper and middle lobes) or from inferior to superior (lower lobes).

Technique overview

Using our approach, it is advantageous to dissect out many of the nodes required for sampling or complete dissection prior to dividing individual hilar structures. For example, if the inferior pulmonary ligament needs dividing to access the inferior pulmonary vein, station 9 is taken radically, which leaves most of this vein skeletonised. We would not simply divide the vein at this stage, but instead remove station 8 nodes posterior and superior to the inferior pulmonary vein and station 11 nodes between the vein and the lower lobe bronchus. This makes for a much simpler division of the vein, and subsequently the dissection of the bronchus. Similarly, we would advocate removal of any further station 10 L and 11 L nodes on the left side prior to division of the bronchus, as this then makes later dissection of the bronchus from the pulmonary artery much easier and safer.

Once the lobectomy specimen is removed there is more room to operate, oozing and back-bleeding is no longer a hindrance, and visualization of the required lymph node zones is simpler. The best approach is now to perform a systematic, if not complete, dissection of the anatomic lymph node stations that have not already been sampled or dissected.

On the right, I begin with the superior mediastinal node stations 2R, 4R and 10R. These can be dissected as a single bloc, or separately dissected from the three zones. If the specimen is removed as a single bloc, it needs to be (somewhat arbitrarily) divided into the three zones before submission to the pathologist, so that accurate staging is achieved. The azygos vein can be divided to facilitate a more radical dissection of the upper mediastinum, but this is not necessary. In most cases I remove station 2R and 4R, together with the azygos vein looped and retracted inferiorly, then remove station 10R with the azygos vein reflected superiorly

Station 7 and 8 can usually be removed as a single bloc, and then separated at the point where the most prominent vagal branch to the lung was previously divided. This anatomical landmark is my own rule, as there is actually no strict definition of where station 7 ends and station 8 begins.

Finally station 9 is taken, although this is probably the least likely to be involved if the resection specimen is not the lower lobe.

On the left, I dissect station 5 and 6 as a single bloc if possible, clearing all of the tissue between vagus and phrenic nerves, and taking care not to damage the recurrent laryngeal nerve. Unless performing a radical dissection for a frozen section-proven positive node at station 5 or 7, I do not routinely dissect station 4 L due to the increasing risks of recurrent laryngeal nerve injury and the decreasing benefits of such radical lymph node excision. When proceeding to dissect station 4 L, I divide the ligamentum arteriosum to obtain better access. Alternatively, if the status of station must be known, it can readily be biopsied pre-operatively by mediastinoscopy or endobronchial ultrasound guided fine needle aspiration.

Advanced access and retraction techniques

Port-site seeding is a rare but recognized risk, which does not appear to be reduced by use of a specimen retrieval bag (1). However, we routinely use wound protectors that completely exclude the chest wall access tissues from the operation, while providing gentle radial retraction. I use a rigid small Alexis® retractor (Applied Medical, CA, USA) for the utility incision, and an extra-extra-small Alexis® retractor with removal tether for the posterior port site. This allows simple removal of the lymph node specimens without the need for multiple specimen retrieval bags.

CMLND is best performed from the highest accessible interspace (preferably the 4^{th}). Therefore, on deciding upon the correct interspace to place the utility incision, I would advise a higher space if there is any doubt. Often a lower lobectomy is more easily performed an interspace below that of an upper lobectomy, and this does steepen the angle of approach of instruments to the superior mediastinal node stations. If this proves to be a significant obstacle, a fourth port can be placed in the auscultatory triangle for this part of the procedure.

We have found that the best instrument for grasping lymph nodes or associated fat is an angled sponge-holder. We then use an endoscopic version of a Cobb periosteal elevator (or a standard Cobb elevator if it reaches) to dissect away the tissues defining the lymph node package and for thinning out lymphatic vascular pedicles.

Haemostasis must be meticulous, as bleeding or chyle leak from the bed of station 7 or 4R can result in an unplanned return to the operating theatre. I use endoscopic clips liberally, although an ultrasonic or other haemostatic energy source could be employed as an alternative. In particular, there is commonly a small vein draining the station 4R package directly into the superior vena cava. This should be sought out and clipped early, and doing so will facilitate a better dissection.

Considerable anterior retraction of the lung is required for access to station 7. This can be a frustrating endeavour, depending on the lobe that has been removed. An angled sponge-holder can be placed through the utility incision to grasp the posterior aspect of the lower lobe and/or upper lobe and then used to pull the lung forward. This can then be left in the base of the utility incision (and even clipped to a drape to maintain retraction) while dissection carries on beside its shaft.

Conclusions

There is no reason that a lobectomy by VATS should have any less optimal SNS or CMLND than by thoracotomy. All anatomical sites are accessible to standard VATS access. Surgeons who can perform VATS lobectomy already have the requisite surgical skills (although may need specific training). Multiple studies have confirmed their oncological equivalence based on lymph node yields and survival.

The emergence of this “dilemma” of lymph node management by VATS at this time, is however fortuitous. It allows the dissemination of latest evidence related to lymph node management (and its importance for adjuvant chemotherapy selection) to both the new generation and the older generation of thoracic surgeons, regardless of whether they choose a VATS approach to lobectomy.

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VATS lymph node dissection

Gavin M. Wright[1,2,3]

[1]Director of Surgical Oncology, St Vincent's Hospital, Melbourne, Australia; [2]Clinical Associate Professor, University of Melbourne, Department of Surgery, St Vincent's Hospital, Melbourne, Australia; [3]Thoracic Surgical Lead, Division of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

Correspondence to: Gavin M. Wright, MD. 5th Floor, 55 Victoria Parade, Fitzroy VIC 3065, Australia. Tel: +61394192477; Fax: +61394171694. Email: gavin.wright@svhm.org.au.

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Introduction

The treatment of lymph nodes has been controversial in the past, but analysis of the highest level of evidence available suggests that in unknown stage or Stage II-IIIA non-small cell carcinoma of the lung, it is associated with a survival benefit (1). Whatever a surgeon's personal node policy may be for open lobectomy, it should be reflected in the approach to VATS lobectomy. There is no particular extra skill required, only intent. The following videos are intended to demonstrate the basic techniques of clearing the minimum node set as set out in the ACOSOG Z0030 trial protocol (2). Throughout these videos I will be referring to the node stations as specified in the same trial. These are station 2R (upper paratracheal), 4R (lower paratracheal), 7 (subcarinal), 8 (paraoesophageal), 9 (inferior pulmonary), 10L/10R (hilar) and 11L/11R (interlobar).

Operative techniques

Video 1 - right-sided dissection

As a general rule, I remove the package of Station 2R and Station 4R as a bloc. The roof of this package is a triangle bounded by the azygos vein (inferior), vagus nerve (posterior) and superior vena cava (anterior). The floor is the trachea, and the apex of the floor is the right subclavian artery. After incising the pleural triangle as described, most of the dissection is blunt, using an implement similar to a blunt periosteal elevator [00 min 30 sec]. There is often a small vein that drains directly from this node-bearing fat into the superior vena cava, and this needs to be clipped and divided. After thinning out the lympho-vascular pedicle tissue, generously apply clips or use ultrasound or impedance-modulated diathermy to reduce bleeding and later lymphatic leakage [01 min 20 sec]. Station 2R lymph nodes are best accessed by simple caudal traction on the entire package, then teasing out and clipping the small draining vessels. If the Station 4R nodes break away, then remove those separately, then re-grasp the lower part of station 2R with a curved sponge-holder [02 min 00 sec]. Whilst it would take quite aggressive dissection to injure the recurrent laryngeal nerve, care must be taken to avoid the intersection of the vagus nerve and subclavian artery at the posterior aspect of the apex of the dissection [02 min 38 sec]. Likewise, the phrenic nerve should be avoided when dissecting along the superior vena cava. At the conclusion all of the boundaries of the superior mediastinum are clearly visible [02 min 48 sec].

Station 10R is dissected by retracting the azygos vein superiorly and incising the hilar pleura. All tissue between the pulmonary artery, right upper lobe bronchus and azygos vein is dissected and removed. A tie can be passed around the azygos vein to facilitate its retraction during the superior mediastinal dissection.

Attention is then turned to Stations 7 and 8. These are often dissected together, clearing all of the tissue between the posterior hilum and oesophagus down to the carina. In the video, the patient has undergone a right middle lobectomy, so access to Station 7 is available from the anterior approach, medial to the bronchus intermedius [03 min 00 sec].

The normal posterior approach is seen in the video of the left-sided dissection. After the station has been cleared, I have retracted the lung forward and opened the posterior space to show that Station 7 is indeed gone, and to search for any Station 8 tissue [05 min 10 sec].

Station 9 is highly variable in quality and quantity. In this right-sided dissection video, there was very little nodal tissue or fat caudal to the inferior pulmonary vein. In contrast, a high volume package was found at the beginning of the video of the left-sided dissection.

Video 2 - left-sided dissection

This patient had a left lower lobe non-small cell lung cancer and, because of previous coronary surgery, required significant division of pleural adhesions prior to commencing any dissection. The dissection therefore commences with station 9, since the inferior pulmonary ligament must be divided in any case. I tend to dissect the entire ligament off the oesophagus and inferior aspect of the inferior pulmonary vein. This leaves it attached to the lower lobe. I then remove the package to label it for the pathologist [02 min 00 sec].

Once the inferior pulmonary vein has been divided [02 min 45 sec], the nodal tissue around the bronchus can be dissected. In fact, this manoeuvre facilitates the lobectomy [04 min 30 sec]. Immediately posterior to the bronchus is Station 8, which must be dissected off the vagus nerve and oesophagus posteriorly. On the bronchus itself is Station 11 L, which may be contiguous with Station 8. There are usually two or three vagal branches to the lung that need to be divided to free up Station 8 [05 min 30 sec].

Rolling the lung forward and dissecting upwards along the underside of the bronchus gives access to station 7 [06 min 40 sec]. The pericardium is swept clean and the package is dissected off the oesophagus. Lastly the subcarinal space is opened by spreading a sponge-holder and the nodal tissue grasped [06 min 40 sec]. All structures suspicious for nodal or bronchial arteries should be clipped as bleeding from a retracted vessel is a considerable nuisance. Station 10L is located between the left main bronchus and the underside of the left pulmonary artery. This is best dissected before division of the bronchus as there is more tissue to grasp for retraction, and it limits the stresses placed directly on the pulmonary artery. After division of the lower lobe bronchus in this case, any remaining nodal tissue can then be cleared from stations 10 L and 11 L [07 min 20 sec].

The lung is next rolled posteriorly to access Stations 5 and 6 [07 min 50 sec]. An incision is made in front of the hilum, behind and parallel to the phrenic nerve. This is continued over the aorta. The nodal tissue between the pulmonary artery and underside of the aorta is Station 5. Care must be taken to stay well anterior to the vagus nerve and not to divide any structure that could possibly be the recurrent laryngeal nerve. Blunt teasing of the tissue inferiorly and anteriorly will usually allow safe removal of these nodes, even if the recurrent nerve is not specifically identified. Station 6 is then grasped and often needs to be dissected off the phrenic nerve [08 min 45 sec].

Comments

Not all surgeons practice, or are comfortable with, complete mediastinal dissection; even in open cases. Therefore a practical compromise is to at least perform a routine minimum node-sampling set. For the right upper and middle lobes, I would recommend a minimum of Station 4R, 7, 8 and 10R. For the right lower lobe, I would recommend Stations 4R, 7, 8 and 9. On the left side for the upper lobe I recommend Stations 5, 6, 7, 8 as a minimum, and for the lower lobe Stations 5, 7, 8 and 9.

I would also comment that often it is simpler and less bloody to removal a whole package at a given site than just a single node, especially if very fatty.

Practice makes perfect for this procedure, and eventually it should add little time to a VATS lobectomy. With routine sampling, there is less than 5% chance of missing a patient with occult N2 disease (2). This is the most critical point, given the known advantage of adjuvant chemotherapy in this setting.

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Efficacy of mediastinal lymph node dissection during thoracoscopic lobectomy

Hanghang Wang, Thomas A. D'Amico

Division of Thoracic Surgery, Duke University Medical Center, Durham, North Carolina 27705, USA

Correspondence to: Thomas A. D'Amico, MD. Professor of Surgery, Duke University Medical Center. Box 3496, Duke South, White Zone, Room 3589, Durham, North Carolina 27710, USA. Tel/Fax: (919) 684-4891. Email: damic001@mc.duke.edu.

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Introduction

While the first description of thoracoscopy occurred as early as 1910 (1), the first successful attempts of video-assisted thoracoscopic (VATS) lobectomy for non-small cell lung cancer (NSCLC) did not take place until the early 1990s (2). As VATS lobectomy continues to gain acceptance as the less invasive alternative to open thoracotomy, extensive research has been conducted to compare its efficacy, postoperative outcomes and oncologic effectiveness to thoracotomy. Despite its many proven advantages, concerns regarding the oncologic effectiveness of VATS lobectomy remain as one of the major obstacles to its wider adoption (3). As an important assessment for accurate staging of NSCLC, adequate evaluation of lymph nodes, especially mediastinal lymph nodes, has been the center of the controversy.

Advantages of VATS *vs.* thoracotomy for lobectomy

The less invasive nature of VATS lobectomy, as compared to lobectomy via thoracotomy, is manifested in less morbidity, including less post-operative pain (4), reduced level of inflammatory response and preserved immune function (4-8), and fewer overall post-operative complications (9-12). Specifically, less post-operative pain with VATS lobectomy is evidenced by reduced amounts of analgesic use and fewer points on the 0-10 pain scale (4). A reduced level of inflammatory response and preserved immune function are demonstrated by lower levels of inflammatory mediators including IL-6 and C-reactive protein, as well as less reduction in levels of CD4 and natural killer cells (4-8). Pulmonary function tests on patients one and two weeks postoperatively have shown faster and improved recovery rates of FVC, FEV1 and vital capacity in VATS lobectomy compared with open lobectomy, supporting preserved pulmonary function (4). While mortality rates are often similar between VATS and open lobectomy, it is conceivable that less pain, reduced inflammation and preserved physiologic function will translate into fewer post-operative complications. This has been illustrated by several studies, including one prospective trial (13), 6 retrospective case control series (9,12,14,15) and one systematic review (7). These studies have shown that VATS lobectomy is associated with lower rates of post-operative complications, including air leak, arrhythmia and pneumonia. In fact, the utilization of the VATS technique has been demonstrated to be a stronger predictor of post-operative morbidity than age and pulmonary function after lobectomy (14,15). The potential to improve oncologic efficacy of VATS lobectomy is suggested in a study demonstrating superior compliance with adjuvant chemotherapy after VATS lobectomy (16). In their study, Petersen *et al.* found that as compared to open lobectomy, patients who underwent VATS lobectomy were more likely to receive planned adjuvant therapy, had fewer delays and reductions in planned doses (16).

Mediastinal lymph node dissection during lobectomy

Guideline recommendations

The controversy concerning the efficacy of mediastinal lymph node dissection (MLND) during VATS lobectomy originates from the lack of strict standards on the technique and extent of lymph node removal for MLN staging in all patients with NSCLC. Current practice guidelines by the National Comprehensive Cancer Network (NCCN) recommend the complete dissection of at least three mediastinal nodal stations (N2) as defined by the most recent staging system (17,18). The European Society of Thoracic Surgeons (ESTS) has published similar guidelines, advising the removal of at least three hilar and interlobar nodes and three mediastinal nodes from three stations, in which the subcarinal station is always included (19). While mediastinal lymph node sampling (MLNS) is the standard of practice among most thoracic surgeons and groups participating in clinical trials in North America (20), debate continues on the efficacy of MLND *vs.* MLNS and focuses on local tumor control, detection of micrometastasis and effects on survival.

MLND *vs.* MLNS

Proponents of MLND argue that with complete removal of all resectable lymph nodes, the proportion of complete R0 resections is increased, leading to reduced local recurrence. This has been supported by several studies, in which the rates of local and overall recurrence were significantly reduced by MLND (19,21-23). Another potential advantage of MLND is more accurate tumor staging through detection of micrometastasis and skip lesions. In their study, Lardinois *et al.* demonstrated significantly higher number of mediastinal lymph nodes harvested by MLND compared with MLNS (17.3±5.3 *vs.* 7.2±2.5) (19). Despite the aforementioned potential advantages, whether MLND is associated with improved survival remains controversial. Some researchers argue that the perceived survival advantage of MLND is in fact a Will Rogers phenomenon - stage migration of patients due to an improved lymph node staging by a more extensive lymphadenectomy (21,24). In a retrospective review by Doddoli *et al.* comparing the effect of MLND (n=258) *vs.* MLNS (n=207) on overall survival of patients with Stage I NSCLC, MLND was found to be a favorable independent prognostic factor on survival (Hazard risk: 1.43, 95% CI 1.00-2.04; P=0.048) (23). Similarly, Lardinois *et al.* demonstrated longer disease-free survival in patients who underwent MLND *vs.* MLNS in stage I NSCLC (60.2±7 *vs.* 44.8±8.1 months, P<0.03) (19). Such results were supported by Keller *et al.* who reported an improved survival in patients who underwent MLND (median survival 57.5 months) *vs.* MLNS (median survival 29.2 months) in patients with Stages II and IIIa NSCLC. Of note, this survival advantage only applied to patients with right lung tumors (25). In a prospective randomized trial by Wu *et al.* comparing MLND *vs.* MLNS through thoracotomy for stages I-IIIA NSCLC (n=532), a significant survival advantage with MLND was again noted for stage I (5-year survival 82.16% *vs.* 57.49%, P=0.02) and IIIA NSCLC patients (26.98% *vs.* 6.18%, P<0.001) (22).

Other studies have not confirmed such survival advantage of MLND. Early retrospective reviews demonstrated no difference in long-term survival after MLND *vs.* MLNS (26-28). A prospective randomized controlled trial by Sugi *et al.* comparing MLND *vs.* MLNS via thoracotomy for T1N0M0 (now T1aN0M0) lesions (n=115) revealed no significant differences in the recurrence rate (10% *vs.* 13%), 3-year (88.1% *vs.* 89.2%) or 5-year (81.4% *vs.* 83.9%) survival. The authors argued that because most recurrences occur distantly, better local control of disease does not translate into improved survival (29). Another prospective randomized controlled trial by Izbicki *et al.* comparing MLND to MLNS (n=169) showed that MLND did not improve survival in the overall group of patients (hazard ratio: 0.78, CI 0.47-1.24), although subgroup analysis showed an improvement in relapse-free survival (58.8% *vs.* 20.7%, P=0.037) in patients with pN1 or N2 disease with one lymph node level involvement (21). Most recently, the randomized, multi-institutional prospective trial by ACOSOG on MLND *vs.* systematic MLNS (Z0030) found no improvement on survival associated with MLND for patients with early-stage NSCLC. However, the authors still recommended MLND for all patients with resectable NSCLC, because of the potential benefits in more accurate staging with no increased mortality or morbidity (30).

Efficacy of MLND during VATS lobectomy

Technique

While the use of instruments may differ, the technique of MLND via VATS follows the same principles as the open approach. As described in detail by D'Amico *et al.*, the most important lymph node stations are levels 2, 4, and 7 for a right upper lobectomy, level 5, 6, and 7 for left upper lobectomy and levels 7, 8, and 9 for lower lobectomies (in addition to the upper lymph node stations) (31).

Lymph node dissection may be performed prior to or following lobectomy, with superior exposure if performed prior to dissection of the hilum. The anterior paratracheal lymph node stations, which include levels 2 and 4, are bordered by the superior vena cava anteriorly, the trachea posteriorly, the pericardium medially, the azygos vein inferiorly and the junction of the innominate artery and the trachea superiorly. The right recurrent laryngeal nerve is at risk of injury during anterior MLND and should be avoided by staying away from the innominate artery. Paratracheal lymph node dissection should be performed en bloc, with respect to the above mentioned borders, and may be performed with a combination sharp dissection, electrocautery, and other energy sources.

On the left side, the VATS approach with magnification facilitates dissection of level 5 and 6 lymph nodes with less risk of injury to the recurrent laryngeal nerve. Using the borders of the left phrenic nerve, the aortic arch, and the left pulmonary artery, all lymph node tissue in the aortopulmonary window should be readily resectable.

To perform subcarinal lymph node dissection (level 7), resection of all nodal tissue bordered by the two main bronchi, esophagus and pericardium is required. On the left side, retraction of the aorta is achieved using long, curved thoracoscopic instruments. Complete subcarinal lymph node dissection is achievable in all cases.

Safety and morbidity

As with open thoracotomy, potential complications from MLND during VATS lobectomy include injuries to the bronchial arteries, tracheobronchial tree and recurrent laryngeal nerves, prolonged air leak, hemorrhage and atrial fibrillation. There may also be risk of pulmonary edema by impairing the lymphatic backflow (23). Studies so far have demonstrated comparable operative mortality and morbidity of MLND by VATS *vs*. open lobectomy, indicating that MLND by VATS is a safe procedure (32).

Results

Several previous studies have examined the extent of MLND by VATS *vs*. open lobectomy. In one study by Kondo *et al*., thoracotomy was performed for reassessment of lymph nodes following MLND using VATS and yielded few additional lymph nodes (mean=1.3 LN, median 0) (33). Similarly, Sugi *et al*. found no difference between the numbers of lymph nodes dissected among VATS (mean=8.4±1.0) *vs*. open (mean=8.2±1.5) group during lobectomy (34). More recently, a retrospective review of 770 patients with cN0-pN2 NSCLC (VATS=450, open=320) by Watanabe *et al*. examined the total number of lymph nodes, number of lymph node stations, number of mediastinal nodes and mediastinal stations by VATS *vs*. open lobectomy, and found no difference in any of these categories (35).

Data from the recent ACSOG Z0030 trial (n=752, VATS=66, open=686) has also confirmed the efficacy of MLND by VATS procedure by demonstrating similar number of LN removed and LN stations assessed (36). So far, few studies have disputed the efficacy of MLND by VATS, with one study by Delinger *et al*. (VATS=79, open=464) showing a fewer number of LN sampled by VATS compared to thoracotomy (7.4±0.6 *vs*. 8.9±0.2, P=0.03) and fewer number of N2 nodes (2.5±3.0 *vs*. 3.7±3.0, P=0.004) (37). In a recent study analyzing data from the NCCN Database by D'Amico *et al*. with a more balanced number of VATS *vs*. open patients (n=388, VATS=199, open=189), VATS and thoracotomy were found to result in similar number of mediastinal lymph node resections (median=4 for both groups) and N2 nodes (median=3 for both groups). The percentage of patients with at least three MLN stations assessed, as recommended for the guidelines, was also similar in the VATS *vs*. open group (66% *vs*. 58%, P=0.12) (38).

Correlation between clinical and pathological staging

In addition to the extent of MLND, the correlation between clinical and pathological staging has been examined by previous investigations and was found to be comparable for VATS *vs*. open MLND. In the study by Sugi *et al*., the incidence of upstaging from N0 to N1 and N2 disease was found to be 4.2% and 2.1%, respectively, for MLND via VATS, and 5.8% and 1.9% for open (P=0.47) (34). This is similar to the research by Denlinger *et al*., in which 1.3% of patients with clinical N0 or N1 disease and treated with VATS had pathologic N2 disease, as opposed to 3.9% treated with thoracotomy (P=0.5) (37). Although the study by Watanabe *et al*. reported higher rates of upstaging for both VATS and open groups of patients with Stage I NSCLC with rate of 20.1% (N0 to N1 or N2 disease) for VATS and 30.3% for open MLND, there was no significant difference between the two groups (32). In the NCCN Database study by D'Amico *et al*., the rate of upstaging from N0 to N1, N2 and N3 disease was 6.4%, 2.3% and 0%, respectively, for MLND via VATS and 6.9%, 7.6% and 0% for thoracotomy (P=0.24). The rate of downstaging from N2 to N1 and N0 disease was 0% and 29%, respectively, for VATS and 8.7% and 17.4% for thoracotomy (P=0.99) (38).

Disease-free survival and overall survival

The definitive proof of efficacy for MLND via VATS

Table 1 Summary of recent studies on the disease-free and overall survival of patients with lobectomy via VATS *vs.* thoracotomy

Study	Disease-free survival (VATS *vs.* thoracotomy)	Overall survival (VATS *vs.* thoracotomy)
Sugi [2000](34)	-	3 yr: 90% *vs.* 93% (P=0.74) 5 yr: 90% *vs.* 85%
Watanabe [2008](35)	5 yr: 60.9% *vs.* 49.6% (P=0.714)	5 yr: 45.4% *vs.* 41.1% (P=0.83)
Denlinger [2010](37)	-	3 yr: 83.3% *vs.* 74.5% (P=0.43)
Flores [2009](9)	-	5 yr: 79% *vs.* 75% (P=0.08)

lobectomy lies in its impact on rate of both disease-free and overall survival. Previous researches have shown equivalent, if not superior, survival rates of VATS lobectomy as compared to thoracotomy (9,35,39,40). In their prospective randomized trial comparing oncologic results of VATS *vs.* open lobectomy, Sugi *et al.* revealed similar 3- and 5-year survival rates (90% *vs.* 93% and 90% *vs.* 85%, respectively) for patients with clinical stage IA lung cancer (34). Additional retrospective analyses and systemic reviews have confirmed these findings (9,39), while one meta-analysis reported a significantly improved 5-year survival rate (RR=0.72, CI 0.45-0.97) associated with VATS lobectomy for early-stage NSCLC (40). A summary of recent studies can be found in *Table 1*.

Conclusions

In conclusion, VATS lobectomy has both physiologic and biologic advantages over open thoracotomy. While controversy still exists concerning its oncologic effectiveness, especially its efficacy in MLND, research to date has confirmed its feasibility, safety, as well as equivalent outcomes as compared to open thoracotomy. In the future, research may help resolve the controversy over the extent of MLND and contribute further to the adoption of VATS lobectomy.

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Single-port video-assisted thoracoscopic surgery for lung cancer

Chao-Yu Liu[1,2,4*], Chen-Sung Lin[1,3,4*], Chih-Hsun Shih[1,4], Chia-Chuan Liu[1,4]

[1]Faculty of medicine, School of Medicine, National Yang-Ming University, Taipei 112, Taiwan; [2]Division of Thoracic Surgery, Department of Surgery, Far Eastern Memorial Hospital, New Taipei City, Taiwan; [3]Division of Thoracic Surgery, Department of Surgery, Taipei Hospital, Ministry of Health and Welfare, New Taipei City, Taiwan; [4]Division of Thoracic Surgery, Department of Surgery, Koo-Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

*Both Dr. Liu CY and Dr. Lin CS contributed equally as co-first authors in this work.

Correspondence to: Chia-Chuan Liu, MD. Division of Thoracic Surgery, Department of Surgery, Koo-Foundation Sun Yat-Sen Cancer Center, 125 Lih-Der Road, Pei-Tou District, Taipei 112, Taiwan. Email: gcliu@kfsyscc.org.

Abstract: In 2004, novel results using pulmonary wedge resection executed through single-port video-assisted thoracoscopic surgery (VATS) was first described. Since that time, single-port VATS has been advocated for the treatment of a spectrum of thoracic diseases, especially lung cancer. Lung cancer remains one of the top three cancer-related deaths in Taiwan, and surgical resection remains the "gold standard" for early-stage lung cancer. Anatomical resections (including pneumonectomy, lobectomy, and segmentectomy) remain the primary types of lung cancer surgery, regardless of whether conventional open thoracotomy, or 4/3/2-ports VATS are used. In the past three years, several pioneers have reported their early experiences with single-port VATS lobectomy, segmentectomy, and pneumonectomy for lung cancer. Our goal was to appraise their findings and review the role of single-port VATS in the treatment of lung cancer. In addition, the current concept of mini-invasive surgery involves not only smaller resections (requiring only a few incisions), but also sub-lobar resection as segmentectomy. Therefore, our review will also address these issues.

Keywords: Lobectomy; lung cancer; segmentectomy; single-port; video-assisted thoracoscopic surgery (VATS)

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A new trend: video-assisted thoracoscopic surgery (VATS) for lung cancer

On October 19, 2013, four live demonstrations of successful single-port VATS lobectomies were performed at Shanghai Pulmonary Hospital. More than 200 chest surgeons witnessed this demonstration and shared their thoughts. Based on this response, it is clear that lung cancer, and, in particular, single-port VATS lobectomy for lung cancer, are popular topics among Asian thoracic surgeons (1,2).

Both the general public and the government are aware of the high incidence, morbidity, and mortality rates (as well as the high medical costs) associated with advanced-stage lung cancer. Several screening tools, including chest radiography and low dose computed tomography (CT) (3,4), have been advocated in high risk patients. As a result, more patients are presenting with early-stage lung cancer. If they can be adequately treated, they usually harbor a better prognostic outcome. These patients are also, potentially, the best candidates for minimally invasive surgery which can reduce their recovery time and suffering after surgery. Thus, we will focus on the role of single-port VATS for lung cancer lobectomy.

Current VATS practice in Taiwan

Before 2000, conventional posterolateral open thoracotomy remained the "gold standard" for the treatment of patients with lung cancer. However, VATS has replaced open thoracotomy and has become the current mainstay of lung cancer surgery (5). Actually, the penetration rate of VATS in Taiwan is extremely high. As surgical creativity and innovation have progressed, three variants of VATS

Table 1 Comparisons among RATS, non-intubated VATS, and single-port VATS

	Special equipment	Cost	Experienced anesthesiologist	Operator skill demands	Experienced cameraman	Experienced assistant	Surgeon's satisfaction	Patient's satisfaction
RATS	Robotic system	+++	–	+	–	For stapling	++	?
Non-intubated VATS	–	–	+++	+	+	–	?	+
Single-port VATS	Double joint instruments	–	–	+++	+++	–	?	++

–, not required; +, low level of requirement; ++, medium level of requirement; +++, high level of requirement; ?, uncertain; RATS, robotic-assisted thoracoscopic surgery; VATS, video-assisted thoracoscopic surgery.

have been developed in our society, the robotic-assisted thoracoscopic surgery (RATS), non-intubated VATS, and single-port VATS (6,7). Differences regarding cost, instrument settings, special anesthesia demands, surgical techniques, patient selection, and insurance coverage among these VATS alternatives are quite difficult to have evidence-based comparison (*Table 1*). Shows the summary based on our interpretation.

For lung cancer surgery, several controversies exist concerning RATS (8), including the high cost, the increased number of utility wounds, and the need for skilled assistants to perform stapling for bronchus and pulmonary vessels. However, with the advances in new instrumentation, especially the endocutter, and the reduced size of the robotic arm which has avoided collisions during surgery, the role of RATS in lung cancer has exceeded our expectations. Although non-intubated VATS did not represent an improvement in surgical technique, it has the advantage of reduction in airway trauma caused by standard double-lumen endotracheal intubation. Furthermore, both the introduction of vagus nerve blockade to inhibit cough reflex and the insertion of an epidural catheter to reduce pain emphasize the need for team work between chest surgeon and anesthesiologist (9,10) during this technique.

Due to high cost limitations associated with RATS or the discomfort associated with mediastinal movement during non-intubated VATS, single-port VATS is another option for chest surgeons who are familiar with the conventional 4-, 3- or 2-ports VATS. In this review, we will assess the various uses of single-port VATS, especially for lobectomy.

Current evidence

Single-port surgery has been adopted in several surgical fields, especially in colorectal and gynecologic training programs (11). In 2004, Rocco *et al.* reported their pioneering work with pulmonary wedge resection through single-port VATS (12). Thereafter, more and more chest surgeons used single-port VATS for pulmonary resection, including wedge resection (12), segmentectomy (13-15), lobectomy (16-19), pneumonectomy (20,21), and pleural surgery (including pleural biopsy and pleural resection or decortication) (22), for both benign or malignant disease (*Table 2*). Lobectomy plus radical mediastinal lymph node dissection remain the "gold standard" for resectable lung cancer. However, pneumonectomy or segmentectomy/wedge resection may be executed based on lung cancer status, according to oncological principles or clinical considerations. Between 2012 and 2013, Gonzalez-Rivas *et al.* shared their innovative experiences with single-port VATS lobectomy, segmentectomy, and pneumonectomy for lung cancer (13,14,17-21). They also explained, in detail, the procedure and necessary equipment for meticulous application of single-port VATS. However, this was only one report from a single institution. The advantages and disadvantages of single-port VATS *vs.* conventional 2-, 3-,or 4-ports VATS, especially for lobectomy or segmentectomy of lung cancer, deserved further re-appraisal.

Our experiences at the Koo Foundation Sun Yat-Sen Cancer Center

We began performing 3-ports VATS lobectomy in 2005, and shifted to 2-ports VATS lobectomy in 2007. As described by Rocco *et al.* (12), surgeons always stand in front of the patient while performing VATS, in contrast to conventional open thoracotomy. Concerning the 2-ports VATS lobectomy that we perform, one port is used for instrument insertion (utility port, 3-5 cm in length, retracted by wound protector) and the other port is used for camera scope insertion (scope port, 1 cm in length, kept by trocar). A 30-degree camera scope was applied to our VATS. Actually, during 2-ports lobectomy, we

Table 2 Summary of the specific issues regarding single-port VATS

Issues of single-port VATS		Reported articles
Pioneer	How to do it	(12)
History/evolution review	Conventional to single-port VATS	(7,16,23)
Geometric configuration	Cranio-caudal perspective	(12,24)
Clinical application		(22)
Clinical diagnosis	Wedge resection/biopsy	(12,25)
Lung cancer/tumor	Wedge resection	(12)
	Segmetectomy	(14,15)
	Lobectomy/sleeve lobectomy	(15,17-19,26)
	Pneumonectomy	(20,21)
Pneumothorax		(12,25,27,28)
Empyema		(29)
Lymph node dissection	Overall number/areas	(19)
	Lobe specific	(15,30)

VATS, video-assisted thoracoscopic surgery.

Figure 1 Two ports VATS—Transection of right superior pulmonary vein.

Figure 2 Single-port VATS—Transection of left superior pulmonary vein.

insert multiple instruments into the utility port, which is the training basis for single-port VATS lobectomy. During upper lobe lobectomy, the straight endocutter is usually shifted to the camera port for the division of superior pulmonary vein, and all other instruments plus thoracoscope are inserted through the utility port (*Figure 1*). More specifically, if we can insert the endocutter through the same wound, i.e., the utility port, it becomes a single-port VATS. The application of the curved endocutter plays an important role in this specific procedure (*Figure 2*).

We began single-port VATS lobectomy in December 2010 (30). The first case we performed was actually a single-port segmentectomy for a centrally located carcinoid tumor over the left common basilar segment of the left lower lung. Because this patient had chronic obstructive pulmonary disease (COPD) with poor lung function, we shifted our tentative single-port VATS lobectomy to a segmentectomy, and this may represent the first single-port VATS segmentectomy reported in the literature (15,30). Despite the severely adherent anthracotic segmental lymph nodes, we completed the procedure smoothly and successfully. Since that time, we have been capable of single-port VATS anatomic lung resection. However, during that period, the concept of single-port VATS lobectomy or segmentectomy was neither popular nor well accepted. Most chest surgeons performed VATS lobectomy through 2-, 3-, or 4-ports procedures, or through a needle scope. Inevitably, however, a small utility wound is necessary for surgical specimen retrieval. Based on the need to reduce surgical trauma, we began our single-port VATS lobectomy/segmentectomy program, depending on careful case selection, the need for resident training, or sufficient surgical time without a tight schedule. Between November 2010 and May 2012, we retrospectively collected 19 cases of single-port VATS lobectomy/segmentectomy at our institute, and we shared our experiences with an emphasis on patient safety and surgical skill during radical lymph node dissection. This preliminary experience demonstrated the feasibility of single-port VATS lobectomy and radical lymph node dissection for benign pulmonary disease and early-stage lung cancer (15).

In Dr. C.C. Liu's practice, single-port lobectomy has become the standard procedure for lung cancer surgery, if there is no chest wall invasion or obvious hilar structural invasion. The size of the tumor is seldom a contraindication, since the larger the tumor, the larger the utility wound needed. Usually, the incision is approximately 3 cm in length if the tumor diameter is less than 3 cm.

Our collection of cases totals 63 single-port VATS lobectomies and 24 segmentectomies. The conversion rate from single-port VATS was low (3.45%, 3 in 87, converted to 2-ports VATS because of adhesion/anthracotic lymph nodes) and no surgical mortality occurred. Post-operative recovery was similar to traditional 2-ports VATS lobectomies.

The concept of minimally invasive surgery is not only preferred for reduction in the size of the external wound but also for reduction in inner trauma, including the extent of tumor resection and lymph node dissection. Therefore, sub-lobar resection (especially segmentectomy) for early stage lung cancer is crucial (31). Regarding the resection planes used in segmentectomy, we prefer the endocutter stapler to seal off air leakage rather than electrical coagulation (32). The segmental structures, including segmental artery, bronchus and veins, are dissected towards the hilum and then divided. The dissected lymph nodes and the resection margins deserve special mention. They are examined by experienced pathologists through frozen section to guarantee a complete resection. One of our patients harbored a ground glass opacity (GGO) lesion over the basal segment of the lower lobe, which proved to be lung cancer during intra-operative pathological diagnosis. The basal segmentectomy was converted to lobectomy due to a close resection margin. At present, we have already performed 24 segmentectomies using endocutter stapler to divide the intersegmental planes. Compared with conventional cauterization along the intersegmental plane and for ligation of branches from intersegmental veins, endocutter stapler is much easier to use. Although transient postoperative lung atelectasis with subsequent fever is not inevitable, this procedure does reduce the incidence of prolonged or delayed air leak (33). With regards to conventional segmentectomies, e.g., superior segmentectomy for the lower lobe, lingular segmentectomy, trisegmentectomy of left upper lobe (lingular sparing) and common basal segmentectomy of lower lobe, they can all be executed using a single-port technique. We have also begun lobe-specific lymph node dissection for early stage lung cancer. It not only reduces the degree of mediastinal trauma and saves more time, but also lessens the complications related to extensive lymph node dissection (15).

OR setting

We use the same setting as used in traditional VATS in our group.

Anesthesia

General anesthesia with double lumen endotracheal tube intubation is applied for right sided procedures. For left sided procedures, in contrast, single lumen endotracheal tube intubation with endobronchial blocker is applied, especially when left subcarinal lymph node dissection is required. A low tidal volume of approximately 350 mL with a PEEP at a setting of approximately 5 mmHg is preferred. Central venous catheter insertion is not our routine. Intercostal nerve block with bupivacaine is injected by the surgeon along the utility wound [including one more intercostal space (ICS) up and down] at the end of surgery.

Patient positioning

We use the same position as used in traditional VATS.

Instruments

Scanlan® VATS instruments, laparoscopic grasp, laparoscopic needle holder, knot pusher, and harmonic scalpel are the main instruments used during single-port VATS. We prefer to use longer instruments to avoid their possible collision due to crowding during manipulation. The surgical field can be viewed clearly through a 10 mm (preferred) or 5 mm 30 degree endoscope. The utility wound is retracted by wound protector (XS in size).

Incision

We prefer to create the utility wound at the sixth ICS that crosses the anterior axillary line for the following reasons:

(I) For upper lobe lobectomy, this incision is away from the superior pulmonary vein and provides adequate space for applying the endocutter;

(II) For lymph node dissection, this incision allows for easier subcarinal lymph node dissection, especially when we encounter a bulky bronchial tree caused by double lumen tube with an inflated balloon or a relatively rigid bronchus;

(III) Such an incision avoids hypersensitive areas or avoids causing paresthesia involving the breast, particularly the nipple, because the nipple is innervated by 4^{th} intercostal nerve;

(IV) The incision may be shifted more laterally along the sixth ICS in female patients, and along the fifth ICS only for left upper lobe $LB_{1+2,3}$ trisegmentectomy for early lung cancer and lobe specific lymph node dissection and the upper mediastinum lymph nodes, rather than the subcarinal lymph nodes.

Handling of instruments

To achieve a smooth surgical procedure, the long curved sucker (Scanlan®) is manipulated by the surgeon's left hand, and the hook, laparoscopic or Scanlan® dissectors are manipulated using his right hand. Such a combination of long straight and long curved instruments can minimize their collision and interference during surgery. Generally, the entire single-port VATS procedure is similar to traditional 2-ports VATS, except for the application of the endocutter through a narrower space that requires more skill. Adequate dissection and release of the surrounding soft tissues of the vascular structures are important steps that provide sufficient space for insertion of the endocutter blade during conventional 3- or 2-ports VATS. The Endo-GIA was originally designed for gastrointestinal anastomosis, rather than pulmonary vascular structures. We feel that it is a problem of instrument design rather than a problem with technique. The newly designed curved-tip endocutter is a useful option when performing division of a vessel, especially the superior pulmonary vein.

Camera scope handling

An experienced cameraman is crucial for a successful single-port VATS lobectomy, and a 30-degree camera scope (10 or 5 mm) is recommended. After an initial inspection of the surgical field from the eagle view through the camera, an impression of the anatomic landmarks should be fully realized. The surgeon can re-adjust the settings to facilitate the exposure and dissection. Usually the surgeon will choose the best position for performing the surgical procedure, and then bring in the camera to take advantage of the 30-degree lens to provide the best view. Every step should be under direct vision in order maintain safety, especially during dissection and application of the endocutter to the great vessels. Concerning the relative positions inside the utility port, grasp and camera scope are usually maintained in the upper part of the port and the surgeon's instruments are in the lower part during dissecting process. However, during application of the endocutter or other specific procedures, a dynamic change in position may be necessary in order to command a clearer view and perform a safer procedure (*Figure 2*).

VATS lymph node dissection

Lymph node dissections on the right side of the mediastinum and left upper mediastinum are similar to traditional 2-ports VATS procedure (*Figures 3,4*). Although usually not difficult, it requires more time and patience to perform. However, the left subcarinal area can be challenging. We developed a special method, called the Liu's maneuver, to facilitate exposure of the left subcarinal space. We placed a non-elastic bandage above the inferior pulmonary vein to hook on the left lower lobe bronchus; thus, the lung parenchyma and hilum can be pulled away from the aorta and esophagus. With this maneuver, we obtain a clearer view of the carina, bilateral main bronchi, bilateral inferior pulmonary veins, pericardium, and esophagus along with right and left vagus nerves, right lung and right mediastinal pleura. In our early series using this maneuver, the average number of dissected lymph nodes for lung cancer was 23, similar to traditional VATS (15).

Learning curve, education, and training

Regarding learning curves, we went through a process similar to that of Diego Gonzalez-Rivas (6,16). As shown in his review articles, he also shifted from 3-ports to 2-ports and then to single-port VATS lobectomy. As a result, this process could be a training model for those who had VATS experience and who wanted to shift to single-port

Figure 3 Relative positions between the surgeon and cameraman during single-portright superior mediastinal lymph node dissection.

Figure 4 Single-port VATS for right subcarinal lymph node dissection.

VATS lobectomy, and for the new learner starting VATS lobectomy.

However, for the new learner without VATS experience, we are not certain about the need for a shift from 3-ports to 2-ports and then to single-port VATS. This question is similar to questions regarding the training required for traditional VATS. An open procedure is not absolutely necessary for the trainee to learn VATS. Similar to Diego Gonzalez-Rivas's group, we found that trainees without previous VATS experience are more open to new ideas and settings using single-port VATS. Actually, they accept these procedures and perform them better and more easily than experienced VATS surgeons who have already performed multiple ports VATS.

There is insufficient supporting data concerning the learning curve associated with VATS. Some thought that experienced VATS surgeons harbored a basic concept for VATS, and thus they could reach the plateau of the learning curve much quicker. However, if we take the Cases/Time curve into consideration when predicting the learning curve, perhaps the new learner will reach the learning plateau quicker than I did as it took me two years to pass the learning curve by accumulating more than 30 cases, which was really slow going in the beginning! This was not due to the difficulty of the technique, but rather the difficulty in making the determination whether or not to do it. To quote a well-known proverb:

The Difficulty lies, not in the new ideas, but in escaping from the old ones

——By John Maynard Keynes

The aggressive mind of the chest surgeon plays an important role in promoting the rapid development of commercial equipment necessary for single-port VATS, including the single-port wound protector, articulating instruments, harmonic scalpel, various sized straight or curved endocutter staplers, and higher resolution camera scopes with less scopic diameter. The mutual interaction between the desire of the surgeon and new manufacturing designs is the stimulus for advances in VATS.

More and more single-port VATS symposiums and conferences are held worldwide. Specific training programs on single-port VATS are also available. Furthermore, there are many single-port VATS videos, including trouble shooting for incomplete fissures, anthracotic lymph nodes, sleeve resection/bronchoplasty, bleeding, etc. These videos are available over the internet through YouTube.

Careful patient selection by the chest surgeon, for either benign or malignant disease, plays an important role when starting a single-port VATS lobectomy program. A single port VATS lower lobe lobectomy can be accomplished as easily as traditional VATS if there are no anthracotic nodes in the hilum nor incomplete fissures. The chest surgeon can then gradually expand his expertise to include all patients with early-stage lung cancer, if there are no specific contraindications.

In conclusion, we have reviewed the feasibility and safety of single-port VATS lobectomy for early-stage lung cancer. Single-port VATS is just another variant of VATS surgery in the modern era. More time and effort is need to procure sufficient evidence to show that single-port VATS is more beneficial to patients compared with standard techniques, in terms of less trauma and less postoperative pain, without compromising ontological outcome.

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Double sleeve uniportal video-assisted thoracoscopic lobectomy for non-small cell lung cancer

Diego Gonzalez-Rivas, Maria Delgado, Eva Fieira, Ricardo Fernandez

Department of Thoracic Surgery, Coruña University Hospital, Coruña, Spain

Correspondence to: Diego Gonzalez Rivas. Department of Thoracic Surgery, Coruña University Hospital, Xubias 84, 15006. Coruña, Spain. Email: diego.gonzalez.rivas@sergas.es.

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Double sleeve (vascular and bronchial) lobectomy is a reasonable alternative to pneumonectomy in patients with centrally located tumors involving the pulmonary artery and bronchus. However, it is a challenging and complex procedure even when performed through thoracotomy.

Despite the advances in thoracoscopic surgery, double sleeve lobectomy by conventional thoracotomy is still the preferred approach because of the technical difficulties of thoracoscopic surgery and the potentially increased operative risks even when performed by experienced video-assisted thoracoscopic surgery (VATS) surgeons. There are very few reported cases of double sleeve lobectomy by VATS using 3-4 incisions (1,2). We present the first report of double VATS sleeve resection by a single incision approach.

Clinical tummary

A 65 year-old male, smoker, was diagnosed with a 7.2 cm left upper lobe adenocarcinoma with vascular and bronchial involvement. The patient received neoadjuvant Platinum based chemotherapy (six sessions) with poor response. A chest computed tomography (CT) scan performed before surgery (*Figures 1* and *2*) showed progression of the tumor (9 cm mass with left upper lobe atelectasis) despite neoadjuvant chemotherapy. The patient was offered left upper lobe resection with uniportal VATS.

Surgical technique

Under general anesthesia, we performed flexible video bronchoscopy. The right-sided airways had normal anatomy with no endobronchial lesions and no significant amount of secretions or pus. In the left-sided airways, there was an obvious tumor mass that had completely occluded the entire orifice of the left upper lobe of the lung and was entering the distal left main bronchus.

The patient was positioned into right lateral decubitus position with the left side up, and a VATS approach using a 5 cm single-incision was made in the 5th intercostal space with no rib spreading (no soft tissue retractor and no direct vision).

The upper lobe was adherent to the chest wall, the mediastinum, and the aorta without signs of invasion, and was detached and freed of its adhesions using cautery. Digital palpation confirmed the presence of a 9 cm mass occupying most of the upper lobe and involving all arterial branches of the upper lobe. There was no other evidence of pleural disease in the chest.

The first step was to expose and control the main pulmonary artery (PA), which was dissected and encircled with a double vessel loop, while the superior pulmonary vein was also dissected free and transected using endostaplers. We then opened the fissure between the upper and lower lobe. The tumor did not involve the fissure or the lower lobe and the artery was dissected and mobilized.

The left main bronchus and the lower lobe bronchus were dissected and cleared, with dissection of the subcarinal lymph node and subsequently the interlobar and peribronchial lymph nodes up towards the specimen. The main bronchus and left lower lobe bronchus were transected with a long handle No. 10 blade (sleeve resection). The inferior pulmonary ligament was released to allow greater mobilization of the lower lobe. Before clamping of the PA, 5,000 units of heparin were given intravenously to prevent clotting. The main PA was occluded using a thoracoscopic D'Amico clamp (Scanlan International, MN, USA) and

Figure 1 Computed tomography scan after chemotherapy showing arterial involvement.

Figure 2 Computed tomography scan after chemotherapy showing bronchial involvement.

the interlobar artery was occluded with a bulldog clamp (Aesculap, Inc., Center Valley, PA, USA). The main PA and the basal artery were transected with scissors (vascular sleeve) to remove the left upper lobe en-block. The specimen was temporarily placed in the lower chest cavity above the diaphragm. We started the double sleeve reconstruction by the bronchial anastomosis using a running, non-absorbable suture (PDS 3/0) for cartilaginous and membranous portions. The posterior wall of the bronchus was sutured first, the anterior wall was sewn up last, and then both sutures were tied together. The lower lobe was inflated and no air leakage was detected underwater. The arterial sleeve anastomosis was performed thereafter by using a monofilament non-absorbable continuous suture (prolene 4/0) in two different rows, with a similar method as for the bronchus (the medial arterial wall was sutured first, followed by the lateral wall). Both suture lines were tied together at the anterior part of the anastomosis using a thoracoscopic knot pusher.

The edges of the anastomosis were everted to enhance arterial intimal interface and maximize the opening of the anastomosis. The bulldog clamp was opened for back bleed to remove the air, and the inflow and outflow were flushed and checked prior to the anastomosis. The clamp from the main PA was slowly opened and no bleeding from the vascular anastomosis was found.

The bronchial anastomosis was then wrapped with a piece of oxidized regenerated cellulose (Surgicel®), to be isolated from the vascular suture. The specimen was inserted into a protective plastic bag and removed by enlarging the incision. A single chest tube was placed at the end of the operation. Frozen section confirmed that all surgical margins were clear, including our bronchial and left main stem bronchus margin. The total surgical time was 260 min and estimated blood loss was 170 cc.

Patient recovery was satisfactory, and the chest tube was removed on the 5th postoperative day. Pathological examination revealed a 7.5 cm adenocarcinoma with bronchial and vascular involvement (free tumoral margins) and no lymph node malignancy (pT3N0M0).

Discussion

The thoracoscopic approach for major lung resection for advanced lung cancer is now gaining wide acceptance worldwide (3). However, lobectomies requiring double sleeve are challenging procedures, even when performed by thoracotomy. As such, it still remains a contraindication for VATS approach, even for experienced thoracoscopic surgeons, primarily due to concerns of vascular injury during thoracoscopy as well as the technical complexity of the procedure for an optimal bronchovascular reconstruction. There are few articles published in the literature describing a double bronchial and vascular sleeve reconstruction by VATS, and all of these cases are reported by using 3-4 incisions (2,3). VATS sleeve lobectomies are still being refined.

Through recent technical advances in VATS lobectomy (instruments and HD cameras) and the skills and experience gained from treating large numbers of patients, these complex procedures can be performed by using only a single incision approach. As a result, advanced procedures such as uniportal sleeve lobectomy (4,5) or uniportal vascular reconstruction (6) have already been published with good postoperative outcomes (7). The advantage of uniportal VATS surgery is that it allows the target tissue to be directly visualised at a similar angle of view as for open surgery (8). Conventional multi-port VATS triangulation creates a new optical plane for the genesis of a dihedral or torsion angle not favorable with 2D monitors. Another advantage of the uniportal VATS technique is that instruments are inserted parallel to the video-thoracoscope, therefore mimicking the maneuvers performed inside the chest during open surgery. This geometric uniportal VATS concept facilitates the double bronchial and vascular anastomosis in complex resections such as the one described in this article.

The use of thoracoscopic instruments with proximal and distal articulation is very useful for sleeve procedures through a single incision approach, especially for clamping the pulmonary artery and for suturing the artery and bronchus. The use of a bulldog clamp placed inside the chest cavity for clamping the basal artery allows surgeons to have more space for instrumentation through a single incision approach. The clamp for the main artery is placed in the anterior portion of the incision and the camera in the posterior portion, making the instrumentation similar as for an open approach for bronchial and vascular anastomosis.

With the single incision thoracoscopic view, the bronchus is located behind the artery, making it easier to perform bronchial anastomosis first, followed by arterial, in order to avoid excessive manipulation and traction to the arterial suture.

Several reports confirm the safety of bronchovascular reconstructions after chemotherapy (9). Video-assisted thoracoscopic sleeve procedures enable faster patient recovery and preserve pulmonary function (10,11). This is especially important in patients receiving induction treatment, as the implementation of a pneumonectomy would increase the rate of postoperative complications (12). In the current literature, there is also evidence supporting the use of neoadjuvant treatment and minimally invasive techniques.

In conclusion, single incision thoracoscopic bronchovascular double sleeve lobectomy is technically difficult, but feasible, when performed by skilled surgeons experienced with the uniportal approach.

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Thoracoscopic double sleeve lobectomy in 13 patients: a series report from multi-centers

Jun Huang[1,2,3]*, Jingpei Li[1,2,3]*, Yuan Qiu[1,2,3], Xin Xu[1,2,3], Dmitrii Sekhniaidze[4], Hanzhang Chen[1,2,3], Diego Gonzalez-Rivas[5,6], Jianxing He[1,2,3]

[1]Department of Thoracic Surgery, Guangzhou Medical University First Affiliated Hospital, Guangzhou 510120, China; [2]Guangzhou Institute of Respiratory Disease, Guangzhou 510120, China; [3]Key cite of National Clinical Research Center for Respiratory Diseases, Guangzhou 510120, China; [4]Thoracic Surgery Department, Regional Oncological Center, Tyumen, Russian Federation; [5]Department of Thoracic Surgery, Coruña University Hospital, Coruña, Spain; [6]Minimally Invasive Thoracic Surgery Unit (UCTMI), Coruña, Spain

*These authors contributed equally to this work.

Correspondence to: Professor Jianxing He, MD, PhD, FACS. Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, 151 Yanjiang Road, Guangzhou 510120, China. Email: drjianxing.he@gmail.com.

Background: This study aims to explore the feasibility and safety of video-assisted thoracic surgery (VATS) double sleeve lobectomy in patients with non-small cell lung cancer (NSCLC).

Methods: Between June 2012 and August 2014, 13 NSCLC patients underwent thoracoscopic double sleeve lobectomy and mediastinal lymphadenectomy at three institutions. A retrospective analysis of clinical characteristics, operative data, postoperative events and follow-up was performed.

Results: Thirteen NSCLC patients (median age, 60 years; range, 43-67 years) underwent thoracoscopic double sleeve lobectomy. There were no conversions to thoracotomy. Left upper lobectomy was most frequently performed (eleven patients). Median operative time was 263 minutes (range, 218-330 minutes), and median blood loss was 224 mL (range, 60-400 mL). The learning curve revealed reductions in both operative times and blood loss of ten cases from one center. Median data were duration of blocking pulmonary artery (PA) 72 minutes (range, 44-143 minutes), resected lymph nodes 24 (range, 10-46), stations of retrieved lymph nodes 6 (range, 5-9), thoracic drainage 1,042 mL (range, 500-1,700 mL), duration of thoracic drainage 5 days (range, 3-8 days), postoperative hospital stay 10 days (range, 7-20 days), and ICU stay 1 day (range, 1-2 days). One patient (1/13, 7.70%) suffered from pneumonia after surgery. There were no deaths at 30 days. Median duration of follow-up was 6 months (range, 1-26 months). And no local recurrences or distant metastasis were reported.

Conclusions: Thoracoscopic double sleeve lobectomy is a technically challenging, but feasible procedure for NSCLC patients and it should be restricted to skilled VATS surgeons.

Keywords: Non-small cell lung cancer (NSCLC); video-assisted thoracic surgery (VATS); sleeve lobectomy; learning curve

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Introduction

Cao and his colleagues (1) reported that video-assisted thoracic surgery (VATS) lobectomy for non-small cell lung cancer (NSCLC) can yield similar long-term survival outcomes with conventional open lobectomy. With the widely application of VATS technique, the indication of this procedure has been greatly broadened, and the technical barriers have been constantly broken (2,3). As an less invasive alternative procedure to total pneumonectomy in patients with locally advanced tumors involving the pulmonary artery (PA) and bronchus (4), sleeve lobectomy by conventional thoracotomy, especially double sleeve lobectomy (vascular and bronchial) is still the preferred approach due to high difficulty in operation and potentially undesirable complications, even when performed by skilled

VATS surgeons.

Since the first reported VATS bronchial sleeve lobectomy was published (5), more and more technical challenges have become reality, which would be VATS angioplasty (6-8), uniportal VATS bronchial sleeve lobectomy (9,10), and even thoracoscopic double sleeve lobectomy (11-13). However, all of these reports were single center experiences, and most series were less than five patients. Hence, the thoracic society urged for a multi-center data of thoracoscopic double sleeve lobectomy to addresses the feasibility and safety of this operation. In this study, we present the first multi-center experiences of thoracoscopic double sleeve lobectomy.

Patients and methods

The medical ethics board of all participating hospitals approved the study. Between June 2012 and August 2014, 13 patients underwent a thoracoscopic double sleeve lobectomy including mediastinal lymphadenectomy for primary NSCLC at the First Affiliated Hospital of Guangzhou Medical University (Guangzhou, China), Coruña University hospital (Coruña, Spain) and Tyumen Regional Cancer Center (Tyumen, Russia). Clinical records of the patients were retrospectively analyzed.

All patients were diagnosed with NSCLC by bronchoscopy. Preoperative staging was determined mainly by enhanced thoracic computerized tomography, brain magnetic resonance or computed tomography (CT), and bone scintigraphy, except that one patient received positron emission tomography/CT (PET-CT). Physical examination, standard laboratory tests, electrocardiograms, and lung function tests were performed in all patients.

There were two patients with clinic N2 disease, and both received induction chemotherapy. One patient with squamous cell carcinoma had four cycles of paclitaxel + cisplatin before surgery (case 6), the other patient with adenocarcinoma had six cycles of pemetrexed + cisplatin (case 11). Two patients rejected to receive adjuvant chemotherapy.

Surgical technique

All patients received a combination of epidural and general anesthesia before the operation. The patients were placed in a lateral decubitus position. All 13 procedures were performed via 3-4 ports, or uniportal. The detailed port design for different methods was described in *Table 1*.

Before dissection, the mediastinal pleura were inspected to assess the mobility of the tumor and its invasion into surrounding structures. Once radical surgery (*Figure 1*) was guaranteed, the superior or inferior pulmonary vein would be dissected and then transected with endostapler (Ethicon Endo-Surgery, Johnson & Johnson, Cincinnati, OH, USA). The main bronchus and distal bronchus were transected with a long handle blade and scissor (*Figure 1A*).

After the main PA was dissected, there were four methods with different port design to clamp the PA: (method A) two patients (case 1-2) underwent three ports thoracoscopic double sleeve lobectomy (*Table 1*). One pair of vascular blocking forceps was placed through the operative port (3.5 cm) on the proximal PA, and the other pair of forceps was placed through the left port (10 mm) on the distal PA (*Figure 2*); (method B) one patients (case 3) underwent three ports thoracoscopic double sleeve lobectomy (*Table 1*). One pair of vascular blocking forceps was placed through the operative port (3.5 cm) on the proximal PA. Different with method A, the other pair of forceps was placed through the camera port (10 mm) on the distal PA (*Figure 3*); (method C) seven patients (case 4-10) underwent four ports thoracoscopic double sleeve lobectomy (*Table 1*). One pair of vascular blocking forceps was placed through a 5-mm port located in anterior chest wall at the level of the proximal PA, and the other pair of forceps was placed through the posterior axillary line port (10 mm) on the distal PA (*Figure 4*); (method D) three patients (case 11-13) underwent uniportal thoracoscopic double sleeve lobectomy (*Table 1*). A bulldog clamp was used for the distal PA while the vascular blocking forceps were used to clamp the proximal PA (*Figure 5*). After the PA clamp was completed, the invasive part of main PA was resected (*Figure 1B*). The surgical technique for PA circumferential sleeve resection is similar to previous reports (11,14). The wedge anastomosis for uniportal approach would only be applied if the tumor invasion was less than 1/3 of the circumference and 2 cm width of the basilar part. After confirming the resected margin of PA, the PA was reconstructed with a primary closure using 4-0 Prolene (Ethicon, Somerville, NJ, USA) (*Figure 1C*). A standard needle holder and a pair of forceps were inserted to complete running suture through the 3.5-5 cm operative port (*Table 1*). After the bronchial margins were confirmed as negative by intraoperative frozen section, the bronchial sleeve reconstruction was performed by using a 3-0 Prolene (Ethicon, Somerville, NJ, USA) for cartilaginous and membranous portions (*Figure 1D,E*). The residual lobe was inflated and no air leakage was

Table 1 The ports design of thoracoscopic double sleeve lobectomy

Method	Case	Ports	Camera port	Operative port	VBF port 1	VBF port 2
A	Case 1-2	3	Midaxillary line/7th ICS/10 mm	Preaxilary line/4th ICS/3.5 cm	Postaxillary line/7th ICS/10 mm	–
B	Case 3	3	Postaxillary line/7th ICS/10 mm	Preaxilary line/4th ICS/3.5 cm	Midaxillary line/7th ICS/10 mm	–
C	Case 4-10	4	Midaxillary line/7th ICS/10 mm	Preaxilary line/3th ICS/3.5 cm	Postaxillary line/7th ICS/10 mm	Anterior chest/ PA level/5 mm
D	Case 11-13	1	Preaxilary line/4th or 5th ICS/4-5cm			

VBF, vascular blocking forcep; ICS, intercostal space; PA, pulmonary artery.

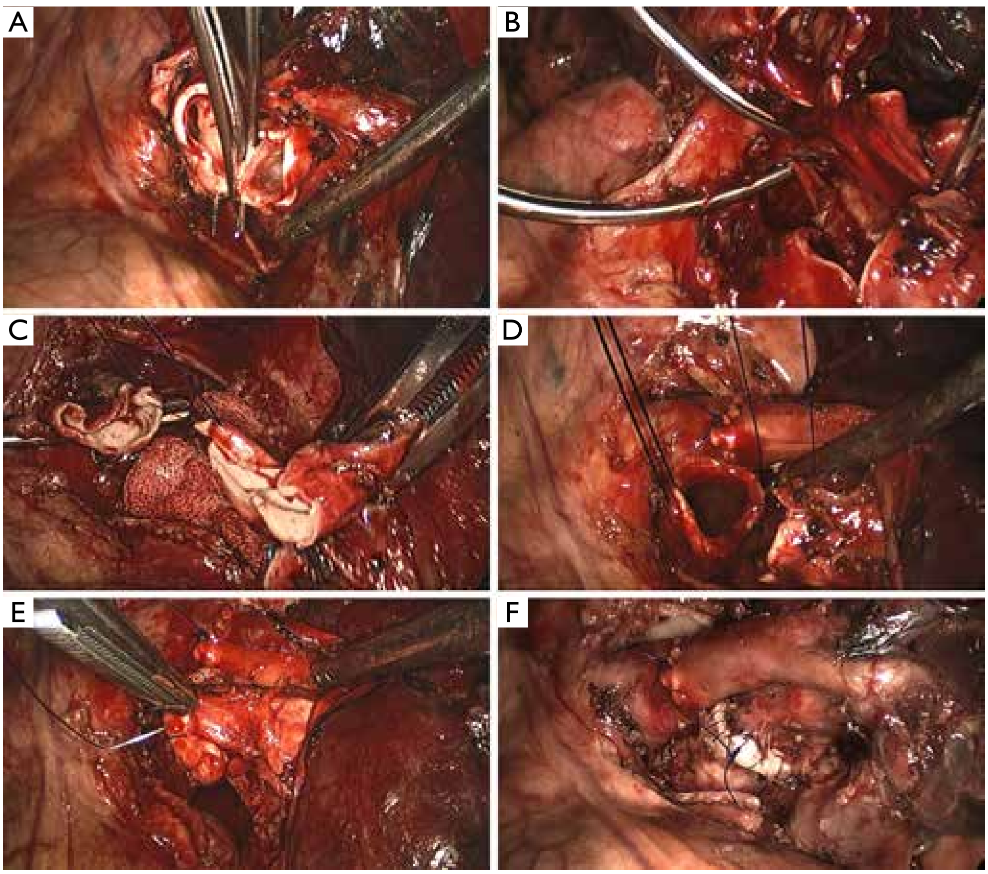

Figure 1 Surgical technique of thoracoscopic double sleeve lobectomy. (A) Transecting the main bronchus; (B) sleeve resecting the blocked PA; (C) sleeve reconstructing the blocked PA; (D) completed vascular reconstruction and starting sleeve bronchial reconstruction; (E) sleeve reconstructing the bronchus; (F) over view of double sleeve reconstruction. PA, pulmonary artery.

detected underwater. Then, the distal clamp was removed before tying the arterial sutures to remove the intravascular air. The proximal clamp was finally removed to ensure hemostasis of the sewn PA (*Figure 1F*).

During uniportal thoracoscopic double sleeve lobectomy, bronchial sleeve reconstruction was completed before angioplasty to avoid traction on the arterial suture. In three cases (case 1, case 3 and case 6), pericardium, pleura and other tissue were used to separate the PA and bronchus to prevent bronchial artery fistula.

Thoracic surgery was completed by placement of one or two intercostal drainage tubes and closure of the thoracic

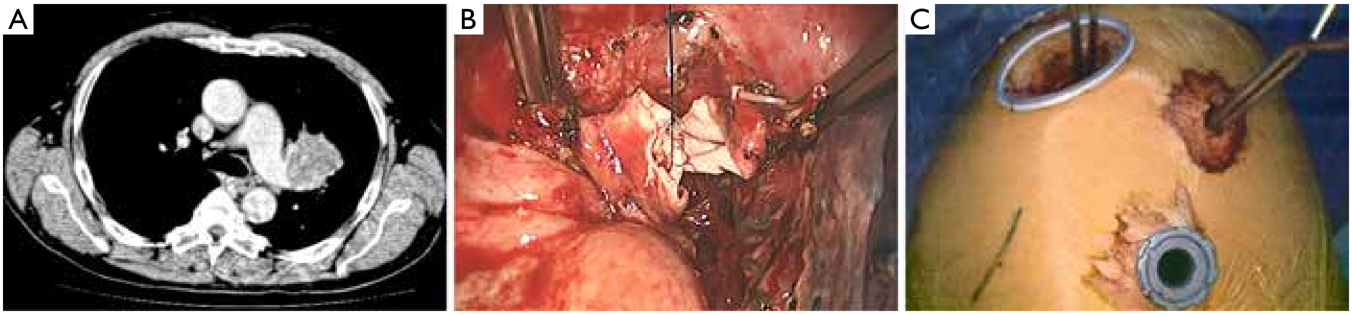

Figure 2 Method A: ports design of thoracoscopic double sleeve lobectomy.

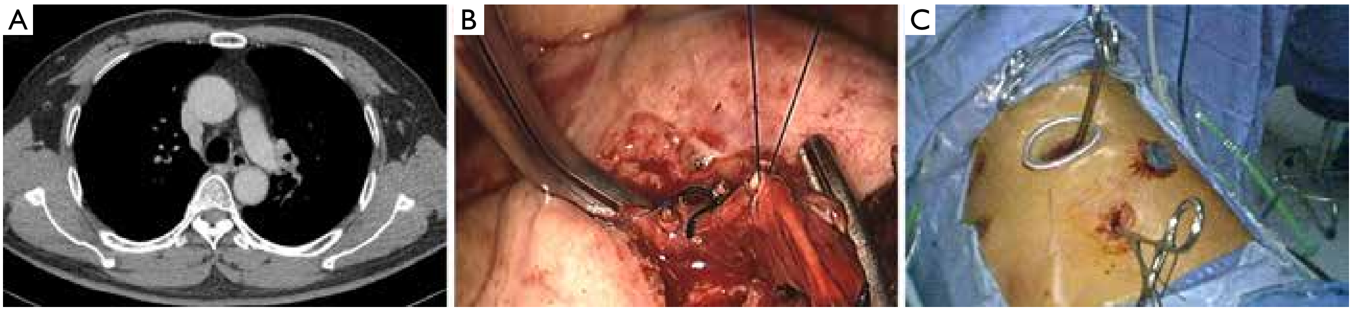

Figure 3 Method B: ports design of thoracoscopic double sleeve lobectomy.

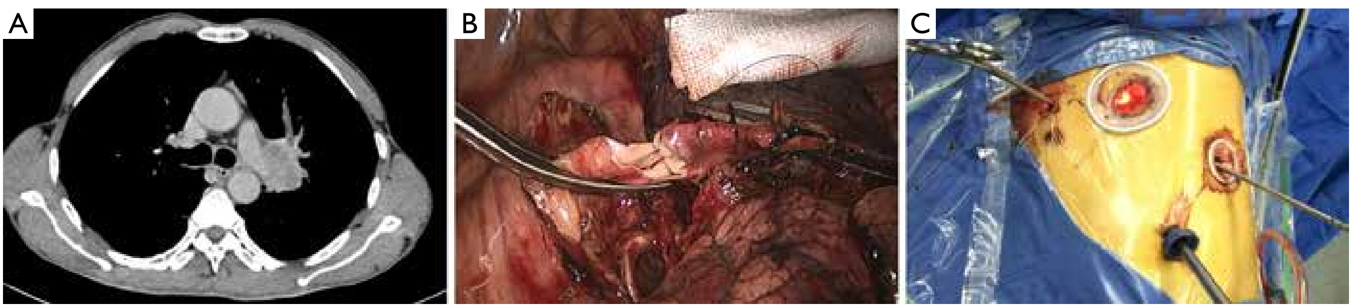

Figure 4 Method C: ports design of thoracoscopic double sleeve lobectomy.

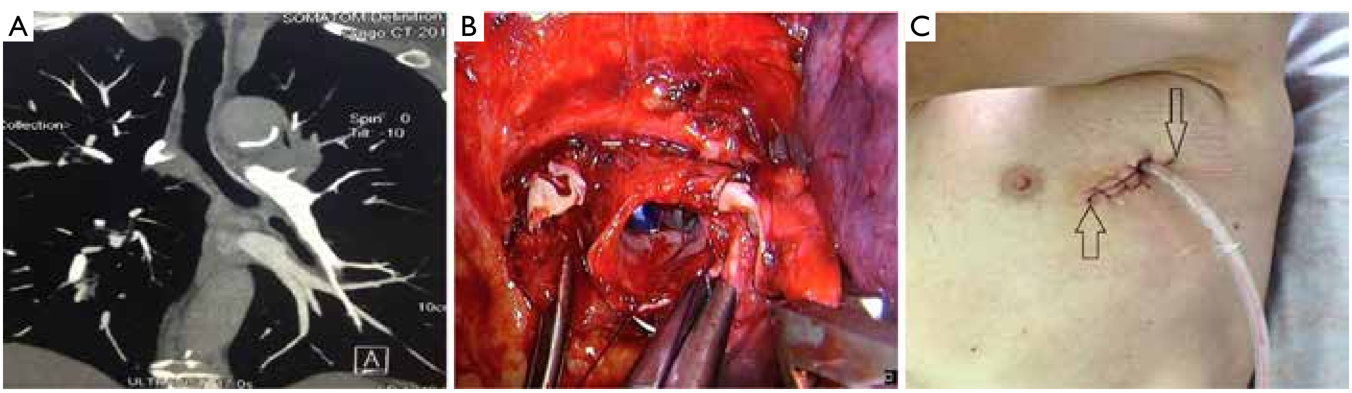

Figure 5 Method D: ports design of thoracoscopic double sleeve lobectomy.

incisions. Postoperative bronchoscopy is then performed to clear the airways of blood and secretions before extubation.

Statistical analysis

Clinical information was recorded in Microsoft EXCEL (Microsoft Corp, Redmond, WA, USA) for further processing. Enumeration data were presented with frequencies and percentages. Measurement data were presented with median and range.

Results

The clinical characteristics of all patients were summarized in *Table 2*. All thirteen patients were males. Median age was 60 years (range, 43-67years). Twelve patients (12/13, 92.3%) had a smoking history. Ten patients (10/13, 76.9%) were diagnosed as squamous carcinoma, while two patients (2/13, 15.4%) were adenocarcinoma, and one patient (1/13, 7.7%) was adenosquamous carcinoma. The location of the tumors was as follow: eleven left upper lobe (LUL) (11/13, 84.6%), one right upper lobe (RUL) (1/13, 7.7%), and one left lower lobe (LLL) (1/13, 7.7%). There were ten invasion of main PA (10/13, 76.9%), and two invasion of branch PA (2/13, 15.4%).

The operative data of all patients were shown in *Table 3*. There were no conversions to thoracotomy. The median operative time was 264 minutes (range, 218-330 minutes). The median blood loss was 224 mL (range, 60-400 mL). There were reductions in both operative times and blood loss of ten cases from one center, which were from 298.5 to 253 minutes, and 300 to 150 mL separately (*Figure 6*). The median duration of blocking PA was 72 minutes (range, 44-143 minutes); the median duration for PA anastomosis time was 45 minutes (range, 26-75 minutes); the median duration for bronchial anastomosis was 31 minutes (range, 15-50 minutes); the median length of resected PA was 2 cm (range, 1-3 cm); the median length of resected bronchus was 2 cm (range, 1.5-3 cm). The median numbers of resected lymph nodes were 24 (range, 10-46), and the median stations of retrieved lymph nodes were 6 (range, 5-9).

Postoperative events were summarized in *Table 4*. One patient suffered from pneumonia after surgery, and no patients died at 30 days. The median postoperative hospital stay was 10 days (range, 7-20 days). The median ICU stay was 1 day (range, 1-2 days). The median duration of thoracic drainage was 5 days (range, 3-8 days); the median thoracic drainage was 1,042 mL (range, 500-1,700 mL). The median duration of follow-up was 6 months (range, <1-26 months). Eight patients had completed four cycles platinum-based adjuvant chemotherapy, the chemotherapy treatment of the remaining three patients is still ongoing. Two patients received at least four cycles of neoadjuvant chemotherapy, and so, did not receive adjuvant chemotherapy. To date, no local recurrences or distant metastasis were reported.

Discussion

In this retrospective multi-center series report, thoracoscopic double sleeve lobectomy was successfully performed to thirteen NSCLC patients. There were no conversions to thoracotomy. The median operative time was 263 minutes. The median blood loss was 224 mL. The reductions in operative times and blood loss of ten cases from one center were promising. The median numbers of resected lymph nodes were 24. The median postoperative hospital stay was 10 days. The median duration of follow-up was 6 months. To date, no local recurrences or distant metastasis were reported.

Although VATS lobectomy has been widely applied (15), double sleeve lobectomy is still a contraindication to VATS in most medical centers (16). To offer potential benefits of VATS to more NSCLC patients, progressively technical innovations have been made, and several institutes have reported their initial experiences of thoracoscopic double sleeve lobectomy (11-13). However, all of these recent reports were same series, or even single patients from one medical center, and they mainly focused on technical feasibility instead of general safety.

Technically, though there were separate methods of clamping the PA for uniportal or multiport procedures, each method was equally effective in blocking PA. In the uniportal procedure, a bulldog clamp is placed inside the chest cavity to clamp the distal artery, which allowed surgeons more operative space. Additionally, once the proximal PA was cut, the exposure and reconstruction of the bronchus could be more convenient through the 4-5 cm operative port, based on the relative anatomical position of the PA and bronchus. For bronchial anastomosis eased subsequent PA reconstruction and reduced vascular tension at the same time. In multiport procedure, an additional 5 mm incision greatly eased the surgical performance, which has already been reported in major thoracic pulmonary resection (17) and minimally invasive cardiac surgery (18,19). Although the choice involving the numbers of port during the procedure is simply based on the surgeons' preference

Table 2 Patient characteristics

Character	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13
Age (years)	60	67	58	57	54	63	62	67	60	43	65	66	52
Gender	Male	Male	Male	Male	Male	Male	Male	Male	Male	Male	Male	Male	Male
Smoking history	40 y, 40/d	30 y, 20/d	35 y, 20/d	35 y, 60/d	25 y, 60/d	50 y, 60/d	40 y, 20/d	30 y, 20/d	40 y, 40/d	No	31 y, 40/d	40 y, 40/d	32 y, 40/d
Histology	Sqa	Ad-Sqa	Sqa	Sqa	Sqa	Sqa	Sqa	Sqa	Sqa	Ade	Ade	Sqa	Sqa
Tumor size	4.5×3.4	5.7×5.3	3.0×2.2	5.8×4.8	4.3×3.2	3.8×2.2	4.8×4.3	3.6×3.5	1.6×1.1	7.6×7.4	7.5×7.5	5	5
Pathological stage	T3N1M0	T3N1M0	T3N0M0	T3N0M0	T3N1M0	T3N1M0	T3N2M0	T3N0M0	T3N2M0	T3N1M0	T3N0M0	T3N1M0	T2aN0M0
Location	LUL	LUL	LUL	LUL	LUL	LUL	LLL	LUL	RUL	LUL	LUL	LUL	LUL
PA invasion	Main	Main	Branch	Main	Main	Main	Main	Main	Branch	Main	Main	Main	–
Pulmonary function													
FEV_1	2.71	2.58	2.67	2.98	2.73	1.79	2.48	2.32	1.86	3.35	NA	NA	NA
FEV_1%	93.33	87.61	88.73	89.17	74.00	63.15	87.52	92.97	69.58	92.53	109	NA	NA
MVV	120.6	88.86	78.43	109.4	100.7	80.9	102.58	96.3	99.51	125.9	NA	NA	NA

Sqa, squamous carcinoma; Ad-Sqa, adenosquamous carcinoma; Ade, adenocarcinoma; LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; PA, pulmonary artery; NA, no available; FEV_1, forced expiratory volume in first second; MVV, maximal ventilatory volume; y, years.

Table 3 The operative data

Character	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13
Blood loss (mL)	200	400	400	60	70	400	200	300	100	200	80	300	200
Operative time (min)	274	323	253	218	222	274	230	256	230	276	260	330	280
Duration of blocking PA (min)	68	108	76	44	45	55	50	60	60	143	110	70	50
Duration of angioplasty (min)	44	60	30	26	35	40	45	41	35	75	60	60	40
Duration of bronchialplasty (min)	35	32	42	30	25	15	30	23	30	24	40	50	30
Length of resected PA (cm)	2	3	1	1	3	2	1	1	1	2	3	3	3
Length of resected bronchus (cm)	2	2	2	1.5	2	1.5	1.5	2	1.5	1.5	1.5	3	3
Numbers of resected LN	37	26	20	46	27	21	19	20	34	24	10	12	13
Stations of retrieved LN	7	7	6	7	9	5	6	7	6	6	5	5	5

PA, pulmonary artery; LN, lymph nodes.

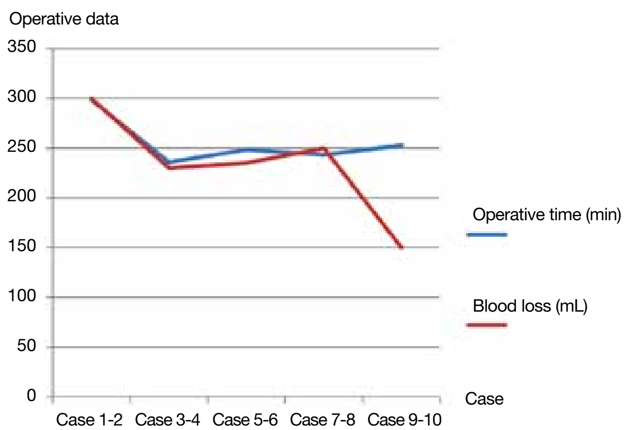

Figure 6 Promising reductions in operative times and blood loss of ten cases from one center.

and experience, it is not a key issue when it comes to the success of thoracoscopic double sleeve lobectomy.

As for surgical trauma, the median operative time and blood loss of this study were 264 minutes and 224 mL, which were consistent with previous reports of thoracoscopic double sleeve lobectomy (11,13,14). And the *Figure 6* also revealed promising reductions in both operative times and blood loss of ten cases from one center, which were from 298.5 to 253 minutes, and 300 to 150 mL separately. Hence, it indicated that thoracoscopic double sleeve lobectomy could be easily done by skilled VATS surgeons with progressive accumulation of surgical experience.

In this series, the median duration of blocking PA was 60 minutes (range, 44-110 minutes) and no complications associated with clamp of the PA occurred. The longest duration of blocking PA among these patients was 143 min, postoperative recovery was uneventful, and no reperfusion injury or thrombosis occurred. Jiang and his colleagues (20) reported a pulmonary vessel blocking model in rabbits that underwent a block of the PA and veins compared to block of the PA alone and found that it might be safe to block the pulmonary vessels up to one hour during pulmonary surgery. In our experience, with satisfactory blocking PA, the arterial reconstruction would be safer and easier during the operation. Since there were no surgical reports concerning this issue, we appeal for further research to determine the proper time for this procedure.

With regard to postoperative complications, only one

Table 4 Postoperative events

Character	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13
Morbidity	–	–	–	–	–	–	–	–	–	–	Pneumonia	–	–
Postoperative hospital stay (d)	7	10	12	8	7	15	8	9	7	13	20	12	9
ICU stay (d)	1	1	1	1	1	1	1	1	1	1	1	2	1
Duration of thoracic drainage (d)	3	6	6	5	3	8	5	4	5	6	5	4	2
Thoracic drainage (mL)	700	1500	1,500	1,330	835	1,700	950	1,100	850	680	700	NA	NA
Adjuvant chemotherapy	TXT/ TO	TXT/ LOP	PAX/ LOP	PAX/ DDP	PAX/ LOP	–	PAX/ DDP	PAX/ DDP	–	–	–	VP-16/ DDP	–
Chemotherapy cycles	4	4	4	4	4	–	4	4	On	On	–	4	On
Follow-up duration (month)	26	15	9	7	4	3	3	3	2	<1	3	6	1
Status	Live	Live	Live	Live	Live	Live	Live	Live	Live	Live	Live	Live	Live

TXT, docetaxe; TO, oxaliplatin; LOP, lobaplatin; PAX, paclitaxel; DDP, cisplatin; VP-16, etoposide; NA, no available.

significant complication was observed and was attributed to effects from the second line of treatment: pneumonia was diagnosed in a patient who received six cycles of neoadjuvant chemotherapy. This suggests that neoadjuvant chemotherapy patients can successfully undergo the operation, but postoperative management needs more attention, especially in regards to anti infection, and nutrition. There were no significant complications observed in the remaining 12 patients. However, there are also several limitations to our study. First, there were only 13 patients in this series, and most tumors of these patients were located in LUL. This might contribute to the surgeons' preference and experience. Second, the median duration of follow-up was only 6 months, and there were still three patients on chemotherapy. The potential long-term benefit of this operation is still unclear. Hence, further experience of both short-term and long-term benefit of thoracoscopic double sleeve lobectomy is needed to be accumulated.

Conclusions

Thoracoscopic double sleeve lobectomy is safe and feasible when performed by a skilled VATS surgeon, although further investigations are needed to confirm this conclusion.

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Video-assisted thoracoscopic lobectomy for non-small cell lung cancer in patients with severe chronic obstructive pulmonary disease

Wei Wang[1,2]*, Zhiqiang Xu[1,2]*, Xinguo Xiong[1,2]*, Weiqiang Yin[1,2], Xin Xu[1,2], Wenlong Shao[1,2], Hanzhang Chen[1,2], Jianxing He[1,2]

[1]Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; [2]Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

*These authors have contributed equally to this work.

Correspondence to: Jianxing He, MD, PhD, FACS. Department of Cardiothoracic Surgery, the First Affiliated Hospital of Guangzhou Medical University, No. 151, Yanjiang Rd, Guangzhou 510120, China. Email: drjianxing.he@gmail.com.

Objective: To assess the feasibility, safety and long-term outcomes of video-assisted thoracic surgery (VATS) lobectomy for the treatment of non-small cell lung cancer (NSCLC) in patients with severe chronic obstructive pulmonary disease (COPD).

Methods: The clinical data of patients with NSCLC and severe COPD (preoperative FEV1% <50%) who underwent VATS lobectomy from January 2000 to January 2011 were retrospectively analyzed to identify their demographic parameters, postoperative complications and outcomes.

Results: The preoperative FEV1/FVC was <70% and FEV1% <50% in all 61 patients in this study, with a mean preoperative FEV1 of 0.99 L (0.54-1.58 L) and mean FEV1% of 38.4% (22-49.82%). All of the 61 patients underwent the VATS lobectomy or sleeve resection plus systemic lymph node dissection. The mean operative time was 218 minutes (120-355 minutes), with a mean intraoperative blood loss of 342 mL (50-1,600 mL). None of the patients converted to thoracotomy. Multivariate statistical analysis revealed that age and TNM staging after tumor resection were independent predictive factors for the 5-year survival in those patients (P=0.014 and 0.013).

Conclusions: With preoperative imaging studies, pulmonary function assessment and target positioning, VATS lobectomy can be safely and effectively performed for patients with NSCLC and severe COPD to achieve a satisfying long-term survival outcome.

Keywords: Non-small cell lung cancer (NSCLC); video-assisted thoracic surgery (VATS); lobectomy; chronic obstructive pulmonary disease (COPD)

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Introduction

A disease of serious harm to human health and life, lung cancer has shown evidently increasing morbidity and mortality worldwide in recent years, and ranked first in both figures in developed and developing countries (1). Although surgery has been recognized as the most effective method of treatment for early-stage non-small cell lung cancer (NSCLC), most patients with lung dysfunction, due to chronic obstructive pulmonary disease (COPD) after a history of smoking, are at a higher risk of complications after lung surgery. Therefore, a history of lung cancer with severe COPD is a contraindication to lobectomy. With the ongoing application of lung volume reduction surgery both at home and abroad, it has been shown that, after the removal of part of the lesions in lung tissue, lung function can be improved to varying extents for some patients with severe emphysema (2). An increasing number of studies have confirmed improvement in the lung function of patients with lung cancer and severe COPD following lobectomy

(3-5). Those findings have shed new light on the indications for lobectomy in patients with lung cancer and COPD.

Video-assisted thoracoscopic lobectomy was first applied for the treatment of lung cancer in 1992. Its greatest advantage included the minimal invasiveness, reduced postoperative pain and less damage to the respiratory muscle and pulmonary function (6). The video-assisted thoracic surgery (VATS) has been reported (7) to allow significantly faster recovery of pulmonary functionality for in the early stages after lobectomy, compared with open-chest surgery, which further suggests that VATS protects lung function more efficiently as it causes less damage to respiratory muscles. With the wide application of VATS and continuous advancement in the technology of anesthesia, intensive care and preoperative respiratory function management, the indications for pulmonary resection are also expanding to include more and more elderly patients or long-term smokers whose lung function is already impaired. At present, favorable short- and long-term outcomes have been reported in a few studies using VATS lung resection to treat patients with lung cancer and severe COPD (8). So far, however, only a small number of such cases undergoing VATS lobectomy have been reported, and the findings are not sufficient to provide a comprehensive evaluation of the safety and effectiveness of this approach in this regard. Hence, this study is conducted to assess the safety and effectiveness of VATS lobectomy based on the findings of 61 patients with lung cancer and severe COPD who underwent this treatment in our department.

Materials and methods

Clinical data

The clinical data of patients undergoing VATS lobectomy in First Affiliated Hospital of Guangzhou Medical College from January 2000 to January 2011 were retrospectively analyzed. Sixty-one patients complicated with COPD were identified and enrolled in this study based on the GOLD classification standard for COPD (9). Upon enrollment, all participants were engaged in a series of preparation before surgery, including quitting smoking, respiratory function exercise, administration of phlegm drugs and chest physiotherapy.

Preoperative examination and surgical methods

Before surgery, all participants received physical examination, routine blood tests, ECG, cardiac color Doppler ultrasound and lower extremity deep venous color Doppler ultrasound. Respiratory function tests include pulmonary ventilation-dispersion function tests and ventilation-perfusion radionuclide scans. Coronary CT or treadmill activity tests were performed in patients with suspected coronary heart disease over the age of 60, as well as coronary interventional examination, if necessary.

Preoperative tumor staging was based mainly on the chest X-ray examination, chest CT, head and abdominal MRI, whole body bone scan, and bronchoscopy. PET/CT scans were recommended for patients considered to be stage II or above. All participants underwent VATS lobectomy and hilar and mediastinal lymph node dissection, of which the specific surgical techniques were already reported in our previous study (10).

Data collection and follow-up

The demographic data, smoking status, lung function test results, operative time, blood loss, postoperative hospital stay, postoperative chest tube residence time, postoperative tumor stage, postoperative complications, and pre- and post-operative ECOG performance status of all enrolled patients were collected. The following postoperative complications were recorded: perioperative mortality (in-hospital mortality or death of any cause in 30 days after surgery), severe complications (surgery-related: second thoracotomy due to postoperative bleeding; Respiratory: ARDS and bronchopleural fistula, pneumonia, pulmonary embolism, empyema, pulmonary edema, tracheostomy or second endotracheal intubation; Cardiac: myocardial infarction, myocardial ischemia or angina pectoris, cerebrovascular event, deep vein thrombosis; Others: acute renal failure, acute gastrointestinal bleeding, etc); and mild complications (atelectasis, postoperative air leakage for more than seven days, pleural effusion, atrial fibrillation or other arrhythmias, wound infection, etc). Long-term follow-up was conducted to identify the breathing status, tumor recurrence and survival of all patients, for a period of 1-60 months.

Statistical analysis

Measurement data were expressed as mean ± standard deviation ($\bar{x}\pm s$). The chi-square test was used in the correlation analysis of changes in the ECOG performance status of the participants, and Kaplan-Meier survival analysis

Table 1 Demographics and clinical data

Characteristics	No (%)
Age, years	64 (range, 46-83)
Male:female	53:8
Smoking	
Yes	51
No	10
Preoperative lung function	
FEV1 (L)	0.99 (0.54-1.58)
FEV1%	38.40 (22-49.82)
FEV1/FVC%	47.88 (25.79-69)
VATS operations	
Lobectomy	57 (93.4)
Sleeve resection	4 (6.6)
Right upper lobe	23 (37.7)
Right middle lobe	3 (5.0)
Right lower lobe	11 (18.0)
Left upper lobe	13 (21.3)
Left lower lobe	11 (18.0)
Mean operative time (mins)	218 (range, 120-355)
Bleeding (L)	342 (range, 50-1,600)
Hospital stay (days)	16 (5-54)
Histology	
Adenocarcinoma	34 (55.7)
Squamous cell carcinoma	20 (32.8)
Others	7 (11.5)
Staging	
IA	9 (14.8)
IB	19 (31.1)
IIA	14 (23.0)
IIB	6 (9.8)
IIIA	13 (21.3)

was conducted to identify the correlation with postoperative survival. The Cox regression model test was performed for each variable with a P value of ≤0.20 in the univariate analysis. The statistical analysis was completed in SPSS 13, with P<0.05 indicating a statistically significant difference.

Results

Clinical data

Sixty-one cases were finally included in the retrospective study, including 53 men (86.9%) and eight women (*Table 1*). The average age was 64 years (46-83 years). Fifty-one patients were long-term smokers. The preoperative FEV1/FVC was <70% and FEV1% <50% in all patients, with a mean preoperative FEV1 of 0.99 L (0.54-1.58 L) and mean FEV1% of 38.4% (22-49.82%).

All of the 61 patients underwent the VATS lobectomy or sleeve resection plus systemic lymph node dissection [right upper lobe in 23 cases (37.7%), right middle lobe in three (5.0%), right lower lobe in eleven (18.0%), left upper lob in thirteen (21.3%) and left lower lobe in eleven (18.0%)]. The mean operative time was 218 minutes (120-355 minutes), with a mean intraoperative blood loss of 342 mL (50-1,600 mL). None of the patients converted to thoracotomy. Postoperative pathology reported 34 cases of adenocarcinoma (55.7%), 20 cases of squamous cell carcinoma (32.8%) and seven of other tumors (11.5%). All participants were subject to pathological and clinical staging according to the TNM Classification of the UICC, 7th edition (11). As a result, there were nine patients of IA (14.8%), nineteen of IB (31.1%), fourteen of IIA (23.0%), six of IIB (9.8%), and thirteen of IIIA (21.3%).

Table 2 Complications

Complication	Patients, No[a]
Mortality	2
Air leak	16
Atrial fibrillation	3
Pneumonia	6
Respiratory failure	3
Atelectasis	2
Empyema	0
Pulmonary embolism	2
Wound infection	0
Bleeding	0

[a], Some patients had more than one complication.

Complications after surgery

Two patients died of ARDS during the perioperative period, and 24 patients (39.3%) presented postoperative complications (*Table 2*). Twenty-two patients (36.1%) had respiratory complications postoperatively, including air leakage in 16 cases (25.8%), pulmonary infection in six, respiratory failure in three, atelectasis in two and pulmonary

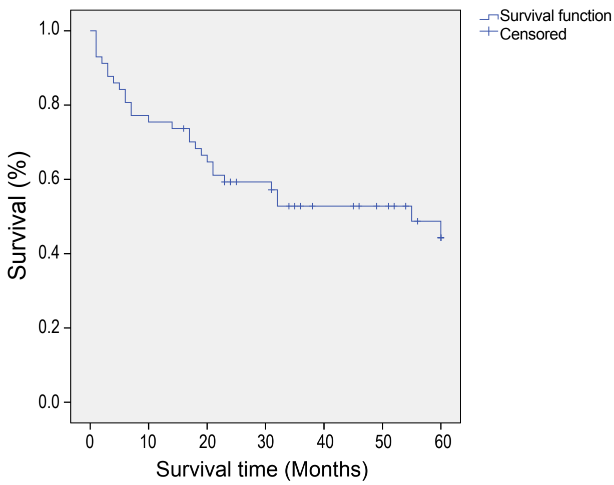

Figure 1 Overall survival (n=56).

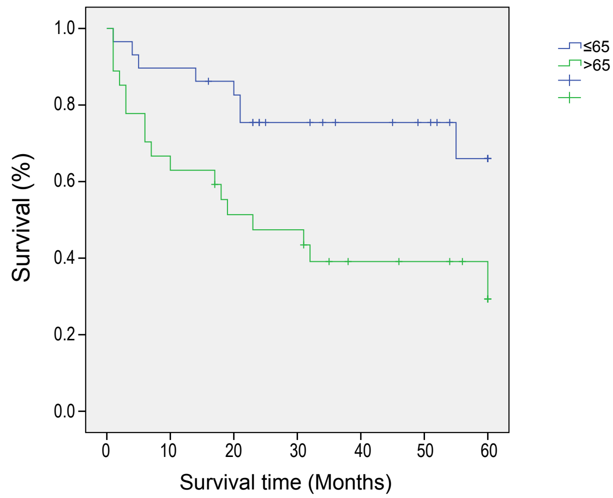

Figure 2 Survival according to age: ≤65 years old (n=27) versus >65 years old (n=29) (P=0.007).

Table 3 Univariate analysis of factors associated with overall survival

	No.	5-y OS rate %, (95% CI)	P Log-rank test
Gender			0.434
Male	50	40.2 (33.3-47.1)	
Female	6	28.7 (12.0-45.3)	
Age			0.007
≤65	29	47.8 (40.2-55.4)	
>65	27	30.6 (20.7-40.4)	
Smoking status			0.335
Nonsmoker	48	40.6 (33.6-47.6)	
Smoker	8	28.0 (13.2-42.8)	
ECOG performance status			0.787
0-1	27	42.0 (32.9-51.0)	
2	29	37.0 (27.5-46.4)	
Histology			0.216
Squamous cell carcinoma	19	47.2 (35.9-58.6)	
Non-Squamous cell carcinoma	37	35.5 (27.6-43.4)	
Lobe location			0.557
Upper lobe	33	40.8 (32.6-49.0)	
Middle-lower lobe	23	37.4 (26.4-48.5)	
pTNM stage			0.006
I	26	49.4 (41.1-57.6)	
II/III	30	30.7 (21.7-39.8)	

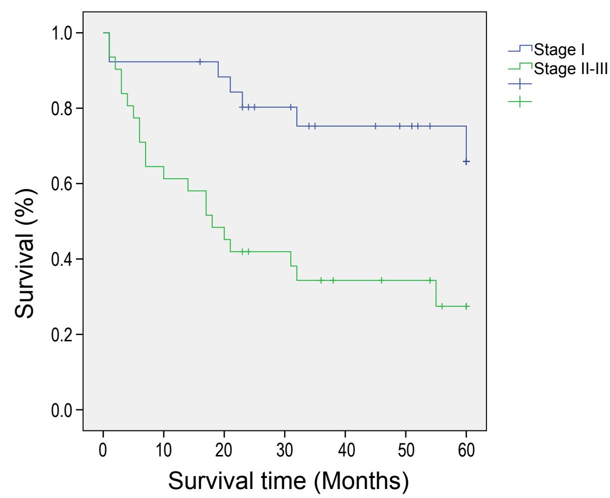

Figure 3 Survival according to stage: stage I disease (n=26) versus stages II/III (n=30) (P=0.006).

embolism in two. The average hospital stay was 16±1.1 days (5-54 days).

Overall survival

During a median follow-up time of 39 months (1-60 months), five patients were lost to follow-up and 27 died. The survival rate was 75.4% in the first year, and 50.9% in five years (*Figure 1*). In the univariate analysis using the

Table 4 Multivariate analysis of overall survival

Factors	Characteristics		Hazard ratio	95% CI	P value
	Unfavorable	Favorable			
Age	>65	≤65	2.899	1.239-6.787	0.014
pTNM stage	II/III	I	3.113	1.273-7.609	0.013

Table 5 Lung resection in poor pulmonary function

References	No. of Patients	Pulmonary function tests	Approach	Hospital stay	Mortality 30 days (%)	Morbidity 30 days (%)	Respiratory complications (pulmonary and pleural) and remarks
Nakajima T *et al*. 2009 (17)	36	Pred FEV% <50%	Open: wedge + segment 4, lobectomy 26, pneumonectomy 6		0	11 (30.6)	Pneumonia 5 Bronchopleural fistula 3 Empyema 3
Garzon *et al*. 2006 (10)	25	Pred FEV1 <0.8 or FEV1% <50%	VATS: lobectomy 13, wedge resection 12	7.4 [2-26] days	0	5 (20.0)	Air leak 2 Atelectasis 2 Pneumonia 1
Linden PA *et al*. 2005 (18)	100	Pred FEV1% <35%	Open: wedge resection 65, lobectomy 10, wedge resection 5, segmentectomy 4, lung volume reduction/ wedge 8. VATS: lobectomy 4, segmentectomy 4	8.37 days	1 (1)	41 (41.0)	Prolonged air leak 22 New oxygen requirement 11 Respiratory failure 4 Pneumonia 4
Magdeleinat *et al*. 2005 (19)	106	Pred FEV% ≤50%	Open: pneumonectomy 16, lobectomy 73, z segmentectomy 7, wedge resection 10	20 days	5 (8.5)	74 (69.8)	Pneumonia 27 Atelectasis 16 Bronchitis 1
Martin U *et al*. 2005 (8)	34	ppoFEV1% <40%	VATS: lobectomy 17, segmentectomy 17	7 [3-31] days	2 (5.8)	10 (29.4)	Pneumonia 3 Air leak 3 Empyema 1
Choong *et al*. 2004 (3)	21	Mean FEV1 =0.7 L mean Pred FEV1% =29%	Open: lobectomy 18, wedge resection 3	9 [5-24] days	0	19 (90.5)	Respiratory failure 2 Air leak 11 Mini-tracheostomy 7
Solli *et al*. 2003 (20)	31	Pred FEV% <50% or DLCO% <50%	Open: pneumonectomy 10, lobectomy 11, z sublobar resection 10, segmentectomy 7, wedge 2	7 [4-21] days	0	16 (31.6)	Respiratory failure 1 Atelectasis 3 Pneumonia 1 Air leak 3
Present study	62	Pred FEV% <50%	VATS: lobectomy 62	16±1 [5-54] days	2 (3.2)	22 (36.1)	Air-leak 16 Pneumonia 6 Respiratory fail 3 Atelectasis 2 Pulmonary embolism 2

FEV, forced expiratory volume; ppoFEV1, predicted postoperative percentage of FEV1; Pred, predicted; VATS, video-assisted thoracic surgery.

Log-rank test, the outcomes were correlated with age and postoperative TNM staging (P=0.007 and 0.006, *Table 3*). The median survival of patients not older than 65 years was 48 months, and reduced to 31 months in those older than 65 (P=0.007, *Figure 2*). Patients with stage I tumors had a median survival of 49 months, while those had stage II/III tumors had only 28 months. The difference was significant between them (P=0.006, *Figure 3*). In the Cox regression model, when taking into account those factors showing significant effect on survival in the univariate analysis, age and TNM staging after tumor resection were independent predictive factors for the 5-year survival in those patients (P=0.014 and 0.013, *Table 4*).

The ECOG scores were recorded three months before and after surgery to evaluate the changes of lung function and quality of life for the patients (12). The results showed that mean ECOG scores of 1.51 and 1.31 before and after surgery, respectively, among the 59 patients, excluding two who died during the perioperative period. The difference between those scores was significant (P<0.05).

Discussion

Lung cancer and COPD are two common diseases of human beings. The presence of both conditions in a patient can increase the risk of complications after lung surgery due to underlying lung function damage. Since lung cancer patients with severe COPD are at a higher risk of postoperative complications, most of they have to receive non-radical partial lung resection (wedge or segmental resection) instead of lobectomy, which is currently recognized as the most effective means of treatment for early stage lung cancer. For patients with lung cancer, however, both pulmonary wedge resection and segmental resection are associated with a significantly increased recurrence rate and lower postoperative survival compared with standard lobectomy (13,14).

With the ongoing application of lung volume reduction surgery, it has been found that partial lung resection can achieve the similar result to volume reduction for patients with lung cancer and emphysema (3), which can minimize or even improve postoperative pulmonary function loss. Those findings have shed new light on the surgical options for patients with lung cancer and severe COPD. With the development of surgical techniques, anesthesia and intensive medical technology, an increasing number of studies have reported that lung resection can be tolerated by patients with lung cancer and severe pulmonary insufficiency, and can lead to satisfying outcomes (3,8,15-18).

Since the early 1990s, VATS has been rapidly developed and widely applied in the world, involving almost all areas of general thoracic surgery. Compared with thoracotomy, VATS enables a smaller incision without removing or stretching the ribs open, sparing respiratory muscles from injures and thus minimizing the loss of lung function. Moreover, with a smaller incision, patients will suffer less pain postoperatively and expectorate more easily, reducing the incidence of postoperative pulmonary infection and complications as well. In view of those advantages, VATS procedures have been used in a growing number of studies to treat patients with lung cancer and severe pulmonary dysfunction (8,19).

Previous studies have shown that, however, patients with lung cancer and COPD have an increased risk of cardiopulmonary complications compared to patients with lung cancer alone (20). In the present study, two patients died of respiratory failure in the perioperative period and 24 patients (39.3%) had postoperative complications, of which 22 (36.1%) had respiratory complications with an average hospital stay of 16 days after surgery. It can be seen that the incidence of postoperative respiratory complications in this study is not unacceptable compared with the previous reports (*Table 5*). According to the existing studies, open chest surgery is associated with a longer postoperative hospital stay and higher incidence of respiratory complications in patients with lung cancer and severe pulmonary dysfunction compared with the VATS procedures, which further demonstrates that the VATS technique is an ideal option for such patients. A possible explanation for the lower risk of postoperative pulmonary complications is that reduced injury to respiratory muscles, smaller chest wall incision and consequently less pain allows patients to cough and expectorate more easily and get out of bed sooner after VATS, and this in turn reduces the likelihood of other complications of the respiratory system. In the present study, pulmonary complications were observed in 36.1% of the patients, which is lower than the report of most studies with open chest surgery (3,16,17) but higher than those with VATS surgery (8). Martin *et al.* (8) carried out VATS lung resection for 34 patients with lung cancer and a FEV1% <40%; Although there were two dead cases, respiratory complications were observed in only ten patients (29.4%). In the present study, although the incidence of postoperative respiratory complications was higher than the above findings (8), systemic radical surgery was administered to all of the patients with lung cancer and severe COPD in the former, while VATS lobectomy accounted for up to 50.2% and 50% (8) in the other two studies. Lobectomy is associated with much greater surgical injury and loss of functional alveolar areas than either wedge resection or segmentectomy, and there were seven patients with extremely severe COPD and a preoperative FEV1% of only 27.8% (22-29.9 %) in this study.

Patients in this study had a relatively long hospital stay, averaging 16 days. Although it is slightly shorter than 20 days as reported by Magdeleinat *et al.* (17), it is longer than all of the other studies, which may be largely due to the surgical approaches. In this study, all 61 patients received either lobectomy or sleeve resection, whereas lobectomy accounts for a relatively small part in all of the remaining studies.

In the present study, both short- and long-term survival rates are observed in patients with moderate COPD who received lobectomy or sleeve resection after a 5-year follow-up. The survival analysis showed a 1-year survival rate of 75.4%, which was basically consistent with the findings of Magdeleinat (17), and a 5-year survival rate of 50.9%, which was higher than the report of Magdeleinat. Further analysis showed significantly better outcomes in patients with stage I lung cancer than in those with stages II or III, with the 5-year survival rates being 73.1% and 32.3%, respectively ($P<0.05$), which were generally consistent with other reports (8,15,17). According to the report by Martin *et al.* (8), the analysis of 34 patients with stage I lung cancer and severe pulmonary dysfunction who underwent VATS lobectomy or segmental resection revealed a 5-year survival up to 69.7%, without significant difference between the two groups. Nakajima *et al.* (15) found a 5-year survival of 57.9% in the stage I group as a part of 36 patients with lung cancer and severe lung dysfunction, but the 5-year survival was merely 11.9% in the more advanced groups.

Lung cancer and COPD are mostly found in elderly people, while patients over the age of 65 years account for about 50% and those over the age of 70 years account for 30-40% of all cases (21). COPD and cardiovascular diseases are the common concomitant diseases in elderly smokers with lung cancer, and the presence of such conditions may directly or indirectly affect their therapy and outcomes. In the study of Janssen-Heijnen *et al.* (22), age was regarded as an independent factor for the survival outcomes of patients with stages I and II NSCLC, though it had no significant impact on the survival outcomes of patients at more advanced stages. Li *et al.* (23) also found that the 5-year survival rate was significantly higher in patients with stage I lung cancer who were not older than 65 years, compared with those older. In our previous study, we also found that age could be a critical factor in predicting the outcomes of those patients (24). A number of studies (15,17,25) have shown that, for patients complicated with severe pulmonary dysfunction, those with stage I lung cancer would have a better outcome than patients with the condition at stages II and III ($P<0.05$). In the present study, multivariate statistical analysis also suggested that age could be an independent prognostic factor for patients with lung cancer and severe COPD, which was consistent with previous reports.

However, there are several limitations in this study due to its retrospective nature. Although it has included the largest number of patients with lung cancer and severe COPD undergoing VATS lobectomy so far, the absolute number is not significantly large. Secondly, the present analysis included only the 5-year survival but not the time to progression, and did not take into account the subsequent treatment patients received after the surgery when calculating the 5-year survival rates. Finally, an objective comparison between the lung function data before and after the surgery is unavailable because some of patients did not receive postoperative pulmonary function tests. Hence, the changes in the quality of life can merely be analyzed based on some relatively objective indicators in the present study. A more comprehensive prospective study will be needed to further determine the safety and effectiveness of VATS lobectomy as the treatment for patients with lung cancer and severe COPD.

In conclusion, VATS lobectomy can be safely and effectively performed for patients with NSCLC and severe COPD to achieve a satisfying long-term survival outcome as good as the routine VATS procedure, with an acceptable incidence of postoperative complications. Therefore, our preliminary conclusion is that for younger patients at an earlier stage (stage I), VATS lobectomy can be used as a more effective treatment option.

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Thoracoscopic minimally invasive surgery for non-small cell lung cancer in patients with chronic obstructive pulmonary disease

Fei Cui[1,2]*, Jun Liu[1,2]*, Wenlong Shao[1,2], Jianxing He[1,2]

[1]Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; [2]Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou, China.

*These authors contributed equally to this work.

Correspondence to: Jianxing He, MD, PhD, FACS. Department of Cardiothoracic Surgery, the First Affiliated Hospital of Guangzhou Medical University. No. 151, Yanjiang Rd, Guangzhou 510120, Guangdong Province, PR China. Email: drjianxing.he@gmail.com.

Objective: To determine the incidence of peri-operative complications in non-small cell lung cancer (NSCLC) patients with co-existent chronic obstructive pulmonary disease (COPD) who undergo lung resection via traditional and minimally invasive techniques.

Methods: A retrospective analysis was conducted of 152 NSCLC patients with COPD who underwent thoracoscopic minimally invasive surgery. Particular attention is given to the relationship between disease severity or surgical approach and the incidence of complications.

Results: The prevalence of respiratory and cardiac complications was significantly higher in patients with severe/extremely severe COPD than those with mild to moderate COPD (respiratory compications: 37.3% *vs*. 20.4%, P=0.022; cardiac complications: 16.9% *vs*. 6.5%, P=0.040). Patients who underwent complete-video assisted thoracoscopic surgery (c-VATS) had a significantly lower overall morbidity of adverse reactions than those who had undergone VATS major resection (26.3% *vs*. 42.1%, P=0.044). Among patients with severe/extremely severe COPD, there was no significant difference in the incidence of any complication between the lobectomy group and wedge resection group (38.8% *vs*. 70.0%, P=0.072). Overall, the occurrence of adverse reactions was significantly lower in patients who underwent c-VATS than in those who had undergone VATS major resection surgery (34.2% *vs*. 61.9%, P=0.038).

Conclusions: VATS techniques are suitable for COPD patients and are demonstrated here to lower the incidence of post-operative complications when compared with more invasive approaches.

Keywords: Non-small-cell lung cancer (NSCLC); chronic obstructive pulmonary disease (COPD); video-assisted thoracic surgery (VATS); thoracic surgery

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Introduction

Lung cancer has been one of the leading causes of death in patients with chronic obstructive pulmonary disease (COPD). In the United States, the incidence of lung cancer in patients with COPD (16.7/1,000 person-years) is much higher than reported in the general population (76.4/1,000,000 in men and 52.7/1,000,000 in women) (1). Whilst surgical resection remains the treatment of choice for patients with non-small cell lung cancer (NSCLC) and co-existing COPD, reduced lung function and poor respiratory reserve make these patients higher risk for surgery. Traditionally, this has resulted in thoracic surgeons adopting a more conservative approach in this patient group, a consequence of which is relatively strict selection criteria for surgical intervention (2). However, recent advances in the field of thoracic surgery, in particular video-assisted thoracic surgery (VATS), have led to a recent decline in the morbidity and mortality associated with surgery in NSCLC patients in comparison to ten years ago

Table 1 General data of the enrolled patients

	No. (%)
Total	152
Age (years)	
<68 years	70
≥68 years	82
Mean (± S.D.)	66.6±8.04
Gender	
Men	140
Women	12
Histological type	
Squamous cell carcinoma	63
Adenocarcinoma	74
Other types	
Adenosquamous carcinoma	4
Large cell carcinoma	4
Bronchioloalveolar carcinoma	4
Pleomorphic carcinoma	3
TMN stage	
I	69
II	52
III	31
Surgical procedures	
VATS major resection	57
c-VATS	95
Resection	
Lobectomy	142
Wedge resection	10

(3,4). There is an increasing body of evidence to suggest that surgery can be performed safely in individuals with both COPD and NSCLC, with emphasis on the need to revise the current selection criteria for these patients (5-7). The aim of this study was to determine whether minimally invasive techniques are beneficial for patients with NSCLC and co-existing COPD.

Patients and methods

Patients

Between March 2000 and September 2010, 152 NSCLC patients with a diagnosis of COPD, in accordance with the Global Guidelines for the Diagnosis and Treatment of COPD (8), were enrolled in the study. Those enrolled included 55 cases of mild COPD [forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) ≤70%, FEV1 ≥80% predicted), 38 cases of moderate COPD (FEV1/FVC ≤70%, 50%≤ FEV1 <80% predicted), 46 cases of severe COPD (FEV1/FVC ≤70%, 30%≤ FEV1 <50% predicted) and 13 cases of extremely severe COPD (FEV1/FVC ≤70%, FEV1 <30% predicted). All tumors were deemed operable based on anatomical location and staging as defined by the Union for International Cancer Control (UICC) guidelines 2007 [1]. Of the 152 patients with NSCLC Sixty-two cases were stage I, fifty-nine were stage II with the remaining thirty-one stage IIIA. There were no patients with significant contraindications of cardiovascular, digestive, urinary, endocrine or other systemic disease. The same surgical team performed the operations, and all cases were divided in two groups with randomly: 57 patients underwent VATS major resection (VATS major resection, approach that used both direct vision and television monitor visualization) whilst the remaining 95 underwent c-VATS (complete VATS) (*Table 1*).

All patients recieved standardized COPD treatment for a minimum of one week, which included pharmaceutical therapy and chest physiotherapy to improve lung function. Intubation via a double-lumen endotracheal tube was used for all patients. Wedge resection was performed in 10 patients with severe/extremely severe COPD whilst the remaining 142 patients underwent standard lobectomy and lymphadenectomy. Patients were postoperatively managed with antibiotics, bronchial relaxation, spasmolytics, phlegm reduction techniques, oxygen therapy and physical expectoration. Patients with poor expectoration were managed with bronchoscopic suctioning, and those who experienced respiratory failure were treated with mechanical ventilation.

Data collection

Preoperative pulmonary function testing, 6-minute walk tests, operation duration and postoperative respiratory complications (lung infections, air leakage, bronchospasm, respiratory function failure, mechanical ventilation and atelectasis) were recorded. Data was also collected regarding cardiac complications (myocardial infarction and arrhythmia), number of deaths, indwelling chest tube duration and length of hospital stay. A repeat 6-minute walk test was conducted four weeks following surgery.

Statistical analysis

Postoperative complications were compared using paired

Table 2 Postoperative complications in the subjects

Complication	n	%
Any complication	49	32.24
Any respiratory complication	41	26.97
Atelectasis	3	0.66
Pulmonary infection	9	5.92
Pulmonary air leak	20	13.16
Respiratory failure	6	3.95
Spasm	21	13.82
Mechanical ventilation	4	1.32
Any cardiac complication	16	10.53
Atrial fibrillation	6	3.95
Atrial flutter	3	1.97
Atrial premature	5	3.29
Ventricular premature	2	1.32
Myoctardial infarction	1	0.66
Death	2	1.32

t-test, and count data were compared using the chi-square test and Fisher exact test in the SPSS13.0. P-values of less than 0.05 were considered to be significant.

Results

Postoperative pulmonary air leak was reported in twenty patients and managed with a prolonged (>14 days) indwelling chest tube, suction (where appropriate) and supportive treatment. Twenty-one patients experienced bronchospasm, which was treated with spasmolytic agents. Six patients were documented as having respiratory failure, hypoxia and carbon dioxide retention. Four of the six still required mechanical ventilation after symptomatic treatment. Two of these patients were discharged after removal of ventilation (three and six days). The other two patients unfortunately passed away (*Table 2*).

Stratified analysis revealed significantly higher complication rates (*Table 3*) in severe/extremely severe COPD patients when compared to the mild to moderate COPD patients (P=0.040). The incidence of any complication was significantly lower in the c-VATS groups than the VATS major resection group (P=0.044). Additionally, there was a significantly higher incidence of any complication in the lobectomy group than in patients undergoing wedge resection (P=0.032).

Patients with mild to moderate COPD had significantly shorter hospital stays than severe/extremely severe COPD patients (P=0.005) (*Table 4*). There was no significant difference in performance pre and post-operatively in the 6 minutes walk tests in the c-VATS group (P>0.05). A significantly reduced distance was observed in the VATS major resection group however (P<0.05) (*Table 5*).

The impact of surgical approach and resection extent on postoperative complications for the 59 severe/extremely severe COPD patients is reported in *Table 6*. Because of the poor lung function, 10 patients underwent a wedge resection considering that they cannot tolerate a lobectomy. A lower incidence of both respiratory and cardiac complications was shown in the c-VATS group compared with the VATS major resection group (P<0.05). No difference was found between the lobectomy group and the wedge resection group (P>0.05).

Discussion

The reported benefits of c-VATS over traditional muscle splitting thoracotomy are many and include a reduction in post-operative pain and complications (9). The minimally invasive nature of the surgery reduces the adverse impact on pulmonary function; a result of limited damage to the chest wall and minimal trauma to the respiratory muscles. Therefore, for lung cancer patients with COPD in whom the risks of surgery are high, thoracoscopic minimally invasive surgery provides a safe alternative to conventional techniques. Even in individuals who can not tolerate radical lobectomy, partial resection via VATS may still be of therapeutic benefit.

In COPD patients who undergo surgery for NSCLC, the most common postoperative complication is parenchymal air leak (10). In the presented study, there was a difference in the morbidity mild to moderate COPD patients and those with severe/extremely severe COPD after surgery (20.4% *vs*. 37.3%, P=0.022), which was mainly attributed to parenchymal air leak (8.6% *vs*. 20.3%). This is likely attributed to the poor quality of the lung parenchyma and the diminished elastic recoil in emphysema, which, in turn, delays healing of the lung tissue. Other complications between the mild to moderate and severe/extremely severe patients included bronchospasm (8.6% *vs*. 23.7% respectively), and respiratory dysfunction (2.2% *vs*. 10.2% respectively). In addition, the rates of cardiac complications differed between the two groups (6.5% *vs*. 16.9%, P=0.040). This could be explained by chronic hypoxia, pulmonary hypertension and associated atrial volume-pressure function

Table 3 Stratified analysis of complications

Stratification factors	Total cases	Any complication n (%)	P value	Respiratory complications n (%)	P value	Cardiac complications n (%)	P value	Death (n)
Gender*			0.525		0.605		1	
Men	140	44 (31.4)		37 (26.4)		15 (10.7)		2
Women	12	5 (41.7)		4 (33.3)		1 (8.3)		0
Age			0.586		0.291		0.738	
≤68 years	70	21 (30.0)		16 (22.9)		8 (11.4)		2
>68 years	82	28 (34.1)		25 (30.5)		8 (9.8)		0
Severity of COPD			0.004		0.022		0.040	
Mild to to moderate	93	22 (23.7)		19 (20.4)		6 (6.5)		0
Severe/extremely severe	59	27 (45.8)		22 (37.3)		10 (16.9)		2
Pathology			0.517		0.801		0.875	
Squamous cell carcinoma	63	20 (31.7)		17 (27.0)		7 (11.1)		1
Adenocarcinoma	74	26 (35.1)		21 (28.4)		8 (10.8)		1
Others	15	3 (20.0)		3 (20.0)		1 (6.7)		0
T stage			0.200		0.547		0.731	
1	36	16 (44.4)		12 (33.3)		5 (13.9)		0
2	88	25 (28.4)		23 (26.1)		8 (9.1)		1
3	28	8 (28.6)		6 (21.4)		3 (10.7)		1
Clinical classification			0.416		0.656		0.926	
1	69	26 (37.7)		21 (30.4)		8 (11.6)		0
2	52	14 (26.9)		12 (23.1)		5 (9.6)		1
3	31	9 (29.0)		8 (25.8)		3 (9.7)		1
Surgical approach			0.044		0.322		0.101	
c-VATS	95	25 (26.3)		23 (24.2)		7 (7.4)		0
VATS major resection	57	24 (42.1)		18 (31.6)		9 (15.8)		2
Resection			0.011		0.064		0.284	
Lobectomy	142	42 (29.6)		32 (22.5)		14 (10.0)		2
Wedge resection	10	7 (70.0)		5 (50.0)		2 (20.0)		0

The number of death was small, and no statistical analysis was performed. *Fisher exact test.

Table 4 Influence of the severity of COPD on the surgery

Severity of COPD	Mild to moderate	Severe/extremely severe	P value
N	93	59	
Surgical duration (min)	256±83.4	211±65.6	0.36
Hospital stay (days)	9.7±4.1	16.0±8.8	0.005
Indwelling chest tube duration (days)	3.6±1.7	6.8±6.5	0.119

Table 5 Influence of surgical approach on the results of 6-minute walk tests

Severity of COPD	Mild to moderate		Severe/extremely severe	
Surgical approach	VATS major resection	c-VATS	VATS major resection	c-VATS
Baseline 6MWT (m)	493±71	473±96	335±64	362±41
Post-operative 6MWT (m)	366±45	416±52	294±58	345±48
P value	0.023	0.327	0.038	0.876

Table 6 Impact of surgical factors on postoperative complications in patients with severe/extremely severe COPD

Stratification factors	Total cases	Any complication n (%)	P value	Respiratory complications n (%)	P value	Cardiac complications n (%)	P value
Surgical approach			0.038		0.033		0.048
c-VATS	38	13 (34.2)		11 (28.9)		2 (5.3)	
VATS major resection	21	13 (61.9)		12 (57.1)		5 (15.8)	
Resection			0.072		0.228		
Lobectomy	49	19 (38.8)		19 (38.8)		4 (8.1)	0.259
Wedge resection	10	7 (70.0)		5 (50.0)		2 (20.0)	

disorders in severe COPD patients. These disorders are known to precipitate arrhythmias and other cardiac complications in the presence of increased load in the right cardiopulmonary circulation.

Longer lengths of hospital stay were reported in the severe/extremely severe COPD group (16.0±8.8 *vs*. 9.7±4.1, P=0.005) as a result of an increase in complication rates. To minimize the effects of these complications, patients were encouraged to expectorate, undergo chest physiotherapy, and therapeutic agents which promote bronchial relaxation were administered during the post-operative period. Fiber-optic bronchoscopy and wound analgesia were also utilised to manage those having difficulty with expectoration. These active interventions are thought to be beneficial in the prevention of post-operative complications.

VATS major resection group and the c-VATS group, and revealed a significant difference (42.1% *vs*. 26.3%, P=0.044). This was particularly evident in patients with severe/extremely severe COPD. In this subpopulation, the frequency of pulmonary and cardiac complications was significantly lower in patients who underwent resection via c-VATS than in the VATS major resection group. These findings reflect the advantages of c-VATS attributed to its minimally invasive nature and are particularly relevant to patients with poor respiratory function as a consequence of severe/extremely severe COPD. It has also been proved that minimally invasive thoracoscopic surgery is reported to have less of an adverse effect to the residual lung function, whilst conventional thoracotomy is associated with a 30-50% decrease in pulmonary function (11-13).

The incidence of air leak in patients undergoing conventional thoracotomy for NSCLC has previously been reported at 52% among 21 severe/extremely severe COPD (10). In the current study, only 13.2% of patients in the c-VATS were reported to have a post-operative air leak. This was potentially related to optimization of our surgical technique where division and suture of pulmonary fissures was completed following the natural anatomical plane. Additionally, margins were trimmed in an inverted U-shape when dissecting the upper lung field. Vacuum suction and intensive bronchial relaxation were administered when appropriate, to improve postoperative lung compliance, reduced airway resistance and promote lung expansion. Optimization of post-operative nutrition was also employed to facilitate wound healing and prevent the occurence of air leakage.

The c-VATS approach was also more efficacious in reducing selective cardiac complications. In the presented study, only 5.3% of the patients with severe/extremely severe COPD in the c-VATS group suffered a cardiac arrhythmia. We have hypothesized that this was related to reduced postoperative pain and improved oxygenation in this subpopulation.

To assess postoperative recovery, quality of life and

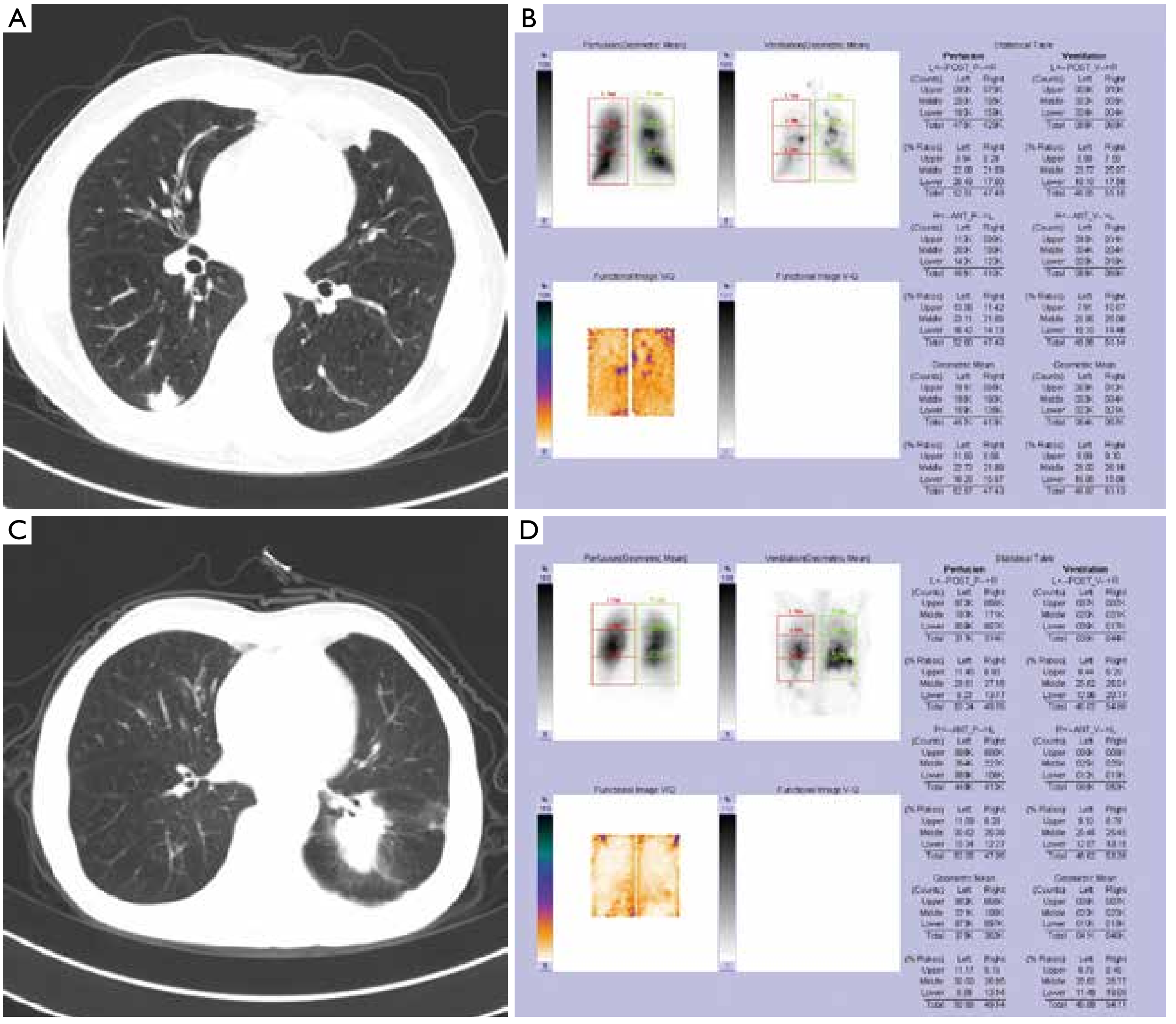

Figure 1 Surgical options for patients with severe COPD. A,B. A 56-year-old man with longstanding COPD, FEV1 0.68 L, FEV1 35% of predicted, and a nodule of 1.2 cm × 1.0 cm in the right lower lung. Biopsy confirmed "invasive adenocarcinoma". Considering the right lower field accounted for almost 20% of the overall ventilation function, the epo FEV1/predicted value =25% Preoperative assessment suggested that the patient could not tolerate lobectomy due to the significant impact on his pulmonary function. Therefore, wedge resection of the right lower lung was performed. The patient was safe and stable throughout the perioperative period. C,D. A 58-year-old man with longstanding COPD, FEV1 0.72 L, FEV1 38% of predicted, and an occupying lesion measuring 5 cm × 4.5 cm in the left lower lobe. Bronchoscopy confirmed squamous cell carcinoma. Radical resection of the lower left lung was conducted. The patient was safe and stable throughout the perioperative period.

cardiopulmonary function in our cohort, we performed 6-minute walk tests before and one month after surgery. We found a remarkable decline in performance in the VATS major resection group regardless of COPD severity. On the contrary, no difference was observed in the c-VATS group before and after surgery. We believe that lung volume reduction contributed to this finding. In patients with severe COPD lung volume reduction can improve elastic recoil, reduce resistance to blood flow and blood perfusion is appropriately redistributed with an associated improvement in the ventilation/perfusion ratio. This has the combined effect of raising the oxygenation capacity.

This benefit is demonstrated to be particularly evident when the tumor is located in an area severely compromised by COPD (10,14).

Standard radical surgery for NSCLC includes anatomical lobectomy plus lymph node dissection. It remains controversial however, as to whether patients with severe/extremely severe COPD can tolerate lobectomy. Sufficient residual lung function is a prerequisite for lung surgery, and good postoperative lung function can reduce both the risk of surgery and postoperative complications (15). Previous studies have suggested that eligibility for surgery in this population relies on a predicted FEV1 of not less than 0.8 L after surgery (16). In the general population a preoperative FEV1 ≥50% or predicted postoperative FEV1 of greater than 40% is generally considered acceptable (17,18). With improved surgical, anesthetic and perioperative care techniques however; the potential for curative surgery in patients with severe pulmonary insufficiency has become a reality. One study of 13 COPD patients undergoing lobectomy with a mean preoperative FEV1 of 49% reported a decline in lung function that was less than expected (19). In another study where radical resection of lung cancer for 29 severe COPD patients was performed, the authors concluded that patients with a predicted postoperative FEV1 of less than 40% could tolerate lobectomy if the tumor was located on the opposite side of emphysema with a perfusion of less than 10% (20). Taking advantage of the protective effects of thoracoscopic minimally invasive techniques, we can further expand the potential for curative surgery in patients with poor lung function. Following consideration of ventilation perfusion imaging, tumor location and size, and tracheal and vascular invasion, patients with preoperative FEV1 of less than 50% can be considered for surgery (*Figure 1*). These patients can be divided into two categories. The first group includes those who have lost the pulmonary function of the lobe where the tumor is located. This is typically seen in larger lesions that occlude the corresponding bronchi and compress the vessels, resulting in reduced perfusion. These patients may tolerate thoracoscopic resection with a FEV1 of <50% or even <30%, as long as there are no signs of respiratory failure. The second group includes patients who have satisfactory pulmonary function in the lobe, which corresponds to the tumor. In these patients, the postoperative lung function is predicted by formal assessment of lung function (pre-operative FEV1), heart function, pulmonary ventilation perfusion, chest CT examination, blood gas analysis, and calculation of the estimated postoperative FEV1 (epo FEV1) based on the BTS guidelines (21). With an estimated postoperative FEV1 of ≥35%, normal Ejection Fraction (EF) and $PaCO_2$ of <50 mmHg, the patients can generally tolerate c-VATS lobectomy. In the case of an estimated postoperative FEV1 <35%, normal EF and $PaCO_2$ of <50 mmHg, c-VATS partial resection is recommended to preserve postoperative pulmonary function. Surgery is contraindicated however if $PaCO_2$ is ≥50 mmHg or contraction dysfunction is present at rest without oxygen administration. In this study, 49 patients (83.1%) successfully tolerated radical resection. This was less well tolerated in the patients with sever/extremely severe COPD. There was no significant difference in the incidence of any complication between those two groups (38.8% *vs.* 70.0%, P=0.072).

In conclusion, despite high incidence rates of postoperative complications in patients with NSCLC and COPD, VATS-guided approaches are suitable for the majority of patients and can significantly reduce post-operative morbidity. Controversy remains in regard to the selection criteria of patients with COPD for thoracoscopic lobectomy. In this population, radical or partial resection based on comprehensive evaluation can benefit patients with severe/extremely severe COPD and provide therapeutic opportunity for a wider subgroup of lung cancer patients with COPD.

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Video-assisted thoracoscopic surgery (VATS) for locally advanced lung cancer

Mark W. Hennon[1,2], **Todd L. Demmy**[1,2]

[1]Department of Thoracic Surgery, Roswell Park Cancer Institute, Buffalo, NY, USA; [2]Department of Surgery, State University of New York at Buffalo, Buffalo, NY, USA

Correspondence to: Todd L. Demmy, MD. Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA. Tel: (716) 845-8675; Fax: (716) 845-7692. Email: todd.demmy@roswellpark.org.

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Introduction

First described over two decades ago, video-assisted thoracoscopic surgery (VATS) is now well established for the treatment of early stage non-small cell lung carcinoma (NSCLC) (1-6). Thoracoscopic approaches are preferred for many common thoracic procedures because of their predictable salutary effect on outcomes likely brought about by perioperative pain reductions. As widespread surgeon experience has grown with VATS, so has reliability. Low conversion rates are now commonplace despite the challenges associated with higher stage tumors and the tissue effects brought on by induction chemoradiotherapy. Tumors once thought unapproachable by thoracoscopic techniques are now frequently resected by VATS.

Video assisted thoracoscopic surgery offers many potential benefits compared to conventional muscle-splitting thoracotomy. Some established examples are decreased postoperative pain, diminished inflammatory response, decreased hospital length of stay (LOS), and faster recovery (7,8). By potentially allowing more patients to receive adjuvant chemotherapy compared to patients who undergo thoracotomy (9), VATS could potentially improve survival of patients with advanced NSCLC. Most large series examining results for VATS in lung cancer have been limited to early stage disease, and thoracotomy remains a staple for the surgical approach to locally advanced NSCLC (10). A variety of concerns regarding the completeness of oncologic resection, technical challenges, and potential safety concerns has limited the incorporation of thoracoscopy for more advanced stages of lung cancer. For patients requiring more extensive resection such as pneumonectomy and/or *en bloc* chest wall resection, thoracoscopic resection is even less common.

As previously demonstrated with many minimally invasive procedures, there is a learning curve with thoracoscopic anatomic resections (11). In general, this learning curve for advanced thoracoscopic cases has been aided by improved video, stapling, hemostatic, and retraction technologies. Excellent exposure is enabled by high-definition camera systems that allow viewing from various different angles (*Figure 1*). Endoscopic staplers have been modified to facilitate negotiation of delicate pulmonary vessels (*Figure 2*). Improved topical hemostatic technologies are useful when dealing with diffuse oozing from extrapleural or inflammatory dissections after induction therapy. Several companies now produce 5 mm low profile lung graspers (*Figure 3*). Up to 4 of these instruments can be placed through a single port incision to replicate the traction and counter-traction employed in open operations.

These technological advances have made thoracoscopic surgery safer allowing for the expansion of indications for thoracoscopic resection. This potentially increases treatment options for patients who otherwise may have previously been considered inoperable with thoracotomy. Here we will discuss key technical points/considerations for thoracoscopic resection for lobectomy in locally advanced non-small cell carcinoma, thoracoscopic pneumonectomy, and thoracoscopic *en bloc* chest wall resection.

VATS lobectomy for locally advanced NSCLC

Thoracoscopic lobectomy for locally advanced NSCL,

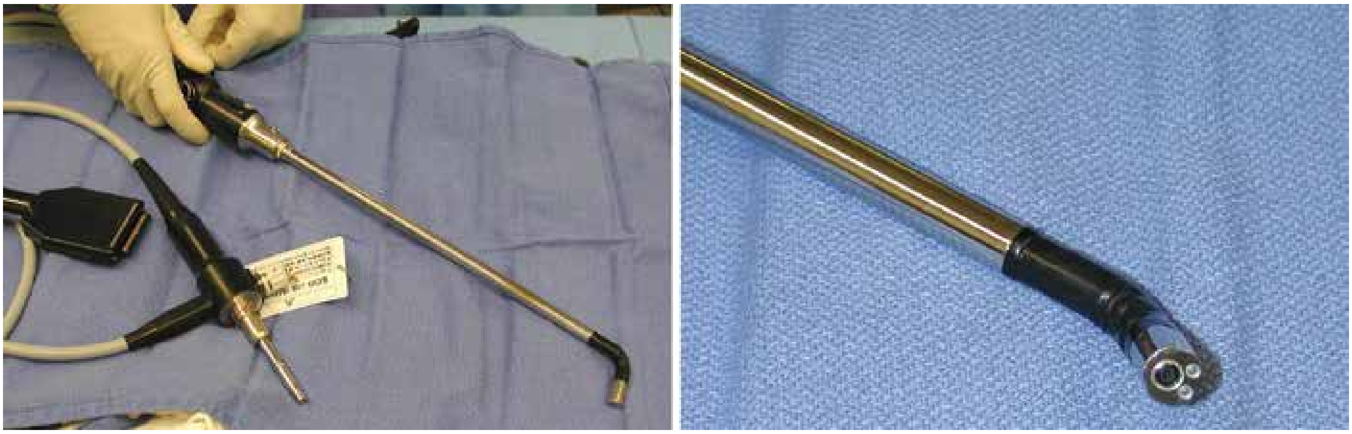

Figure 1 High definition, thoracoscopic video camera with deflectable tip. (Olympus Surgical and Industrial America Inc., Center Valley, PA).

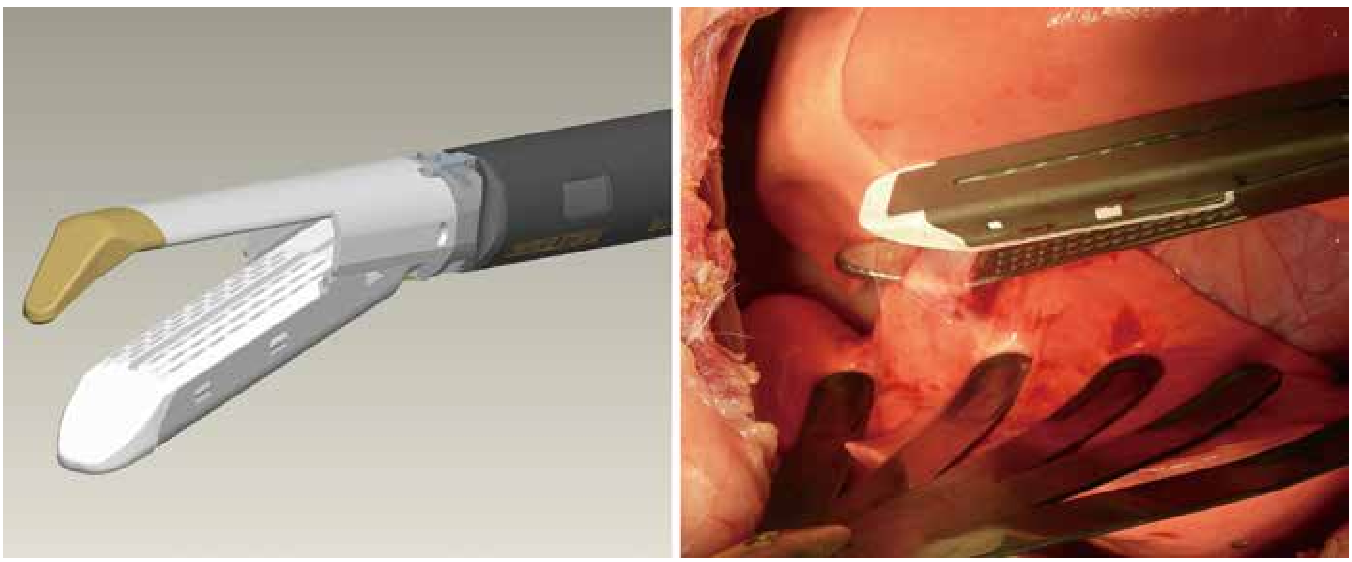

Figure 2 Curved-tip stapler technology which facilitates improved passage around anatomic structures. (Covidien, Inc., Mansfield, MA).

though not as common as resection for early stage disease, has been reported (12). We consider tumors that are greater than 4 cm in diameter, T3 or T4 tumors (based on the American Joint Committee on Cancer, 7th edition), or tumors requiring neoadjuvant treatment to be locally advanced. Though a 4 cm tumor today may not seem advanced, original indications for VATS lobectomy during its evolution were for peripheral tumors less than 3 cm in diameter. Also, patients with tumors of this size were shown to have a survival advantage with adjuvant chemotherapy by Cancer and Leukemia Group B (CALGB) 9,633, suggesting more aggressive tumor characteristics in this subgroup of patients (13).

As surgical techniques have become refined and surgical instrumentation becomes more advanced, VATS has become our preferred approach for most forms of locally advanced NSCLC. We expect the demonstrated benefits associated with thoracoscopic resection for early stage NSCLC to translate to resections involving more locally advanced disease, provided overall tissue trauma remains less than for open procedures. Thoracoscopic lobectomy for advanced lung cancer can be performed safely with an acceptable morbidity and mortality (12). Perioperative complications were equal in patients undergoing thoracoscopic resection when compared to those having a thoracotomy, and a higher proportion of patients who underwent VATS resection were

Figure 3 5 mm low profile thoracoscopic instruments. (Sontec Instruments, Centennial, CO).

Figure 4 Adjustable laparoscopic liver retractors that can be positioned around the bronchus to facilitate specimen retraction for division of the bronchus. (Cardinal Health, Dublin, OH).

able to go on to receive adjuvant therapy. No difference was observed for disease-free and overall survival.

Thoracoscopic resections for locally advanced diseases pose challenges not encountered when performing typical VATS operations for early stage disease. Centrally located tumors and those in close proximity to major vascular structures, granulomatous or other lymphadenopathy, and post-neoadjuvant therapy effects increase thoracoscopic dissection complexity and difficulty. Tumors may invade the fissure requiring an *en bloc* segmental resection of an adjoining lobe. While completing the fissures first can be occasionally challenging, this ultimately leads to an easier, safer dissection of the lobe's vascular and bronchial structures. For instance, such methods improve the exposure to vessels like the ascending posterior artery to the right upper lobes. They also make performance of a sleeve resection easier by removing other intervening anatomic structures. Practicing fissure division techniques on less challenging cases increases operator capability when confronted by difficult tumor anatomy.

With larger tumors and difficult anatomic dissections, having proper traction and counter-traction on structures is of paramount importance. Usually when difficulty arises during a dissection, one can find inadequate retraction angles to be the source of trouble. Proper retraction angles to facilitate safe dissection are now easier to create, and quickly adjust, with newer low profile 5 mm round shaft thoracoscopic instruments (*Figure 3*). Another concern regarding thoracoscopic approaches for technically difficult cases is that increased operative time, with prolonged general anesthesia, will prove detrimental to the patient and negate any proposed benefits of a thoracoscopic approach. In our previously reported data for VATS lobectomies for locally advanced NSCLC, median operative time for the thoracoscopic group was 231 minutes (96-574), compared to 202 minutes for the open group (105-317) (12). We feel these operative times are not unreasonable. Previous concerns regarding the duration of general anesthesia exposure and its impact on patient results may not be as relevant if the operation can be completed with VATS. For instance, increased resources like extended operative times with thoracoscopy may be justified if avoiding thoracotomy in a frail patient reduces the need for prolonged convalescence.

VATS Pneumonectomy

While thoracoscopic lobectomy is an established operation, the safety and potential benefits of thoracoscopic pneumonectomy are uncertain. Thoracoscopic pneumonectomy utilizing a traditional 3-incision VATS approach has been described (14), and recently single-port pneumonectomy has recently been reported (15). Whether the well-defined benefits noted with thoracoscopic lobectomy translate to thoracoscopic pneumonectomy is uncertain.

We reported the intention-to-treat results from our modest experience and demonstrated that thoracoscopic pneumonectomy is a safe alternative to open pneumonectomy. Results were equivalent to those patients undergoing pneumonectomy using a standard thoracotomy approach (16). Median blood loss was equal, as well as median ICU length of stay and hospital length of stay. Operations were longer, and though operative blood loss was similar, transfusions were increased in the thoracoscopic pneumonectomy group. Major complications were similar for both groups. Though a significant conversion rate of 25% was noted, there were no significant differences in any postoperative complications between the thoracoscopic group and the group requiring emergent conversion (16). When long-term survival was examined in patients undergoing thoracoscopy versus thoracotomy for elective pneumonectomy, results were equivalent (17). *Table 1* summarizes technical challenges

Table 1 Technical challenges and hurdles associated with VATS pneumonectomy

Challenge	Solution
Concern regarding the possibility of stapler induced injury or stapler misfire when coming across and dividing main pulmonary artery with limited vascular control	Guiding stapler with red rubber "leader" facilitates safer passage across the main pulmonary artery
Safety of pulmonary artery dissection	Dissection onto the mainstem bronchus when performing mediastinoscopy/Transcervical Extended Mediastinal Lymphadenectomy (TEMLA) will make vascular dissection easier/safer at time of VATS resection
Tissue coverage for the bronchial stump	Creation of a pericardial fat pad and/or pleural flap is safe Thoracoscopic intercostal muscle flap is also feasible
Getting proximal division point on the main stem bronchus, especially with a left pneumonectomy	Lung retraction instrumentation now allow for aggressive retraction for proximal division of the bronchus Use of Transcervical Extended Mediastinal Lymphadenectomy (TEMLA) before resection
Technical consideration of retracting the whole lung when dividing the mainstem bronchus	A laparoscopic adjustable liver retractor (Snowden-Pencer Diamond-Flex) placed around the main stem bronchus allows for retraction of the entire lung (*Figure 4*)
Removing the specimen from the chest cavity	Larger 8 inch by 10 inch Nylon extraction sac Facilitates removal of the entire lung

associated with performing VATS pneumonectomy and solutions for overcoming them.

VATS Resection with *en bloc* chest wall resection

Performing thoracoscopic *en bloc* chest wall resection at the time of lobectomy constitutes another area of potential expansion for VATS techniques. As noted with the expansion of techniques and indications for VATS lobectomy and pneumonectomy, improved instrumentation has made thoracoscopic chest wall resection feasible. Our initial experience indicates that it is technically safe, but large single center series are not yet available to define refined techniques on this subject.

Technical maneuvers already exist that enable minimally invasive approaches to the chest wall for tumors and other pathology related to thoracic bone anatomy. Special bone cutting tools have been developed by surgeons in other subspecialties including minimally invasive devices to procure bone grafts (18). For chest wall resections in which a large chest wall defect will be expected, minimally invasive options now exist. Muscle flaps commonly required in complex thoracic chest wall resections for coverage like the latissimus dorsi have been mobilized by videoendoscopy (19). Few reports have good comparison groups when evaluating postoperative recovery effects. Advantages for VATS over open thoracotomy may be counterintuitive in the context of chest wall resections, however pain physiology theories exist to explain why pain would be potentially less with approaches that "on the surface" are less invasive (20). This is because the innervation for that area is removed by the resection and the remainder of the wound space stimulation, which in its totality induces chronic pain, is minimized.

Patient selection criteria for whom to apply a thoracoscopic approach for chest wall resection are not clearly defined and will be influenced by surgeon experience. As was our approach when expanding indications for VATS lobectomy and pneumonectomy, our preferred group for extending thoracoscopic indications includes those frail patients expected to have the most difficulty with thoracotomy. This similar ideology has been applied by another group for less invasive laser resection for T3 chest wall tumors in 10 patients who had poor pulmonary function (21). Since improved exposure begets operative precision, we are confident that surgical planning by adding an internal VATS view of rib invasion before or during thoracotomy is an improvement over the traditional reliance on normal-appearing external landmarks.

Because the experience with thoracoscopic approaches for tumors is limited largely by the infrequent nature

Table 2 Technical challenges and considerations for en bloc chest wall resection

Challenge	Solution
Division of the ribs/bone	Thoracoscopic bone shears (Sofamor-Danek™) exist to facilitate rib division. Standard bone cutting tools can be used for division near utility incision
Chest wall soft tissues	Standard thoracoscopic cutting energy devices allow for division of muscle and the neurovascular bundle
Location of tumor invasion related to standard VATS incisions	Utility port location may need to be altered in some cases. Moving it towards the anterior thorax may aid in dissection as well as extraction of the specimen (due to the wider intercostal space)
Pancoast Tumors/ Spine Invasion	Combined approach with surgical spine team utilizing posterior spine approach, followed by VATS approach to lung resection is feasible
Extraction of the specimen	Sturdy 8 by 10 in Nylon extraction sac. Orientation of the rib block perpendicular to the extraction site while delivering the ribs through the port first. An alternative site for extraction may be necessary

of suitable cases, validating long terms results will be challenging. This will require substantial time and a cooperative framework to determine if there are any long-term advantages for a thoracoscopic approach to tumors with chest wall invasion, or even primary chest wall tumors. In the meantime, knowledge of the techniques that will be useful for experienced VATS surgeons who encounter complex anatomic situations will continue to expand and be refined. *Table 2* summarizes technical considerations for thoracoscopic chest wall resection.

Summary

Initial fears regarding the oncologic equivalence of the thoracoscopic and open techniques for resecting NSCLC have not been realized. Reported data to date indicate that even in advanced NSCLC requiring pneumonectomy, the overall and disease free survival are equivalent for patients undergoing VATS versus thoracotomy. Furthermore, these results have occurred during a time where the complex procedures are still in a relatively early stage of refinement and we sense that results will improve as we make adjustments to speed the operations and further reduce conversions and complications. VATS lobectomy for early stage disease produces oncologically similar results with open techniques, and long term studies will determine if the same hold true for more advanced case. Early indications are favorable. This finding is in accordance with others who have hypothesized that the reduced inflammatory response associated with thoracoscopy may be associated with equivalent or even improved long-term survival (22,23).

VATS lobectomy, pneumonectomy, and chest wall resection for advanced lung cancer can be performed safely with an acceptable mortality rate. VATS offers the benefit of increased tolerance for adjuvant therapy so if high VATS reliability is achieved, it may be reasonable someday to consider resection first for some patients who currently undergo induction chemoradiotherapy for their disease. The low morbidity of VATS reported for early stage lung carcinoma, though not definitively proven for advanced stage NSCLC, will be expected as experience builds.

Further analyses of outcomes for thoracoscopic resection of advanced stage disease are ongoing. This is particularly important given the large number of frail patients with advanced stage disease who require multimodality therapy, which can be difficult to tolerate. Conversions, though increased in frequency, are not associated with a significant change in short-term or long-term outcomes. Continued improvements in instrument technology and surgical technique will only continue to expand the possibilities for minimally invasive pulmonary resections, as well as those for primary chest wall tumors.

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Feasibility of complete video-assisted thoracoscopic surgery following neoadjuvant therapy for locally advanced non-small cell lung cancer

Jun Huang[1,2], Xin Xu[1,2], Hanzhang Chen[1,2], Weiqiang Yin[1,2], Wenlong Shao[1,2], Xinguo Xiong[1,2], Jianxing He[1,2]

[1]Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; [2]Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China

Correspondence to: Jianxing He, MD, PhD, FACS. Department of Cardiothoracic Surgery, the First Affiliated Hospital of Guangzhou Medical University, No. 151, Yanjiang Rd, Guangzhou 510120, Guangdong Province, PR China. Email: drjianxing.he@gmail.com.

Objective: To explore the feasibility of complete video-assisted thoracoscopic surgery (c-VATS) following neoadjuvant therapy (chemotherapy, targeted therapy and radiotherapy, either alone or in combination) for the treatment of patients with non-small cell lung cancer (NSCLC).

Methods: The clinical data of 43 NSCLC patients undergoing c-VATS following neoadjuvant therapy were retrospectively analyzed, including the preoperative functional indicators, staging, concurrent diseases, surgical techniques, operation time, number of lymph nodes dissected and postoperative drainage time and quantity, postoperative hospital stay, postoperative complications, and survival.

Results: From January 2006 to March 2012, a total of 43 patients with stage IIA-IIIB NSCLC were included in this study (IIIA: 27 cases, 62.8%; IIIB: 11 cases, 25.6%), including 32 males (74.4%) and 11 females (25.6%). Forty-two patients were operated successfully, 28 underwent pulmonary lobectomies (including 9 bronchial sleeve resections), 5 had double lobectomies, 5 had wedge resections, and 4 had total pneumonectomies. Seven patients were referred to undergo Hybrid VATS (7/42, 16.7%). The mean length of the operation was 160.48±16.52 min (range, 130-180 min); the intraoperative blood loss was 253.57±117.08 mL; the number of lymph nodes dissected was 16.88±10.93; the postoperative drainage time was 1-7 d (mean: 2.62±0.96 d); and the postoperative hospital stay was 3-7 d (mean: 5.45±1.30 d). The incidence of postoperative complications was 9.5% (4/42), and the perioperative mortality was 2.4% (1/42). The 1-, 2-, and 3-year overall survival rates were 94%, 79%, and 65%, respectively.

Conclusions: c-VATS following neoadjuvant therapy is safe and feasible for the treatment of locally advanced NSCLC.

Keywords: Non-small-cell lung cancer (NSCLC); neoadjuvant chemotherapy; targeted therapy; complete video-assisted thoracoscopic surgery (c-VATS)

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Introduction

Neoadjuvant therapy (preoperative chemotherapy, targeted therapy and radiotherapy, either alone or in combination) can significantly improve the resection rate for patients with locally advanced non-small cell lung cancer (NSCLC) and can prolong their survival (1). However, there is also concern that neoadjuvant therapy may promote pleural adhesion and vascular fragility, which is unfavorable to the anatomy and hemostasis and may increase the postoperative complication rate and perioperative mortality (2). The toxic effects of neoadjuvant therapy may undermine the constitution of

Table 1 Characteristics of 43 patients with stage IIa-IIIb NSCLC who underwent c-VATS following neoadjuvant therapy

Characteristic	No. (%)
Gender	
Male	32 (74.4)
Female	11 (25.6)
ECOG PS	
0	21 (48.8)
1	22 (51.2)
Method for definite diagnosis of histological types	
EBUS	29 (67.4)
CT-guided biopsy	11 (25.6)
Mediastinoscopy	3 (7.0)
Histological types	
Adenocarcinoma	21 (48.8)
Squamous cell carcinoma	20 (46.5)
Adenosquamous carcinoma	2 (4.7)
Degree of differentiation	
Undifferentiated	5 (11.6)
Poorly differentiated	21 (48.8)
Moderately differentiated	16 (37.2)
Highly differentiated	1 (2.3)
Clinical TNM staging approach	
PET-CT	13 (30.2)
CT	37 (86.0)
EBUS	11 (25.6)
Mediastinoscopy	3 (7.0)
Clinical TNM staging	
IIa	3 (7.0)
IIb	2 (4.6)
IIIa	27 (62.8)
IIIb	11 (25.6)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; EBUS, Endobronchial Ultrasound; PET-CT, Positron Emission Tomography-Computed Tomography.

patients and affect the patients' ability to heal, making it difficult for patients to tolerate the conventional open thoracotomy (3), and the neoadjuvant therapy thus is not conducive to patients who were planed to undergo the surgical resection.

Compared with the conventional open thoracotomy, complete video-assisted thoracoscopic surgery (c-VATS) is less invasive and allows a faster recovery among patients (4,5). Theoretically, certain patients with poor physical fitness can still receive c-VATS after neoadjuvant therapy, even if they are unable to tolerate open thoracotomy. VATS has been performed in our center since 1994. To date, we have an accumulated experience of more than 1,000 cases of VATS (c-VATS, Hybrid VATS) lobectomies (6-10), including more than 150 cases of VATS sleeve lobectomies (7). Since 2006, we have attempted to perform c-VATS in locally advanced NSCLC patients after neoadjuvant therapy. To the best of our knowledge, there was no report on the feasibility and clinical effectiveness of c-VATS following neoadjuvant therapy for the treatment of locally advanced NSCLC. In this study, we explored the feasibility of c-VATS following neoadjuvant therapy (chemotherapy, targeted therapy and radiotherapy, either alone or in combination) for the treatment of patients with locally advanced NSCLC, and its perioperative complications.

Patients and methods

Patients

A total of 43 IIA-IIIB NSCLC patients, who were treated in our center from January 2006 to March 2012, were included in this study. All patients were stratified based on their ECOG performance status [0-1]. These patients completed preoperative chemotherapy, targeted therapy, and radiotherapy (alone or in combination) and underwent c-VATS. There were 32 men and 11 women in the study, aged 35-76 years (mean: 56.30±10.15 years; median: 57 years).

All cases were histopathologically diagnosed as NSCLC preoperatively. The histological diagnosis was confirmed by fibrobronchoscopy, EBUS and CT-guided percutaneous needle biopsy. The diagnoses included adenocarcinoma (n=21, 48.8%), squamous cell carcinoma (n=20, 46.5%) and adenosquamous carcinoma (n=2, 4.7%). The types included undifferentiated carcinoma (n=5, 11.6%), poorly differentiated carcinoma (n=21, 48.8%), moderately differentiated carcinoma (n=16, 37.2%) and highly differentiated carcinoma (n=1). The clinical stages were clinically assessed and intraoperatively confirmed through PET-CT, MRI, and CT. Cases of clinical stages N2 or N3 were staged through mediastinoscopy or EBUS. TNM staging was based on the 2009 UICC staging criteria (7^{th} edition) (11) with 27 cases of Stage IIIA (62.8%) and 11 cases of stage IIIB (25.6%) (*Table 1*).

Neoadjuvant therapy

The patients were requested to select a neoadjuvant

Table 2 Neoadjuvant treatment regimens of the 43 patients with stage IIa-IIIb NSCLC and evaluation of their effectiveness

Treatment regimen	Effectiveness, n (%)			
	CR	PR	SD	PD
Targeted therapy (Gefitinib)	2 (4.7)	2 (4.7)	1 (2.3)	–
Neoadjuvant chemotherapy				
NP	–	1 (2.3)	–	–
GP	–	5 (11.6)	–	–
DocCarbo	1 (2.3)	2 (4.7)	2 (4.7)	–
PexCarbo	1 (2.3)	5 (11.6)	6 (14.0)	–
Concurrent chemoradiotherapy				
NP + radiotherapy (40 gy)	–	1 (2.3)	–	–
GP + radiotherapy (40 gy)	–	1 (2.3)	–	–
DP + radiotherapy (40 gy)	1 (2.3)	9 (20.9)	–	–
Sequential chemoradiotherapy				
GP + radiotherapy (40 gy)	–	2 (4.7)	–	–
DP + radiotherapy (40 gy)	–	1 (2.3)	–	–

Gefitinib Tablets, AstraZeneca UK, 250 mg (one tablet) once daily, taken with food or after fasting; GP (gemcitabine + cisplatin): gemcitabine 1,000 mg/m^2, intravenous infusion, d1, d8; total cisplatin 90 mg/m^2, intravenous infusion, d1-3, 21 days as one cycle; NP (vinorelbine + cisplatin), vinorelbine 25 mg/m^2, intravenous infusion, d1, d8; total cisplatin 90 mg/m^2, intravenous infusion, d1-3, 21 days as one cycle; DocCarbo (docetaxel + carboplatin), docetaxel injection, administered by intravenous infusion, 75 mg/m^2 intravenous infusion, d1, AUC (area under the curve) method to calculate the carboplatin dose, AUC =5.5, 21 days as one cycle; DP (docetaxel + cisplatin), docetaxel injection, intravenous infusion, 75 mg/m^2, intravenous infusion, d1, total cisplatin 90 mg/m^2, intravenous infusion, d1-3, 21 days as one cycle; PexCarbo (pemetrexed + carboplatin), pemetrexed injection, administered by intravenous infusion, 75 mg/m^2, intravenous infusion, d1, AUC (area under the curve) method to calculate the carboplatin dose, AUC=5.5, 21 days as one cycle.

treatment regimen based on the expression of Predictive Molecular Markers, including TS (12), RRM1 (12), ERCC1 (13) and TUBB3, BRCA1, and TYMS protein, as determined by ICH and/or gene mutation test results. The neoadjuvant treatment approaches that were adopted included preoperative targeted therapy, preoperative chemotherapy, preoperative concurrent radiochemotherapy, and preoperative sequential radiochemotherapy (*Table 2*). Five patients positive in the EGFR gene mutation detection received gefitinib treatment. Other regimens included GP (n=8, gemcitabine + cisplatin), DocCarbo (n=6, docetaxel + carboplatin), DP (n=10, docetaxel + cisplatin), and PexCarbo (n=12, pemetrexed + carboplatin). Twenty-two patients received preoperative chemotherapy alone, 13 received concurrent radiochemotherapy, and 3 received sequential radiochemotherapy (*Table 2*). Patients underwent 2-3 cycles of neoadjuvant therapy. Four weeks after the end of treatment, the patient received CT scan again. If disease progression was confirmed by imaging, surgical treatment was not given; if staging down-regulation or no lesion progression was confirmed by the imaging, c-VATS was performed. The mean length of time from the end of the neoadjuvant therapy to the operation was 31.21±20.17 d (range: 3-79 d).

C-VATS surgical techniques

Body position

The patients underwent a double-lumen endotracheal intubation under general anesthesia; in a contralateral supine position, the upper limb of the affected side was positioned on the hand bracket.

Incision selection

The observation hole was positioned at the level of the 7th or 8th intercostal space on the posterior axillary line with the main manipulative incision 3 cm to the anterior axillary line as the center, an upper lobectomy at the 4th intercostal space and a lower lobectomy at the 5th intercostal space, which allowed two surgical tools to enter or leave simultaneously. The harmonic scalpel was operated together with the suturing instrument and the aspirator. The auxiliary manipulative incision, measuring approximately 1 cm in length, was made at the same intercostal space posterior to the posterior axillary line as the observation hole for the auxiliary operation.

Surgical approaches

The surgeon stood in front of the patient, completing the procedures through the manipulative incision via the screen without using the rib distractor during the operation or operating under direct vision. The veins, arteries, and bronchia were separated anatomically, and the lymph nodes in stations 10 and 11 were dissected. The specimen bags were inserted to remove lung tissue, and the mediastinal lymph node dissection was subsequently performed again (on the left, stations 4, 5, 6, 7, 8, and 9; on the right, stations 2, 4, 7, 8, and 9). For patients whose tumor masses were closely related to blood vessels or bronchia, bronchial/vascular sleeve resection was selected as appropriate, and the patients were transferred to Hybrid VATS when necessary. The specific procedures were conducted in accord with the literature (4,11). The volume of the fluid replacement was strictly monitored intraoperatively, and the tracheal catheter was extubated in a routine manner after the operation.

Observation indicators and follow-up

The c-VATS resection rate, rate of conversion to thoracotomy, operation time, intraoperative blood loss, number of lymph nodes dissected, postoperative catheter drainage time, postoperative hospital stay, and postoperative complications (e.g., air leakage, bronchopleural fistula, and wound infection) were observed. Patients received follow-up regularly after discharge. The first follow-up was conducted postoperatively at 2-4 w. During the first three years, patients were followed up every 3-6 months and every 6-12 months thereafter. Patients' survival was followed up via telephone, written communication, or site visit. Patients received routine outpatient examinations of a chest CT and abdominal B ultrasound. A brain MRI was conducted if necessary.

Statistical analysis

A survival analysis was conducted using the Kaplan-Meier method, and survival was calculated beginning with the point in time that point patients were diagnosed with NSCLC. Follow-up continued until May 17, 2002. $P<0.05$ is considered to be statistically significant. Data were entered into the database and statistically analyzed using SPSS13.0 software (SPSS, Inc, Chicago, IL).

Results

Clinical efficacy and toxic effects of neoadjuvant therapy

All 43 patients were followed up. There was no disease progression from the neoadjuvant therapy to the surgery; the postoperative histopathological stages of 25 patients were lowered, demonstrating the effectiveness of the neoadjuvant therapy; 18 patients had no changes in staging either before or after neoadjuvant therapy; 11 of these patients showed smaller lumps or lymph nodes with regard to imaging performance but did not reach PR. Among 25 patients who were responsive to the neoadjuvant therapy, one was pathologically completely response (pCR) after the operation (*Table 2*).

The most important adverse reactions of neoadjuvant targeted therapy were rashes and constipation. The primary adverse reactions of preoperative chemotherapy included leukopenia, nausea/vomiting, and hair loss, including grade I-II leukopenia (n=17), grade III leukopenia (n=3), grade I-II nausea and vomiting (n=8) and grade III nausea and vomiting (n=3), which were alleviated after symptomatic treatment. The common side effects of preoperative concurrent radiochemotherapy and sequential radiochemotherapy also included radiation esophagitis (n=2) and radiation pneumonia (n=5).

Surgical results and complications

Forty-two of the 43 patients underwent successful resections with a resection rate of 97.7% (42/43). Seven patients were transferred to receive Hybrid VATS (7/42, 16.7%). The operation time was 130-180 min (mean: 160.48±16.52 min); the intraoperative blood loss was 253.57±117.08 mL; the number of lymph nodes dissected was 16.88±10.93; the postoperative drainage time was 1-7 d (mean: 2.62±0.96 d); and the postoperative hospital stay was 3-7 d (mean: 5.45±1.30 d). The surgical approaches included c-VATS lobectomy (n=28, including 9 cases of bronchial sleeve resection), c-VATS double lobectomy (n=5), c-VATS wedge resection (n=5), and c-VATS total pneumonectomy

Table 3 Surgical outcomes of 42 patients undergoing c-VATS

Item	No.	Operation time (min)	No. of lymph nodes dissected	Intraoperative blood loss (mL)	Postoperative drainage days (days)	Postoperative hospital stay (days)
Surgical procedure						
Lobectomy	19	156.32±13.83	18.32±13.18	247.37±88.94	2.79±0.71	5.26±1.15
Double lobectomy	5	162.00±20.49	19.40±6.12	280.00±164.31	2.60±1.14	5.40±1.52
Wedge resection	5	158.00±14.83	16.60±12.32	190.00±22.36	2.20±1.10	5.80±1.10
Total pneumonectomy	4	165.00±19.15	16.25±9.85	200.00±70.71	2.75±0.50	5.50±1.00
Sleeve resection	9	167.78±19.86	12.89±7.96	311.11±169.15	2.33±1.09	5.67±0.87
Surgical results						
R0	40	160.50±16.94	16.80±11.20	258.75±117.06	2.68±0.86	5.10±1.17
R1	1	160.00	20.00	200.00	3.00	5.00
R2	1	160.00	17.00	100.00	3.00	1.00
Resection						
Right upper lobe	14	163.57±14.47	17.14±9.33	292.86±139.86	2.36±1.01	4.50±1.40
Right middle lobe	4	162.50±12.58	18.50±6.56	237.50±47.87	2.00±0.82	4.75±0.50
Right lower lobe	4	165.00±10.00	24.00±23.71	175.00±50.00	3.50±0.58	5.75±1.26
Left upper lobe	7	157.14±22.15	9.43±4.20	271.43±111.27	2.29±0.95	4.86±1.46
Left lower lobe	4	142.50±15.00	21.25±15.22	200.00±81.65	3.25±0.96	5.50±1.00
Left whole lung	3	167.67±23.09	13.67±10.26	200.00±86.60	3.00±0.00	5.67±1.16
Double lobectomy	6	161.67±14.83	17.83±6.20	266.67±164.32	2.67±1.14	5.50±1.52
Postoperative TNM staging						
No tumor	1	140.00	14.00	200.00	3.00	5.00
Ia	3	156.67±5.77	15.67±7.10	233.33±115.47	3.00±1.00	5.33±2.08
Ib	6	161.67±22.29	10.50±3.78	325.00±204.33	2.17±0.98	4.83±1.72
IIa	9	156.67±18.03	18.00±10.71	227.78±66.67	2.78±0.97	5.78±1.09
IIb	6	170.00±16.73	14.83±9.64	241.67±102.06	2.50±1.38	4.50±1.22
IIIa	12	156.67±13.71	19.67±14.26	233.33±65.13	2.50±1.00	4.67±1.30
IIIb	5	170.00±14.14	19.60±13.10	300.00±183.71	2.80±0.45	5.20±0.45
Total	42	160.48±16.52	16.88±10.93	253.57±117.08	2.62±0.96	5.45±1.30

(n=4).

In terms of surgical complications, 5 patients developed postoperative complications (11.6%). Air leakage, chylothorax, wound infection, and respiratory failure were observed in five different patients. Another 67-year-old male patient died of heart failure three days after the operation. The patient had a history of preoperative hypertension and had received sequential radiochemotherapy. The patient continually suffered from radiation esophagitis, but his symptoms were remitted after symptomatic treatment. The operation went smoothly. On the second postoperative day, the patient died of sudden heart failure due to the inability to control the volume of fluid replacement. This patient represented the only perioperative death in this study (*Table 3*).

Postoperative survival rate

Patients in this study were all followed up for 4-68 months (mean: 20.78±16.89 months). Eleven patients suffered from a recurrence or metastasis after the operation: skull metastasis (n=5), bone metastasis (n=3), adrenal metastasis (n=2), and recurrence (n=1). The recurrent patient underwent an R2 resection. Among the 11 patients with a recurrence or metastases, 10 died, and one simultaneously underwent gamma knife treatment whole brain radiotherapy after brain metastasis and has survived for 23 months. The median overall survival (OS) in this study was 33.0 months (95% CI, 14.7-51.4 months) with a 1-year survival rate of 94%, a 2-year survival rate of 79%, and a 3-year survival rate of 65%.

Discussion

Studies have shown that c-VATS has validated advantages in the treatment of early-stage NSCLC; it has been applied in treating locally advanced NSCLC (7,14-16). In recent years, a series of studies have suggested that surgical resection following neoadjuvant therapy for patients with locally advanced NSCLC can significantly improve the surgical resection rate and survival (1). However, neoadjuvant therapy will inevitably lead to tissue adhesion, an indistinct interface and increased vascular fragility, and it will have a definite impact on patients' ability to heal. The incidence of surgical complications after neoadjuvant therapy has been reported to be as high as 35-43.5% (2,17). Therefore, the safety of surgical resection following neoadjuvant therapy remains a clinical concern. Theoretically, the difficulty of performing c-VATS following neoadjuvant therapy is greater than without neoadjuvant therapy. In fact, the length of the operation time is one of the commonly used indicators to evaluate the feasibility of c-VATS. The length of the operation time of c-VATS in this study was 130-180 min (mean: 160.93±16.59 min), which was consistent with times (130-168.6 min) in the previous published studies (15,18,19).

The postoperative drainage time and the length of the postoperative hospital stay can reflect the effects of surgery on patients' ability to heal. In our current study, the postoperative drainage time was 1-7 d (mean: 2.56±0.98 d), and the postoperative hospital stay was 3-7 d (mean: 4.98±1.32 d). Tomaszek *et al.* (18) reported that the postoperative drainage time in their study was 1-12 d (mean: 2 d), and the postoperative hospital stay was 1-12 d (mean: 4 d). The postoperative drainage time of the majority of other c-VATS procedures are in line with our results (14,15,20).

The rate of conversion to thoracotomy is another important indicator to evaluate the safety of VATS procedures. The literature shows that the rate of c-VATS conversion to thoracotomy ranges from 0-15.7% (14). No patient was converted to conventional thoracotomy in our study, but 7 patients were converted to Hybrid VATS with a conversion rate of 16.7%. It is believed that the preoperative adjuvant therapy (especially preoperative radiotherapy) has an obvious effect on a patient's body. In fact, this treatment can easily induce local tissue inflammation, edema and organization and thus increase the tissue's fragility, which can cause gap fuzziness and dense adhesion, making the surgery even more difficult. In this regard, Hybrid VATS has the advantages of thoracotomy under direct vision and a large operational space and at the same time can avoid the limitations of c-VATS; therefore, this therapy can replace thoracotomy in operations including tissue isolation, anatomic lobectomy, and systematic lymph node dissection (20). Lymph node dissection can be performed on different stations in line with the standards in this study with an average dissection number of lymph nodes of 16.88±10.93, which fully meets the criteria of conventional c-VATS and thoracotomy (14,15,21).

In this study, the incidence of postoperative complications and the mortality rate were 11.9% (5/42) and 2.4% (1/42), respectively, similar to those of thoracotomy following neoadjuvant therapy [Gilligan *et al.* (22): 10%, 224/229] and similar to those reported for other pure c-VATS procedures [McKenna *et al.* (16): 15.3%; Kim *et al.* (23): 9.1%]. A common concern is that adhesion due to neoadjuvant therapy can often result in a long operation time, high operational risk, and a high incidence of postoperative complications. However, this phenomenon was not observed in our study, which may be due to the following factors: (I) c-VATS is minimally invasive and less painful and predisposes patients to coughing. This treatment can therefore reduce infection, atelectasis, respiratory failure, and other complications caused by poor expectoration. In our current study, the mean postoperative drainage time did not exceed 3 days, which is more conducive to postoperative expectoration and also reduces the incidence of infections of the drainage opening; (II) c-VATS has a locally magnifying ability, which is not only beneficial to the identification of intraoperative vessels and bronchia but also conducive to the detection of small bleeding spots, lung fissures and bronchial fistulas, thereby reducing the occurrence of operation-related complications; (III) The surgeon's experience in managing complex and highly difficult procedures under c-VATS is also important to reduce the occurrence of postoperative complications and to lower the operative mortality. Our rich experience in VATS lobectomies (3) facilitated the launching of this study, which enrolled nine patients who received bronchial sleeve resection/plasty, four of whom received c-VATS (completed), 5 of whom were converted to Hybrid VATS (completed), and only one of the nine patients experienced chylothorax but without a bronchopleural fistula; (IV)

The application of neoadjuvant therapy was based on gene mutation detection and drug gene (protein) test results, which are conducive to increasing the tumor response rate and reducing the damage to normal tissues. In this study, all five of the EGFR mutation-positive patients selected gefitinib therapy; TS enzyme expression-negative patients selected pemetrexed therapy (12); all of the patients without remarkable clinical significance in multi-drug gene (protein) expression selected the third-generation platinum-based chemotherapy with an overall response rate of 58.1%. These approaches can avoid poor impacts (e.g., poor target effects, strong impact on normal tissue, and impaired immunity) due to less optimized neoadjuvant therapy; (V) Because the impact of the different neoadjuvant therapy regimens on postoperative recovery differs, it is important to reduce the difficulty of the operation by selecting neoadjuvant therapy regimens based on genetic testing and drug gene (protein) detection results while reducing the proportion of preoperative radiotherapy. As shown by our study, the pre-operative application of targeted therapy drugs had a minimal impact on human tissues and typically did not cause remarkable tissue adhesion, scarring, or edema while maintaining a vascular toughness that was close to normal. On the contrary, radiotherapy often leads to breast tissue edema or adhesion, thus increasing the difficulty of the procedures. Among the 16 patients receiving preoperative radiotherapy, 6 patients (6/16, 37.5%) were converted to Hybrid VATS; among the remaining patients who did not receive radiotherapy, only one patient (1/27, 3.7%) was converted to Hybrid VATS. In addition, several scholars (17) have argued that a preoperative radiotherapy dose of >45 Gy might significantly increase the incidence of postoperative complications. This finding was validated in our current study: the incidence of postoperative complications was not high among patients receiving preoperative radiotherapy, which might be observed because the radiotherapy dose in this study was not higher than 40 Gy.

The long-term efficacy of this study was satisfactory with a 1-year survival rate of 94%, a 2-year survival rate of 79%, and a 3-year survival rate of 65%, which may be observed because c-VATS is minimally invasive. After neoadjuvant therapy, patients may still tolerate c-VATS, even with a poor constitution or impaired lung function. Therefore, more patients can receive this procedure, and the overall survival rate is also increased. Patients can recover from c-VATS faster and were able to complete postoperative adjuvant radiochemotherapy. Lymph node dissection of c-VATS is not inferior to conventional thoracotomy. The rational combination of c-VATS with neoadjuvant treatment improves the overall response rate. However, a larger sample size is warranted to validate this conclusion further.

This study investigated the impact of neoadjuvant therapy on c-VATS among NSCLC patients, but it failed to compare the findings with those of thoracotomy. Furthermore, the success of c-VATS is highly dependent on the surgeon's experience and skills. The postoperative complications and long-term efficacy differ if the c-VATS is performed by different surgeons. Additionally, the small sample size of this study can easily cause bias. Neoadjuvant therapy for tumors has become increasingly popular (24), and in our current study, we assessed neoadjuvant treatment regimens based on the results of genetic tests and drug molecular detection and assessed the relevant indicators. However, these detection methods also resulted in a diversity of neoadjuvant treatment regimens, causing the statistical analysis to be more difficult. No definite conclusion was reached on the impact of diverse neoadjuvant regimens on the perioperative and long-term survival rates of c-VATS. Finally, because this study was initiated in 2006, during which both the 6th and the 7th editions of the TNM staging system were adopted, and although the 7th edition of the system was used during patient enrollment, the criteria used for assessing the efficacy of neoadjuvant therapy were not fully consistent. Thus, multi-center, prospective, randomized and controlled trials with larger sample sizes are warranted to clarify further the role of c-VATS following neoadjuvant therapy in the treatment of NSCLC.

In conclusion, c-VATS following neoadjuvant therapy is safe and feasible for the treatment of locally advanced NSCLC, and its long-term efficacy is satisfactory. In our current study, the application of multiple preoperative assessment methodologies, including fibrobronchoscopy, EBUS, PET-CT, mediastinoscopy, and chest CT, improved the outcomes by displaying the scope of the intrabronchial and peripheral tumor invasion and enabling the assessment of the effectiveness of the surgical regimens. Furthermore, the routinely performed intraoperative frozen pathological examination of the resection margins ensured a cancer-negative surgical margin and effectively reduced postoperative local recurrences.

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Nonintubated thoracoscopic surgery: state of the art and future directions

Ming-Hui Hung[1,2], Hsao-Hsun Hsu[3], Ya-Jung Cheng[1], Jin-Shing Chen[3,4]

[1]Department of Anesthesiology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; [2]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan; [3]Division of Thoracic Surgery, [4]Division of Experimental Surgery, Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

Correspondence to: Jin-Shing Chen, MD, PhD. Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; 7, Chung-Shan South Road, Taipei 10002, Taiwan. Email: chenjs@ntu.edu.tw; Ya-Jung Cheng, MD, PhD. Department of Anesthesiology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; 7, Chung-Shan South Road, Taipei 10002, Taiwan. Email: chengyj@ntu.edu.tw.

Abstract: Video-assisted thoracoscopic surgery (VATS) has become a common and globally accepted surgical approach for a variety of thoracic diseases. Conventionally, it is performed under tracheal intubation with double lumen tube or bronchial blocker to achieve single lung ventilation. Recently, VATS without tracheal intubation were reported to be feasible and safe in a series of VATS procedures, including management of pneumothorax, wedge resection of pulmonary tumors, excision of mediastinal tumors, lung volume reduction surgery, segmentectomy, and lobectomy. Patients undergoing nonintubated VATS are anesthetized using regional anesthesia in a spontaneously single lung breathing status after iatrogenic open pneumothorax. Conscious sedation is usually necessary for longer and intensively manipulating procedures and intraoperative cough reflex can be effectively inhibited with intrathoracic vagal blockade on the surgical side. The early outcomes of nonintubated VATS include a faster postoperative recovery and less complication rate comparing with its counterpart of intubated general anesthesia, by which may translate into a fast track VATS program. The future directions of nonintubated VATS should focus on its long-term outcomes, especially on oncological perspectives of survival in lung cancer patients. For now, it is still early to conclude the benefits of this technique, however, an educating and training program may be needed to enable both thoracic surgeons and anesthesiologists providing an alternative surgical option in their caring patients.

Keywords: Thoracoscopy; lung cancer; intubation, anesthesia, intercostal nerve block; thoracic epidural anesthesia

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Introduction

In the past two decades, video-assisted thoracoscopic surgery (VATS) has become a common and globally accepted alternative in place of thoracotomy to surgically treated patients with various thoracic conditions involving lungs, pleura and mediastinum (1-3). A minimally invasive approach is demonstrated to be superior in shortening length of hospital stay, alleviating postoperative pain, improving postoperative lung function and reducing overall morbidities after surgery (4-6). Traditionally, intubated general anesthesia with one-lung ventilation, using a double-lumen tube or an endobronchial blocker, has been considered mandatory during VATS to obtain a quiet, optimally visualized and better surgical environment (7). In spite of well-tolerated, complications and adverse effects following intubated general anesthesia and one-lung ventilation are inevitable, including intubation-related airway trauma, ventilation-induced lung injury, residual neuromuscular blockade, impaired cardiac performance, and postoperative nausea and vomiting (8-10).

Recently, interests and efforts have been made to adopt a thoracoscopic technique without tracheal intubation for avoidance of intubation-related complications and for a smoother postoperative recovery. Successful results are accumulating not only from anecdotal case reports of difficult and high-risk patients not suitable for an intubated general anesthesia (11-14), but also from a systemic application of this technique to various thoracic procedures, including management of pneumothorax, wedge resection of pulmonary tumors, excision of mediastinal tumors, lung volume reduction surgery, segmentectomy, and lobectomy (15-35). Encouragingly, the safety and feasibility of this surgical modality were well established in previous studies. Although its short- and long-term benefits comparing to standard intubated general anesthesia are not clearly addressed yet, several prospective studies are recruiting patients by now to answer this issue.

In this article, we revisit the current literature about anesthetic management and results of nonintubated VATS in various thoracic diseases, and suggest its future role in the field of thoracic surgery.

Anesthetic management of nonintubated VATS

Nonintubated VATS entails thoracoscopic procedures performed under regional anesthetic techniques, with or without consciousness sedation, in spontaneously breathing patients. The anesthetic techniques consist of local anesthesia, intercostal nerve blocks, paravertebral blocks or thoracic epidural anesthesia. Mostly, thoracic epidural anesthesia can be enough to serve solo for nonintubated VATS (36).

To be feasible and safe in performing nonintubated VATS, anesthetic management should meet the considerable physiological derangements during the procedure. The pathophysiological disturbances are mainly attributed to spontaneous one-lung breathing in an open pneumothorax status, influence of the chosen anesthetic techniques and type of surgical manipulations (37).

Open pneumothorax after trocar insertion can cause the nondependent lung to collapse gradually so that nonintubated VATS can be performed. In the meantime, patients may become dyspneic or tachypneic because of open pneumothorax. In such circumstances, awake patients should be reassured and coached to slow their breath. However, sedation may be necessary occasionally if patients become anxious and panic. In patients with conscious sedation, incremental titration of opioid can also be used to attenuate the respiratory responses after open pneumothorax.

Hypoxemia and hypercapnia are always major concerns during one-lung ventilation in thoracic surgery, which may also develop in nonintubated VATS. On contrary to one-lung ventilation during intubated general anesthesia with neuromuscular blockade, efficient contraction of dependent hemidiaphragm in spontaneous one-lung breathing during nonintubated VATS preserves favorably match of ventilation and perfusion in a lateral decubitus position. However, a paradoxical respiratory pattern may cause carbon dioxide rebreathing from nondependent, collapsed lung while mediastinal shifting after open pneumothorax may decrease the compliance and tidal volume of the dependent lung. Fortunately, although hypercapnia may occur, they are usually mild and well-tolerated. After returning to two-lung breathing after surgery, the level of carbon dioxide returns to the normal level. In addition, oxygenation is usually satisfactorily maintained with supplemental oxygen via a facemask (29).

Current results of nonintubated thoracoscopic surgery

Management of lung tumor

As progresses in cancer screening and treatment, patients with lung tumors are increasing, and requiring thoracoscopic management of their lung tumors either for diagnostic or therapeutic purposes. Surgical treatment of lung tumors includes wedge resection, anatomical segmentectomy, lobectomy or pneumonectomy with or without mediastinal lymph node dissection, depending on the nature of the lung tumors (38).

In 2004, Pompeo and his coworkers evaluated the feasibility of awake thoracoscopic resection of solitary pulmonary nodules in 30 patients under sole thoracic epidural anesthesia (15). Comparing to patients with intubated general anesthesia, their results showed that awake technique were safely feasible with better patient satisfaction, less nursing care and shorter in-hospital stay. However, it is important to note that two of the awake patients were converted to intubated general anesthesia because of lung cancer requiring lobectomy via thoracotomy approach (15). Similar results were obtained in patients with metastatic lung tumors using awake VATS metastasectomy (19) and even via a single-port VATS approach (39).

For surgical management of primary lung cancer, major pulmonary resections such as segmentectomy or lobectomy with mediastinal lymph node dissection are usually necessary (38). However, these procedures are associated with longer operating time, frequent lung traction and intense hilar manipulation, which can trigger cough reflex in awake patients. When thoracic epidural anesthesia is used, the reactivity of coughing response can be exaggerated because of an unbalanced parasympathetic activity after sympathetic block (36). While Al-Abdullatief *et al.* used stellate ganglion block to attenuate cough reflex (18), Chen and his colleagues used ipsilateral intrathoracic vagal block to achieve effective control of cough reflex (29-33,40). In addition, intravenous opioid and propofol were titrated with monitoring of anesthesia depth to further control respiratory rate and alleviate anxiety of patients. Using their nonintubated methods, they reported that nonintubated VATS lobectomy and segmentectomy with mediastinal lymphadenectomy for early stage non-small cell lung cancer could be safely performed (29-33). Rates of conversion to intubated general anesthesia were reported to be between 2.3% to 10.0%, depending on the type of procedure and which could be further decreased as the learning curve progressed (29-33). In addition to be feasible and safe, nonintubated thoracoscopic lobectomy for lung cancer using thoracic epidural anesthesia also offered better postoperative pain control, lower rates of sore throat, earlier resumption of oral intake and shorter length of hospital stay with better noncomplication rates, when comparing to its counterpart of intubated general anesthesia (29,30,32), especially in geriatric lung cancer patients (32).

Spontaneous pneumothorax

Nonintubated VATS for wedge resection of blebs and pleural abrasion have been reported in several studies for management of either primary or secondary spontaneous pneumothorax with satisfactory results (11-13,20,39,41-48). High-risk patients with pneumothorax are usually considered difficult, and might be harmful, to maintain adequate respiratory function during intubated one-lung ventilation, including patients after pneumothorax (11,13,41,42), lung transplantation (47) or those pregnant women (43,46). Successful results are obtained in these high-risk patients using either local anesthesia, intercostal blocks, or thoracic epidural anesthesia.

In a small randomized trial performed by Pompeo *et al.*, 43 awake patients with spontaneous pneumothorax were anesthetized with sole thoracic epidural anesthesia to received VATS bullectomy and pleural abrasion (20). Their results have shown that the awake procedures were not only easily feasible, but also shorten the hospital stay, reduced the cost with comparable clinical outcomes to patients anesthetized with intubated general anesthesia (20). Noda *et al.* reported similar results in 15 patients with secondary spontaneous pneumothorax with shorter operating room stay and less respiratory complications in awake patients (42).

Recently, awake single-access (uniportal) VATS was also reported feasible for management of spontaneous pneumothorax (39,43,45), even in a case of bilateral pneumothorax (45).

Pleural effusion and empyema

Patients with pleural effusion are frequently associated with medical comorbidities. These patients therefore carry additional risks for intubated general anesthesia. However, chronic collapse of operated lung enables these patients to favorably tolerate surgical pneumothorax during spontaneous one-lung breathing. As a result, they rarely develop significant hypoxemia requiring additional ventilatory support and seem to be the optimal candidate for nonintubated VATS (49).

When management of pleural effusions with medical thoracoscopy, local anesthesia with or without sedation has been widely reported (16,21,50-53). In addition, thoracic paravertebral block or epidural anesthesia are also useful and reported for more accurate pleural biopsies or extensive pleurodesis to be easily performed by nonintubated VATS (14,22).

Moreover, Tacconi *et al.* had reported 19 cases with thoracic empyema treated with awake VATS decortication under sole thoracic epidural anesthesia or paravertebral block (24). Notably, conversion to lateral thoracotomy was performed in four patients because of thick pleural adhesions. The oxygenation was satisfactory during surgery except permissive hypercapnia developed in three patients but no need of conversion to intubated general anesthesia. Their results are successful and no recurrence requiring another surgery in all patients (24). Nonetheless, thoracic epidural catheterization in patients with empyema should be cautiously evaluated to avoid of epidural abscess resulting from bacterial contamination (54).

Emphysema and lung volume reduction surgery

Resectional lung volume reduction surgery is a palliative surgical treatment in severe emphysema patients with impaired exercise tolerance to improve pulmonary function, exercise capacity, and quality of life (55,56). However, it still carries high rates of mortality and morbidity, especially prolonged air leak after surgery (57,58). In 2006, Mineo *et al.* developed a novel nonresectional technique to perform awake lung volume reduction surgery in awake patients under thoracic epidural anesthesia (17). Their further studies including a randomized trial showed that awake nonresectional lung volume reduction surgery caused significantly functional improvement, including absolute increase in forced expiratory volume in one second, functional vital capacity and residual volume, improvement in exercise capacity index and 6-minute walking test. These improvements lasted for more than 24 months (26,27,59). Comparing to conventional intubated general anesthesia, durations of postoperative air leak and hospital stay were significantly shorter in awake technique, while 3-year survival was comparable (26,60). Similar results were also reported in patients with bullous emphysema (25,61).

Lung biopsy for interstitial lung diseases

Patients with interstitial lung disease are usually associated with impaired respiratory function (62). Although precise histopathologic characterization by surgical lung biopsy can help orient therapy and reliably predict prognosis, VATS biopsy using intubated general anesthesia still carries not negligibly mortality rate (63). In 2012, Pompeo and his colleagues reported 30 awake patients completed VATS biopsy for interstitial lung disease using thoracic epidural anesthesia or intercostal blocks without operative mortality and only one minor complication (3.3%) (28). In addition, precise histopathologic diagnosis was achieved in 29 (97%) patients. They concluded that awake VATS lung biopsy by regional anesthesia might become the safest and most accurate surgical method for obtaining precise histopathologic diagnosis, and potentially leading to better management of interstitial lung diseases (28).

Myasthenia gravis/thymectomy and biopsy of mediastinal masses

Patients with myasthenia gravis are usually sensitive to neuromuscular blockade and perioperative uses of muscle relaxants are associated prolonged mechanical ventilation or re-intubation in these patients. In addition, risks of intubated general anesthesia are increased when anterior mediastinal mass compresses the airway. The rationale of avoiding use of muscle relaxants in these patients, both Matsumoto *et al.* (64) and Al-Abdullatief *et al.* (18) reported satisfactory feasibility and results of awake VATS thymectomy using thoracic epidural anesthesia. VATS biopsy of anterior mediastinal masses could also be satisfactorily achieved with high diagnostic yield and no mortality and limited morbidity (23).

Other nonintubated VATS procedures were also reported to manage pericardial effusion (14) and treat palmar hyperhidrosis via thoracic sympathectomy (65).

Potential advantages of nonintubated VATS and its future directions

Although thoracic surgery has its traditional root under regional anesthesia without tracheal intubation, modern thoracoscopic surgery benefits and fundamentally develops under the establishment and safety practice of intubated general anesthesia with effective one-lung ventilation (7). Still, critically ill patients are sometimes challenging and their risks for an intubated general anesthesia are not negligible (9). For instance, prolonged use of mechanical ventilator and stay of intensive care unit are not uncommon for patients with compromised lung function or neuromuscular diseases such as myasthenic patients. Renaissance of nonintubated techniques for VATS, either in awake or sedative patients, are naturally applied not only on anecdotal difficult cases but also broadly on a variety of VATS procedures.

Current reported studies in the literature support the feasibility and safety of nonintubated VATS for management of pleural, mediastinal and pulmonary diseases. Potential advantages of nonintubated VATS are faster postoperative recovery and less over-all complication rates, by which enhance a short length of hospital stay. Therefore, use of nonintubated VATS may translate into a fast track protocol bypassing intensive care or postoperative ventilator support. For patients with high risks for an intubated general anesthesia, this technique may offer better chances for surgical treatment.

In addition to these beneficial early outcomes, nonintubated VATS under thoracic epidural anesthesia are also demonstrated to attenuate surgical stress responses as decreased level of stress hormones and preservation of function of natural killer cells, comparing to intubated general anesthesia (66,67). It is recently hypothesized

Table 1 Suggested indications and contraindications of nonintubated VATS

Indications
Patients with significant risks for an intubated general anesthesia
Simple and easy-to-perform procedures
Major pulmonary resections (requiring experienced surgical team consisting of both surgeons and anesthesiologists)
Contraindications
Hemodynamically unstable patients
Expected difficult airway management
Obesity (body mass index >30)
Expected dense and extensive pleural adhesions (previous ipsilateral chest surgery, pulmonary infection etc.)
Inexperienced and poorly cooperative surgical team
Large and central pulmonary lesions (>6 cm) for pulmonary resections
Thoracic spinal deformity and coagulopathy when thoracic epidural catheterization considered

that regional anesthesia and analgesia may protect cancer patients from recurrence or metastases after surgery (68-70). This implies that further investigation including long-term outcomes (recurrence-free survival or over-all survival) by large controlled trial is needed in attempts to develop safer, more effective and less invasive surgical strategies for an optimal treatment of lung cancer patients.

For institution applying this technique, we suggest that collaborative thoracic surgeons and anesthesiologists should select their patients carefully in the early phase of learning curve. Individualized decisions should be made according to the intended procedure, anesthetic method and characteristics of patients without jeopardizing the safety of patients. Suggested indications and contraindications of nonintubated VATS are listed in *Table 1*. Notably, nonintubated thoracoscopic experiences can be accumulated from simple and minor procedures. When both surgeon and anesthesiologist getting familiar with this technique, major pulmonary resections for lung tumors, such as segmentectomy or lobectomy, are feasible. However, we suggest an effective sedative anesthetic care and blockade of cough reflex are imperative in nonintubated procedures for major pulmonary resections. Monitoring of anesthetic depth and adequacy of ventilation are important for patients' safety, which requiring the continuing vigilance of caring anesthesiologists through the procedure. Even so, conversion to intubated general anesthesia may occasionally mandatory. Plans and equipment for a prompt conversion to intubated general anesthesia should be available immediately and performed without hesitation to decrease the risk of emergency intubation (29).

Conclusions

In a modern era of minimally invasive thoracoscopic surgery, we are encouraged that tracheal intubation with double lumen tube or bronchial blocker is no longer regarded as a prerequisite for single lung ventilation in series of reported studies. Nonintubated thoracoscopic surgery is feasible and safe in a variety of thoracic procedures, including pulmonary resection, empyema, and excision of pleural and mediastinal tumors. Although the risks and benefits of this technique are not clear yet, it seems to offer an equally effective and safe alternative for those patients with high risks to intubated general anesthesia. Postoperative recovery is faster with less complication rates. Nonetheless, further studies are still necessary to clarify the indications and true benefits of this technique and its potential beneficial role against postoperative recurrence in lung cancer patients.

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Anesthetic consideration for nonintubated VATS

Jen-Ting Yang[1], Ming-Hui Hung[1,2], Jin-Shing Chen[3,4], Ya-Jung Cheng[1]

[1]Department of Anesthesiology, [2]Graduate Institute of Clinical Medicine, [3]Division of Thoracic Surgery, [4]Division of Experimental Surgery, Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

Correspondence to: Ya-Jung Cheng, MD, PhD. Department of Anesthesiology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; 7, Chung-Shan South Road, Taipei 10002, Taiwan. Email: chengyj@ntu.edu.tw.

Abstract: In the recent decade, nonintubated-intubated video-assisted thoracoscopic surgery (VATS) has been extensively performed and evaluated. The indicated surgical procedures and suitable patient groups are steadily increasing. Perioperative anesthetic management presents itself as a fresh issue for the iatrogenic open pneumothorax, which is intended for unilateral lung collapse to create a steady surgical field, and the ensuing physiologic derangement involving ventilatory and hemodynamic perspectives. With appropriate monitoring, meticulous employment of regional anesthesia, sedation, vagal block, and ventilatory support, nonintubated VATS is proved to be a safe alternative to the conventional intubated general anesthesia.

Keywords: Anesthesia; thoracoscopy; nonintubated; thoracic epidural anesthesia (TEA); intercostal nerve block; bispectral index

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Introduction

For the conventional idea of video-assisted thoracoscopic surgery (VATS), ventilation control and lung separation/isolation was presumably thought to be vital for the safety and feasibility of the procedure (1). With the advent of modern imaging and monitoring technology, nonintubated VATS has brought a new possibility of breakthrough to this tenet.

In the recent decade, nonintubated VATS has been intensively researched and reported, which has been advocated to be a rising alternative to the conventional intubated VATS with general anesthesia from several perspectives, such as surgical and anesthetic feasibility and safety (2-10), perioperative immunology (11,12), and outcome analysis (13-17).

The aim of this article is to introduce the major anesthetic consideration and the management experience of our group with a problem-based fashion, in the hope of improvement of mutual understanding between surgical and anesthetic personnel, and thus the coordination of the teamwork.

Who and which procedures are suitable for nonintubated VATS?

According the experience of the major research groups, the general patient exclusion criteria includes American Society of Anesthesiologists score 4 and higher, bleeding disorders, sleep apnea, unfavorable airway or spinal anatomy, need for contralateral lung isolation, clinically significant sputum production, bronchiectasis, asthma, extreme of body mass index (BMI), preoperative decompensated heart disease, severe pleural adhesion over targeted hemithorax, and noncompliance to the procedure or patient refusal (5,14).

With the maturation of the technique, Wu and colleagues (18) had evaluated the feasibility of geriatric patients (age ranging from 65 to 87) undergoing lobectomy, which showed comparable safety profile with control group, and opened up the possibility of nonintubated VATS on the old age group.

Initially, nonintubated VATS was tested on simpler diagnostic procedure or management of solitary and peripheral lung lesion (2,9,19,20). With the increasing body of evidence and experience, nonintubated VATS has been extensively promoted and proved safe for treatment of pleural/pericardial effusion, empyema thoracis, bullous emphysema, non-resectional lung volume reduction surgery, spontaneous pneumothorax, biopsy of interstitial lung disease, wedge resection of lung nodules, segmentectomy and lobectomy for lung cancer, mediastinal biopsy and tumor excision (5-8,14,20,21).

What's the anesthetic goals and the corresponding management?

The main difference of the nonintubated VATS from conventional intubated general anesthesia, is to create an iatrogenic pneumothorax, a subsequently collapsed lung to be operated on, and to maintain patients' spontaneous ventilation sufficiently at the same time. Conscious sedation is sometimes required due to emotional stress or prolonged procedure-related discomfort.

Monitoring

In order to handle the physiologic derangement and the complexity of the surgical/anesthetic procedure aforementioned, standard monitoring with pulse oximeter, electrocardiogram, sphygmomanometer, and end-tidal CO_2 should always be in place. In addition, invasive arterial pressure monitor is set for most patients in our group for its versatility on monitoring arterial blood gas, real-time hemodynamic index, and fluid status inclination. For the occasion in which sedation is part of the planning, bispectral index (BIS) is highly recommended for evaluation of sedation level and advanced judgement of anesthetic depth.

Ventilatory

The goal of ventilatory manipulation is to maintain a smooth, non-effort, spontaneous respiratory pattern, aiming respiratory rate over 12 to 20 times/minute for acquiring a satisfactory surgical field with adequately collapsed lung (5).

In awake patients, preoperative communication for reassuring the patients, intraoperative coaching, mental support, verbal communication with medical personnel, and comfortable environment with low-volume music might all contribute to calm the patients down with acceptable respiration (16,22).

In sedated patients of our group, premedication with opioid agent followed by deliberate titration had been proved to control respiratory rate effectively. Meticulous use of nasal airway could be of great benefit if upper airway obstruction raises clinical concerns. If significant hypoventilation should happen, modest assisted ventilation by a mask might be required after notification of the surgical team.

Oxygenation could be facilitated with O_2 supplement by nasal cannula 3-4 liters/minute or by Venturi Mask. Overly hypercapnia should be avoided, a good-quality end-tidal CO_2 trace and serial arterial blood sampling before/after iatrogenic open pneumothorax should mostly suffice for close monitoring.

Analgesia

The target of the analgesia is to block the unpleasant sensation throughout the surgical manipulation. With the temporal sequence, VATS ports are first to be set, which bring about painful sensation from skin to parietal pleura; after ports are set, the manipulation of lung and traction of intrathoracic structures would cause irritation over visceral pleura.

Regional anesthesia had been long reported to be effective for analgesia covering chest cage and parietal pleura (23). Various approaches have been developed and proved feasible, including the current mainstream of thoracic epidural anesthesia (TEA), paravertebral nerve block, and percutaneous or thoracoscopic intercostal nerver block, intrapleural analgesia. In our group practice, we add vagus nerve block and intravenous narcotic to minimize the visceral component of irritating sensation.

Traditionally, before minimal invasive procedure era, thoracotomy was traumatic procedure with large incision, and thus epidural anesthesia was favored for its better quality of postoperative pain control and reduction of respiratory and cardiac complication (23). But with the paradigm shift to VATS, Yie *et al.* (24) had reported Epidural anesthesia holds no superior postoperative analgesic benefits over narcotic-based intravenous patient-controlled analgesia (IVPCA). The optimal postoperative analgesia remains an open issue, other promising modalities such as continuous intercostal-intrapleural analgesia or continuous paravertebral block worth more attention and further investigation (25,26).

Amnesia

Surgery, more or less, could bring forth mental stress to the patients, which might consequently has detrimental effects on patient's physiology (27) and even jeopardize the safety of surgery by panic attack. Sedation with amnesia could offer a stress-free environment even for the relatively vulnerable groups, especially with the prolonged procedure like lobectomy, which makes keeping same position for hours intolerable.

For sedation, our group employs BIS for monitoring sedation level. Empirically speaking, premedication with 50 to 100 mcg fentanyl, followed by propofol with target controlled infusion (TCI), aiming for BIS over 40 to 60, would mostly create a balanced status without significant ventilatory or hemodynamic disorder.

Areflexia

When approaching central intrathoracic lesion, cough reflex is an inevitably encountered problem that requires effective but temporary suppression of the reflex. On the other hand, as an intrinsic protective mechanism, recovery of cough reflex is beneficial on reduction of postoperative respiratory complication.

Pre-operative inhalation of aerosolized lidocaine (28) and ipsilateral stellate ganglion block (29) had been proposed to reach cough control in some extent. In our group experience, Chen and colleagues (5) has routinely performed intraoperative thorascopic vagal block, which has been proved effective on cough reflex suppression without causing hemodynamic instability. For more swift procedures, for the sake of decreasing cough suppression duration, incremental intravenous fentanyl is applied in place of vagal block.

Prepare for conversion to general anesthesia

Despite of extra vigilance and preparation aforehand, intraoperative conversion to intubated general anesthesia is inevitable occasionally due to significant bleeding, pleural adhesion, and insufficient anesthesia (5,30). Plan B should always be in hand.

Intubation in lateral decubitus position with VATS instruments in place presents itself as a technical challenge to anesthesiologists. Direct laryngoscopy might stands a chance, but fiberoptic bronchoscopic intubation, video-assisted system, and laryngeal mask airway (LMA) are the trustworthy back-up plan.

How are intraoperative hemodynamic and ventilatory index change?

The hemodynamic and ventilatory index are the core of perioperative monitoring and evaluation. Different protocols would naturally bring out diverse outcomes. During one lung ventilation, heart rate, respiratory rate, PaO_2 and CO_2 elimination will change significantly but they can be kept physiologically adequate.

Generally speaking, the hemodynamic and ventilatory index remained in the acceptable range without causing detrimental hypotension, hypoxemia, hypercapnia, nor acidosis.

Conclusions

Nonintubated VATS has been extensively and safely applied to various surgical procedures involving pleura, lung, and mediastinum. The main challenges for anesthesiologists are coping with the physiologic derangement upon iatrogenic open pneumothorax and balancing the benefits and risks of different anesthesia techniques. With a well-controlled, well-monitored anesthetic combinations of regional anesthesia, sedation, and postoperative pain service, nonintubated VATS has been proved to be safe and feasible amongst a wide variety of patient groups.

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A systematic review and meta-analysis on pulmonary resections by robotic video-assisted thoracic surgery

Christopher Cao[1,2,3], Con Manganas[3], Su C. Ang[3], Tristan D. Yan[1,2]

[1]The Systematic Review Unit, The Collaborative Research (CORE) Group, Sydney, Australia; [2]The Baird Institute for Applied Heart and Lung Surgical Research, Sydney, Australia; [3]Department of Cardiothoracic Surgery, St George Hospital, Sydney, Australia

Correspondence to: Christopher Cao, MBBS. The Systematic Review Unit, The Collaborative Research (CORE) Group, Sydney, Australia. Email: drchriscao@gmail.com. Tristan D. Yan, MBBS, MS, MD, PhD. The Systematic Review Unit, The Collaborative Research (CORE) Group, Sydney, Australia. Email: tristanyan@annalscts.com.

Background: Pulmonary resection by robotic video-assisted thoracic surgery (RVATS) has been performed for selected patients in specialized centers over the past decade. Despite encouraging results from case-series reports, there remains a lack of robust clinical evidence for this relatively novel surgical technique. The present systematic review aimed to assess the short- and long-term safety and efficacy of RVATS.

Methods: Nine relevant and updated studies were identified from 12 institutions using five electronic databases. Endpoints included perioperative morbidity and mortality, conversion rate, operative time, length of hospitalization, intraoperative blood loss, duration of chest drainage, recurrence rate and long-term survival. In addition, cost analyses and quality of life assessments were also systematically evaluated. Comparative outcomes were meta-analyzed when data were available.

Results: All institutions used the same master-slave robotic system (da Vinci, Intuitive Surgical, Sunnyvale, California) and most patients underwent lobectomies for early-stage non-small cell lung cancers. Perioperative mortality rates for patients who underwent pulmonary resection by RVATS ranged from 0-3.8%, whilst overall morbidity rates ranged from 10-39%. Two propensity-score analyses compared patients with malignant disease who underwent pulmonary resection by RVATS or thoracotomy, and a meta-analysis was performed to identify a trend towards fewer complications after RVATS. In addition, one cost analysis and one quality of life study reported improved outcomes for RVATS when compared to open thoracotomy.

Conclusions: Results of the present systematic review suggest that RVATS is feasible and can be performed safely for selected patients in specialized centers. Perioperative outcomes including postoperative complications were similar to historical accounts of conventional VATS. A steep learning curve for RVATS was identified in a number of institutional reports, which was most evident in the first 20 cases. Future studies should aim to present data with longer follow-up, clearly defined surgical outcomes, and through an intention-to-treat analysis.

Keywords: Robotics; video-assisted thoracic surgery; systematic review; meta-analysis; minimally invasive surgery

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Introduction

The 'minimally invasive' revolution that began in the 1980s has made a significant impact in many specialties of surgery. The first pulmonary resections by video-assisted thoracic surgery (VATS) were described in the early 1990s (1,2). Since then, there has been growing evidence to suggest that similar or improved long-term oncologic efficacy and survival can be achieved with superior perioperative outcomes by VATS compared to conventional thoracotomy for selected patients with early-stage non-small cell lung cancers (NSCLC) (3,4).

With technological innovation in the form of robotic surgery, robotic video-assisted thoracic surgery (RVATS) emerged as an alternative technique for pulmonary resections in the early 2000s (5,6). Proponents of RVATS emphasize its superior imaging and improved maneuverability compared to conventional VATS, as well as technical advantages such as movement scaling and tremor filtration (7). However, critics of this novel procedure cite its lack of robust clinical evidence as well as its high cost relative to conventional VATS (8). The present systematic review aims to assess the safety and efficacy of pulmonary resections by RVATS, with particular focus on perioperative outcomes, long-term survival and recurrence for malignant lesions. In addition, cost and quality of life (QoL) studies were also systematically evaluated.

Methods

Literature search strategy

Electronic searches were performed using Ovid Medline, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Database of Abstracts of Review of Effectiveness from their date of inception to March 2012. To achieve the maximum sensitivity of the search strategy and identify all studies, we combined “robotics” or “robotic surgery” or “computer-assisted surgery” as Medical Subject Headings (MeSH) terms or keywords with “lung” or “VATS” or “video-assisted thoracic surgery” or “lobectomy” as MeSH terms or keywords. The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies. All relevant articles identified were assessed with application of predefined selection criteria.

Selection criteria

Eligible studies for the present systematic review included those in which patients with histologically proven NSCLC underwent pulmonary resection by RVATS. For studies that included patients who had NSCLC as a subset of patients who had other pathological entities, results for patients who had NSCLC were extracted if possible. When centers have published duplicate trials with accumulating numbers of patients or increased lengths of follow-up, only the most updated reports were included for qualitative appraisal. It is acknowledged that criteria for patient selection for RVATS varied amongst institutions and sometimes within an institution in different time periods. All publications were limited to human subjects and in English language. Abstracts, case reports, conference presentations, editorials and expert opinions were excluded. Studies that included ten or less patients who underwent pulmonary resections by RVATS were also excluded.

Data extraction and critical appraisal

Findings from initial scoping searches were used to decide outcomes for the present review. The primary outcomes included perioperative mortality and morbidity. Secondary outcomes included quality of life assessment, cost analysis, conversion rate, operating time, intraoperative blood loss, duration of chest drainage, duration of hospitalization, recurrence rate and long-term survival. All data were extracted from article texts, tables, and figures. Two investigators (C.C. and S.A.) independently reviewed each retrieved article. Discrepancies between the two reviewers were resolved by discussion and consensus. The final results were reviewed by the senior investigators (T.D.Y. and C.M.).

Statistical analysis

Meta-analysis was performed by combining the results of reported incidences of any assessed outcomes in comparative studies. The relative risk (RR) was used as a summary statistic. X^2 tests were used to study heterogeneity between trials. I^2 statistic was used to estimate the percentage of total variation across studies, due to heterogeneity rather than chance. All statistical analysis was conducted with Review Manager Version 5.1.2 (Cochrane Collaboration, Software Update, Oxford, United Kingdom).

Results

Quantity of trials

A total of 393 records were identified through the five electronic database searches. After removal of duplicates and limiting the search to humans and English language, 317 articles remained to be screened. Exclusion of irrelevant studies resulted in 36 articles, which were retrieved for

Table 1 Summary of relevant studies identified in the present systematic review on robotic video-assisted thoracic surgery for pulmonary resections

Institutions	Author	Reference Number	Publication year	Study period	Study type	n	Follow-up (months)
MSKCC, NY, USA	Park*	(9)	2012	2002–2010	ROS	123	27
Milan, Italy				2006–2010		82	
Pisa, Italy				2004–2010		120	
Milan, Italy	Veronesi	(10)	2011	2006–2010	ROS	91	24
Milan, Italy	Veronesi	(11)	2010	2006–2008	ROS	54	NR
Pisa, Italy	Melfi	(12)	2008	NR	ROS	107	NR
Pisa, Italy	Melfi	(13)	2002	2001-2001	ROS	11	NR
MSKCC, NY, USA	Park	(14)	2008	2007–2007	ROS	12	NR
MSKCC, NY, USA	Park	(15)	2006	2002–2004	ROS	34	NR
Birmingham, USA	Cerfolio*	(16)	2011	2010–2011	ROS	168	NR
Birmingham, USA	Cerfolio	(17)	2011	2009–2010	ROS	62	NR
Miami, USA	Dylewski*	(18)	2011	2006–2010	ROS	200	NR
Miami, USA	Ninan	(19)	2010	2008–2009	ROS	76	10.2
Goyang, Korea	Jang*	(20)	2011	2009–2009	ROS	40	NR
Innsbruck, Austria	Augustin*	(21)	2011	NR	ROS	26	27
Rochester, USA	Fortes*	(22)	2011	2008–2010	ROS	23	7
Chicago, USA	Giulianotti*	(23)	2010	2001–2009	ROS	29	60
Grosseto, Italy						9	
Washington DC, USA	Gharagozloo*	(24)	2009	2004–2008	ROS	100	32
Washington DC, USA	Gharagozloo	(25)	2008	2004–2007	ROS	61	28
City of Hope, USA	Anderson*	(26)	2007	2004–2006	ROS	21	9.8

ROS, Retrospective observational study. NR, not reported. *, Updated study included for detailed analysis.

more detailed evaluation. Manual search of references identified three additional potentially relevant studies. After applying the selection criteria, 18 articles remained for assessment (9-26). A summary of these studies from 12 institutions are presented in *Table 1*. After selecting studies with the most updated data, nine reports were examined in detail, including 941 patients from 12 institutions.

Surgical technique and patient selection

All nine studies selected for detailed analysis used the same master-slave robotic system (da Vinci, Intuitive Surgical, Sunnyvale, California). The majority of resections were lobectomies, but a smaller proportion of bilobectomies, pneumonectomies, sleeve lobectomies, segmentectomies and wedge resections were also performed. The number of ports used in each institution, as well as the size of the access port/incision used for specimen retrieval, varied between studies. Similarly, the number of lymph node stations dissected and the total number of lymph nodes removed differed between institutions. The majority of patients selected for pulmonary resection had a preoperative histological diagnosis of primary NSCLC with early clinical staging. Other indications for surgery included metastatic disease and carcinoid tumors. A summary of patient baseline characteristics and surgical details are presented in *Table 2*.

Assessment of perioperative outcomes

The perioperative mortality rates ranged from 0 to 3.8%. Overall morbidity rates ranged from 10% to 39% and major morbidity rates ranged from 0 to 5% in three studies (9,20,26). The most commonly reported postoperative complications included tachyarrhythmias (3-19%) (9,16,18,21,22,24,26), prolonged air leak (4-13%) (16,18,20-24), pneumonia (1-5%) (18,24) and acute

Table 2 Summary of surgical details and baseline characteristics of patients who underwent robotic video-assisted thoracic surgery

Author	Age	Gender (Male)	Primary NSCLC	Staging^	Resection type					Lymph nodes		Access	Port
					LR	BR	PR	SR	WR	Stations	Number		
Park	66 [30-87]	63%	325/325	cI	324	1	0	0	0	5 [2-8]	NR	< 8 cm	3 or 4
Cerfolio	67 [21-87]	45%	168/168	NR	106	0	0	16	26	8	17	>15 mm	4 or 5
Dylewski	68 [20-92]	45%	125/200	cIA	160*	4	1	35	0	5 [4-8]	NR	2-4 cm	4
Jang	64±10	58%	40/40	cI	40	0	0	0	0	7 [2-10]	22 [7-45]	2-5 cm	3
Augustin	65 [47-82]	54%	24/26	cI	26	0	0	0	0	NR	NR	5-7 cm	3
Fortes	70 [51-86]	48%	16/23	cI-II	18	1	0	1	3	4	12 [2-50]	2-3 cm	3 or 4
Giulianotti	66 [16-78]	50%	24/38	cI-II	32	3	3	0	0	NR	8 [1-18]	4-5 cm	3 or 4
Gharagozloo	65±8	42%	100/100	cI-II	100	0	0	0	0	4R; 5L	12 ± 3	2-3 cm	3 or 4
Anderson	67 [36-86]	52%	19/21	cI	14	2	0	5	1	NR	16 [2-58]	3-4 cm	4 or 5

*, Includes 154 lobectomies, 3 sleeve lobectomies and 3 en bloc resection with lobectomies; ^, Majority of patients; NR, Not reported. Resections types: LR, Lobectomy; BR, Bilobectomy; PR, Pneumonectomy; SR, Segmentectomy; WR, Wedge resection; R, Right-sided disease; L, Left-sided disease.

Table 3 Summary of perioperative outcomes for patients who underwent robotic video-assisted thoracic surgery

Author	Mortality	Morbidity			Conversion rate	Operating time (min)	Blood loss (mL)	Chest drain (days)	Length of stay (days)
		Total	Major	Minor					
Park	0.3%	25%	4%	22%	8.3%	206 [110-383]	NR	3 [1-23]	5 [2-28]
Cerfolio^	0%	26%	NR	NR	11.9%	132±60	30±26	1.5 [1-6]	2 [1-7]
Dylewski	1.5%	26%	NR	NR	1.5%	175 [82-370]	70 [25–500]	1.5 [1-35]	3 [1-44]
Jang	0%	10%	0%	10%	0%	240±62	219±123	NR	6 [4-22]
Augustin	3.8%	15%	NR	NR	19.2%	228 [162-375]	NR	7 [3-15]	11 [7-53]
Fortes	0%	39%	NR	NR	4.3%	238 [156-323]	133 [0-2000]	2 [1-12]	3 [1-13]
Giulianotti	2.6%	11%	NR	NR	15.8%	209±66	NR	NR	10 [3-24]
Gharagozloo	3%	21%	NR	NR	1%	216±27	NR	NR	4 [3-42]
Anderson	0%	29%	5%	33%	0%	216 [60-384]	100 [2-600]	2 [1-5]	4 [2-10]

NR, Not reported; ^62 patients excluded from analysis by author due to conversion (n=13), irresectable disease (n=7) or sublobar resections (n=42).

respiratory distress (1-4%) (16,22-24). The conversion rates from RVATS to open thoracotomy ranged from 0 to 19.2%. Average operating time varied between 132 to 238 minutes, whilst blood loss ranged from 30 to 219 mL. The median length of hospitalization was from 2 to 11 days and the duration of chest drainage was 1.5 to 7 days. A summary of perioperative outcomes are presented in *Table 3*. Jang *et al*. conducted a three-arm retrospective study comparing 40 patients who underwent RVATS to 40 patients who underwent conventional VATS at the beginning of their institutional experience and 40 patients who underwent conventional VATS after two years of experience, performed by the same surgeon. Their results indicated superior perioperative outcomes for RVATS compared to the first 40 patients who underwent conventional VATS, with fewer complications, shorter hospital stays and lower conversion rates. However, RVATS resulted in similar perioperative outcomes when compared to 40 patients who underwent conventional VATS after 2 years of surgical experience (20). Two retrospective propensity-score analyses comparing RVATS with open thoracotomy for patients with early-stage NSCLC were reported (11,16). A meta-analysis of these two comparative studies assessing perioperative morbidity outcomes identified a trend favoring RVATS compared to

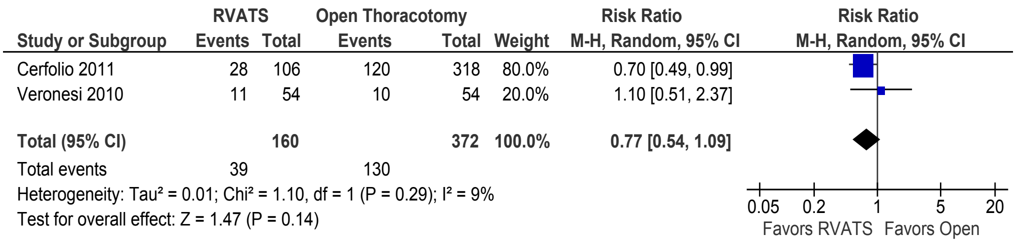

Figure 1 Forest plot of the relative risk (RR) of postoperative morbidity after robotic video-assisted thoracic surgery (RVATS) versus open thoracotomy for patients with early-stage non-small cell lung cancer. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics

Table 4 Summary of long-term survival and recurrence outcomes for patients who underwent robotic video-assisted thoracic surgery for non-small cell lung cancer

Author	5-year survival	Overall recurrence	Local recurrence	Systemic recurrence	Both local and systemic
Park	80%	9.8%	2.8%	5.2%	1.8%
Cerfolio	NR	NR	NR	NR	NR
Dylewski	NR	NR	NR	NR	NR
Jang	NR	NR	NR	NR	NR
Augustin	63.6%	7.7%	3.8%	0%	3.8%
Fortes	NR	0%	0%	0%	0%
Giulianotti	71.4%	4.8%	0%	4.8%	NR
Gharagozloo	NR	6%	0%	6%	0%
Anderson	NR	NR	0%	NR	NR

NR, Not reported.

conventional thoracotomy (24% *vs.* 35%, P=0.14), as shown in *Figure 1*. The length of hospitalization was significantly shorter after RVATS compared to propensity-matched patients who underwent open thoracotomy in both studies. However, RVATS consistently required a significantly longer operative time.

Assessment of overall survival and recurrence

Survival was calculated from the date of surgery. Of the three studies that presented data on long-term survival for patients with malignant disease, the overall 5-year survival rates ranged from 64% to 80% (9,21,23). An additional study reported an overall survival of 99% after a median follow-up of 32 months (24). Overall recurrence ranged from 0% to 9.8%, including 0% to 4.8% local recurrence, 0% to 6% systemic recurrence, and 0% to 3.8% for both local and systemic recurrence at the time of the latest follow-up. These outcomes are summarized in *Table 4*.

Assessment of costs

Park and Flores conducted the only cost analysis to date, comparing conventional VATS (n=87) to RVATS (n=12) to open thoracotomy (n=269) in a retrospective study (14). All direct and indirect expenditures were included to calculate the average hospitalization costs, and the surgeon's fee was added to calculate the overall cost. This study reported that RVATS was on average $3,981 more expensive than conventional VATS, but $3,988 cheaper than open thoracotomy. After taking into account the amortized cost of employing the robot for each case, an additional $1,715 was required for each patient who underwent RVATS. The increased cost of RVATS compared to conventional

VATS occurred almost exclusively on the first day of hospitalization, the reasons for which remained uncertain. Suggested explanations included additional robotic-related equipment and increased likelihood of performing additional procedures, such as bronchoscopy and adhesiolysis. The main factor in reducing the costs of VATS and RVATS compared to thoracotomy was the reduced length of hospitalization.

Assessment of quality of life

Cerfolio *et al*. reported a quality of life assessment in their propensity-score analysis involving 106 patients with NSCLC who successfully underwent RVATS lobectomy and 318 patients who underwent rib- and nerve-sparing thoracotomy (16). The participants were given the 12-item Short Form Health Survey (SF-12) with supplemental questions about analgesic control at 3 weeks and 4 months postoperatively. Results of this study reported a significantly higher mental QoL score for the RVATS cohort at 3 weeks postoperatively (53.5 *vs*. 40.3, P<0.001) and a similar trend favoring RVATS for physical QoL score at the same time interval (40.1 *vs*. 34.1, P=0.07). However, both the mental and physical QoL scores were similar between the two groups at 4 months postoperatively. Pain scores out of 10 was also significantly lower in the RVATS group at 3 weeks (2.5 *vs*. 4.4, P=0.04). The authors of this study conceded that patients were informed that RVATS was a 'new and less invasive' technique, which may have contributed to bias in their reporting.

Discussion

Since the first case-series report on pulmonary resection by RVATS was published in 2002, a number of studies have demonstrated the feasibility of this novel technique with encouraging results (13). Advantages of RVATS compared to conventional VATS include the additional four degrees of freedom (internal pitch, internal yaw, rotation and grip), the elimination of the fulcrum effect, superior 3-D vision from binocular camera, reduced human tremor and improved ergonomic position for the surgeon (12). With these technological improvements, RVATS has the potential to allow more complex procedures such as sleeve lobectomies and chest wall resections to be performed, where conventional VATS might fail (17,27). Indeed, many advocates of RVATS consider it as the leading edge of the swinging pendulum in the paradigm shift towards minimally invasive thoracic surgery (9). On the other hand, critics of RVATS cite the lack of tactile feedback, personnel and cost commitments, as well as prolonged operating time as significant disadvantages of this surgical technique.

The present systematic review identified nine updated retrospective observational studies, mostly from institutions in the United States and Italy involving patients with early-stage NSCLC who underwent lobectomy procedures. These studies reported comparable perioperative outcomes to the results of a recent systematic review on conventional VATS (4). The most common postoperative complications from RVATS, such as tachyarrhythmia, prolonged air leak, pneumonia, and acute respiratory distress, were similar to complications identified for conventional VATS (3). A meta-analysis involving two propensity-score analyses revealed a trend towards fewer complications after RVATS compared to open thoracotomy for selected patients with early-stage NSCLCs. Unfortunately, robust long-term oncologic outcomes such as 5-year survival and disease recurrence rates for patients with malignancies are relatively scarce, with only one small case-series reporting follow-up of more than three years (23). Finally, there is limited but important evidence suggesting superior outcomes in cost and quality of life for selected patients who underwent RVATS compared with propensity-matched patients who underwent open thoracotomy (11,16).

The effect of a steep learning curve for RVATS has been well documented. Perioperative outcomes such as operating time and conversion rates have been shown to significantly improve after the initial learning period. A study by Veronesi estimated the number of operations considered necessary to attain adequate skill in RVATS to be approximately twenty, which is supported by two other institutional experiences (10,13,24). Melfi pointed out that early experiences in RVATS were disadvantaged by a lack of standardized surgical techniques, limited training opportunities, as well as underdevelopment of robotic instrumentation (12). The importance of specialized training for scrub nurses and anesthetists were also highlighted in other studies (12,17). Results from the present systematic review identified the studies with the highest conversion rates (21,23) and operating times (21) were from institutions with fewer than thirty reported cases. This suggests that perioperative outcomes are likely to improve in specialized centers after the initial steep learning curve period. Similarly, these findings may advocate that RVATS should only be performed in tertiary high-volume referral centers with an adequately trained and specialized team of RVATS staff.

A number of limitations exist in the present systematic review. Firstly, it should be acknowledged that publication bias is inherently associated with novel surgical techniques, and unpublished outcomes may differ to the results reported from the selected tertiary centers. Secondly, patient inclusion in each institution was highly selective and variable, and results should be interpreted with caution in view of a lack of randomized-controlled trials comparing RVATS to conventional VATS or open thoracotomy. In addition, many studies presented surgical outcomes without standardized definitions or an intention-to-treat analysis. Examples include the variable definition of 'conversion rates', morbidity outcomes, and the exclusion of patients with extensive disease or those who required conversion from statistical analysis. For example, Giulianotti *et al.* reported one of the highest conversion rates from RVATS to open thoracotomy (6/38, 15.8%) (23). However, three of these conversions were decided after exploratory thoracoscopy and before the robot was docked. In contrast, the multi-institutional report by Park *et al.* reported a conversion rate of 8.3%, with a definition of 'conversion' as the use of open thoracotomy after docking the robot to the patient and initiation of robotic dissection (9). Finally, Cerfolio and colleagues excluded all patients who had conversions (13/168) and those who had metastatic pleural disease (n=7) in their propensity-score analysis comparing RVATS to open thoracotomy (16). Inconsistent reporting of morbidity outcomes was also evident, with only three studies presenting data according to standardized morbidity definitions (9,16,20).

Overall, the current literature suggests that minimally invasive pulmonary resections by RVATS is feasible and can be performed safely for selected patients in specialized centers. However, important questions remain to be answered. Long-term oncologic efficacy compared to open thoracotomy for patients with NSCLC remains to be seen, and the perioperative superiority of RVATS compared to conventional VATS, which is now performed in many centers at a significantly lower cost, is thus far unconvincing. Until such evidence is presented in the form of well-designed randomized controlled trials or a large multi-institutional registry, the role for RVATS will continue to be questioned. Nonetheless, proponents of RVATS highlight the indirect benefits of robotic technology in encouraging the thoracic community to accept and adopt minimally invasive surgery in general (17). Future studies should aim to present long-term follow-up data and use clearly defined surgical outcomes in the form of an intention-to-treat analysis.

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A complete video-atlas of five robotic-assisted lobectomies

Bernard J. Park

Division of Thoracic Surgery, Hackensack University Medical Center, 30 Prospect, Avenue, Suite 5636, Hackensack, NJ 07601, USA

Correspondence to: Bernard J. Park, MD, FACS. Division of Thoracic Surgery, Hackensack University Medical Center, 30 Prospect, Avenue, Suite 5636, Hackensack, NJ 07601, USA. Tel: 551-996-4218; Fax: 551-996-4833. Email: bpark@hackensackumc.org.

Editor's Key Points

1. These narrated videos are extremely valuable materials demonstrating the detailed surgical techniques of each of the five robotic-assisted lobectomies
2. Dr Park described an approach based on a video-assisted thoracoscopic surgery (VATS) lobectomy incision strategy, which could be reproducible for VATS surgeons
3. For those used to the conventional open technique, the very intuitive and user-friendly robotic interface may be easier to master than the different set of hand-eye skills demanded by VATS, hence, the robotic system may provide the non-VATS surgeons an excellent route into the world of minimally invasive thoracic surgery
4. Promising results have been reported by a small number of specialist centers with particular experience using the robotic systems

--T.D.Y.

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Advances in technology have allowed minimally invasive approaches for pulmonary lobectomy to be utilized increasingly over traditional thoracotomy for the purported benefits of decreased surgical trauma resulting in shorter hospital stay, quicker recovery, less pain and decreased morbidity. While video-assisted thoracic surgery (VATS) lobectomy was initially developed in the early 1990s, it has taken two decades for VATS lobectomy to become a more widely available and reproducible technique. This is in part because of the training required to teach and learn a different approach to handle hilar dissection in a closed chest. It may also be because of the limitations of VATS technology and instrumentation.

Telerobotic surgical technology with a binocular visual system and wristed instrumentation was developed in order to overcome the limitations in the established minimally invasive technology. While initially developed and first reported for closed chest coronary revascularization, robotics has enabled rapid and nearly uniform adoption of a minimally invasive approach for pelvic procedures, such as prostatectomy and hysterectomy, where vision and maneuverability are limited. The capital costs of these systems and the question of whether clear-cut benefits exist, aside from those to the operating surgeon, are important and unresolved issues.

In the arena of general thoracic surgical procedures, the development of robotic approaches has been slowly increasing, as more emphasis is placed on minimally invasive surgery. However, much like the early experiences with VATS lobectomy there only a few centers of excellence in robotic thoracic surgery exist worldwide. Teaching materials, training courses and opportunities for mentoring are sparse.

These narrated videos represent an effort to demonstrate one approach in utilizing robotic technology to perform minimally invasive lobectomy. *Video 1* reviews the docking process. *Videos 2* to 6 demonstrate the technical aspects of right upper lobectomy (*video 2*), right middle lobectomy (*video 3*), right lower lobectomy (*video 3*), left upper lobectomy (*video 5*) and left lower lobectomy (*video 6*), respectively. The approach is based on a VATS lobectomy incision strategy consistent with the CALGB 39802 registry study. In this regard, it is a reproducible technique for those individuals who already have some advanced VATS experience. In many ways the two-dimensional video clips cannot adequately represent the three-dimensional nature of the robotic dissection, but the viewer should focus on how the robotic system is implemented to achieve a precise bimanual hilar dissection.

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Robotic lobectomy for non-small cell lung cancer (NSCLC): Multi-center registry study of long-term oncologic results

Bernard J. Park

Division of Thoracic Surgery, Hackensack University Medical Center, 30 Prospect Avenue, Suite 5636, Hackensack, NJ 07601, USA

Correspondence to: Bernard J. Park, MD, FACS. Division of Thoracic Surgery, Hackensack University Medical Center, 30 Prospect Avenue, Suite 5636, Hackensack, NJ 07601, USA. Tel: 551-996-4218; Fax: 551-996-4833. Email: bpark@hackensackumc.org.

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Introduction

Minimally invasive video-assisted thoracic surgery (VATS) lobectomy has proven to be feasible and oncologically acceptable for non-small cell lung cancer (NSCLC) and a number of other conditions. Multiple studies have demonstrated clear benefits of VATs over a traditional thoracotomy approach, such as decreased length of stay, decreased short-term postoperative pain and fewer complications (1-4). Despite this, however, a VATS approach to anatomic resection is still not the current standard and is only slowly being implemented more widely. The explanation is likely multifactorial including: (I) technical issues, such as two-dimensional imaging and limited maneuverability of instrumentation; (II) lack of adequate training; and (III) concerns about the consequences of major vascular injury with a closed chest approach.

In order to address the perceived technical limitations of conventional minimally invasive platforms a master-slave robotic surgical system was developed (da Vinci Surgical System, Intuitive Surgical, Sunnyvale, California). The major advantages were in the three-dimensional visual system that re-establishes binocular vision and instrumentation capable of seven degrees of freedom enabling wristed movement for dissection. The initial intent for this robotic system was for use in closed chest coronary surgery, but this has not eventuated. Instead, the major applications have been for pelvic procedures, such as prostatectomy and hysterectomy. Use of robotics for general thoracic surgical procedures dates back to initial case reports in the early 2000's, but it was not until 2004 and 2006 that actual series of robotic lobectomies were reported by Melfi and colleagues and Park and coauthors, respectively (5,6). These centers reported the initial technique and experience demonstrating feasibility and concordance of outcomes with the largest series of VATS lobectomies. However, long-term data are lacking in a larger cohort of patients.

Rationale and methods

Early in the development of thoracic robotic surgery it was clear that there were only a handful of centers throughout the world utilizing robotics for major pulmonary resection. In order to evaluate a large cohort of patients that underwent robotic lobectomy to analyze both the perioperative and long-term survival results a multicenter retrospective registry was created using prospectively collected data from the thoracic surgery divisions of three institutions active in robotic pulmonary resection: Memorial Sloan-Kettering Cancer Center, New York, New York, USA, The European Institute of Oncology, Milan, Italy and Ospedale Cisanello, Pisa, Italy. Eligible patients were those with biopsy-proven or suspected primary NSCLC isolated to the chest who subsequently underwent attempted robotic lobectomy for primary NSCLC. Patients with carcinoid tumor, small cell lung cancer, benign or metastatic lesions were excluded. Information regarding preoperative characteristics, operative details, hospital course, pathologic findings and postoperative follow-up were recorded prospectively and sent to one institution (Milan) for analysis.

Techniques of robotic lobectomy

One of the strengths of the study was that the patient selection and surgical approach was virtually uniform despite the retrospective design. The majority of patients had clinical early stage disease with no prior treatment,

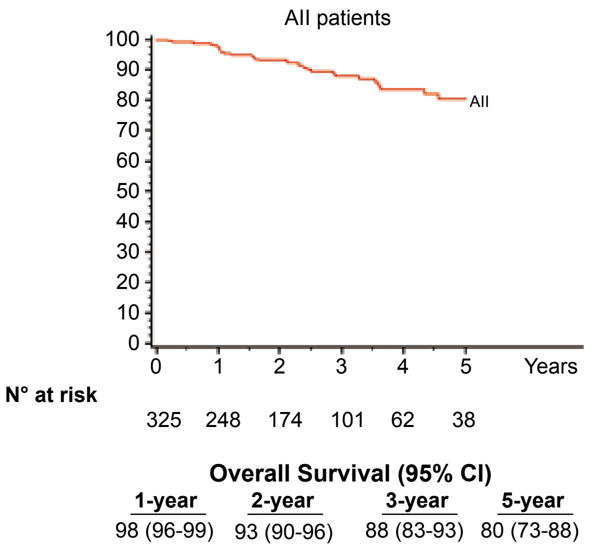


Figure 1 Overall survival for the group.

and patients gave informed consent to undergo robotic surgery. Each surgeon performed robotic lobectomy employing a technique that conformed to the CALGB 39802 consensus criteria for VATS lobectomy (7): use of non-rib-spreading incisions with a 3-4 cm utility incision, videoscopic guidance and traditional hilar dissection. Two of the surgeons employed a total of 4 incisions while the third used 3 incisions, and all phases of dissection were performed with robotic instrumentation. Patients underwent systematic hilar and mediastinal lymph node dissection. Operative times were measured from first incision to closure, and conversion was defined as use of a rib-spreading thoracotomy at any point after docking of the robot to the patient and initiation of robotic dissection.

Results

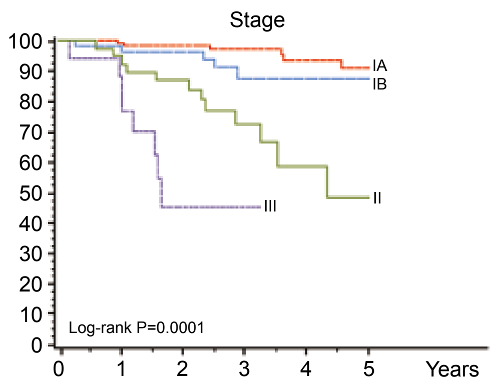
From November 2002 through May 2010 325 patients underwent robotic lobectomy for primary NSCLC at three centers. Sixty-three percent of the patients were male and 85% were former or current smokers. Fifty-one percent of the procedures were upper lobectomies (92 RUL, 75 LUL), and 40% were lower lobectomies (71 RLL, 57 LLL). The majority of cases were subtypes of adenocarcinoma (73%), and most patients were clinical stage I (247 IA, 63 IB) and had no preoperative therapy.

Median operative time was 206 minutes, ranging from 110 to 383 minutes. There were no intraoperative deaths and the conversion rate to thoracotomy was 8% (27/325). Three patients (0.9%) had conversion for minor bleeding that did not require intraoperative or postoperative transfusion. Overall morbidity rate was 25.2% (82/325), and 12 patients had major complications (3.7%), including bronchopleural fistula (2), pulmonary embolism (3), acute renal insufficiency (3), hemorrhage (2) and myocardial infarction (2). Supraventricular tachycardia was the most common postoperative complication, occurring in 37 patients (11.4%). Median chest tube duration was 3 days (range, 1-23 days) and length of stay was 5 days (range, 2-28 days). There was one in-hospital death in a patient that developed acute renal insufficiency followed by a pulmonary embolism and death on postoperative day 12, with a mortality rate of 0.3%.

Seventy-six percent (248/325) of patients were pathologic stage I (176 IA, 72 IB), and 68 (21%) patients were upstaged. The median tumor size was 2.2 cm (range, 0.7-10.2 cm) and the median number of lymph node stations dissected was 5 (range, 2-8). Sixty-one patients (19%) had metastatic nodal disease and 67 patients received adjuvant cytotoxic chemotherapy. At a median follow-up of 27 months 280 patients (86%) were without evidence of disease and 32 patients (10%) had recurred with 25 dead of their disease. The majority (72%) were distant (17 distant only, 6 locoregional + distant) and 28% (9/32) were locoregional only. Overall 5-year survival for the group was 80% (*Figure 1*) and stage-specific survival is shown in *Figure 2*.

Impact and significance

This study is important for several reasons. First, it is the largest experience of totally robotic lobectomies reported to date. Previous initial feasibility studies had small numbers of patients, and like those this report shows perioperative results consistent with large VATS lobectomy experiences with short chest tube duration and length of stay, as well as low major morbidity (3.7%) and in-hospital mortality (0.3%) rates. Second, it is a multicenter, international experience with one center in the United States and two in Italy employing similar patient selection criteria, surgical technique and prospective evaluation of perioperative and long-term outcome. This demonstrates not only feasibility of the technique, but reproducibility as well. Third, this report is the first to look at the long-term oncologic outcome of robotic lobectomy for early NSCLC. The overall and stage-specific survivals are consistent with both the largest series of VATS lobectomies and the most recent data used for the revisions to the lung cancer staging system.



N° at risk

	0	1	2	3	4	5
IA	176	143	105	64	41	27
IB	72	52	37	22	15	6
II	54	36	28	14	6	5
III	20	15	2	1	–	–

Overall Survival (95% CI)

	1-year	2-year	3-year	5-year
IA	99 (98-100)	99 (97-100)	97 (94-100)	91 (83-99)
IB	97 (93-100)	97 (93-100)	88 (77-98)	88 (77-98)
II	96 (90-100)	87 (76-98)	72 (56-88)	49 (24-74)
III	89 (75-100)	43 (16-69)	43 (16-69)	–

Figure 2 Overall survival for stage-specific survival.

There are, however, limitations of this study and questions regarding the role of robotic technology in thoracic surgery. As this is a retrospective review, there are inevitable biases in patient selection and unknown differences between centers despite the fact that the patient characteristics and surgical techniques appear similar. Another limitation is the lack of other short- and long-term outcome measures, such as postoperative pain, respiratory function, rates of post-thoracoscopy pain and quality of life. Lastly, a comparative arm of VATS and/or thoracotomy patients is lacking. If utilization of robotic technology for thoracic surgical procedures increases, it will be important for future studies to attempt to discern differences between robotic and non-robotic approaches (VATS and thoracotomy) with respect to important outcomes, such as postoperative pain, quality of life and cost.

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Robotic lobectomy is a feasible, safe and oncologically sound surgical treatment for early-stage lung cancer. The technique is reproducible across multiple centers and yields results consistent with the best seen with conventional VATS. It should not be considered experimental, but an accepted minimally invasive thoracic surgical technique. Future evaluation of differences between robotic versus VATS versus thoracotomy approaches to thoracic diseases is warranted.

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Cost concerns for robotic thoracic surgery

Bernard J. Park

Division of Thoracic Surgery, Hackensack University Medical Center, 30 Prospect Avenue, Suite 5636, Hackensack, NJ 07601, USA

Correspondence to: Bernard J. Park, MD, FACS. Division of Thoracic Surgery, Hackensack University Medical Center, 30 Prospect Avenue, Suite 5636, Hackensack, NJ 07601, USA. Tel: 551-996-4218; Fax: 551-996-4833. Email: bpark@hackensackumc.org.

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In an era of increasing scrutiny of expenditure on healthcare, the cost of technological developments such as robotic surgery is an important consideration. Prior studies have shown that robotic thoracic procedures can be performed safely with perioperative results that are comparable to thoracotomy and VATS approaches (1-3). Whether this technology adds benefit at a cost that is reasonable is an unanswered question. Given the high capital and maintenance costs of these systems, it is necessary to analyze their cost to the healthcare system. Assessing the cost and value of robotic surgery is, however, a complex undertaking.

In attempting to elucidate the cost implications of robotic technology, one strategy would be to perform a cost comparison between robotic, VATS and thoracotomy procedures. This approach has been demonstrated in a recent retrospective study comparing VATS and thoracotomy for lobectomy (4). In this study, thoracotomy was on average $700 more per procedure in terms of hospital cost, despite the fact that operating room (OR) time was lower than with VATS. The likely difference was due to shorter hospital stay and complications in the VATS cohort. A similar study was performed for robotic, VATS and thoracotomy for lobectomy (5). Even without taking into consideration the indirect and amortized costs, robotic surgery adds additional direct OR costs compared with conventional VATS or thoracotomy.

There are two main sources of disposable costs at the time of the procedure. The first is the cost of the drapes, valued at approximately $200 USD. The second is the cost of the instruments. This varies depending on how many and what type of instruments are employed. On average each instrument used for a procedure costs $200 USD, with the expense of instruments ranging from at least $400 to $1,000 USD. The total additional disposable cost of employing robotics is therefore between $600 and $1,200. In the case of robotics compared with thoracotomy, however, this added OR cost did not result in greater overall cost of the entire hospital stay. We have previously shown that the average cost of robotic lobectomy was more expensive than VATS, yet substantially less expensive than thoracotomy.

Unlike the VATS study, this observation was made taking into account two additional costs of robotics that are more difficult to calculate in a consistent manner. The first is the direct OR cost, i.e. the cost associated with increased time associated with system setup and increased operative time. While there is no doubt that early in the development of robotic procedures this component adds substantial increased cost, it is also likely that with continued refinement in technique and experience of both surgeon and OR team, this will be minimized. Moreover, the difference between different surgeons and centers is difficult to ascertain. The second is the amortized cost of the robotic system. This is calculated by the following formula: (total capital cost of the system + total service costs over the life of the system)/total number of cases performed with the system. At best the amortized cost is an estimate based on a large number of assumptions: duration of use of a particular system, total service costs, total capital costs and total number of cases performed with a given system. It is inaccurate to assign a fixed additional amortized cost to each robotic procedure.

For example, in our previous analysis the amortized cost of each case was calculated by adding the following: the initial purchase cost, the service costs (assuming a 10-year life span of the system) and dividing by an estimate of the total number of cases performed. In order to determine the latter, the actual number of cases performed with the system was added to the projected additional number of cases for the remainder of the 10-year life span of the system assuming utilization at a fixed level from the most recent year. However, soon after the study the institution acquired 3 new systems, returning the original system and receiving credit. Should this be subtracted from the capital cost of the original or from the subsequent systems? If from the subsequent systems, should it be applied to the cost of a single system or to all of the new systems? Does this now mean that the actual cases performed with the original system are now more or less costly?

Perhaps the best method to evaluate the cost implications of any technology for thoracic surgical procedures is a formal cost effectiveness analysis. This has not been done for VATS technology. For a cost analysis between robotics, VATS and thoracotomy one would have to assume that the three approaches are equivalent in clinical efficacy. This may be problematic given that there is no level I evidence showing that any minimally invasive approaches are equivalent to conventional thoracotomy. Outcome data for robotic lobectomy are only beginning to emerge and are largely drawn from single arm retrospective experiences (6). While VATS lobectomy series are greater in number, the majority are retrospective, with few cohort studies comparing VATs to thoracotomy. The few cohort studies that do exist focus largely on perioperative outcome (7-9), showing an advantage for VATS, but there has been recent evidence that suggests that for the surgical treatment and staging of early stage lung cancer, a VATS approach may be associated with a lower rate of accurate hilar lymph node assessment compared with thoracotomy (10).

Moreover, there are two areas of potential cost benefit not likely to be included in cost analyses of robotic technology. The first is the impact of robotics on the volume of cases in general and for a particular institution. What is the cost benefit if a patient decides to pursue surgical therapy at a particular hospital based on the availability of a minimally invasive robotic approach? Second, what is the cost benefit of robotics if it allows wider implementation of a potentially more cost effective alternative, i.e. minimally invasive lung resection instead of thoracotomy? A recent analysis of the voluntary Society of Thoracic Surgery (STS) database demonstrated that, while the percentage of all lobectomies performed by VATS has been increasing, the overall percentage of cases performed by VATS during the 3-year study period ending in 2006 was only 20%. Furthermore, another recent analysis of a non-voluntary national insurance database indicated that <6% of lobectomies were performed via VATS. The fact remains that the majority of major lung resections performed in the United States are still via thoracotomy. If robotic technology can result in a more widespread adoption of a minimally invasive approach in a safe and appropriate manner that has not been achieved with VATS, the added cost may be justified by all the potential benefits over traditional open surgery. This point also addresses the issue of the cost benefit of robotic technology to those patients who are able to undergo minimally invasive surgery instead of thoracotomy. It is important to take into account the cost benefit to the patient of faster recovery, quicker return to preoperative activity level such as return to work, as well as less expenditure for management of postoperative complications and outpatient services like visiting nurse and rehabilitation.

The capital cost of robotic surgical systems, particularly as there is currently only a single supplier, is significant. This cost must be evaluated critically because of the implications on healthcare expenditures in general. However, the financial impact of robotics is no less significant than other seemingly less costly technological innovations that are implemented without the same attention to cost or efficacy that surgical robotics receives. It is incumbent upon all healthcare practitioners to critically evaluate the costs and benefits of any new technology in order to determine the appropriate utilization of our limited healthcare resources.

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Perspectives on robotic pulmonary resection: It's current and future status

Robert J. Cerfolio, Ayesha S. Bryant

Division of Cardiothoracic Surgery, University of Alabama at Birmingham, Birmingham, AL 35294, UK

Correspondence to: Robert J. Cerfolio, MD, FACS, FCCP. Professor of Surgery, Chief of Thoracic Surgery, JH Estes Family Endowed Chair for Lung Cancer Research, Division of Cardiothoracic Surgery, University of Alabama at Birmingham, 703 19th St S, ZRB 739, Birmingham, AL 35294, UK. Tel: 205-996-7561; Fax: 205-975-2815. Email: rcerfolio@uab.edu.

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Current status of robotic pulmonary resection

Currently robotic pulmonary resection, as described in the previous chapter by Dr. Parks, is performed in select centers in the United States, Europe, and other parts of the world. It still represents less than 1% of how pulmonary resections are performed, with the main reason relating to the limited platform availability of the robot to thoracic surgeons. A few hospitals have robots, and are mostly used by urologists and gynecologic surgeons. However, thoracic surgeons are using it more frequently. In fact, recent data from Intuitive Surgical suggests that the greatest growth in robotic use over the past year is by thoracic surgeons.

There are several ways to perform robotic pulmonary resections including completely portal robotic lobectomy; meaning only trocars are placed through the incisions. An international writing committee has submitted a suggested nomenclature for robotic pulmonary resection. In this yet to be published article, completely portal is abbreviated as CPR and robotic assisted is abbreviated as RA. This nomenclature differentiates the different ways to perform robotic pulmonary resection. The important point is that the robot has now been used on almost a thousand patients to safely perform pulmonary resections and provides a minimally invasive surgical method.

A few of the advantages of the robot over VATS are obvious and they include: improved visualization, improved instrumentation that provide the surgeon more degrees of movement, better lymph node visualization and dissection, the ability to teach using a dual console, and the simulator. However, a few disadvantages include: limited platform availability as well as the capital and maintenance costs and expensive software incurred with the robot. An additional drawback is the fact that instruments have to be replaced after 10-20 uses based on whether they are 5 or 8 mm respectively. Finally, a complete portal approach does not allow the surgeon to palpate the lung whereas a robotic-assisted approach (such as VATS) allows the surgeon to feel the outer one-third of the lung.

Obviously, the enthusiasm for the robot has stemmed from its success in mediastinal resections and esophageal resections. Although this textbook is limited to pulmonary resections, we would be remiss and incomplete if we did not mention the success the robot has had in the mediastinum and esophagus for both malignant and benign esophageal lesions. This is a main reason why the thoracic surgeon has extended the use of the robot for pulmonary resection.

Future status of robotic pulmonary resection

The future of robotic surgery is exciting. There are several technical problems with robotic pulmonary resection. The primary limitation is the fact that the bedside assistant is placing the stapler on the pulmonary arteries and pulmonary veins. A robotic stapler that can be controlled by the surgeon is almost ready for release (planned release date is mid-June 2012).

Perhaps the most important instrument that will be released in the next year is a robotic vessel sealer, which is similar to the robotic harmonic scalpel but is a wristed instrument. This vessel sealer will allow the surgeon to go through the fissure, to seal and cut small pulmonary arteries and veins that are 7 mm or smaller and to seal the base of lymph nodes. Some surgeons are currently using the robotic

Harmonic scalpel for lymph node dissections during VATS or robotic surgery. However, the edges of this instrument are extremely hot and can damage surrounding tissue.

Another exciting instrument that has just made its way to the market in March 2012 is the robotic suction irrigator. It is a major advance that allows the surgeon to control both the suction and irrigation in the operative field. It can also be used for blunt dissection.

A promising area that the robot provides exclusively is the use of fluorescence of tissue. A special robotic camera can be placed into the operative field and allows the surgeon to view the tissue in a different color. Currently, indigotine (Indigo carmine) is the fluorescence agent of choice. It is given intravenously to the patient and by a specialized robotic camera the surgeon views vascularized tissue as green in the monitor and non-vascularized tissue as brown. Its current clinical usefulness is during partial nephrectomy by the urologist. However, we envision a more sophisticated use of the fluorescence of tissue. The ability to tag specific antigens such as Thymic ones, may allow the thoracic surgeon to be able to see the difference between thymus gland and the surrounding fat using the da Vinci monitor and the specialized camera. Fluorescence may also be able to help identify small pulmonary nodules that are embedded in the deep pulmonary parenchyma.

Other new techniques are being developed to help find small pulmonary nodules. These include placing magnetic coils or clips into or near small pulmonary nodules or by placing seeds or clips that emit a very low level of radiation. Specialized instruments are then hooked to the robotic arms that guide the surgeon to the nodule in question even though it cannot be seen or palpated.

There are many obstacles to adoption of the robot. The most important one is the lack of standardized credentialing. Some surgeons often try to perform pulmonary resections before the surgeons and/or their surgical teams have mastered easier robotic operations such as mediastinal tumor resection or lymph node biopsy. It is our belief there should be a standardized pathway or progression toward credentialing (1). This stepwise progression starts with inanimate object training, followed by on-line credentialing, followed by cadaver work, followed by the performance of level one surgical operation such as removal of small mediastinal tumors and lymph node biopsies. After 2 or 3 of these have been performed, level two operations should be performed next. These include wedge resection of the lung for interstitial lung disease and the enucleation of benign esophageal tumors. Once the team and the surgeon are comfortable with level I and II operations, the more complicated pulmonary lobectomy and pulmonary segmentectomy can be attempted. It is important to note that the credentialing may be required not only for the surgeon but rather the entire surgical team. Surgeon credentialing should apply to various surgical operations and not to all chest operations, i.e. a surgeon may be capable of safely performing a robotic wedge resection, but the surgeon may not be capable of safely performing a robotic lobectomy. All these issues need to be further addressed and resolved at a national level.

There have been several robotic surgeons who have misrepresented robotic surgery and had marginal results. Credentialing currently is not promulgated by a national board and is essentially in the hands of individual hospitals. This has led to misinterpretation, confusion, and some controversy. Clearly, a consensus statement from the STS, AATS, and ESTS is needed on credentialing for robotic surgery. Other impediments to adoption include the cost of buying a robot, the fee for maintenance of robot and its equipment and the limited platform availability to the thoracic surgeon.

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Robotic-assisted pulmonary resection—Right upper lobectomy

Robert J. Cerfolio, Ayesha S. Bryant

JH Estes Family Endowed Chair for Lung Cancer Research, Division of Cardiothoracic Surgery, University of Alabama at Birmingham, UK

Correspondence to: Robert J. Cerfolio, MD, FACS, FCCP. Professor of Surgery, Chief of Thoracic Surgery, JH Estes Family Endowed Chair for Lung Cancer Research, Division of Cardiothoracic Surgery, University of Alabama at Birmingham, 703 19th St S, ZRB 739, Birmingham, AL 35294, UK. Tel: 205-996-7561; Fax: 205-975-2815. Email: rcerfolio@uab.edu.

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Introduction

General thoracic surgery is the fastest growing sector of robotic surgery. The reason is advantage the robot offers in mediastinal work such as thymectomy, resection of esophageal leiomyoma, removal of bronchogenic or esophageal duplication cysts, and even diaphragmatic plication. Once general thoracic surgeons try the robot and see the improved visualization they are often willing to continue to learn to do more with it. We have now applied it to pulmonary resections.

There are multiple published articles that have shown the efficacy and safety of robotic pulmonary resection including lobectomy, segmentectomy, and even several reports of pneumonectomy (1-4). However, there are difficulties in learning robotic surgery. It is a "team sport" where the bedside assistant is the one currently placing the stapler on the arteries and the veins, which makes everyone anxious. Another difficulty relates to the high capital cost of a robotic surgery program, including purchasing a robot, the additional expenses of buying a second console and replacing robotic surgical equipment and finally getting time on the robotic platform for the patients.

Despite the debate, cardiac and thoracic surgeons are currently learning many robotic surgery techniques. We recently helped design and develop a CPRL-4 technique and have published the world's largest experience with it - in over 100 lobectomies. We now have completed over 180 robotic lobectomies with only one 30 or 90 day mortality. In addition, with other authors, we have written an international nomenclature paper on this issue (JTCVS 2012, publication pending) and have proctored many surgeons and trained two robotic surgery fellows. We have also published the largest series on robotic Ivor Lewis esophageal resection with a two-layered hand-sewn anastomosis. In addition, we have the world's largest series on the robotic resection of posterior mediastinal tumors.

Based on our experience, we know all too well the difficulties in establishing robotic programs in North America. Some of these difficulties include: anesthesia push- back because of the safety concerns, and increased time, the limited degree of robot platform availability, and the fact that teams are best if they perform several robotic operations a week to get experience. In this *Art of Operative Technique Teachers' Section*, we will display the specific step-by-step approach for a robotic right upper lobectomy.

Operative techniques - robotic right upper lobectomy

Port placement (*Figure 1*)

1. Start with the creation of a 5 mm port to facilitate port

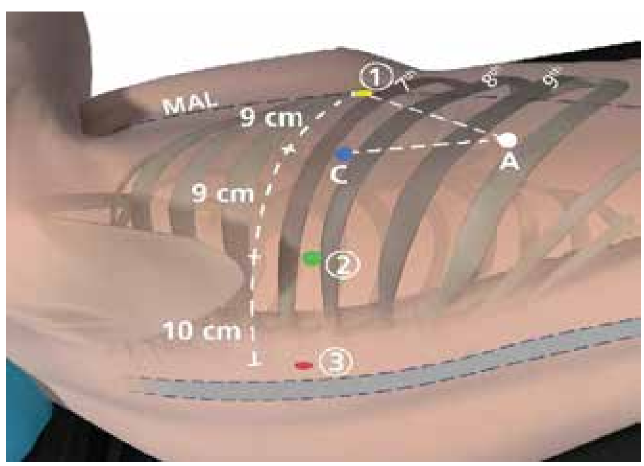

Figure 1 da Vinci Right Lobectomy port placement.

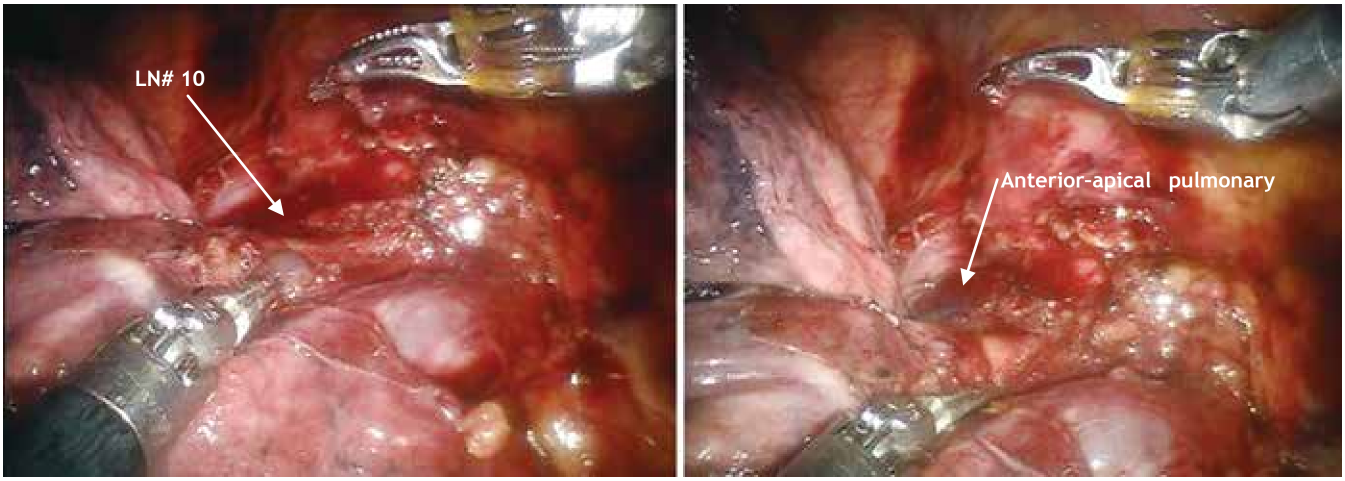

Figure 2 Identification of LN # 10 at anterior–apical pulmonary artery branch.

placement in the midaxillary line (MAL) placed over the 7th rib into the 6th intercostal space (ICS). Later this will become *da Vinci* Instrument Arm ① port.

2. Use a 5 mm videoscope through this port to ensure entry into the pleural space and to visualize placement of *da Vinci* and assistant ports. Start CO_2 insufflation (warmed and humidified) to displace the diaphragm inferiorly.
3. Mark the spinous processes of the vertebral bodies on the patient (grey zone in *Figure 2*). Did not understand the grey zone! Perform a paravertebral block posteriorly with a local anesthetic (21 gauge needle) from ribs three to eleven under the pleural surface (0.25% Marcaine with epinephrine).
4. *da Vinci* Instrument Arm ③ Port, 5 mm (Red): Place port in the ICS that is two rib spaces inferior to the major fissure and slightly anterior to the spinous process of the vertebral body. Distance to *da Vinci* Instrument Arm ② port should be at least 10 cm.
5. *da Vinci* Instrument Arm ② Port, 8 mm (Green): Placed in the 7th ICS. Distance to *da Vinci* Instrument Arm ③ port is 10 cm and to the camera port should be at least 8-9 cm. If stapler access from this location is deemed necessary, dilate this port to a 13 mm *da Vinci* cannula during the surgery.
6. Assistant Port, 15 mm (White): Use a small 21-gauge needle to identify the most anterior and inferior aspect of the chest that is just above the diaphragmatic fibers. Port location should be chosen so that a triangle is established with Camera Port and Arm ① Port with the Assistant Port at the tip equidistant to each port. It should be two or three ribs lower than and as distant to the *da Vinci* ports as possible to maximize assistant workspace. Keeping this port off the trajectory lines for those ports will facilitate the Patient-side assistant's access for retraction, etc.

Right upper lobectomy

- ❖ Instrumentation: 0° and/or 30° down endoscope, 5 mm Thoracic Grasper (left ③), Cardiere Forceps (left ②) and Permanent Cautery Spatula or Curved Bipolar Dissector (right ①)
- ❖ First inspect the pleural space and explore to ensure that there are no metastatic lesions on the diaphragm or the parietal or visceral pleura.
- ❖ Dissection is started at the N2 mediastinal lymph nodes. If the lung deflates well the nodes #9, #8 and then #7 can be completely removed (*Figure 3*). If the lung does not deflate sufficiently it is best to start at the #7 station and then move cephalad toward the trachea and remove #10R and separate the azygous vein off of the trachea. Removal of the lymph nodes first opens up the anatomy and affords visual inspection of the N2 nodes.
- ❖ The dissection is carried down between the hilar structures and the phrenic nerve.
- ❖ Sweep phrenic nerve gently down to remove the #10R lymph node avoiding the small phrenic vein that goes to the large #10R lymph node that is routinely found in this area.
- ❖ Develop the bifurcation between middle and upper

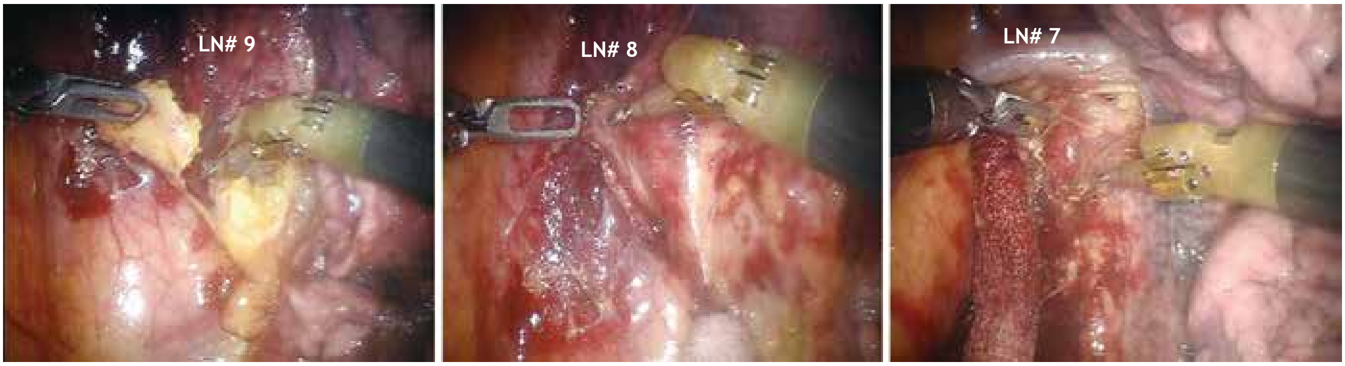

Figure 3 N2 mediastinal lymph node resection.

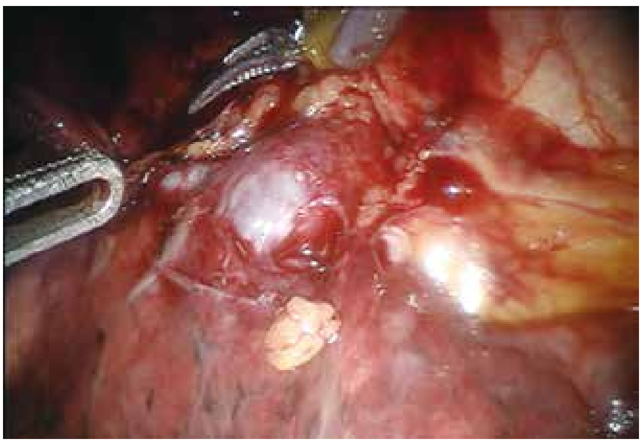

Figure 4 Identification of superior pulmonary artery.

lobe veins by bluntly dissecting it off of the underlying pulmonary artery. It can be easily encircled with the Cardiere Forceps or Curved Bipolar Dissector and a vessel loop; and subsequently stapled with a vascular stapler (*Figure 4*).

- ❖ The #10R lymph node between the anterior-apical pulmonary artery branch and the superior pulmonary vein should be removed or swept up towards the lung. This exposes the anterior apical pulmonary artery branch (*Figure 2*).
- ❖ Continue en bloc dissection of the hilar tissue to cleanly expose the main pulmonary artery.
- ❖ Encircle the superior pulmonary vein with an 8 cm vessel loop and retract it off the pulmonary artery behind it. Using the vessel loop as a guide, the linear stapling device is passed across the right superior pulmonary vein and fired (*Figure 5 A-D*).
- ❖ Next the anterior apical trunk pulmonary artery branch is encircled with a vessel loop and transected with a linear stapler in the same fashion as the vein (*Figure 6*). Exposure might be improved by using the left hand *EndoWrist* instrument to deflect the trachea downward and enable the tip of the stapler device to go above the trachea.
- ❖ The operation is now changed to a posterior approach in contrast to continue this anteriorly as done commonly via VATS lobectomy.
- ❖ The RUL bronchus' anatomy is exposed from posterior one. This is not possible or difficult to do with VATS in an anterior to posterior approach. However, the robot allows us to operate from either ways as seen here. The upper aspect of the RUL bronchus is easily seen coming off the trachea. The dissection is continued inferiorly to expose the inferior edge of the RUL bronchus and free it from the bronchus intermedius. Once the anatomy is identified, a Cardiere Forceps can be placed under the RUL bronchus to confirm complete dissection (*Figure 7*).
- ❖ Lymph node dissection (10R and 11R, hilar and interlobar) is continued along the right main bronchus and the bifurcation between the bronchus intermedius and the upper lobe bronchus identified (*Figure 8*).
- ❖ Encircle the right upper lobe bronchus with a vessel loop and transect with a linear stapler (gold or purple load). Care must be taken to apply only minimal retraction on the specimen to avoid tearing of PA branches (*Figure 9*).
- ❖ Next the posterior segment of the pulmonary artery is exposed. The surrounding N1 nodes can be removed and the posterior artery can be encircled with a vessel loop and taken with a vascular stapler. A vessel-sealing device or Titanium clips applied by the *EndoWrist* Small Clip Applier could be used if the vessel is less than 6

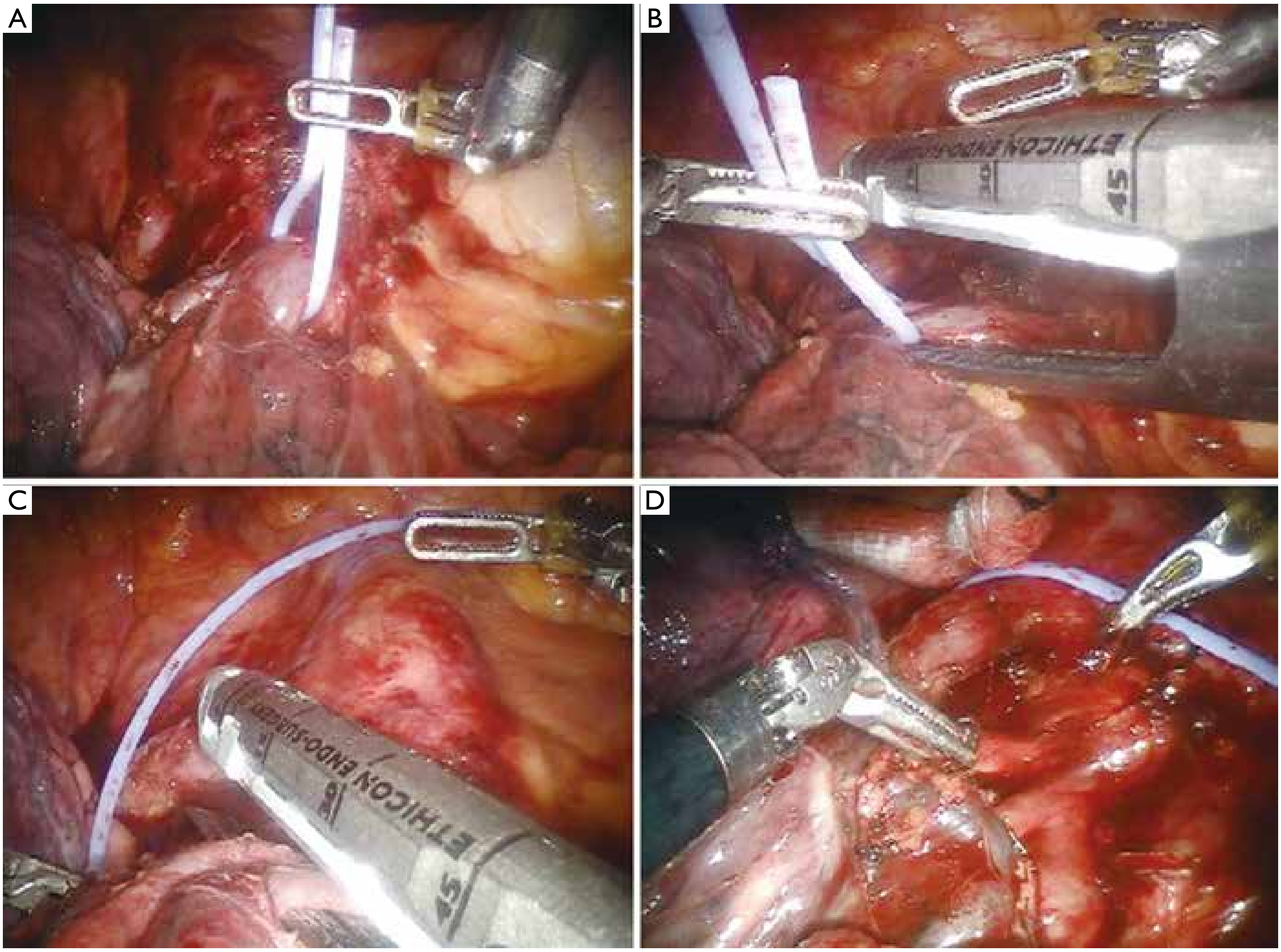

Figure 5 Transection of right superior pulmonary vein: A. vessel loop placed; B. Vessel loop guiding stapler; C. stapler placed; D. vein transected.

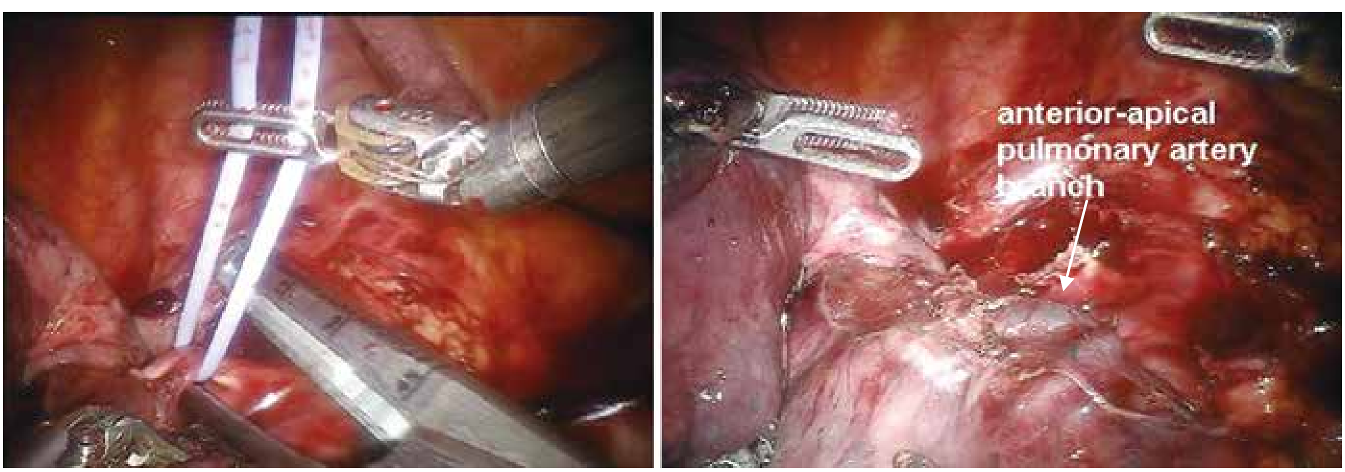

Figure 6 Transection of anterior apical pulmonary artery branch.

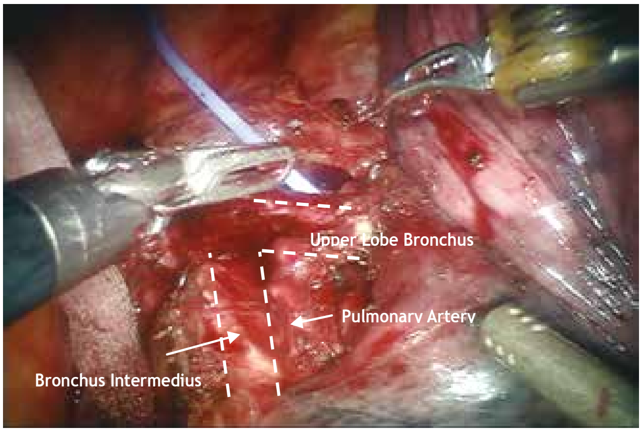

Figure 7 Identification of RUL bronchus, bronchus intermedius and Pulmonary Artery.

Figure 8 Removal of hilar and interlobar lymph node stations (10R & 11R).

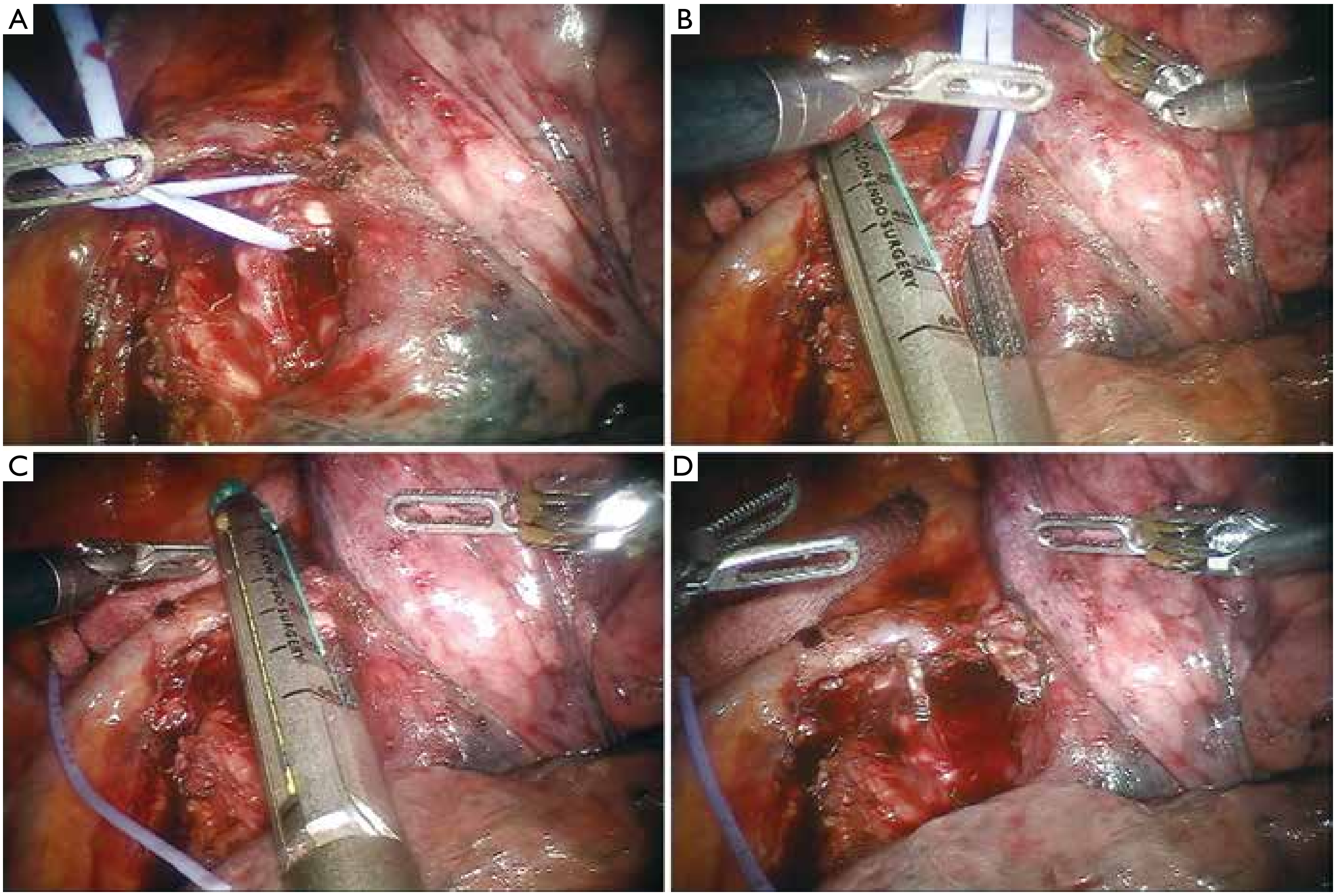

Figure 9 Transection of right upper lobe bronchus: A. vessel loop placed; B. Vessel loop guiding stapler; C. stapler placed; D. bronchus transected.

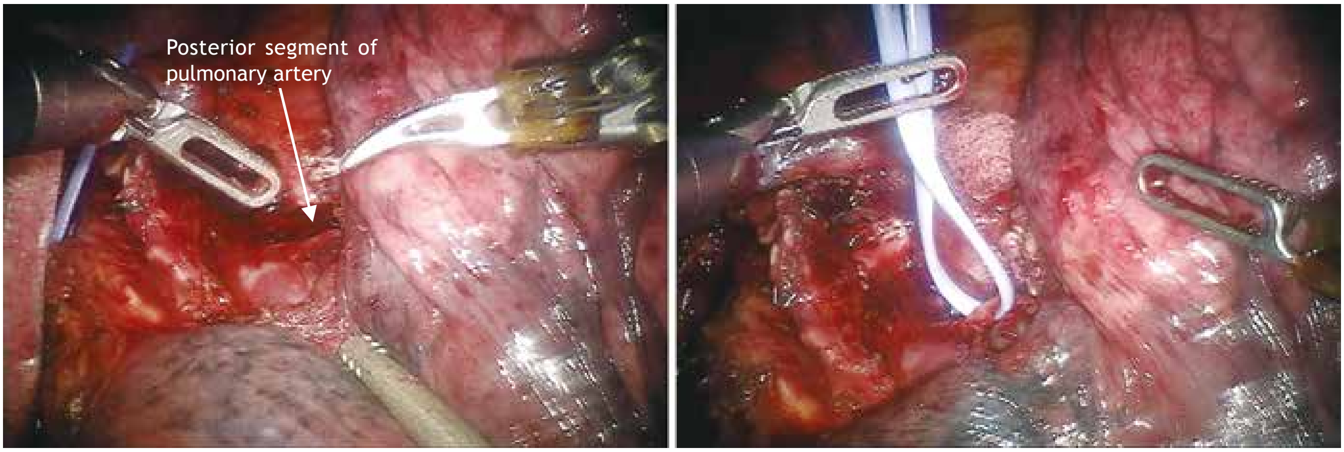

Figure 10 Identification of posterior segment of pulmonary artery.

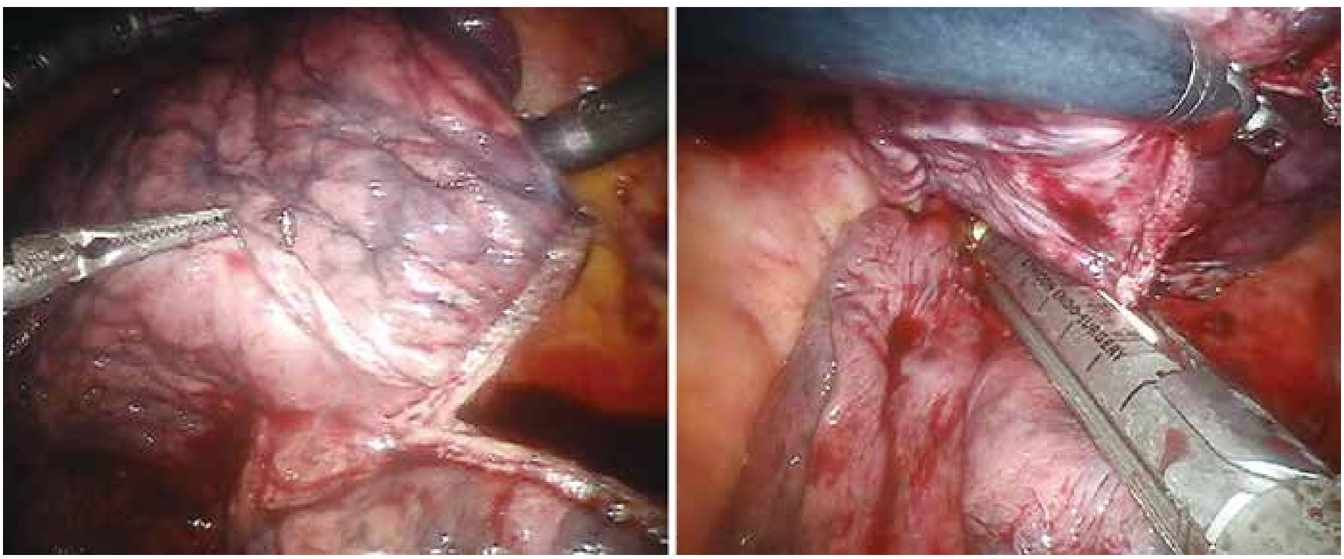

Figure 11 Transection of minor fissure.

mm in size (*Figure 10*).

- ❖ Prior to finishing the operation by stapling the fissure last, the anterior aspect of the pulmonary artery is carefully inspected to ensure that there are no PA branches remaining. If so these are usually quite small and can be easily torn and hence must be carefully ligated.
- ❖ The fissure between the right upper lobe and the right middle lobe is now taken with a gold or purple stapler (*Figure 11*). Usually this is done anterior to posterior, however if the space between the PA and the Right Middle Lobe vein is already developed it can be done in the reverse direction as shown in *Figure 11*.
- ❖ As the fissure is completed the main pulmonary artery should be seen and the stapler should be placed just above it and again ensuring that all small PA branches to the RUL have been taken. The right middle lobe PA branch can be easily seen and should be preserved. The RUL must be lifted up to ensure the specimen bronchus is included in the resected specimen.
- ❖ To delineate the minor fissure, the upper lobe is retracted superiorly and the middle - lower lobe pushed inferiorly (*Figure 12*).
- ❖ Minor fissure is divided with a gold or purple load linear stapler (*Figure 13*).

Figure 12 Minor fissure exposed for transection.

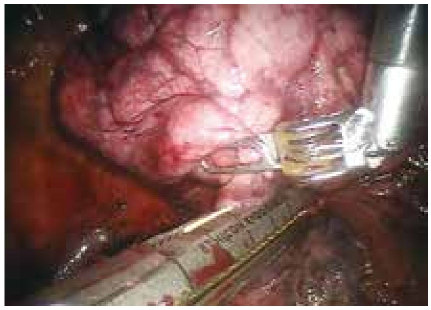

Figure 13 Transection of minor fissure.

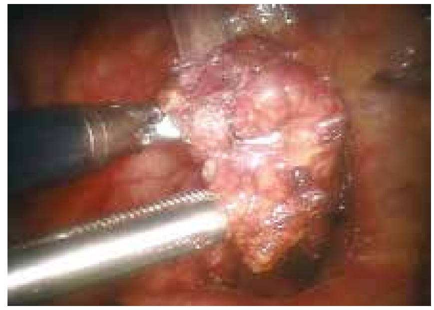

Figure 14 Removal of superior mediastinal lymph node stations.

Figure 15 “Anchor” bag inserted through assistant port.

- ❖ The lobe, now free of any attachments is placed remotely anteriorly and the remaining LN dissection of station 2R and 4R should be performed (*Figure 14*).

Specimen removal

- ❖ Instrumentation: 0° endoscope, 5 mm Thoracic Grasper (left ③), Cardiere Forceps (left ②) and 5 mm Thoracic Grasper (right ①) With completion of the lymph node dissection and the lobe completely resected, an “Anchor” bag is inserted into the chest from the assistant port in the 9^{th} ICS (*Figure 15*).
- ❖ The lobe is then held up freely in the dome of the chest by the Thoracic Grasper. This is to utilize gravity to facilitate bagging of the lobe (*Figure 16*).
- ❖ The open Anchor bag is placed below the freely hanging lobe (*Figure 17*).
- ❖ The lobe is then dropped and pushed into the bag. Visualize that the complete specimen is contained in the bag while the assistant slowly closes the “Anchor” bag (*Figure 18 A-C*).
- ❖ The straps of the bag are brought out though the 15 mm access port.
- ❖ A small 20 Fr chest tube is placed apically and posteriorly via the most anterior port and guided into position by the *EndoWrist* instrument in arm ②. Once completed, CO_2 is turned off and the right thorax vented.
- ❖ *EndoWrist* instruments are removed, the *da Vinci* arms are undocked and Patient cart pushed back.
- ❖ Extend the assistant port in the 9^{th} ICS to an appropriate size needed to remove the tumor en bloc.
- ❖ Pull tissue straight out of thoracic cavity. Once specimen is removed use traditional VATS if needed:
    - o Check for bleeding
    - o Check cannula sites under endoscopic view for hemorrhage.
- ❖ Fill chest with warm saline solution, expand lung to 20 cm H_2O and check for air leaks if not done already previously.
- ❖ If one is found a 5-0 polypropylene with an RB-1 needle can be used to provide an airtight closure of the

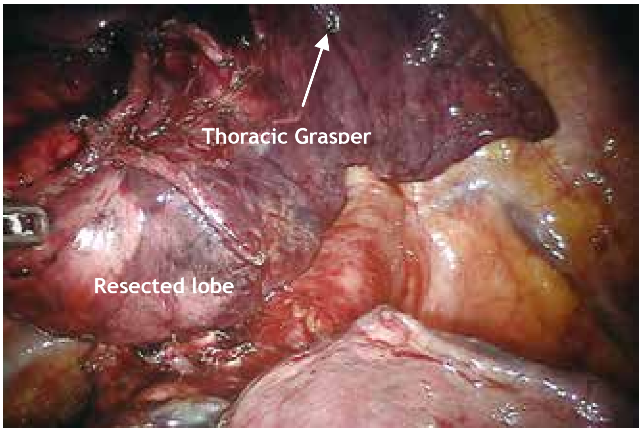

Figure 16 Thoracic Grasper lifting resected lobe for "bagging".

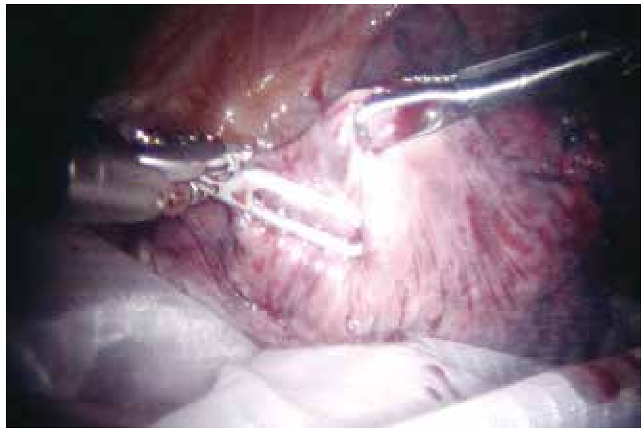

Figure 17 Open "Anchor" bag below free lobe.

Figure 18 A. lobe pushed into bag opening; B. closing of the bag; C. Visual confirmation that specimen is in bag.

bronchial stump.

- ❖ Chest tube is employed as per surgeon's standard routine.
- ❖ Close incisions with absorbable suture:
  - o All cannula sites 8 mm or greater with size 0 suture at the fascia level
- ❖ Skin closed with subcuticular absorbable suture without knots.

Comments

As shown above via the specific operative techniques, pictures, and graphics there is outstanding visibility of the anatomic structures during robotic surgery. Many people worry about encircling the vessels because of the lack of proprioception; however, the reality is that the enhanced visibility allows one to start with a blunt instrument such as a Caudier in a safe plane. The key is starting in a safe plane. For example, when encircling the superior pulmonary vein it is best to dissect the middle lobe vein from the upper lobe vein. Then identify and dissect the plane of the upper lobe vein off of the underlying pulmonary artery. The entrance point for the blunt Caudier and the exit point for the blunt Caudier should be clearly identified. Then the clamp is gently placed just under the vein and you can clearly see it come under the view and above the artery. The key to doing this safely is by first dissecting out both the entry and exit part; secondly, by using the blunt instrument (such as a Caudier; and thirdly, by having a vessel loop and rolled up Ray-Tec available to dissect the tissue off of the clamp as it comes under the vein and a Ray-Tec so compress is immediately available in case of injury and bleeding. Then a vessel loop is placed under the vessel. The vessel is retracted upwards in order to dilate the space with an open Caudier that is gently spread under the vessel. We prefer to use the vessel loop to help guide the stapler around.

The bottom line is the future of robotic surgery is extremely bright. Multiple new instruments are coming to market soon to make the operations safer and more efficient. There are even new robotic surgical techniques being developed, including the use of FIREFLY, immunofluorescence, and fluorescence of specific antigens and perhaps organs (such as the thymus). Careful studies are necessary to provide a responsible cost-benefit analysis of this interesting and exciting era of robotic thoracic surgery.

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Robotic thoracic surgery: from the perspectives of European chest surgeons

Alper Toker

Department of Thoracic Surgery, Istanbul Medical School, Istanbul University, Istanbul, Turkey

Correspondence to: Alper Toker, MD, Professor of Thoracic Surgery. Hamidiye Mah. Barisyolu Cad Agaoglu MyCountry Sitesi G/5 Blok No:3 Cekmekoy, Istanbul, Turkey. Email: aetoker@superonline.com.

Abstract: Although thoracic surgery is one of the fastest growing programs, the results of robotic thoracic surgery reports are presented very rarely. In this manuscript, the development of robotic thoracic surgery programs in Europe and the initial results are discussed. Several European countries lead the development of robotic surgery in the world, especially for lung cancer surgery and for thymus—thymoma surgery. Yet, we may not recognize any major advantage in the outcome when compared to video-assisted thoracic surgery (VATS). But, certainly, the superior capabilities of the intraoperative instrumentation of robotic surgery will be beneficial. More experience in robotic surgery may provide superior results in oncological, physiological and life quality measurements.

Keywords: Lobectomy; robotic surgery; video-assisted thoracic surgery (VATS); lung cancer

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Video-assisted thoracoscopic surgery (VATS) has been a strong alternative to thoracotomy for lobectomy in patients with early stage lung cancer. The success of improved endoscopic video systems and endoscopic staplers has increased the thoracic surgeons' capabilities to perform complicated thoracic procedures since 2000. In the current era, the world wide experience with VATS resections for lung cancer is sufficiently large to compare the outcome with open thoracotomy, which was unforeseen in 1993 by an experienced author of the North America (1). Miller predicted that VATS would be a tool to be used in 25-30% of all activities of an active, general thoracic surgeon's practice. More than this, he did not believe lung cancer surgery could have ever been a common indication for VATS.

In 2008, a comprehensive and methdological review and survey demonstrated that VATS lobectomy was not a commonly used procedure among European surgeons, with a rate of not more than 5% using the VATS technique among the surgeons who filled out the survey (2). Although in current practice, there are several European thoracic surgery clinics performing VATS lobectomy at a rate higher than 50% in all lung cancer patients (personal communications). However, there is still a lack of adoption of the technique. This may be attributed to several factors, including a lack of oncological control by means of lymph node dissection and experience, and limitations in instrumentation and depth sensation. In addition to the above mentioned concerns, a fear of hemorrhage and an inability to control the bleeding has made thoracic surgeons hesitate to adopt the minimally invasive lobectomy. All of these have occurred within the past two decades.

To overcome these limitations in minimally invasive resections, robotic surgery has been designed. With the development of the surgical robot (Intuitive, Da Vinci, Inc, Sunnyvale, CA, USA), the performance of urologic, gynecologic and cardiac operations has been proven to be safe and feasible. Robotic thoracic surgery reports were presented within the past decade very rarely (3-6). Several European countries—Italy, France, Austria, Germany, Switzerland and Belgium—lead the development of robotic surgery in the world, especially Italy for lung cancer surgery and Germany for thymus—thymoma surgery. This manuscript describes the development of a robotic thoracic surgery program in the context of Europe.

European surgeons and their contributions to robotic surgery platform

Several European thoracic surgery centers did important contributions to Robotic thoracic surgery. University of Pisa was the first to perform a robotic lobectomy in Europe with da Vinci Robotic Systems in February 2001 and published this initial experience in 2002 (3). They summarized their robotic lobectomy experience in 2008 on 107 good-risk patients. They reported that all their patients returned to preoperative levels of physical activity within 10 days (7). From November 2006 through September 2008, 54 patients with suspected or proven clinical stage 1 or 2 lung cancer were recruited to undergo robotic lobectomy. Veronesi was the sole surgeon to perform these lobectomies in several European centers. She concluded that the robotic lobectomy with lymph node dissection is practicable, safe and associated with shorter postoperative hospitalization than open surgery. She found that the robotically dissected mediastinal lymph nodes were similar in number to those of open surgery and robotic lobectomy could be applied to early lung cancer treatment (8). In 2013, a large robotic thymectomy series was published by the University of Padua. Authors described the robotic thymectomy technique as a safe and effective procedure. They observed a neurological benefit in great number of patients and a better clinical outcome was obtained in patients with early stages of clinical conditions (9). Four European centers collected their data on robotic thymoma resections. They analyzed 79 patients with early stage thymoma who were operated on between 2002 and 2011. They indicated that the robotic enhanced thoracoscopic thymectomy for early stage thymoma was a technically sound and safe procedure with a low complication rate and short hospital stay (10). The oncologic outcomes seemed good (10).

VATS and robotics and VATS versus robotics

A lobectomy with systematic mediastinal lymph node dissection remains the "gold standard" for the treatment of early-stage NSCLC (11). Although this concept was already accepted during the era of open thoracotomies, lobectomies with VATS continues to be questioned. With the advancement of minimally invasive surgery, many surgeons have developed capabilities to perform lobectomy with VATS. After a decade of collecting data on VATS lobectomies, comparisons of open versus VATS have become available. When a VATS lobectomy is compared with that of thoracotomy, VATS is shown to have a decreased hospital stay, an improved postoperative pulmonary function, decreased pain, and a lower morbidity (12-14). However, concerns remain over the oncological principles of lung cancer surgery and VATS' ability to respect them. The published research favors the abovementioned benefits of the new technology VATS over the open approach (15). Finally, the survival data establishes that VATS is at least equivalent to thoracotomy for the early-stage of NSCLC. Despite the development of new instrumentation for the VATS approach, the standardization of the VATS technique, and the superior outcomes of VATS, a review of the STS database shows a limited adoption (16). Yet, due to the challenges of learning and practicing the techniques, we do not have enough evidence to say that VATS is the "standard-of-care" for the treatment of early stage lung cancer.

Although both VATS and robotics are minimally invasive techniques using a comparable number of ports, there tends to be a comparison or split of the data. While robotic surgeons site VATS' results and benefits, VATS surgeons often deny the similarities, instead demanding the original data provided by the robotic surgeons. As there are not many reports on robotic lung cancer surgeries, it is too early to know and compare the long term survival rates. Recently published reports suggest that there may be certain advantages of the robotic approach over VATS. It is suggested that the robotic surgery offers better instruments and a better view of the operative field: 3-dimensional rather than 2-dimensional; 10× magnification rather than 2× or 3×; and less fogging, therefore less camera manipulation required. Most surgeons who passionately try to learn both the VATS and robotic techniques agree that the robot provides clear advantages for mediastinal and esophageal operations (17). The advantages for robotic lung surgery may include better dissection of enlarged or metastatic N1 lymph nodes off the pulmonary artery, more precise and thorough N2 lymph node dissection, and less operative blood loss. The robot may be less painful than VATS and leads to fewer conversions. However, there are no reports that clearly support these "advantages" and improved outcomes for robotic resections.

There are several large series of lung cancer resection. The robotic group had a reduced morbidity, a lower mortality, an improved mental health, and a shorter hospital stay when comparing the 106 patients who had a lobectomy with robotic surgery with the 318 propensity-matched patients who underwent lobectomy via nerve and rib-sparing thoracotomy (17). According to the author of this paper, robotic surgery is clearly superior to the open approach. Therefore, the concern is not that robotic surgery is superior to the open approach, but if there are any superiorities to the VATS technique.

Swanson and co-workers analyzed the STS data to compare the VATS to robotics. The results indicate that robotic lobectomy and wedge resection seem to have higher hospital costs and longer operating times, without any differences in the adverse events (18). This study shows some noteworthy limitations (18). These include the lack of preoperative data—patient body mass index and smoking habits—and postoperative data—pain scores, quality of life, morbidity, and time to return to work. Furthermore, intraoperative data regarding the precision of surgery—the surgical margins, the adequacy of lymph node dissection, the amount of bleeding, and adverse events during surgery—were not evaluated.

Results of robotic lung cancer surgery

Previous reports demonstrate the safety of robotic pulmonary resections (19,20). Veronesi and associates from Milan report the safety of a 4-arm robotically assisted (not completely portal) lobectomy (with a 3- to 4-cm access incision, such as the one used by VATS surgeons) in 54 patients (8). Ninan and coworkers report the effectiveness of a completely portal 3-arm robotic lobectomy in 74 patients (19). Another study by the same group reports that robotic video-assisted pulmonary resection was accomplished in 197 of 200 patients: a total of 154 patients underwent lobectomy; 4 patients required bilobectomy, and 35 patients underwent segmentectomy. One patient received a left pneumonectomy. Three patients required conversion to a thoracotomy. The median operative time was 90 minutes. The median length of hospital stay was 3 days. The 60-day mortality and morbidity rates were 2% and 26%, respectively. Robotic VATS (RVATS, as the group names the technique) lung resection is technically feasible and safe. Their results indicate that the procedure is associated with a reduced length of stay, and a low morbidity and mortality (20). Our operative results and complications show similarities with this report.

One of the most influential manuscripts presented the long term outcomes of 325 robotic lobectomy patients who were operated on at three thoracic surgery centers (two from Italy and one from the US) from 2002 to 2010 (21). They concluded that the robotic lobectomy was a safe procedure for early stage lung cancer patients. The long term stage specific survial was acceptable and consistent with prior results for VATS and thoracotomy (21).

Learning, education and future perspectives

There are two recently published papers questioning the transition from VATS to robotics.

The second paper evaluates an established VATS single surgeon's learning curve in a robotic lobectomy program (22). This retrospective review was conducted on patients undergoing minimally invasive lobectomy (robotics or VATS) for lung cancer. It concludes that, based on the clinical outcomes, there does not seem to be a significant advantage for an established VATS lobectomy surgeon to transition to robotics. The learning curve for robotic upper lobectomies seems to be significantly more difficult than that for lower lobectomies (22). Although our program demonstrates similarities in terms of starting a robotic thoracic program after an established VATS program, we don't share the conclusions given in this paper. We believe the advancement of the technology brings superior health care. Today we may not recognize these differences as they happened during the initial development of VATS. Today, we may not yet provide the data necessary to demonstrate the superiority of the robotic technology over VATS. But the next generation of surgeons, with their enthusiasm and computer-based capabilities, will decide. Forecasting the future trends, one may clearly see that standardization in surgical education may only be provided through computer-based systems, rather than the classical Halstedian learning systems (see one—do one—teach one). The apprenticeship style of learning may fade away within two decades. Instead, the next generation may rely on simulators, learning through simulation rather than on patients; they may even be recognized and certified as surgeons by the computer-enhanced accreditation systems. Even today, simulators and robots have the capability to differentiate an expert from a novice (23). In this study, the authors describe an open-ended longitudinal study and automated motion recognition system capable of objectively differentiating between the clinical and technical, operational skills in robotic surgery.

The robot measures and collects data on the skill paramaters of the trainees operating it. As the novices gain practice during the training protocols, their results, measured by the robot, converge to be the same as those of expert robotic surgeons (23).

The robotic technology may bring new surgical educational standards worldwide. Through the standardization of these

Table 1 Characteristics of the patients

Patient characteristics	n=87 (%)
Male/female	62/25
Median age, years	56 [7-84]
Median tumor diameter	2.4 cm (0.5-8.5)
Lobectomy	35 (40.2)
Pneumonectomy	2 (2.2)
Segmentectomy	26 (29.8)
Wedge resection (metastasectomy—diagnostic resection for solitary pulmonary nodule)	11 (13)
Mediastinal mass (including bronchogenic and enteric cysts)	12 (13.7)
Giant bullectomy	1 (1.1)

Figure 1 Docking from posterio-superior of the patient for a right lobectomy patient.

techniques, patients may be operated on in a standard way around the world. The computer enhanced programs may allow monitoring of the quality of surgery. Telesurgical apprenticeship or assistance may be provided to those who need mentorship or assistance during a particular surgery. Yet we may not have the data to prove the clear benefits of robotic surgery unless more surgeons adopt the techniques.

From the discussion, it is clear that European chest surgeons credited robotic thoracic surgery and created the most of the literature and the data behind it. We believe that robotic thoracic surgery will be developed by the enthusiastic chest surgeons all around the world. The European Society of Chest Surgeons will start to organize robotic surgery courses and will help dissemination of the knowledge in the upcoming years.

Robotic surgery experience in our center

We started our thoracic robotic program after an established experience of VATS surgery program. Our VATS program included >300 anatomical lung resections and >350 thymectomies and >60 thymomectomies. The idea of the start of a thoracic robotic program relied on the difficulties of some anatomical VATS lung resections. Here, in this manuscript, we presented our experience in the first 29 months of experience. We still continue to perform VATS anatomical resections for lung cancer and other pathologies, which may enable comparative studies in the upcoming years. Our case series demonstrates a nice distribution among pathologies and type of operations. This may provide the evidence of similarities with VATS abilities. We may also claim that the rate of segmentectomy is relatively higher when compared to lobectomy, which may be a sign that the robot could be used for even more precise dissection of small vessels and bronchi.

Between October 2011 and March 2014, 87 consecutive patients (25 females and 62 males) underwent a robotic assisted thoracic surgery. We preferred docking from superior and posterior to the patient in all lung resections (*Figure 1*). The patient characteristics are listed in *Table 1*. Thirty-five patients underwent an anatomical lobectomy. Only two patients underwent lobectomy for benign lesions: one patient with bronchiectasis and one patient with pulmonary aspergilloma. All other patients were operated on for lung cancer. Four patients had a neoadjuvant treatment due to single node N2 disease prior to the scheduled robotic operations. Two patients underwent left pneumonectomy, one patient for invasive N1 lymph node, and the other one for a hilar located, sleeve impossible lesion.

Twenty-six patients were operated on using formal segmentectomies: 13 from the right lung and 13 from the left lung. Eleven patients had a segmentectomy from the upper lobes and 15 patients from the lower lobes. The mean duration of chest tube drainage and postoperative hospital stay were 3±3.1 [1-10] days and 4±1.8 [2-7] days, respectively. Out of 74 lung resection operations, four patients required conversions to a muscle-sparing mini-thoracotomy due to bleeding (two patients) and difficulties (two patients). In our series, upper-lobe NSCLC lesions predominated, with the right upper lobe being the most common tumor site.

No patient required an epidural catheter for postoperative pain control. The median length of stay in the intensive

Table 2 Complications after anatomical lung resections in 63 patients (wedge resections are excluded)

Perioperative events in anatomical lung resections	n=63 (%)
30-day mortality	1 (1.5)
Supraventricular arrhythmia	3 (4.7)
Prolonged air leaks (>5 days)	8 (12.6)
Heart failure	2 (3.1)
Conversion for difficulty	2 (3.1)
Conversion for bleeding	2 (3.1)

care unit (ICU) was 1 (range, 0-1) day. The complication rate for the study cohort was 20 out 87 patients (*Table 2*). Most complications occurred in patients who underwent a lobectomy (9/35). The most common complications were air leaks for more than five days (five patients) and atrial fibrilation (three patients). One patient died within 30 days of the operation; he was discharged after a right upper lobectomy for squamous cell lung cancer. He was readmitted one week later with an infiltration of the contralateral lung and leucocytosis of 88.000/mL. He was diagnosed with a concurrent lymphoblastic lymphoma through the bone marrow aspiration biopsy, and died of chemotherapy side effects.

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Technical strategy for dealing with bleeding during thoracoscopic lung surgery

Zhi-Lan Xiao*, Jian-Dong Mei*, Qiang Pu, Lun-Xu Liu

Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China

*Drs. Zhi-Lan Xiao and Jian-Dong Mei have contributed equally to this article.

Correspondence to: Lun-Xu Liu. Department of Thoracic Surgery, West China Hospital, Sichuan University, No. 37, Guo Xue Alley, Chengdu 610041, China. Email: lunxu_liu@aliyun.com.

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Introduction

Uncontrollable bleeding caused by vascular injury is an important reason for conversion to thoracotomy during thoracoscopic lung surgery. Demmy *et al*. (1) summarized several effective methods for dealing with bleeding, such as the use of thrombostatic material, biological sealant, or discreet utilization of energy sources. However, managing more severe bleeding is quite challenging even for experienced thoracoscopic surgeons.

The most common solution for this situation is compression or tamponade of the injured site while converting to open thoracotomy (1,2). We have previously described a series of skills named the "suction-compressing angiorrhaphy technique (SCAT)" for dealing with severe bleeding due to vascular injury during thoracoscopic lung surgery (3). Bleeding control and angiorrhaphy were both achieved through thoracoscopy in most of the cases of vascular injury in our center. Here, we present our technical strategy for dealing with bleeding and vascular injury during thoracoscopic lung surgery with a video series.

Minor bleeding

Mild bleeding is usually not a troublesome problem and can typically be solved easily. Some biological materials can be used to stop bleeding as previously mentioned in the literature (1,2). However, we generally use the electrocoagulation hook or Harmonic scalpel to achieve exact hemostasis. Titanium or Hemlock clips may also be used to stop bleeding from some visible small blood vessels. The situation which needs to be highlighted is bleeding of the vascular stump after transecting the pulmonary vessels with an endostapler. We choose the electrocoagulation hook to stop bleeding in this situation. The hook is inserted at the bleeding point of the stump to perform a quick electrocoagulation. Special attention is needed to avoid melting the staple and causing additional injury to the vessels.

Major bleeding

The most common etiology of major bleeding is vascular injury, especially injury of major pulmonary artery branches. This is a more serious situation that usually leads to conversion. Dunning *et al*. (4) introduced their "swab-on-a-stick" method to control bleeding temporarily. The method generated a secure interval for emergent thoracotomy. We usually use a suction to control bleeding in these cases before further manipulation of the accident. The next step can be divided into several stages, including transecting the injured vessel after temporary control of bleeding, performing angiorrhaphy with suction-compressing bleeding control, performing angiorrhaphy after proximally clamping the injured vessel, and converting to open thoracotomy.

Transect the injured vessel after temporary control of bleeding

In the first part of *Video 1*, we performed a right lower lobectomy for a 35-year-old female patient with pulmonary sequestration. The anomalous artery of the sequestrated lung located in the inferior pulmonary ligament was mistaken for dense adhesions and was injured by electrocoagulation hook when dissecting the inferior pulmonary ligament. We used two curved Kelly forceps to clamp the injured vessel to stop bleeding first. The distal Kelly forceps was then replaced by a Titanium clip to make sufficient room for the endostapler. Finally, the vascular bundle was directly transected using an endostapler.

The next section of *Video 1* shows an example of clamping the injured site before performing angiorrhaphy. An accidental injury to the truncus anterior occurred during thoracoscopic right upper lobectomy for a patient with adenocarcinoma. The operation was carried out with the single-direction technique as previously described (5). Hilar structures of the upper lobe were transected in the order of superior pulmonary vein, truncus anterior and the upper lobe bronchus. The truncus anterior was injured by the electrocoagulation hook during this procedure. We used the curved Kelly forceps to clamp the vascular laceration temporarily. The superior pulmonary vein was transected for better exposure of the injured artery. We then sutured the injured site with the SCAT method (situations 1 and 2), followed by transecting the truncus anterior using the endostapler.

In these two cases, both of the injured vessels were planned to be transected. However, a temporary bleeding control was still needed to ensure the safety of the operation and to reduce blood loss. For the first case, the injured vessel was relatively long enough to allow the use of an endostapler, even with a pair of Kelly forceps on the vessel. Thus, there was no need to suture the laceration. Angiorrhaphy was needed to control bleeding instead of the Kelly forceps because of limited room for the involvement of an endostapler. The decision whether to use a clip or perform a suture was made according to the convenience of the operation.

Perform angiorrhaphy with suction-compressing bleeding control

If the injured vessels are to be preserved, a more careful angiorrhaphy is needed. As for the situation of a relatively minor injury, side compression of the injured site with the suction tip is usually enough to control bleeding and offers a chance to perform angiorrhaphy directly. In some cases, if the laceration is larger, usually more than 5 mm but not exceeding one-third of the vascular circumference, or if additional preparation is needed before performing angiorrhaphy, we may use a pair of Allis forceps or curved Kelly forceps to clamp the vascular wound. Instances of performing angiorrhaphy directly, with the technique of side compression via suction for bleeding control (SCAT situation 1) are shown in the accompanying video.

In the first case, the patient had a lymph node adherent to the superior vena cava, and injury occurred to the wall of the superior vena cava from the scissors during sharp dissection. We used the suction tip to compress the injured site to avoid blood loss. Angiorrhaphy was then carried out directly. The lymph node was confirmed, by intraoperative frozen section, to be without metastasis and was partially left *in situ*.

The second example presents a case of injury to the azygos vein. The suction was used to compress the injured site immediately, followed by suturing the wound directly. In contrast to the previous case we used a "rotating-technique" when performing angiorrhaphy in this case. The first suture was done on one side of the wound after slightly rotating the suction tip to expose the injury. The second suture was then performed on the other side of the wound after rotating the suction towards the opposite direction.

Perform angiorrhaphy after proximally clamping the injured vessel

Occasionally, an unexpected major laceration of pulmonary artery which exceeds one third of the circumference of the vessel may occur during the operation. Furthermore, sometimes, it may be inconvenient or unsafe to perform suturing directly with a pair of curved Kelly forceps or Allis forceps clamping the vascular laceration. In these cases, we choose to dissect the proximal artery and clamp the vessel. Angiorrhaphy is completed with the method summarized as SCAT situation 3 (3). In this video, we were performing a thoracoscopic left upper lobectomy for a patient with proven adenocarcinoma using the Single-direction method (5). After transecting the superior pulmonary vein and left upper lobe bronchus, we found dense adhesions surrounding the pulmonary artery. The adventitia of the pulmonary artery was then carefully dissected first to get a better exposure of the lingular artery. When we tried to dissect the lingular artery bluntly, an accidental laceration emerged at the crux of lingular artery and the main pulmonary artery. The suction tip was immediately introduced to compress the wound site for bleeding control. A pair of Allis forceps was used to clamp the vascular wound for further manipulation, instead of using the suction for bleeding control. The left main pulmonary artery was then dissected and clamped with endoscopic atraumatic vascular clamp. Angiorrhaphy was then carried out with continuous suture using 5-0 Prolene stitch. After the knot was made, we carefully removed the vascular clamp. The lingular artery was then carefully dissected and transected, followed by transecting the posterior ascending artery and the oblique fissure.

Convert to open thoracotomy

This is considered as the last line of defense to guarantee the safety of thoracoscopic lung surgery. Though most of the bleeding and vascular injury can be successfully managed with the above skills in our daily work, emergent conversion to open thoracotomy is still sometimes unavoidable, for example, when the vessel is unexpectedly transected or there is insufficient room to get a satisfactory proximal clamping of the injured vessel. If an emergent conversion is unavoidable, we often use the suction tip to compress the injured vessel to control bleeding during thoracotomy.

In short, patient safety should always be the top priority during thoracoscopic lung surgery. When it is technically difficult to control the bleeding according to the surgeon's own experience, a timely conversion should be adopted. The emergent conversion is not a label of unsuccessful operation. Instead, it is an important step of thoracoscopic lung surgery when needed.

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Pulmonary artery bleeding caused during VATS lobectomy

Joel Dunning[1], William S. Walker[2]

[1]Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK; [2]Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK

Correspondence to: Joel Dunning, MD, PhD, FRCS. Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK. Tel: 00447801548122; Fax: 00441642815761. Email: joeldunning@doctors.org.uk.

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VATS lobectomy is a very successful procedure with proven benefits over open lobectomy, including reduced hospital stay, reduced tube drainage and better compliance with post operative chemotherapy (1-4).

But there is a learning curve with this operation as with all complex procedures and thus surgeons must be aware of the particular complications that may face them, and the novel methods that are required to try to overcome them (5-7).

In the case presented in this video, we were performing a left upper lobectomy for a proven T1bN0M0 adenocarcinoma. The patient was 73 years old and had COPD with an FEV1 of 40%. He had undergone all routine preoperative tests including a CT Head and a mediastinoscopy to exclude N2 disease.

The video clip commences after the posterior oblique fissure has been opened up, the pulmonary artery has been dissected out and its sheath opened up and we had already dissected out and divided the lingular artery and the posterior segmental artery. The artery that we were now isolating was an anteroapical truncal artery, as in this particular patient there was not further artery after the apical segmental artery to the left upper lobe, and this artery was therefore supplying both segments.

In the video you will see that we had successfully gone round the artery with a 30 cm Roberts artery forcep. We then attempted to introduce the endo GIA stapler with a white 2.5 mm insert in order to divide this vessel. However you may also see that the angle of the stapler is not correct and it is pushing into the crux of the apicoanterior segmental artery and the main pulmonary artery. While attempting to pass the stapler round this vessel a sudden gush or dark blood is seen as the pulmonary artery is breached.

The first step is to introduce a swab mounted on a rampleys forceps. This is our first move for any significant bleeding and such a 'swab-on-a-stick' should always be available in case of significant bleeding. It should be remembered that the pressure in the pulmonary artery is often 1/3rd or less of systemic pressure and therefore pressure via the anterior working port will most often control the bleeding. We pressed on this area for 10 minutes and during that time we first cleared the area of blood and secondly as the bleeding was now controlled, we performed some further dissection in order to gain us better access to the area of the tear. This is an important point in trying to obtain control. When you have temporary control of the bleeding point, you have time to inform your staff about the event, obtain additional instruments if required, make sure that you are ready to perform a thoracotomy, ensure that blood is available, and that any additional instruments such as artery forceps are available.

We then removed the swab and as quite often occurs in these cases, the bleeding had actually stopped. This again allowed us to further mobilize around this vessel, in the hope that we might again be able to pass the stapler and obtain haemostasis endoscopically.

Unfortunately it can be seen that on investigation by the sucker, the PA started to bleed again. While using the suction to investigate this area, a rampleys forcep was placed on the left upper lobe so that bleeding could be quickly covered and pressed on, which was the case.

After this bled for a second time, the decision was made to perform a thoracotomy, but in a balanced and timely manner.

On examination there was a large tear 50% of the diameter of the segmental vessel right at the crux with the main PA. We used a side biting clamp to resect the pulmonary artery branch, we then completed the lobectomy, and finally we placed a small bovine pericardial patch over the defect and sutured this in place with 5.0 prolene. We also covered this with coseal and the patient made an uncomplicated recovery.

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Troublesome bleeding at mediastinoscopy

Joel Dunning[1], William S. Walker[2]

[1]Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK; [2]Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, UK

Correspondence to: Joel Dunning, MD, PhD, FRCS. Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK. Tel: +447801548122; Fax: +441642815761. Email: joeldunning@doctors.org.uk.

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We present in this video a case of troublesome bleeding at mediastinoscopy. Video Mediastinoscopy is a vital part of the pre-operative evaluation of patients prior to lung resection. A full staging mediastinoscopy with lymph node sampling from stations 2L, 2R, 4L, 4R, and 7 are key to competent staging and for the avoidance of lobectomy or pneumonectomy in patients with N2 disease for which there is little or no benefit with surgery alone (1,2).

The case presented in the video is just such a case, with a 67 years old patient who has a right upper lobe T2aN0M0 adenocarcinoma. The PET scan was negative in the mediastinum but we embarked on a staging mediastinoscopy for the reasons highlighted above.

Surgeons will often be most concerned about accidental biopsy of the major vessels including the innominate artery anteriorly, superior vena cava on the right, the left and right pulmonary artery distally, or the aorta to the left, but often the most troublesome bleeding does not come from these major structures. For example, bleeding may occur an exception to that comes when a malignant lymph node has eroded through a major structure and thus pulling on the node disrupts the structure behind which there is an already weakened vessel wall. Thus extra caution should be taken when the mediastinoscopy is performed to confirm already suspected established or extensive N2 disease rather than to look for micrometastases.

One additional caution is paid to the azygous vein. This vessel joins the SVC from posteriorly and it lies close to the 4R lymph nodes.

In this video, all these structures were easily identified and avoided. However, a very large bronchial artery was encountered, which in our experience causes troublesome bleeding much more often than the major structures.

We note that with some additional aforementioned equipment available and some experience, these can often be successfully addressed without resorting to sternotomy.

In our case, early efforts were made to avoid the bronchial artery but as we were reaching over this artery to reach station 7 it started to bleed, perhaps at the site of a side branch to it. We used the suction diathermy to control it initially and then placed and adrenaline soaked swab over it to attempt to vasoconstrict the vessel. While waiting for the adrenaline soaked swab to work, we continued the mediastinoscopy, taking samples from 4R and 4L.

On removal of the swab, the vessel was still bleeding significantly. But during that time we had brought into theatre a 5 mm endoscopic clip applicator which fits easily down the mediastinoscope. Then, using the suction diathermy to control the bleeding, we eventually managed to achieve hemostasis with a 5 mm clip. We continued with the procedure and took samples from station 7 before exiting the mediastinum, leaving behind a surgicel haemostat for further haemostasis.

Acknowledgements

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Prevention and management of postoperative air leaks

Bryan M. Burt, Joseph B. Shrager

Division of Thoracic Surgery, Stanford University School of Medicine, Stanford, USA

Correspondence to: Joseph B. Shrager, MD, Professor of Cardiothoracic Surgery, Chief. Division of Thoracic Surgery, Stanford University School of Medicine, Stanford Hospitals and Clinics, 300 Pasteur Drive, Falk Building CV-207, Stanford, CA 94305, USA. Email: shrager@stanford.org.

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Introduction

A contemporary, practical definition of prolonged air leak (PAL) is an air leak that lasts beyond postoperative day 5. This is consistent with the definition used in the Society of Thoracic Surgeons database and represents a leak whose duration exceeds the average length of stay (LOS) for lobectomy. The reported incidence of PAL ranges from 8% to 26% (1), but the definition of PAL has varied amongst reports. PAL increases the LOS, increases hospital costs, and is associated with elevated rates of empyema and other complications. The most consistently reported risk factors for PAL include poor pulmonary function, use of steroids, performance of an upper lobectomy, presence of a pneumothorax coinciding with an air leak, and the presence of pleural adhesions (1,2). With regard to sublobar resection, although it has yet to be studied scientifically, we believe that segmentectomy may have a higher risk of PAL compared to wedge resection due to the increased thickness of some intersegmental planes and the more extensive dissection involved.

Safeguards and pitfalls

Intraoperative prevention of air leaks

Though less often a problem after sublobar resection compared with lobectomy, attaining pleural apposition without having to resort to high levels of suction appears to be an effective strategy for preventing PALs. There are several techniques that are commonly used to minimize residual space. Mobilization of all intrapleural adhesions and division of the inferior pulmonary ligament is often practiced and likely helpful. Creation of an apical pleural tent at the time of upper lobectomy is a proven technique for decreasing PAL (3). Creation of pneumoperitoneum at the time of lower lobe resection has also been shown to decrease PAL, time of chest tube drainage, and LOS, although not without potential complications (4). Transient diaphragmatic paralysis via injection of the phrenic nerve with a local anesthetic has been described and may serve a similar purpose.

The use of sealants and buttressing material in pulmonary resection has been recently and comprehensively reviewed (5). Whereas synthetic sealants more reliably decrease the occurrence, magnitude, and duration of air leak than do fibrin sealants, this does not translate consistently into a substantial reduction in the duration of chest tube drainage or hospital stay. Similarly, routine use of staple-line buttressing has shown variable results. For surgery in the setting of severe emphysema (e.g., LVRS), randomized data has suggested that buttressing is effective, and one study also suggests that sealants may in fact be useful in patients with severe emphysema (6). Other often practiced, but less studied, techniques for intraoperative prevention of air leak include minimizing dissection within the fissure, minimizing inspiratory pressures when re-inflating the lung, careful attention to avoid overlapping parenchymal staple lines, and closing the surgical stapler slowly in thick tissues. Our opinion is that attention to these intraoperative details may be at least as effective as the commercially available approaches.

Postoperative chest tube management

The balance of evidence from randomized trials addressing water seal or reduced suction algorithms suggest that some version of reduced or part-time suction likely decreases the duration of air leak after pulmonary resection in most patients (1). Although high level evidence is not available specifically for patients with severe emphysema, expert consensus and extensive clinical experience (in LVRS) suggest that patients with an FEV_1 <40% predicted are optimally treated with water seal in the absence of a large, symptomatic, or growing pneumothorax; progressive subcutaneous emphysema; or clinical deterioration. The traditional use of –20 cm water of suction is counterproductive in these patients. For patients without severe emphysema, available evidence suggest that either a lower amount of suction (7) or preferably water seal are reasonable, with the same contraindications, in patients with a less than large or symptomatic air leak (1).

Non-invasive management of prolonged air leak (PAL)

It is rare that aggressive re-interventions are required to treat PALs. The treatment strategy of watchful waiting is largely successful. Approximately 95% of PALs that permit waterseal will resolve within a few weeks of operation with chest tube drainage alone, with only rare development of empyema (1). For patients with no more than a small, stable, and asymptomatic pneumothorax on water seal, PALs can be managed in the outpatient setting using a one-way valve attached to the drain. If it is necessary to differentiate air leak from residual space evacuation, the patients can be admitted for a "provocative clamping" trial, and the majority of these patients will be able to safely have their chest tubes removed.

If a period of watchful waiting is unsuccessful in treating a PAL, or if water seal is not tolerated due to a larger leak, one must consider active interventions to mechanically seal the site of the leak. Most of these options are supported by expert consensus with variable amounts of published data. If the residual lung is fully expanded, chemical pleurodesis with instillation via the thoracostomy tube of tetracycline, doxycycline, or talc can promote pleural symphysis and leak closure. Autologous blood patch is another simple and often effective treatment, although some reports suggest an associated increased risk of intrathoracic infection.

Invasive management of prolonged air leak (PAL)

Invasive procedures are indicated to treat PALs if more conservative measures fail. Pneumoperitoneum instilled through a transabdominal catheter has been reported to be effective in some cases. Unidirectional endobronchial valves, originally studied for treatment of emphysema, have emerged as a useful intervention for some patients with PAL (8). Although data are currently limited, these devices have received Humanitarian Device Exemption approval from the Federal Drug Administration for this purpose.

Surgical re-exploration is rarely needed but must be considered when other approaches have failed. The choice of operation depends upon multiple factors. Bronchoscopy should be done to rule out a bronchial rather than a parenchymal fistula. If the residual lung is relatively normal, the leak can be re-stapled or oversewn with good results. Decortication of surrounding lung may be required to facilitate full lung expansion. Parietal pleurectomy or mechanical pleurodesis can be added when pleural apposition can be achieved. If a residual space is present, that space should be obliterated with either muscle or omental transposition. Following sublobar resection, completion lobectomy may be necessary on rare occasions. Thoracoplasty or the creation of an open window can be considered under extreme circumstances.

Comments

A variety of options are available to prevent and manage PALs. Intraoperative technical details are likely important in reducing their incidence. Pleural tents and pneumoperitoneum are helpful when residual spaces are likely; commercial buttresses and sealants have shown mixed results outside of severe emphysema and are expensive. Optimal postoperative management of chest tubes appears to include less than the traditional –20 cm H_2O of suction in most patients. Non-invasive approaches to resolve PALs are almost always effective, but when required, operative intervention is largely successful.

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The application of capnography to differentiate peri-chest tube air leak from parenchymal leak following pulmonary surgery

Jonathan D. Oparka, William S. Walker

Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, Edinburgh, UK

Correspondence to: Jonathan D. Oparka. 51 Little France Crescent, Old Dalkeith Road, EH164SA Edinburgh, UK. Email: jonoparka@hotmail.com.

Abstract: Prolonged air leak is a common complication of pulmonary resection. However, while a bubbling chest drain is commonly related to parenchymal air leakage, it may also be caused by air entering the pleural cavity via an incomplete seal of the tissues at the chest tube insertion site. Examination alone is not sufficient to guide the surgeon as to which of the above complications is responsible for drain bubbling. We describe a simple method, whereby a CO_2 monitoring device is attached to the chest drain to determine whether the air loss observed is in fact due to a pulmonary air leak.

Keywords: Lung cancer surgery; lobectomy; pleural air leak; surgery complications; postoperative care

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Introduction

Air leaks represent a common complication following pulmonary resection (1,2). In most individuals, these will resolve in the early postoperative period but persistent air leaks are demonstrated to result in prolonged hospital stays, increased costs and risk of infection (3-5). Attention has been given to intraoperative measures to limit the incidence of air leaks such as sealants and staple line buttresses; however, their efficacy remains unclear (6).

The postoperative management of chest tubes therefore remains an essential component of patient care. Whilst it is acceptable to manage persistent air leaks on an outpatient basis with a Heimlich valve or similar compact drainage device, this can be uncomfortable for patients and is demonstrated to lower patient satisfaction (7). The goal of the surgeon is therefore to optimize the inpatient assessment of air leaks and ensure safe and early removal of chest tubes.

Previously, there was little to guide the surgeon in the timing of chest tube removal other than clinical experience. Recent developments have led to the use of digital air leak devices, which give a quantitative measure of the air leak size (8). However, these devices are costly, and often clinical decisions remain subjectively based on the observation of bubbles in the chest drain (9). A major limitation of this approach is the inability to determine whether the bubbles are representative of a pulmonary air leak or of air drawn into the pleural cavity via an incomplete seal of the tissues around the chest tube. The latter occurs due to the negative intra-thoracic pressures generated during respiration, and is particularly evident in thin patients in whom tissue closure often fails to achieve an adequate seal during prolonged drainage.

In this article, we describe a simple method to determine the nature of chest drain bubbling which, in our practice, has optimized the postoperative management of pulmonary resection patients.

Methods

Following observation of chest drain bubbling, clinical examination is performed, with attention given to auscultation and percussion of the chest and the inspection of any surgical wounds. If necessary, a plain chest radiograph is performed to confirm the presence or absence of a significant pneumothorax. Whilst a pneumothorax may be evident, these routine interventions cannot confirm an associated pulmonary air leak.

The technique described here relies on the detection of raised CO_2 levels in the chest drainage system to confirm a pulmonary air leak. If chest drain bubbling is a result of air entering the pleural space via the chest tube wound, then the levels of CO_2 in the chest drainage system are expected

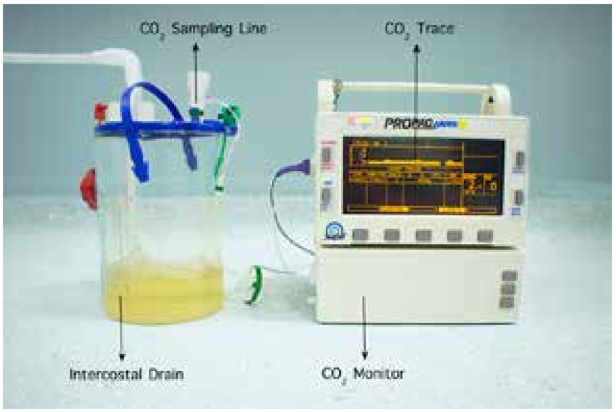

Figure 1 Arrangement of equipment.

Figure 2 CO_2 waveform in the presence of parenchymal air leak.

to be normal [similar to the atmosphere].

A Propaq® Encore Vital Signs Monitor (WelchAllyn® NY, USA) is attached to the chest drain via a standard CO_2 sampling line. Alternative handheld vital signs monitors used in the intensive care unit settings may also be suitable for this task. The elbow connector of the sampling line is attached to the exhaust of the chest drain system (*Figure 1*).

The sidestream CO_2 option is selected, which will display the measured CO_2 levels as both a waveform and a numeric value. The patient is then asked to take some controlled, deep breaths whilst the resultant waveform is observed. In the event of a pulmonary air leak, the monitor will display a characteristic CO_2 waveform (*Figure 2*). Conversely, it is assumed that chest tube bubbling is a result of air drawn through the chest tube wound in the absence of a CO_2 waveform.

Comment

This simple technique can prevent chest tubes being left in unnecessarily and has greatly improved our management of chest drainage systems in postoperative patients. Using this technique has also reduced the number of patients discharged home with compact chest drainage systems. Whilst described here as an aid to managing drains following pulmonary resection, the technique is equally applicable to other surgical procedures including bullectomy and lung biopsy. In summary, we have found the technique described here to be safe, cost-effective and reliable at confirming the presence or absence of a pulmonary air leak following pulmonary resection.

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Meta-analysis of intentional sublobar resections versus lobectomy for early stage non-small cell lung cancer

Christopher Cao[1,2], Sunil Gupta[1], David Chandrakumar[1], David H. Tian[1], Deborah Black[3], Tristan D. Yan[1,4]

[1]The Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia; [2]Department of Cardiothoracic Surgery, Prince of Wales Hospital, Sydney, Australia; [3]Faculty of Health Sciences, University of Sydney, Sydney, Australia; [4]Department of Cardiothoracic Surgery, Royal Prince Alfred Hospital, Sydney, Australia

Correspondence to: Christopher Cao. Collaborative Research (CORE) Group, Macquarie University, Sydney, Australia. Email: drchriscao@gmail.com.

Background: Surgical resection is the preferred treatment modality for eligible candidates with non-small cell lung cancer (NSCLC). However, the selection of sublobar resection versus lobectomy for early-stage NSCLC remains controversial. Previous meta-analyses comparing these two procedures presented data without considering the significant differences in the patient selection processes in individual studies. The present study aimed to compare the overall survival (OS) and disease-free survival (DFS) outcomes of patients who underwent sublobar resections who were also eligible for lobectomy procedures with those who underwent lobectomy.

Methods: An electronic search was conducted using five online databases from their dates of inception to December 2013. Studies were selected according to predefined inclusion criteria and meta-analyzed using hazard ratio (HR) calculations.

Results: Twelve studies met the selection criteria, including 1,078 patients who underwent sublobar resections and 1,667 patients who underwent lobectomies. From the available data, there was no significant differences in OS [HR 0.91; 95% confidence interval (CI) 0.64-1.29] or DFS (HR 0.82; 95% CI 0.60-1.12) between the two treatment arms. In addition, no significant OS difference was detected for patients who underwent segmentectomies compared to lobectomies (HR 1.04; 95% CI 0.66-1.63, P=0.86).

Conclusions: Using the available data in the current literature, patients who underwent sublobar resection for small, peripheral NSCLC after intentional selection rather than ineligibility for greater resections achieved similar long-term survival outcomes as those who underwent lobectomies. However, patients included for the present meta-analysis were a highly selected cohort and these results should be interpreted with caution. The importance of the patient selection process in individual studies must be acknowledged to avoid conflicting outcomes in future meta-analyses.

Keywords: Sublobar resection; segmentectomy; non-small cell lung cancer (NSCLC); meta-analysis

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Introduction

The primary and preferred treatment of early stage non-small cell lung cancer (NSCLC) remains to be surgical resection for eligible candidates. Traditionally, this was performed by lobectomy or greater resection procedures (1). However, sublobar resections in the form of wedge resections or segmentectomies have been reported as an alternative surgical technique, especially in patients with significant comorbidities or limited pulmonary function.

Conflicting outcomes for sublobar resections versus lobectomies have been reported previously, and the issue remains controversial, despite a randomized-controlled trial published by the Lung Cancer Study Group (LCSG) in 1995 (2). Importantly, differences in patient selection and baseline characteristics in the two treatment groups have obscured the evidence for these surgical approaches. It is important to recognize that survival outcomes of patients who were allocated to sublobar resections due to significant comorbidities rather than intentional selection must be vastly different, and any analysis must take into account of the patient selection process to either the lobectomy or sublobar resection groups.

The aim of the present meta-analysis was to compare the overall survival (OS) and disease-free survival (DFS) outcomes of patients who underwent either a lobectomy or a sublobar resection in a population that could have tolerated either procedure. That is, assessing patients who were intentionally allocated to the sublobar resection group rather than deemed inoperable by the lobectomy approach. A subgroup analysis was performed to compare the OS of segmentectomy versus lobectomy in this study cohort.

Methods

Literature search strategy

A systematic electronic search was performed using Ovid Medline, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Database of Abstracts of Review of Effectiveness from their dates of inception to December 2013. To achieve the maximum sensitivity of the search strategy and identify all potentially relevant studies, we combined "segmentectomy" or "sublobar" or "limited" or "sublobectomy" or "wedge resection" as Medical Subject Headings (MeSH) terms or keywords with "lobectomy" and "survival" or "mortality" and "NSCLC" or "lung cancer". All relevant articles identified were assessed with application of predefined selection criteria.

Selection criteria

Eligible studies included those in which comparative outcomes were presented for patients with early-stage NSCLC who underwent sublobar resections or lobectomies. Sublobar resections included anatomical segmentectomies or wedge resections, and subgroup analysis was performed for segmentectomies when data was available. To minimize differences between baseline patient characteristics, studies in which patients were allocated to the sublobar resection group due to increased comorbidities were excluded from analysis. When centers published duplicate trials with accumulating numbers of patients or increased lengths of follow-up, only the most updated reports were included for qualitative appraisal. When data were presented separately for different stages of disease, early-stage NSCLC were selected where possible. All publications were limited to human subjects and in English language. Abstracts, case reports, conference presentations, editorials and expert opinions were excluded.

Data extraction and critical appraisal

The primary outcomes included OS and DFS. All data were extracted from article texts, tables, and figures. Two investigators (D.C. and S.G.) independently reviewed each retrieved article. Discrepancies between the two reviewers were resolved by discussion and consensus. The final results were reviewed by the senior investigators (C.C. and T.D.Y.).

Statistical analysis

Meta-analysis was performed by combining the results of reported OS and DFS. Hazard ratio (HR) and associated variance were obtained or calculated from each selected study using techniques described by Tierney and Parmar (3,4). When direct calculations were not possible due to a lack of presented data, HRs were estimated using Kaplan-Meier graphs. Calculations were performed independently by two researchers (C.C. and D.H.T.) and discrepancies were discussed to reach consensus. The summary statistical analysis was conducted with Review Manager Version 5.1.2 (Cochrane Collaboration, Software Update, Oxford, United Kingdom). I^2 statistic was used to estimate the percentage of total variation across studies, due to heterogeneity rather than chance.

Results

Quantity and quality of trials

A total of 1,387 records were identified through the five electronic database searches, with three additional studies identified through other sources. After removal of duplicates and limiting the search to humans and English language, 913 articles remained to be screened. Exclusion of irrelevant studies resulted in 145 articles, which were retrieved for more detailed evaluation. After applying the selection criteria, 12 articles remained for assessment, including 1,078 patients who underwent sublobar resections and 1,667 patients who underwent lobectomies (2,5-15). A summary of the search strategy is presented in *Figure 1* and a review of study characteristics is presented in *Table 1*. Baseline patient characteristics included in the present meta-analysis appeared to show similar age and gender distribution between the two surgical treatment groups. However, tumor size was found to be generally smaller in the patients who underwent sublobar resection. A summary of these findings are presented in

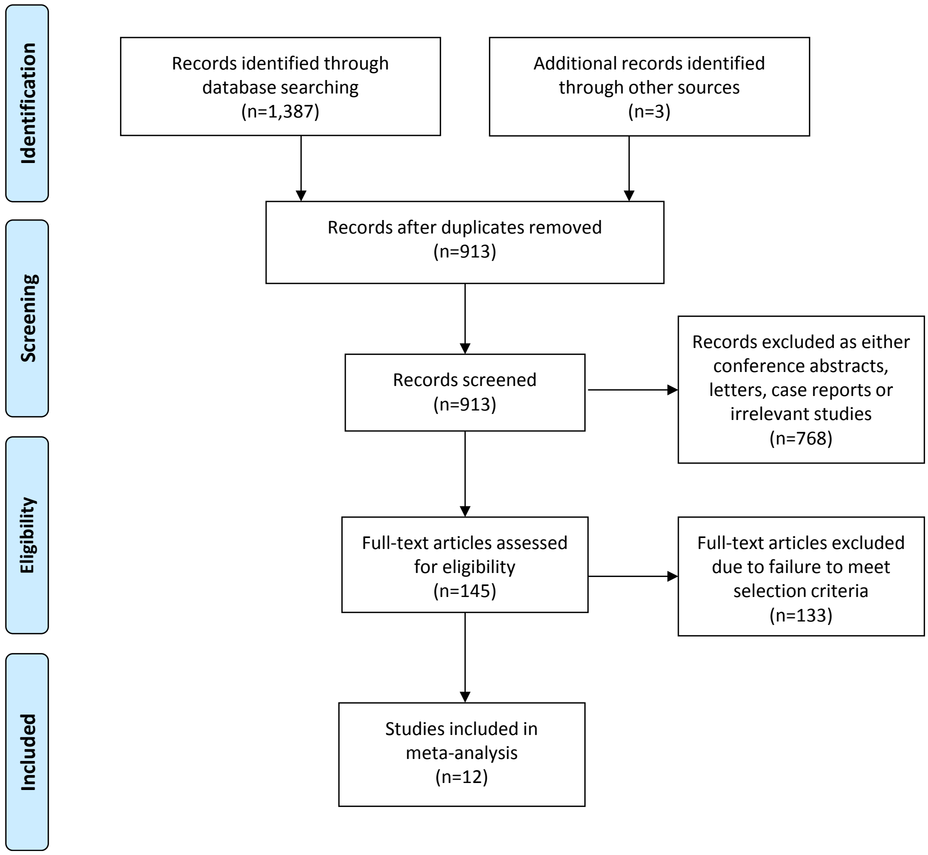

Figure 1 Summary of search strategy performed to identify relevant comparative studies on sublobar resections *vs.* lobectomies for early-stage NSCLC. NSCLC, non-small cell lung cancer.

Table 2. Adenocarcinomas accounted for the majority of pathological findings in all of the included studies, and nearly all studies were limited to stage I disease. A summary of histopathological and staging data for the selected studies is presented in *Tables 3* and *4*, respectively.

Of the twelve studies identified for inclusion in the present meta-analysis, one study was a randomized controlled trial that compared 122 patients who underwent sublobar resections with 125 patients who underwent lobectomy (2). The remaining 11 studies were observational comparative studies, including three studies that reported prospectively collected data (10,11,15). One recent report by Tsutani *et al.* utilized propensity score analysis to adjust for potential differences in patient characteristics between the segmentectomy and lobectomy treatment groups (15). Reported median follow-up periods ranged from 30 to 98 months, but there was variation according to the treatment group and a lack of routine imaging to detect disease recurrence. Individual studies were also limited by the population size, which was generally less than 150 patients in each treatment arm, as summarized in *Table 1*.

Sublobar resections *vs.* lobectomies

Using the available data in the existing literature, 12 studies involving 1,078 patients who underwent sublobar resections were compared to 1,667 patients who underwent lobectomies to assess the OS from the date of surgery. The combined HR for OS was 0.91 [95% confidence interval (CI) 0.64-1.29; P=0.61], as shown in *Figure 2*. DFS was reported in five studies involving 600 patients who underwent sublobar resections and 1,039 patients who underwent lobectomies. Comparative data demonstrated no significant differences as the HR for DFS was 0.82 (95% CI 0.60-1.12; P=0.21), as shown in *Figure 3*.

Segmentectomies *vs.* lobectomies

A subgroup analysis was performed for segmentectomies

Table 1 Study characteristics of relevant articles identified for meta-analysis comparing sublobar resection versus lobectomy for patients with NSCLC

Author	Year	Institution	Study period	Sublobar (n)	Lobectomy (n)	Selection for sublobar approach	Follow-up (median months)
Read (5)	1990	McClellan Memorial Veterans Hospital, USA	1966-1988	113 (S:107, W:6)	131	NR	Sub: 42, Lob: 54^{M}
Warren (6)	1994	Rush-Presbyterian-St. Luke's Medical Centre	1980-1988	38 (S:38, W:0)*	34*	Small and peripherally located lesions	NR
Ginsberg (2)	1995	North American Lung Cancer Study Group Institutions, USA	1982-1988	122 (S:82, W:40)	125	Randomized study	>54
Kodama (7)	1997	Osaka Medical Center, Japan	1985-1996	46 (S:46, W:0)	77	Well-defined peripheral tumor <2 cm	Sub: 30, Lob: 83
Koike (8)	2003	Niigata Cancer Centre Hospital, Japan	1992-2000	74 (S:60, W:14)	159	Clinical T1 peripheral NSCLC <2 cm	Sub: 53 ± 22^{M} Lob: 50 ± 32^{M}
Okada (9)	2006	Hyogo Medical Center for Adults, Niigata Cancer Centre Hospital & Osaka Medical Centre, Japan	1992-2001	305 (S:NR, W:NR)	262	Clinical T1 peripheral NSCLC <2 cm	Sub: 72, Lob: 71
Kodama (10)	2008	Osaka Medical Center, Japan	1997-2002	58 (S:25, W:33)	80	<2 cm and GGO ratios	Sub: 91, Lob: 98
Sugi (11)	2010	Yamaguchi-Ube Medical Centre, Japan	2001-2004	33 (S:33, W:0)	111	Tumors <2 cm with high GGO and >2 cm from periphery	60
Ichiki (12)	2011	University of Occupational and Environmental Health, Japan	2001-2008	35 (S:18, W:17)	104*	Adenocarcinoma <10 or 11-20 mm in which >50% GGO	>60
Yamashita (13)	2012	Oita University Hospital, Japan	2003-2011	90 (S:90, W:0)	124	NR	30
Hamatake (14)	2012	Fukuoka University School of Medicine, Japan	1995-2011	66 (S:32, W:34)	77	Pure GGO on CT and <1 cm in size. Wedge if close to pleura, segmentectomy if non-peripheral lesion	NR
Tsutani (15)	2013	Hiroshima University, Kanagawa Cancer Center, Cancer Institute Hospital & Hyogo Cancer Center, Japan	2005-2010	98 (S:98, W:0)	383	Peripheral lesion that could be completely resected by segmentectomy	43.2

NSCLC, non-small cell lung cancer; *, stage T1a disease analyzed; ^{M}, mean; S, segmentectomy; W, wedge resection; Sub, sublobar; Lob, lobectomy; GGO, ground glass opacity; NR, not reported.

Table 2 A summary of patient baseline characteristics in comparative studies on sublobar resection versus lobectomy for patients with NSCLC

Author	Age (mean)		Male gender, n [%]		Mean tumor size (cm)	
	Sublobar	Lobectomy	Sublobar	Lobectomy	Sublobar	Lobectomy
Read (5)	62.4±7.5		242 [99]		2.03±0.6	
Warren (6)	63.9±9.8	63.8±9.9	44 [67]	67 [65]	2.23±0.97	3.28±1.71
Ginsberg (2)	>60^{M}	>60^{M}	149 [61]		≤3	
Kodama (7)	61^{M}	61^{M}	31 [67]	46 [60]	1.67±0.50	2.29±0.52
Koike (8)	64.2±7.2	65.3±9.5	38 [51]	80 [50]	1.5±0.4	1.7±0.4
Okada (9)	63.2	64	167 [55]	146 [56]	1.57	1.62
Kodama* (10)	60^{M}		90 [50]		NR	NR
Sugi (11)	61.6±9.4	64.8±9.4	19 [44]	31 [33]	1.42±0.44	2.33±0.69
Ichiki (12)	67.9	67.1	15 [43]	64 [56]	<2	<2
Yamashita (13)	69^{M}	68^{M}	41 [46]	73 [59]	1.5^{M}	2.0^{M}
Hamatake (14)	64		62 [43]		0.8	
Tsutani (15)	67^{M}	66^{M}	45 [46]	169 [44]	1.7^{M}	2.2^{M}

Data is presented as numbers with percentage of study population in brackets. NSCLC, non-small cell lung cancer; ^{M}, median; NR, not reported; *, baseline characteristics in this study included patients operated on for reasons other than NSCLC.

versus lobectomies, which included seven studies involving 551 patients in the segmentectomy group and 999 patients who underwent lobectomies. There was no statistically significant difference between the two surgical intervention groups, and the combined HR for OS was 1.04 (95% CI 0.66-1.63, P=0.86), as shown in *Figure 4*.

Discussion

The selection of the appropriate surgical resection procedure for patients with small, peripheral NSCLC remains controversial. On one hand, lobectomy is commonly considered to be the standardized approach to achieve long-term oncological efficacy and minimize the risks of local recurrence (16). Conversely, sublobar resections have been demonstrated to preserve lung function without compromising DFS (9). Unfortunately, the presentation of the clinical evidence on long-term outcomes has been unclear, partly due to the collation of clinical data without considering the variable patient selection processes of comparative studies. The primary focus of the present meta-analysis was to compare patients who underwent sublobar resections who were also eligible for lobectomy procedures. Patients who underwent segmentectomy or wedge resection because they were considered too frail or had insufficient lung capacity for lobectomy resection were excluded from analysis. This analytical approach for NSCLC has not been performed previously in the medical literature.

According to our findings, patients who intentionally underwent sublobar resections did not demonstrate any significant OS or DFS differences compared to patients who underwent lobectomy. Furthermore, patients who underwent segmentectomy also had similar survival outcomes compared to the lobectomy approach. It is important to emphasize that patients included in the individual comparative studies selected for the present analysis generally had early-stage NSCLC and often with ground glass opacities. This cohort of patients is increasingly being diagnosed after the initiation of more aggressive and accurate imaging screening programs in selected countries (17,18). In addition, the level of evidence was relatively low, with only one RCT and the rest of the studies consisting of level IV evidence. Our findings contradict previous meta-analyses that combined patients who underwent sublobar resections due to significant comorbidity or limited pulmonary functions with those who underwent intentional resection for comparison with lobectomy procedures (19,20).

The only completed randomized controlled trial was conducted by the LCSG from 1982 to 1988 (2). Computed tomography was not routinely performed and positron emission tomography was not available. In addition, T1N0 criteria at the time included tumors less than 3 cm, and patients who underwent sublobar resections were

Table 3 The histopathological subtype of tumors in comparative studies of sublobar resection versus lobectomy for patients with NSCLC

Author	Adenocarcinoma		Squamous cell		Bronchoalveolar		Large cell		Adenosquamous		Neuroendocrine		Other	
	Sub	Lob	Sub	Lob	Sub	Lob	Sub	Lob	Sub	Lob	Sub	Lob	Sub	Lob
Read (5)	NR	NR	137 [56]		NR	NR	NR	NR	NR	NR	NR	NR	107 [44]§	
Warren (6)	44 [67]	53 [51]	15 [23]	35 [34]	0 [0]	0 [0]	2 [3]	9 [9]	0 [0]	0 [0]	0 [0]	0 [0]	5 [8]	6 [6]
Ginsberg (2)	NR	NR	30 [25]	33 [26]	NR	NR	NR	NR	NR	NR	NR	NR	92 [75]§	92 [74]§
Kodama (7)	36 [78]	61 [79]	8 [17]	13 [17]	0 [0]	0 [0]	2 [4]	3 [4]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]
Koike (8)	68 [92]	141 [89]	5 [7]	17 [11]	NR	NR	NR	NR	NR	NR	NR	NR	1 [1]	1 [1]
Okada (9)	276 [90]	229 [87]	27 [9]	30 [12]	0 [0]	0 [0]	0 [0]	0 [0]	2 [1]	3 [1]	0 [0]	0 [0]	0 [0]	0 [0]
Kodama (10)	58 [100]	70 [88]	0 [0]	4 [5]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	6 [8]
Sugi (11)	2 [5]	21 [22]	2 [5]	8 [8]	NR	NR	0 [0]	4 [4]	0 [0]	2 [2]	NR	NR	39 [91]*	60 [63]*
Ichiki (12)	35 [100]	114 [100]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]
Yamashita (13)	26 [29]	51 [41]	11 [12]	20 [16]	48 [53]	52 [42]	NR	NR	NR	NR	NR	NR	5 [6]	1 [1]
Hamatake (14)	127 [89]		7 [5]		0 [0]		0 [0]		1 [1]		0 [0]		9 [6]	
Tsutani (15)	98 [100]	383 [100]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]	0 [0]

Data is presented as numbers with percentage of study population in brackets. NSCLC, non-small cell lung cancer; §, non-squamous origin; *, tumors classified according to the Noguchi classification system; NR, not reported.

Table 4 Staging of lung cancer in comparative studies for sublobar resection versus lobectomy

Author	Sublobar resection						Lobectomy					
	Stage I	Stage IA	pT1a [<2 cm]	pT1b [2-3 cm]	Stage IB	>Stage I	Stage I	Stage IA	pT1a [< 2 cm]	pT1b [2-3 cm]	Stage IB	>Stage I
Read (5)	113 [100]	NR	NR	NR	NR	0 [0]	131 [100]	NR	NR	NR	NR	0 [0]
Warren (6)	66 [100]	51 [77]	38 [58]	13 [20]	15 [23]	0 [0]	103 [100]	44 [42]	34 [33]	10 [10]	59 [56]	0 [0]
Ginsberg (2)	122 [100]	122 [100]	NR	NR	NR	0 [0]	125 [100]	125 [100]	NR	NR	NR	0 [0]
Kodama (7)	46 [100]	46 [100]	46 [100]	0 [0]	0 [0]	0 [0]	77 [100]	77 [100]	NR	NR	0 [0]	0 [0]
Koike (8)	74 [100]	74 [100]	74 [100]	0 [0]	0 [0]	0 [0]	159 [100]	159 [100]	159 [100]	0 [0]	0 [0]	0 [0]
Okada (9)	273 [90]	266 [87]	305 [100]	0 [0]	7 [2]	32 [10]	227 [87]	217 [83]	262 [100]	0 [0]	10 [4]	35 [13]
Kodama (10)	58 [100]	58 [100]	58 [100]	0 [0]	0 [0]	0 [0]	62 [78]	62 [78]	80 [100]	0 [0]	NR	18 [22]
Sugi (11)	40 [93]	40 [93]	40 [93]	0 [0]	0 [0]	0 [0]	80 [84]	80 [84]	NR	NR	NR	9 [9]
Ichiki (12)	35 [100]	35 [100]	35 [100]	0 [0]	0 [0]	0 [0]	99 [87]	96 [84]	114 [100]	0 [0]	3 [3]	15 [13]
Yamashita (13)	90 [100]	90 [100]	76 [84]	14 [16]	0 [0]	0 [0]	124 [100]	124 [100]	72 [58]	52 [42]	0 [0]	0 [0]
Hamatake (14)	NS*	NS*	66 [100]	0 [0]	NR	NR	NS*	NS*	77 [100]	0 [0]	NR	NR
Tsutani (15)	97 [99]	97 [99]	NR	NR	0 [0]	1 [1]	339 [89]	339 [89]	NR	NR	0 [0]	44 [11]

Data is presented as numbers with percentage of study population in brackets. *, 136 (95%) of the entire cohort (sublobar and lobectomy patients) were stage I & stage IA; NR, not reported; NS, not specified.

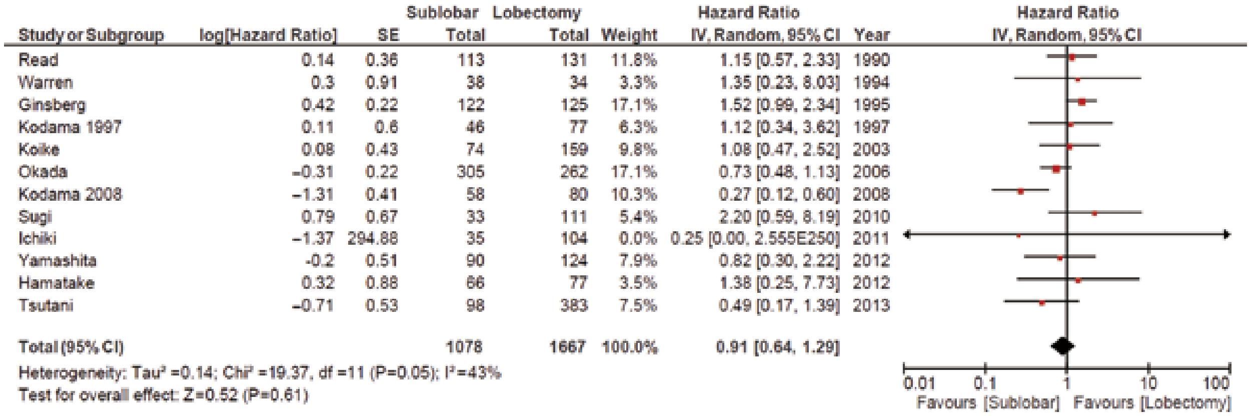

Figure 2 Overall survival: sublobar *vs*. lobectomy. CI, confidence interval.

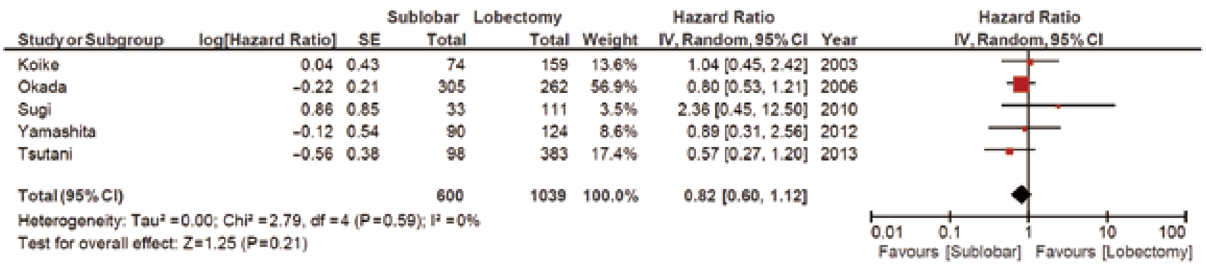

Figure 3 Disease-free survival: sublobar *vs*. lobectomy. CI, confidence interval.

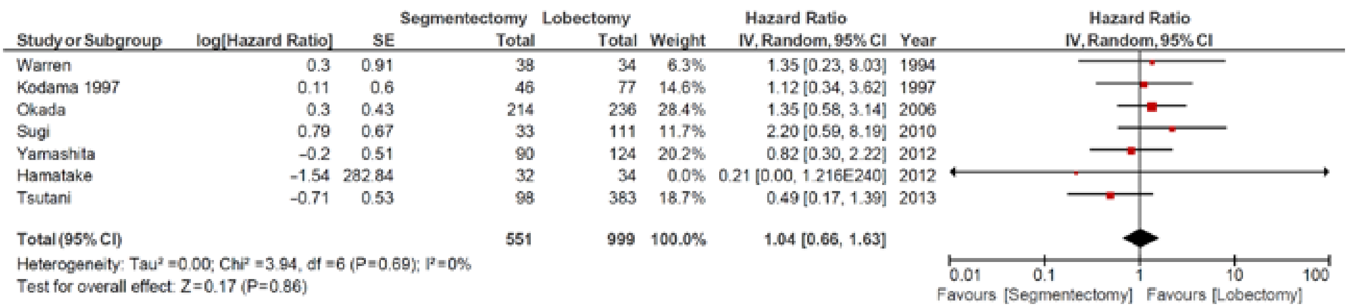

Figure 4 Overall survival: segmentectomy *vs*. lobectomy. CI, confidence interval.

not differentiated between segmentectomies and wedge resections. Furthermore, data was unavailable for almost a third of the patients, and the initial presented data were inaccurate, as highlighted by a recent letter by Detterbeck (21). The updated results of this study found lobectomy to confer a significant survival benefit as well as a decrease in the recurrence rate compared to the sublobar resection group. Despite its many limitations, results of the LCSG study formed the basis of many current guidelines.

More recently, a number of case series reports have demonstrated encouraging outcomes for patients undergoing sublobar resections following strict patient selection protocols. A number of Japanese studies have shown that patients with small, peripheral lesions with various degrees of GGO can achieve similar or superior survival outcomes (10-12,14). These results have revived interest in the debate of lobectomy versus sublobar resections in T1N0M0 NSCLC. Currently, RCTs are underway to compare patients who undergo segmentectomy (22) or sublobar resection (CALGB 140503) versus lobectomy. Outcomes of these trials will no doubt have a strong impact on the surgical management of patients with small, peripheral NSCLC.

Furthermore, in an era of growing enthusiasm for minimally invasive surgery, the comparison of clinical outcomes after video assisted thoracoscopic (VATS) sublobar resections versus VATS lobectomies may be of immense value.

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Open, thoracoscopic and robotic segmentectomy for lung cancer

Chi-Fu Jeffrey Yang, Thomas A. D'Amico

Department of Surgery, Duke University Medical Center, Durham, North Carolina, USA

Correspondence to: Thomas A. D'Amico, MD, Professor and Vice Chairman. Department of Surgery, Duke University Medical Center, Durham, North Carolina, USA. Email: damic001@mc.duke.edu.

Abstract: While lobectomy is the standard procedure for early stage lung cancer, the role of sublobar resection is currently under investigation for selected patients with small tumors. In this review, studies reporting outcomes on open, thoracoscopic and robotic segmentectomy were analyzed. In patients with stage I lung cancer, with tumors <2 cm in diameter and within segmental anatomic boundaries, segmentectomy appears to have equivalent rates of morbidity, recurrence and survival when compared to lobectomy. Segmentectomy also resulted in greater preservation of lung function and exercise capacity than lobectomy. It appears reasonable to consider segmentectomy for patients with stage I lung cancer (particularly in air-containing tumors with ground glass opacities) where tumors are <2 cm in diameter and acceptable segmental margins are obtainable, especially in patients with advanced age, poor performance status, or poor cardiopulmonary reserve. The results of two ongoing randomized controlled trials (CALGB 140503 and JCOG0802/WJOG4607L) and additional well-designed studies on open, thoracoscopic, and robotic segmentectomy will be important for clarifying the role of segmentectomy for lung cancer.

Keywords: Lung cancer surgery; minimally invasive surgery; thoracoscopy/video-assisted thoracoscopic surgery (VATS); segmentectomy

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Introduction

The first segmentectomy, a lingulectomy, was performed by Churchill and Belsey in 1939 for the treatment of bronchiectasis (1). Over the subsequent decades, segmentectomy was increasingly applied to small primary lung cancers (2,3). However in 1995, the Lung Cancer Study Group (LCSG) performed a randomized controlled trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer (NSCLC) and found that limited pulmonary resection for tumors <3 cm in size resulted in increased locoregional recurrence compared to lobectomy (4). Subsequently in North America, the use of segmentectomy for NSCLC was generally limited to patients with marginal cardiopulmonary function (5).

The LCSG trial is the only randomized controlled trial of lobectomy versus limited resection for lung cancer to date, and is indeed a landmark study. However, it enrolled patients from 1982-1988 (4) and the landscape of thoracic oncology has changed considerably. Since then, there have been new developments leading to renewed interest in segmentectomy for small primary lung cancer tumors (5). Firstly, there is now strong evidence that low-dose computed tomography (LDCT) screening in high-risk patients reduces lung cancer deaths. Importantly, the screening protocols have identified greater numbers of smaller lung tumors (<2 cm), which are more frequently operable and curable (6,7). Of note, the LCSG trial did not specifically assess the effect of lobectomy versus segmentectomy on smaller tumors, as 30% of patients in that study had tumors that were larger than 2 cm (4). Secondly, since 1995, newer staging modalities have emerged which will likely improve patient selection for anatomic lung resection (4). Thirdly, surgeons have advanced the fields of video-assisted thoracoscopic surgery (VATS) and robotic surgery, with increasing experience at applying those approaches to segmentectomy. These new developments have led to a growing number of studies investigating the use of open, minimally invasive and robotic segmentectomy for carefully selected patients with smaller tumors less than 2 cm in size, especially in patients with marginal cardiopulmonary function (5).

A previous review of these studies demonstrated that when compared to thoracoscopic lobectomy, thoracoscopic segmentectomy had equivalent rates of morbidity, recurrence and survival in selected patients (5). When compared to open segmentectomy, thoracoscopic segmentectomy was found to have equivalent oncologic results, with shorter length of stay, reduced rates of morbidity, and lower cost. There have since been additional studies on segmentectomy, including further reports on uniportal and robotic approaches. This review is an update on the current role of segmentectomy and will focus on the most relevant recent studies on open, minimally invasive and robotic segmentectomy for lung cancer.

Open segmentectomy *vs.* open lobectomy

Since the LCSG study, although there have been no new randomized trials, there have emerged several retrospective studies comparing open segmentectomy to open lobectomy (8). In contrast to the LCSG trial, which enrolled patients from 1982-1988 and included 30% of patients with tumors >2 cm, these studies reflected a more current medical and surgical practice, and focused on examining the role of segmentectomy for tumors >2 cm in diameter. These studies reported similar outcomes and have found no significant differences in morbidity, mortality, locoregional recurrence or survival between segmentectomy and the lobectomy (8).

Most of these studies had groups well-matched for pulmonary function, but an important limitation of these studies is that many did not include information on preoperative co-morbidities. Three recent retrospective studies on segmentectomy *vs.* lobectomy did however include preoperative comorbidities and pulmonary function tests in their analysis. In 2011, Schuchert and colleagues compared the results of 107 patients undergoing resection for stage IA NSCLC (≤1 cm) via lobectomy (n=32), segmentectomy (n=40) or wedge resection (n=35) (9). Preoperative forced expiratory volume in 1 second (FEV1) was significantly lower in the sublobar resection (segmentectomy, wedge) groups compared with the lobectomy group; but age, sex distribution, tumor size, histology and preoperative comorbidities were similar between groups. Mean follow-up was 42.5 months and there was no statistically significant difference in overall disease recurrence or estimated 5-year disease-free survival (lobectomy, 87%; segmentectomy, 89%; wedge, 89%; P>0.402). While the authors note that a VATS approach was used more often than an open approach (57% *vs.* 43%) they did not specifically study the effects of open *vs.* VATS approach on outcomes.

Carr and colleagues conducted a retrospective study comparing the outcomes of 429 patients undergoing resection of stage I NSCLC via lobectomy or anatomic segmentectomy (10). The segmentectomy group (n=178) was older and had more co-morbidities—more likely to have coronary artery disease (18.5% *vs.* 12.8%, P=0.036) or chronic obstructive pulmonary disease (26.4% *vs.* 14.4%, P=0.0001)—than the lobectomy group (n=251). The segmentectomy group also had worse pulmonary function than the lobectomy group (FEV1 81.1±17.6 *vs.* 71.8±25.6, P=0.02). The authors found no difference in 30-day mortality (1.1% *vs.* 1.2%), recurrence rates (14.0% *vs.* 14.7%, P=1.00), or 5-year cancer-specific survival (T1a: 90% *vs.* 91%, P=0.984; T1b: 82% *vs.* 78%, P=0.892) when comparing segmentectomy and lobectomy for pathologic stage IA non-small cell lung cancer, when stratified by T stage. Of note, this study included patients who underwent both open and VATS approaches, and an open approach was used less often with segmentectomy than with lobectomy (41% *vs.* 60.6%, P=0.0001). The authors did not specifically evaluate outcomes by type of approach.

With regard to the role of open segmentectomy in the elderly, Kilic and colleagues conducted a retrospective review of 78 patients >75 years of age who underwent segmentectomy *vs.* lobectomy for stage 1 NSCLC. The segmentectomy group included more patients with chronic obstructive pulmonary disease (COPD) and diabetes. The tumors were significantly larger in the lobectomy group (3.5 *vs.* 2.5 cm, P<0.0001). The authors found no significant difference in 5-year disease-free survival between segmentectomy and lobectomy (11). Outcomes associated with an open *vs.* VATS approach were not specifically evaluated.

In addition to the single-institution retrospective studies described above, there has been one population-based study of open segmentectomy and lobectomy for stage I NSCLC. In 2011, Whitson and colleagues analyzed 14,473 patients undergoing anatomic segmentectomy or lobectomy for stage I NSCLC derived from the Surveillance Epidemiology and End Results (SEER) database. The authors were unable to stratify by open or VATS approach, but presumably most of the operations were performed open. Lobectomy was demonstrated to be associated with improved overall ($P<0.0001$) and cancer-specific ($P=0.0053$) 5-year survival compared with segmentectomy. After adjusting for tumor size, this improvement in survival remained. However, it is difficult to draw specific conclusions from this study because, in addition to its retrospective nature, the study did not have data on patient preoperative co-morbidities and pulmonary function—important variables which may have significantly affected both procedure selection and postoperative outcomes.

Advantages of open segmentectomy *vs.* open lobectomy

Since the 1995 LCSG randomized trial, there have been numerous retrospective studies that have shown that there are no differences in recurrence and survival between open segmentectomy and open lobectomy, even in patients with greater co-morbidities and worse pulmonary function (10), patients older than 75 years of age (11), and patients with larger tumors between 2 and 3 cm in size (10). Furthermore, in one study, open segmentectomy was found to preserve postoperative pulmonary function at 90%±12% of preoperative levels (12). There is one recent population-based analysis which found that patients undergoing anatomic segmentectomy had a decreased survival rate when compared to those undergoing lobectomy for stage I NSCLC. However, this study did not include information about patient comorbidities or cardiopulmonary function; patients in segmentectomy could have had reduced cardiopulmonary function, greater co-morbidities or other factors that affected survival.

Advantages of segmentectomy *vs.* wedge resection

With regard to the outcomes of patients undergoing an open segmentectomy versus wedge resection for stage I NSCLC, multiple reports show a decreased risk of recurrence and equivalent or improved survival in patients undergoing open segmentectomy compared to those undergoing wedge resections (8). When compared with the wedge resection, segmentectomy has also been shown to be associated with a larger parenchymal margin (13,14), a higher yield of lymph nodes and rate of nodal upstaging (14), and reduced risk of locoregional recurrence (15). Based on these studies, segmentectomy would be the preferred procedure for patients considering sublobar resection.

Predictors for prognosis and recurrence

With regard to predictors for prognosis and recurrence for patients with NSCLC who underwent segmentectomy, Koike and colleagues found age >70 years, gender (male), >75% consolidation/tumor ratio on high-resolution CT, and lymphatic permeation to be independent poor prognostic factors, and lymphatic permeation to be an independent predictor for recurrence (16). Yamashita and colleagues found KI-67 proliferation index to be a predictor of early cancer death (17). Traibi and colleagues have also shown male gender, FEV1 ≤60% and open (as opposed to VATS) surgery to be risk factors for postoperative complications (18).

In 2013, Koike and colleagues reported risk factors for locoregional recurrence and survival in patients undergoing sublobar resection (patients who underwent segmentectomy or wedge resection in the analysis) (15). They found four independent predictors of locoregional recurrence: wedge resection, microscopic positive surgical margin, visceral pleural invasion, and lymphatic permeation. Independent predictors of poor disease-specific survival were smoking status, wedge resection, microscopic positive surgical margin, visceral pleural invasion, and lymphatic permeation.

Thoracoscopic segmentectomy *vs.* open segmentectomy

Since the 1995 LCSG randomized trial, there have been significant advancements in thoracoscopic surgical techniques, including a better understanding of the potential advantages of the thoracoscopic lobectomy and segmentectomy for anatomic pulmonary resection (5). The studies included in the present review will use the definition of thoracoscopic segmentectomy as the completion of sublobar anatomic pulmonary resection, with individual vessel ligation and without the use of a utility thoracotomy, retractors or rib-spreading (5). Studies using a "hybrid" segmentectomy with mini-thoracotomy fall into the category of open surgery and are not included in this section.

The first retrospective study comparing outcomes of thoracoscopic and open segmentectomy was performed by Shiraishi and colleagues in 2004 (19). The authors selected patients with clinical stage IA peripheral tumors (<2 cm) and reviewed the outcomes of 34 patients who underwent VATS segmentectomy versus 25 who underwent open segmentectomy. They found no significant differences in postoperative complications and perioperative deaths. Long-term survival was not evaluated in this study.

In 2007, Atkins and colleagues conducted a retrospective study comparing the results of 48 patients who underwent VATS versus 29 who underwent an open approach (20). The authors found no significant differences in preoperative co-morbidities, pulmonary function, operative time, estimated blood loss, nodal stations sampled and chest tube duration between the two groups. In addition, no significant differences were seen in locoregional recurrences between the open (8.3%) and the VATS (7.7%) approaches (P=1.0). However, there was a significantly decreased length of hospital stay for the VATS group when compared to the thoracotomy group (4.3±3 *vs.* 6.8±6 days; P=0.03). At approximately 30 months postoperatively, it was found that the VATS group had improved long-term survival when compared with the thoracotomy group (P=0.0007), although the groups were not matched oncologically.

Schuchert and colleagues performed a retrospective review of patients who underwent VATS segmentectomy (n=104) versus those who underwent thoracotomy (n=121) (21). There were no significant differences between the two groups in age, gender, histology, and pulmonary function as measured by FEV1 and DLCO. The VATS group had slightly smaller tumor sizes than the thoracotomy group (2.1±1.1 *vs.* 2.4±1.2 cm, P=0.05) and there were fewer lymph nodes harvested during VATS segmentectomy when compared with open segmentectomy (6.4. *vs.* 9.1, P=0.003). The VATS group also had a decreased length of hospital stay compared to the thoracotomy group (5 *vs.* 7 days, P<0.001). There were significantly fewer perioperative pulmonary complications in the VATS group as well (15.4% *vs.* 29.8%; P=0.012) but both groups, VATS and open, had similar rates of postoperative complications. Most importantly, regarding margins, it was demonstrated that a margin: tumor size ratio >1 was associated with a decrease in recurrence (14.7%) when compared to a ratio <1 (28.9%, P=0.037). In addition, the authors performed a propensity analysis that showed no significant difference in recurrence-free or overall survival. Interestingly, there were also no significant differences in locoregional or overall survival between groups with tumors >2 cm and tumors <2 cm.

In another analysis, Leshnower and colleagues conducted a retrospective review of 17 patients who underwent VATS segmentectomy versus 26 who underwent a thoracotomy approach for patients with primary lung cancer and metastatic disease (22). The two groups were similar with regards to age, tumor size, gender, body-mass index, co-morbidities and pulmonary function. An average of 3 lymph node stations were sampled in both groups and there were no significant differences in numbers of lymph nodes sampled (VATS 4.0±3 *vs.* open 6.1±5, P=0.40). There was also no significant difference between the groups in operative time. There were 2 (4.8%) deaths within 30 days after surgery in the thoracotomy group but none in the VATS group. Furthermore, the VATS group had decreased chest tube duration (VATS 2.8±1.3 *vs.* open 5.2±3 days, P=0.001) and reduced hospital length of stay (VATS 3.5±1.4 *vs.* open 8.3±6 days, P=0.01). In addition, the authors found that average hospital costs were approximately $1,700 less for the VATS group, although this finding was not statistically significant.

Advantages of thoracoscopic segmentectomy *vs.* open segmentectomy

In summary, the above studies comparing VATS segmentectomy with open segmentectomy show that VATS segmentectomy for stage I NSCLC is feasible and safe (19-22). VATS segmentectomy appears to be associated with an equivalent survival rate when compared to the open approach: all studies report 0% 30-day mortality for the VATS group, compared to 1.7-7.7% 30-day mortality for open segmentectomy, and there is no apparent difference in long-term survival. The VATS approach was also found to be associated with shorter length of stay, lower costs, reduced rates of overall complications, including fewer cardiopulmonary complications and reduced length of chest tube duration (5). At this time, it appears that there are no significant differences in operative times between the VATS *vs.* open approach: one study has shown a longer operative time (19), and the other three have shown similar operative times (20-22).

Thoracoscopic segmentectomy *vs.* lobectomy *vs.* wedge resection

Evaluation of thoracoscopic segmentectomy *vs.* thoracoscopic lobectomy or wedge resection for NSCLC is also under current investigation. Harada and colleagues conducted an analysis of pulmonary function for patients undergoing VATS segmentectomy (n=38) or VATS lobectomy (n=45) for stage I NSCLC (23). The authors found that 50% fewer segments were resected in the segmentectomy group and that the number of resected segments was associated with reduced forced vital capacity (FVC) and FEV1 at 2-

and 6-month postoperatively (P<0.0001). Consequently, at six months after surgery, the segmentectomy group had regained exercise capacity while the lobectomy group continued to have a 10% loss in exercise capacity.

In 2004, Iwasaki and colleagues performed a retrospective review of patients who underwent VATS lobectomy (n=100) or VATS segmentectomy (n=40) for stage I and II NSCLC (24). The authors found no significant differences in 5-year survival between the segmentectomy and lobectomy groups (77.8% *vs*. 76.7%, P=0.47). Shapiro and colleagues also conducted a retrospective study of VATS segmentectomy (n=31) *vs*. VATS lobectomy (n=113) but solely for stage I NSCLC (25). The segmentectomy group was found to have a longer smoking history and reduced pre-operative pulmonary function when compared to the lobectomy group (FEV1 83% *vs*. 92%, P=0.04). Despite differences in baseline patient fitness between the segmentectomy and lobectomy groups, there were no significant differences in complication rates, perioperative mortality, hospital length of stay, local recurrence (3.5% *vs*. 3.6%) and total recurrence rate (17% *vs*. 20%). In terms of lymph nodes dissected, segmentectomy was equivalent to lobectomy, with both groups having approximately five nodal stations sampled and ten lymph nodes resected. Mean follow-up for the segmentectomy and lobectomy groups were 21 and 22 months respectively, and both groups had similar overall and disease-free survival rates (P>0.5).

In 2010, Sugi and colleagues conducted a retrospective study of 159 patients who underwent VATS wedge resection (n=21), VATS segmentectomy (n=43) or VATS lobectomy (n=95) for stage I NSCLC (26). The lobectomy group had a higher percentage of patients with pathological stage greater than pT1N0 when compared to the segmentectomy group (18% *vs*. 8%, P=0.07). Follow-up was five years and the groups had similar 5-year recurrence-free and overall surviva, although there were differences in tumor size between the groups—the VATS wedge group had tumors <1.5 cm, the segmentectomy group had tumors <2 cm and the lobectomy group had tumors >2 and <3 cm. Yamashita and colleagues compared the results of VATS segmentectomy (n=38) or VATS lobectomy (n=71) with systemic lymphadenectomy (27). Both groups had similar recurrence-free and overall survival, although there were differences in tumor size between the segmentectomy and lobectomy groups (1.5 *vs*. 2.5 cm, P<0.0001).

Nakamura and colleagues performed a retrospective review of patients undergoing VATS lobectomy (n=289), VATS segmentectomy (n=38) or VATS wedge resection (n=84) for stage I NSCLC (28). The authors found differences in the mean tumor size between the lobectomy (2.57 cm), segmentectomy (1.98 cm) and wedge resection groups (1.85 cm). In this study, 5-year survival was lower for the wedge resection group (71.2%), compared to the lobectomy (90%) and segmentectomy (100%) groups. However, compared to the other groups, the wedge resection group comprised sicker patients with more co-morbidities.

Yamashita and colleagues evaluated the results of patients undergoing VATS segmentectomy (n=90) or VATS lobectomy (n=124) for stage IA NSCLC (29). There was a higher percentage of T1a tumors in the segmentectomy group when compared with the lobectomy group (84% *vs*. 58%, P<0.001). The segmentectomy group had a smaller median tumor size (15 *vs*. 20 mm). However, both groups were similar with regards to operative time, intraoperative blood loss, chest tube duration, and hospital stay. There were fewer numbers of dissected lymph nodes in the segmentectomy group when compared to the lobectomy group (12.1 *vs*. 21, P<0.0001) but both groups were also similar with regards to morbidity, 30-day mortality, recurrence, disease-free and overall survival.

Zhong and colleagues conducted a retrospective review of patients undergoing VATS segmentectomy (n=81) or VATS lobectomy (n=120) for stage IA NSCLC (30). There were no significant differences between the groups in pre-operative co-morbidities, pulmonary function, tumor size or histology. Both groups had similar operative times, similar rates of postoperative complications and no perioperative deaths. There were no differences between VATS segmentectomy and lobectomy with regards to lymph nodes resected (11.2±6.5 *vs*. 14.5±8.1, P=0.18). Length of hospital stay was also similar between both groups. There were no significant differences in local recurrence rates and 5-year overall or disease-free survivals. Multivariate Cox regression analyses also showed that tumor size was the only independent prognostic factor for disease-free survival. Another study compared the results of 73 VATS trisegmentectomies for stage IA (n=45) and IB (n=11) lung cancer with 266 VATS left upper lobe lobectomies for stage IA (n=105) and IB (n=73) lung cancer (31). There were no significant differences in overall complication rates or survival between patients undergoing VATS trisegmentectomy and those undergoing lobectomy for either stage IA lung cancer or stage IB lung cancer.

A retrospective review of patients undergoing VATS segmentectomy (n=26) or VATS lobectomy (n=28) for stage

IA NSCLC was also conducted by Zhang and colleagues (32). Again, there were no significant differences in operative time, estimated blood loss, number of lymph nodes resected and postoperative complications. Both groups had similar local recurrence rates and 3-year survival. Of note, the authors did find a significantly decreased length of hospital stay in the VATS segmentectomy group by approximately three days (P=0.03). Postoperative FEV1 was also decreased to a lesser degree in the VATS segmentectomy group. Tumor size, however, was not reported in this study.

Zhao and colleagues compared the results of patients undergoing VATS segmentectomy (n=36) or VATS lobectomy (n=138) for stage I NSCLC (33). There were no significant differences in blood loss, operative time, chest tube duration and length of hospital stay between the two groups. There was also no significant difference in local recurrence and in recurrence-free survival between the two groups, although the study was limited by a relatively short follow-up of less than one year and by not including tumor size data.

Advantage of thoracoscopic segmentectomy over thoracoscopic lobectomy and wedge resection?

These studies demonstrate that although thoracoscopic segmentectomy is a more complex procedure than the thoracoscopic lobectomy (5), the rates of morbidity, recurrence and survival are similar among patients with tumors >2 cm in diameter. Specifically, there were no significant differences in overall complication rates (25,26,29,30,32,33), local recurrence rates (25,26,29,30,32,33), 5-year recurrence-free survival (26,27,29,30) and 5-year survival rates (24,26,27,29,30). The studies also show no difference in operative time between the two groups (29,30,32,33). In addition, the segmentectomy groups had similar (25,29,30,33), or reduced lengths of hospital stay (32) when compared to the lobectomy groups. It appears that thoracoscopic segmentectomy is able to preserve more lung function (23,32) and exercise capacity (23) than thoracoscopic lobectomy, although long-term follow-up data is needed.

There are, however, important limitations to the abovementioned studies. Firstly, some studies did not report the tumor size data (31-33). Of the studies that did, most found that the lobectomy groups had significantly larger tumors than the segmentectomy groups (23-29). This difference in tumor size limits interpretation of results because tumor size is known to be a prognostic factor of survival for NSCLC (30,34). However, in one recent study where both thoracoscopic segmentectomy and lobectomy groups were well-matched in tumor size, histology, preoperative co-morbidities and pulmonary function (30), both groups had similar local recurrence rates, disease-free and overall survival. This is consistent with previous data from the open segmentectomy literature. For example, in 2006, Okada and colleagues conducted a multi-center study of 567 patients with tumor size <2 cm who underwent open segmentectomy or lobectomy (35). Mean tumor size for the segmentectomy and lobectomy groups were 1.57 cm and 1.62 cm (P=0.056), respectively. The segmentectomy was associated with equivalent 5-year survival when compared to the lobectomy (83.4% *vs.* 85.9%, respectively).

Another limitation of the above-referenced studies is that many of them, with the exception of four studies (27,29,30,33), did not report the percentage of patients with bronchoalveolar carcinoma or adenocarcinoma *in situ*. This is an important variable to account for (5), as demonstrated by a study performed by Nakayama and colleagues that examined the results of 63 patients with adenocarcinoma who underwent open sublobar resection of clinical stage IA NSCLC (36). The authors classified the patients' tumors as either "air-containing type" (n=46) or "solid-density type" (n=17) according to the tumor shadow disappearance rate on high-resolution CT. After resection, 38 of the 46 air-containing tumors were identified as bronchoalveolar carcinomas whereas all solid-density type tumors were non-bronchoalveolar carcinomas. Air-containing tumors were associated with better overall 5-year survival than solid-density tumors (95% *vs.* 69%, P<0.0001).

The VATS wedge resection procedure yields a smaller parenchymal margin, reduced number of resected lymph nodes and reduced sampling of nodal stations when compared to segmentectomy (14). There have also been two studies comparing the survival outcomes of this procedure with that of the VATS segmentectomy and lobectomy. However, in the wedge resection group, the tumors were smaller (26,28) or the patient population had greater co-morbidities, which limits interpretation of results (28); further studies with groups that are better matched will be needed prior to making any conclusions regarding the role of VATS wedge resection role in NSCLC.

Further study is also needed regarding selection criteria for the thoracoscopic segmentectomy. Based on the reviewed evidence, it appears reasonable to consider segmentectomy for patients with small, peripheral tumors (in particular air-containing tumors with ground glass opacities suggesting bronchoalveolar histology) that are less than 2 cm in diameter when an acceptable segmental margin is obtainable (margin ≥ tumor diameter), especially in patients with advanced age, poor performance status, or poor cardiopulmonary reserve. Future retrospective studies would benefit from controlling for tumor size, operative co-morbidities, type of cancer, tumor location (including distance from the margin to the edge of the tumor and resection margin) and propensity score matching. There are two ongoing randomized trials (discussed below) that will clarify the role of the thoracoscopic segmentectomy in lung cancer.

Feasibility of mediastinal lymph node dissection (MLND)

Mediastinal lymph node assessment is a critical component of segmentectomy for NSCLC. Mattioli and colleagues reported that open segmentectomy procures an adequate number of N1 and N2 nodes for pathologic examination (37). When comparing the thoracoscopic segmentectomy to the thoracoscopic lobectomy, two studies preliminarily demonstrate no significant differences in lymph nodes harvested or nodal stations sampled (25,30) while one reported fewer lymph nodes harvested with the segmentectomy (29). When comparing open *vs*. thoracoscopic segmentectomy, one study found no difference in lymph nodes harvested (22), while another reported fewer lymph nodes harvested with the VATS approach (21).

In addition, two studies compared the completeness of lymph node evaluation during anatomic resection of primary lung cancer by open and VATS approaches (38,39). Most of the analyses performed in these studies grouped segmentectomies together with lobectomies, thereby limiting the ability to draw any conclusions specifically regarding segmentectomy. However, in one of the studies which reported analyses of nodal upstaging from the Society of Thoracic Surgery national database, the authors did report one subset analysis that showed off the 170 VATS segmentectomies analyzed, upstaging from cN0 to pN1 was seen in 4% of patients compared with 5.3% among 280 open segmentectomies (38). The authors noted that the differences in upstaging between VATS and open approaches may have been the result of approach bias, and that equivalent nodal staging may be possible with increasing experience with VATS (38).

Preliminarily, based on the available evidence, it appears that it is possible to achieve adequate lymph node dissection with segmentectomy, but that surgeon experience does play an important role, particularly in the case of the thoracoscopic segmentectomy. More detailed investigation on lymph node evaluation in VATS versus open segmentectomy and VATS segmentectomy *vs*. VATS lobectomy is therefore needed.

Other types of thoracoscopic segmentectomy

Totally thoracoscopic segmentectomy

There have been a few small case series reported on the “totally thoracoscopic” or “complete VATS” technique for segmentectomy (39-46). In this technique, there is no access incision, and the specimen is retrieved through one of the port sites that is enlarged at the end of the procedure; only video-display and endoscopic instrumentation are used (47). There is no evidence that there are advantages associated with this approach, although it does allow the surgeon to use carbon dioxide insufflation. The largest series reported is from Gossot and colleagues, who performed totally thoracoscopic anatomic segmentectomy on 117 patients (48). The authors reported five conversions to thoracotomy with mean operative time of 181±52 minutes, mean intraoperative blood loss of 77±81 mL, and postoperative complication rate of 11.7%. The mediastinal lymph node harvested and nodal stations sampled were 21±7 and 3.5±1. The average length of hospital stay was 5.5±2.2 days. Preliminarily, it appears that totally thoracoscopic segmentectomy is feasible and safe, although further studies with longer follow-up that compare this technique with traditional open and VATS approaches are needed.

Uniportal segmentectomy

VATS segmentectomies are typically performed via two to three incisions, but Gonzalez-rivas and colleagues presented the first case report demonstrating that the procedure is feasible with one incision and through one port (49). Subsequently, they reported their initial results for 17 uniportal VATS anatomic segmentectomies. Mean operative time was 94.5±35 minutes, 4.1±1 nodal stations were sampled and 9.6±1.8 lymph nodes were resected. There were no conversions. Median tumor size was 2.3±1 cm, chest tube duration was 1.5 days (range, 1-4 days) and the median length of stay was 2 days (range, 1-6 days) (50). Wang and colleagues also demonstrated their experience, performing thoracoscopic lobectomy (n=14) and segmentectomy (n=5) with radical MLND through a single small (3- to 5-cm) incision (51). Mean operative time was 156±46 minutes, median number of lymph nodes harvested was 22.9±9.8, and blood loss was 38.4±25.9 mL. There were no conversions and 30-day mortality was 0%. The authors did not assess for differences by type of operation and there was no long-term follow-up. Preliminarily, it appears that single-incision segmentectomy is feasible and safe, although further studies comparing single-port to traditional open and VATS approaches are needed.

Robotic segmentectomy

A recent review of a national database demonstrated that robotic pulmonary resections have increased from 0.2% in 2008 to 3.4% in 2010 (52). The vast majority of robotic procedures are lobectomies, but there has been a small increase in robotic segmentectomies performed as well.

A retrospective study of 35 patients who underwent robotic thoracoscopic segmentectomy was performed, including 12 patients who had stage IA NSCLC (53). In this series, median age was 66.5 years, tumor size was 1.4 cm, operative time was 146 minutes and number of lymph node stations sampled was 5 (54). Four patients had perioperative complications, and 60-day mortality was 0%, while length of hospital stay was two days. Pardolesi and colleagues reported the initial results of 17 patients who underwent robotic segmentectomy at three institutions (55). The authors used a 3- or 4-incision strategy with a 3-cm utility incision in the anterior fourth or fifth intercostal space. Mean age was 68.2 years and mean duration of surgery was 189 minutes. There were no major intraoperative complications and no conversions were needed. Postoperative morbidity rate was 17.6%, median postoperative stay was five days and postoperative mortality was 0%.

Based on these reports, robotic segmentectomy appears to be a safe and feasible operation although additional studies comparing the outcomes of the robotic segmentectomy with the open and VATS approaches, as well as with the lobectomy, will be needed.

Limitations

There were several key limitations to the studies discussed above. Firstly, because the studies were retrospective in nature, there was the potential for surgeons' bias to affect the type of operation a patient received, which could have affected outcomes. In addition, often, the studies did not compare groups that were well-matched—which could have affected results. For example, in studies where patients in the VATS segmentectomy group were sicker than those in the comparison group (9-11,21,25), the benefits of VATS segmentectomy could have been underestimated. In studies where the VATS group had slightly smaller tumors than those in the comparison group (21,24,26-29), there may have been an overestimation of the benefits of VATS segmentectomy.

To reduce the impact of treatment-selection bias and confounding in estimating the effects of segmentectomy *vs.* lobectomy, randomized controlled trials should continually be performed (described below). Future retrospective studies should also aim to match variables that have confounding effects, use stratification or multivariate regression analysis where appropriate, and incorporate propensity score matching when possible (56,57).

Future research

In the studies reviewed above, there was no data reported on the tolerance of patients for resection of secondary cancers. This would be an important area for future research because up to 11.5% of patients who undergo pulmonary resection for stage I NSCLC develop additional primary lung cancers (25,58). By causing less trauma than open segmentectomy, and preserving more lung function than lobectomy, VATS segmentectomy theoretically would offer patients higher tolerance for resection of secondary cancers when compared to the open segmentectomy or open or VATS lobectomy (5).

In addition, future studies should aim to include data on the number and type of nodal stations sampled or lymph nodes dissected. Only four of the studies in this review (22,25,29,30) reported specific information on lymph node sampling with segmentectomy. The effect of surgeon experience on outcomes in segmentectomy also deserves attention, as there is currently no published data on the topic.

There are two ongoing large-scale randomized controlled trials that will improve our understanding of the outcomes of limited resection for NSCLC: CALGB 140503 and JCOG0802/WJOG4607L (59,60). CALGB 140503, sponsored by the Alliance for Clinical Trials in Oncology, will evaluate the outcomes of patients who are randomly assigned to undergo limited resection (segmentectomy or wedge resection) or lobectomy, with the VATS or thoracotomy approach determined by the surgeon (60). JCOG0802/WJOG4607L, sponsored by the Japan Clinical Oncology Group and the West Japan Oncology Group, will evaluate outcomes of patients who are randomly assigned to undergo segmentectomy (wedge resections are excluded) or lobectomy (59). Both studies will clarify the role of segmentectomy for NSCLC but will have some limitations as well. CALGB 140503 may be limited in its final analysis because the limited resection group includes not only patients undergoing segmentectomy, but also patients undergoing wedge resection. And in both CALGB 140503 and JCOG0802/WJOG4607L, the operative approach—VATS *vs*. open—will not be a primary outcome variable.

Conclusions

Based on the reviewed evidence, it appears reasonable to consider segmentectomy for patients with stage I NSCLC tumors (particularly in air-containing tumors with ground glass opacities) that are <2 cm in diameter when an acceptable segmental margin is obtainable (at least 2 cm), especially in patients with advanced age, poor performance status, or poor cardiopulmonary reserve. The outcomes of CALGB 140503 and JCOG0802/WJOG4607L and additional well-designed studies on open, thoracoscopic, and robotic segmentectomy will be important for further clarifying the role of segmentectomy for NSCLC.

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Segmentectomy versus lobectomy for clinical stage IA lung adenocarcinoma

Morihito Okada[1], Takahiro Mimae[1], Yasuhiro Tsutani[1], Haruhiko Nakayama[2], Sakae Okumura[3], Masahiro Yoshimura[4], Yoshihiro Miyata[1]

[1]Department of Surgical Oncology, Hiroshima University, Hiroshima, Japan; [2]Department of Thoracic Surgery, Kanagawa Cancer Center, Yokohama, Japan; [3]Department of Thoracic Surgery, Cancer Institute Hospital, Tokyo, Japan; [4]Department of Thoracic Surgery, Hyogo Cancer Center, Akashi, Japan

Correspondence to: Morihito Okada, MD, PhD. Department of Surgical Oncology, Research Institute for Radiation Biology and Medicine, Hiroshima University, 1-2-3-Kasumi, Minami-ku, Hiroshima City, Hiroshima 734-0037, Japan. Email: morihito@hiroshima-u.ac.jp.

Background: Despite the increasing prevalence of the early discovery of small-sized non-small cell lung cancers (NSCLCs), particularly adenocarcinoma, sublobar resection has not yet gained acceptance for patients who can tolerate lobectomy.

Methods: We compared the outcomes of segmentectomy (n=155) and lobectomy (n=479) in 634 consecutive patients with clinical stage IA lung adenocarcinoma and in propensity score-matched pairs. Those who had undergone wedge resection were excluded.

Results: The 30-day postoperative mortality rate in this population was zero. Patients with large or right-sided tumors, high maximum standardized uptake value (SUVmax), pathologically invasive tumors (with lymphatic, vascular, or pleural invasion), and lymph node metastasis underwent lobectomy significantly more often. Three-year recurrence-free survival (RFS) was significantly higher after segmentectomy compared to lobectomy (92.7% *vs*. 86.9%, P=0.0394), whereas three-year overall survival (OS) did not significantly differ (95.7% *vs*. 94.1%, P=0.162). Multivariate analyses of RFS and OS revealed age and SUVmax as significant independent prognostic factors, whereas gender, tumor size and procedure (segmentectomy *vs*. lobectomy) were not. In 100 propensity score-matched pairs with variables adjusted for age, gender, tumor size, SUVmax, tumor location, the three-year RFS (90.2% *vs*. 91.5%) and OS (94.8% *vs*. 93.3%) after segmentectomy and lobectomy respectively were comparable.

Conclusions: Segmentectomy with reference to SUVmax should be considered as an alternative for clinical stage IA adenocarcinoma, even for low-risk patients.

Keywords: Adenocarcinoma; segmentectomy; sublobar resection; lung cancer; lobectomy

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Introduction

Sublobar resection for intentionally treating patients with small non-small cell lung cancer (NSCLC) who are able to withstand lobectomy has remained highly controversial, although lobectomy is considered a standard procedure even for sub-centimeter lung cancers. The Lung Cancer Study Group (LCSG) revealed a three-fold increase in local recurrence rates and poorer survival in patients who had undergone sublobar resection rather than lobectomy in a singular randomized phase III study published in 1995 (1). The dogma that lobectomy is the standard of care for stage I NSCLC has been upheld until recently. However, several current investigations have found equivalent outcomes of sublobar resection and lobectomy when NSCLC are ≤2 cm (2-7).

Sublobar resection consists of segmentectomy and wedge resection, which are quite different from each other as curative surgery for lung cancer, since segmentectomy is more likely to provide sufficient margins and allows access to subsegmental and hilar lymph nodes. The present study retrospectively compared the outcomes of segmentectomy, not wedge resection and lobectomy among patients with clinical stage IA lung adenocarcinoma, and adjusted for clinical factors to minimize selection bias of patients. This analysis is an extended and updated version of our previous investigation (8).

Patients and methods

We analyzed data from 634 patients who had undergone lobectomy and segmentectomy for clinical T1N0M0 stage IA lung adenocarcinoma since October 2005. All patients were assessed using high-resolution computed tomography (HRCT) and F-18-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT). Patients with incompletely resected (R1 or R2) or multiple tumors were excluded from the prospectively maintained database that was analyzed herein. All patients were staged according to the TNM Classification of Malignant Tumors, 7th edition (9). Platinum-based chemotherapy was administered to patients with pathological lymph node metastasis after surgery. The institutional review boards of the participating institutions approved the study and the requirement for informed consent from individual patients was waived because the study was a retrospective review of a database. Chest images were acquired by multi-detector HRCT independently of subsequent FDG-PET/CT examinations. Tumor sizes and maximum standardized uptake values (SUVmax) were determined by radiologists at each institution. Because of the heterogeneity of PET techniques and performance, we corrected inter-institutional errors in SUVmax resulting from PET/CT scanners of variable quality based on outcomes of a study using an anthropomorphic body phantom (NEMA NU2-2001, Data Spectrum Corp, Hillsborough, NC, USA) that conformed to National Electrical Manufacturers Association standards (10). A calibration factor was analyzed by dividing the actual SUV by the gauged mean SUV in the phantom background to decrease inter-institutional SUV inconsistencies. Postoperative follow-up of all patients from the day of surgery included physical examinations and chest X-rays every three months, as well as chest and abdominal CT and brain MRI assessments every six months for the first two years. Thereafter, the patients were assessed by physical examinations and chest X-rays every six months, and annual CT and MRI imaging.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences software version 10.5 (SPSS Inc., Chicago, IL, USA). Continuous variables were compared using t-tests and Mann-Whitney U tests in all cohorts and Wilcoxon tests for propensity-matched pairs. Frequencies of categorical variables were compared using the χ^2 test and propensity-matched pairs were analyzed using McNemar tests. Propensity score matching was applied to balance the assignments of the included patients and to correct for the operative procedures (lobectomy or segmentectomy) that confounded survival calculations. The variables of age, sex, tumor size, SUVmax, side and lobe were multiplied by a coefficient that was calculated from logistic regression analysis, and the sum of these values was taken as the propensity score for each patient. Lobectomy and segmentectomy pairs with equivalent propensity scores were selected by a 1-to-1 match.

We defined recurrence-free survival (RFS) as the time from the day of surgery until the first event (relapse or death from any cause) or last follow-up, and overall survival (OS) as the time from the day of surgery until death from any cause or the last follow-up. The durations of RFS and OS were analyzed using the Kaplan-Meier method, and differences in RFS and OS were assessed using the log-rank test. Both RFS and OS were assessed by multivariate analysis using the Cox proportional hazards model.

Results

Of the 634 patients analyzed in this study, 479 and 155 underwent lobectomy and segmentectomy, respectively (*Table 1*). Patients with large tumors, right-sided tumors, pathologically invasive tumors, (presence of lymphatic, vascular, or pleural invasion), high SUVmax, and lymph node involvement were significantly more often treated by lobectomy. However, age and gender did not differ significantly between the two procedures. *Table 2* shows the segments that were removed during segmentectomy.

None of the patients died within 30 days of surgery, and tumors recurred in 54 patients at a median postoperative follow-up period of 34.2 months. Twenty recurrences were local only and 34 were distant (with or without local recurrence). Local recurrence occurred in 17 patients after

Table 1 Patient characteristics

Variables	Lobectomy (n=479)	Segmentectomy (n=155)	P value
Age	66 [30-89]	66 [31-89]	0.37
Gender			
Male	223 (46.6%)	74 (48.1%)	0.78
Tumor size (cm)	2.2 (0.7-3.0)	1.5 (0.6-3.0)	<0.001
SUVmax†	2.1 (0-16.9)	1.1 (0-9.8)	<0.001
Side			
Right	325 (67.8%)	81 (52.3%)	<0.001
Lobe			<0.001
Upper	254 (53.0%)	82 (52.9%)	
Middle	48 (10.0%)	0 (0%)	
Lower	177 (37.0%)	73 (47.1%)	
Lymphatic invasion	97 (20.3%)	10 (6.5%)	<0.001
Vascular invasion	111 (23.3%)	10 (6.5%)	<0.001
Pleural invasion	66 (13.9%)	8 (5.2%)	0.0024
Lymph node metastasis	50 (10.6%)	3 (1.9%)	<0.001

†, maximum standardized uptake value.

Table 2 Details of segmentectomy (n=155)

Site	Number
Right (n=81)	
S1	11
S1+2	1
S2	13
S3	7
S6	31
S7	3
S8	8
S9	1
S10	1
S7+8	1
S8+9	2
S9+10	1
S7+8+9+10	1
Left (n=74)	
S1+2	17
S3	9
S1+2+3	10
S1+2+3c	1
S4	5
S5	1
S4+5	7
S6	15
S8	2
S9	5
S10	1
S8+9+10	1

lobectomy (hilar lymph node, n=1; mediastinal lymph node, n=11; pleura, n=2; hilar and mediastinal lymph nodes, n=1; bronchial stump and mediastinal lymph node, n=1; mediastinal lymph node and pleura, n=1) and in three patients after segmentectomy (bronchial stump, n=1; pleura, n=1; residual lung and mediastinal lymph node, n=1).

The 3-year OS rates between patients who underwent lobectomy and segmentectomy were similar (94.1% *vs.* 95.7%, P=0.162), whereas three-year RFS rates significantly differed (86.9% *vs.* 92.7%, P=0.0394; *Figure 1*). *Table 3* shows that the multivariate analyses of RFS and OS selected age and SUVmax as significant independent prognostic factors, but not sex, tumor size, or procedure (lobectomy *vs.* segmentectomy).

Propensity score-matching based on clinical variables of age, gender, tumor size, SUVmax, side and lobe, allowed good matches of 100 lobectomy and segmentectomy pairs in terms of clinical and consequently pathological factors, except for more advanced age and higher SUVmax in the segmentectomy group (*Table 4*). Patients who underwent middle lobectomy were excluded from matching for a fair comparison, since tumors located in a middle lobe were never treated by segmentectomy. *Figure 1* shows that the three-year RFS and OS did not significantly differ between propensity score-matched patients after lobectomy or segmentectomy (91.5% *vs.* 90.2% and 93.3% *vs.* 94.8%, respectively).

Discussion

The RFS and OS curves of patients with clinical stage IA lung adenocarcinoma seemed better after segmentectomy than lobectomy, although the clinical and pathological backgrounds significantly differed and would obviously affect their survival (11-16). Multivariate analyses of the clinical background for RFS and OS demonstrated that procedure (lobectomy *vs.* segmentectomy) was not a significant prognostic factor. The clinical features or

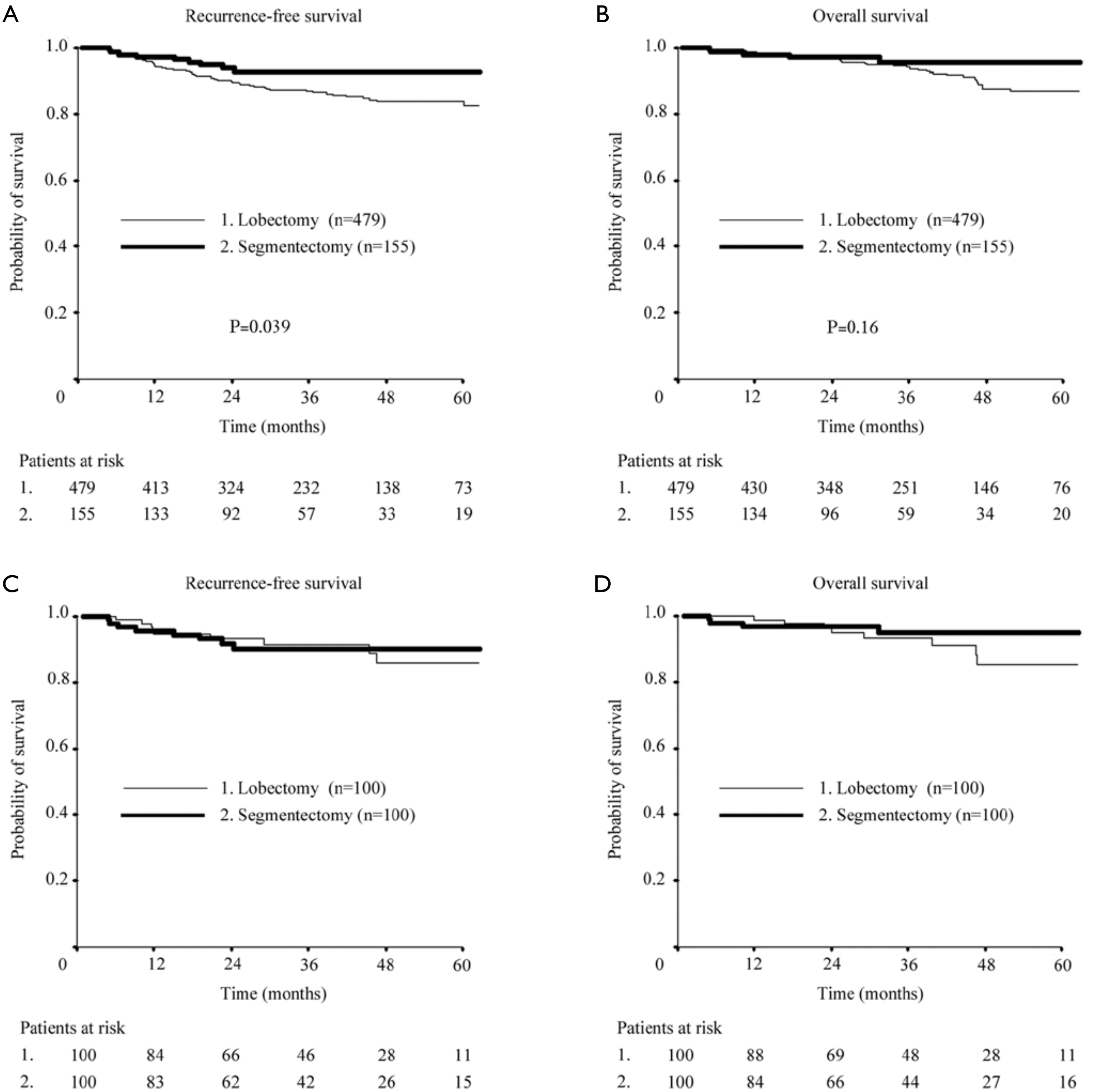

Figure 1 Recurrence-free (RFS) and overall survival (OS) curves of patients after lobectomy and segmentectomy. Three-year RFS (A) and OS (B) after lobectomy and segmentectomy were 86.9% *vs*. 92.7% (P=0.0394) and 94.1% *vs*. 95.7% (P=0.162), respectively, in all cohorts. Three-year RFS (C) and OS (D) in propensity score-matched patients after lobectomy and segmentectomy were 91.5% *vs*. 90.2% and 93.3% *vs*. 94.8%, respectively.

pathological factors of lymphatic, vascular or pleural invasion, or lymph node metastasis were similar in propensity score-matching analyses that matched for potentially confounding variables of age, sex, tumor size, SUVmax, tumor location to minimize selection bias. Only age and SUVmax significantly differed. The three-year RFS and OS rates after segmentectomy and lobectomy group were similar in the matched model, although the former

Table 3 Multivariate analyses for RFS and OS

Variables	HR (95% CI)	P value
Multivariate analysis for RFS[†]		
Age	1.04 (1.01-1.07)	0.011
Gender		
Male *vs*. female	1.20 (0.74-1.93)	0.46
Tumor size (cm)	1.36 (0.86-2.14)	0.19
SUVmax[‡]	1.17 (1.09-1.25)	<0.001
Procedure		
Lobectomy *vs*. segmentectomy	0.72 (0.34-1.52)	0.39
Multivariate analysis for OS[#]		
Age	1.05 (1.01-1.09)	0.0082
Gender		
Male *vs*. female	1.10 (0.49-1.70)	0.78
Tumor size (cm)	1.23 (0.67-2.26)	0.50
SUVmax[‡]	1.13 (1.04-1.24)	0.0068
Procedure		
Lobectomy *vs*. segmentectomy	0.68 (0.25-1.82)	0.44

RFS, recurrence-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval. [†], recurrence-free survival; [‡], maximum standardized uptake value; [#], overall survival.

Table 4 Propensity score-matched comparison of clinical and pathologic factors between patients who underwent lobectomy and segmentectomy

Variables	Lobectomy (n=100)	Segmentectomy (n=100)	P value
Clinical factors			
Age	63 [33-82]	66 [32-89]	0.030
Gender			
Male	46 (46%)	50 (50%)	0.67
Tumor size (cm)	1.6 (0.7-3.0)	1.6 (0.6-3.0)	0.28
SUVmax[†]	1.2 (0-8.7)	1.2 (0-9.8)	0.047
Side			0.27
Right	62 (62%)	53 (53%)	
Lobe			0.10
Upper	62 (62%)	50 (50%)	
Lower	38 (38%)	50 (50%)	
Pathologic factors			
Lymphatic invasion	11 (11%)	7 (7%)	0.45
Vascular invasion	9 (9%)	9 (9%)	1.0
Pleural invasion	10 (10%)	7 (7%)	0.61
Lymph node metastasis	7 (7%)	3 (3%)	0.34

[†], maximum standardized uptake value.

were significantly older and had a higher SUVmax. These data suggest that segmentectomy could be an alternative strategy for treating clinical stage IA lung adenocarcinoma when HRCT and FDG-PET/CT findings are taken into consideration.

This investigation has several limitations and the results should be interpreted with care. Information in the database analyzed herein included surgical procedures; however, further details such as indications for segmentectomy—that is, whether or not patients who were treated with segmentectomy could have tolerated lobectomy—are difficult to obtain. In addition, patients who underwent segmentectomy tended to have less invasive, smaller tumors, with small tumor size or low SUVmax, and thus a lower frequency of pathologically invasive factors such as lymphatic, vascular, pleural or nodal involvement. Therefore, we used propensity score-matched analysis to adjust the patients' backgrounds as much as possible. However, we could not compare the surgical outcomes of patients with a relatively low SUVmax, implying that patients with a high SUVmax require close scrutiny. The database also did not include information about lung function. The key advantage of segmentectomy is the preservation of lung function, and several studies have shown that segmentectomy has functional advantages over lobectomy (5,17,18).

The target tumors of most previous studies that compared the outcomes of segmentectomy and lobectomy were T1 N0 M0 NSCLC of ≤2 cm (4-6). However, the present study included patients with clinical T1b tumors of 2 to 3 cm. Patients with T1b lung adenocarcinomas with a sufficient surgical margin could be candidates for sublobar resection if selected based on HRCT and FDG-PET/CT findings (12).

The ongoing, multicenter phase III clinical trials of propriety of radical segmentectomy in the United States (CALGB-140503) and Japan (JCOG0802/WJOG4607L) should be carefully monitored. The primary end-point of the Japanese study is OS (disease-free survival in the US study), and wedge resection is not permitted as a sublobar resection, as it differs from radical segmentectomy. The Japanese study (19) aims to compare the surgical outcomes of lobectomy and segmentectomy for T1 N0 M0 NSCLC measuring ≤2 cm, excluding radiologically less-invasive tumors such as ground-glass opacity (GGO)-dominant tumors on HRCT (20), and thus can show the true colors of segmentectomy compared with lobectomy. Segmentectomy is more procedurally demanding than either lobectomy or wedge resection, and thus incorrect outcomes of these clinical trials due to technical errors, such as recurrence at resection lines or excessive loss of lung function, might be a concern. Surgeons must carefully avoid local failure at the margin and fully expand adjacent segments to maximize postoperative lung function.

Current understanding of radical segmentectomy can be summarized as follows. Firstly, the indication for segmentectomy should be limited to T1 tumors ≤3 cm in diameter, and HRCT and PET-CT findings must be taken into consideration, particularly for T1b tumors (21-23). Whenever nodal involvement or an insufficient margin is confirmed intraoperatively, segmentectomy should be converted to lobectomy with complete nodal dissection. Secondly, radical (intentional) and compromising indications for segmentectomy must be independently discussed. The former is for low-risk patients who can tolerate lobectomy. Thirdly, segmentectomy is more valuable than wedge resection from an oncological perspective because it allows nodal dissection at the hilum. Thus, the decision of the most suitable procedure, such as whether or not to intraoperatively convert to lobectomy, should consider precise staging and the lower rate of local recurrence resulting from sufficient surgical margins. Therefore, segmentectomy must be clearly separated from wedge resection amongst the categories of sublobar resection for lung cancer. Surgeons must become adept and master segmentectomy as a keynote procedure because small lung cancers are being detected with increasing frequency.

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Lobectomy *vs*. segmentectomy for NSCLC (T<2 cm)

Nestor Villamizar, Scott J. Swanson

Department of Thoracic Surgery, Brigham and Women's Hospital, Boston, Massachusetts, USA

Correspondence to: Nestor Villamizar, MD. Department of Thoracic Surgery, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA. Email: nvillamizarortiz@partners.org.

Abstract: The extent of surgical resection for peripheral clinical T1N0M0 non-small cell lung cancer (NSCLC) ≤2 cm continues to be a matter of debate. Eighteen years ago, a randomized controlled trial (RCT) established lobectomy as the standard of care for peripheral clinical T1N0M0 NSCLC. However, numerous publications since then have reported similar outcomes for patients treated with segmentectomy or lobectomy for peripheral clinical T1N0M0 NSCLC 2 cm or smaller in size. The majority of these publications are retrospective studies. Two ongoing RCTs aim to resolve this debate, one in Japan and the other in the United States. This manuscript is a comprehensive review of the literature that compares lobectomy to segmentectomy for peripheral clinical T1N0M0 NSCLC 2 cm or smaller in size. Until data from the ongoing RCTs become available, this literature review provides the best evidence to guide the thoracic surgeon in the management of these patients.

Keywords: Segmentectomy; lobectomy; lung cancer; 2 cm

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Lobectomy was established in 1995 as the standard of care for optimal oncologic resection of stage I non-small cell lung cancer (NSCLC), after the results of the Lung Cancer Study Group (LCSG) reported a significantly higher rate of recurrence and associated trend toward lower cancer-specific survival in patients undergoing sublobar resections (1). Since then, several investigators have challenged this dogma by demonstrating equivalent oncologic outcomes of segmentectomy and lobectomy for stage IA NSCLC. A large proportion of studies have integrated segmentectomy and wedge resection under the category of limited resection when making comparisons to lobectomy (2). However, recent publications have focused on comparisons between segmentectomy and lobectomy excluding cases of wedge resection (3-6).

Potential advantages of segmentectomy over lobectomy include preservation of lung function and reduced morbidity and disability. Preservation of lung function may be particularly important for elderly patients, those with borderline preoperative cardiopulmonary function, and patients with synchronous or metachronous cancers that would require repetitive resections over the course of their lifespan. The incidence of a second primary lung cancer may be as high as 3% per year (7); thus, patients who survive five or more years after their first resection would face a significant cumulative risk of second cancers. On the other hand, lobectomy may provide a lower recurrence rate that could translate into longer disease free survival, particularly in young patients who are good surgical candidates.

The main objective of this manuscript is to review the literature that compares lobectomy versus segmentectomy for NSCLC less than 2 cm in size. The data provided here is intended to help in the decision-making process about which of these two surgical approaches should be used based on tumor and patient characteristics.

Lung Cancer Study Group (LCSG) trial

This randomized controlled trial (RCT) enrolled patients from February 1982 through November 1988 and compared open lobectomy to sublobar resection for patients with lung cancer ≤3 cm with absence of lymph node involvement (1). There were 247 patients eligible for analysis: 122 received a limited resection and 125 underwent lobectomy. Of the 122 patients who underwent a limited resection, 40 (32.8%) had a wedge resection and 82 (67.2%) had a segmentectomy. There were no significant differences for all stratification variables, selected prognostic factors, perioperative morbidity, mortality, or late pulmonary function. The rate of local recurrence in the limited resection group was 6.3%, which was significantly higher than the 2.1% observed in the lobectomy group (P=0.008), and the 5-year survival rate in the limited resection group was 83.1%, which was slightly poorer than the 89.1% observed in the lobectomy group. In addition, postoperative pulmonary function was not significantly different in the two groups, even at one year after surgery. The authors concluded that, compared with lobectomy, limited pulmonary resection does not confer improved perioperative morbidity, mortality, or late postoperative pulmonary function. Furthermore, due to higher death rates and locoregional recurrence rates associated with limited resection, lobectomy must be considered the surgical procedure of choice for patients with peripheral T1N0 NSCLC.

It must be acknowledged that a considerable number of wedge resections (32.8%) were included in the limited resection group; tumor sizes ranging from 2 to 3 cm were included in the analysis; and routine computed tomographic examination of the lung was not required either preoperatively or for postoperative surveillance. Several publications have demonstrated a lower rate of loco-regional recurrence after segmentectomy compared to wedge resection for stage IA NSCLC (8-10). An adequate body of literature has also demonstrated that T1b tumors (2-3 cm) have lower survival rates than T1a tumors (≤2 cm) (11,12). Moreover, advances in imaging and optimal pre-resection surgical mediastinal staging have improved staging accuracy since the LCSG trial was published (13). This trial was done in an earlier era when tumors were often more central, many were squamous cell cancers, and they were larger stage I tumors (14).

Extended segmentectomy for stage I lung cancer

Since the results of the LCSG were published, several Japanese investigators have studied the role of sublobar resection for stage I NSCLC. The Study Group of Extended Segmentectomy for Small Lung Tumors was created and their final report was published in 2002 (15). This prospective multicenter study enrolled 55 patients with peripheral clinical T1N0M0 (cT1N0M0) NSCLC (≤2 cm) from January 1992 to December 1994. All patients were in physical conditions to tolerate a lobectomy. Extended segmentectomy involves the development of the intersegmental plane, by keeping inflated the segment to be resected after ligation of the segmental bronchus, while the adjacent segments are collapsed. The resection is then performed on the side of the collapsed segments in order to optimize lateral margins, and a complete lymph node dissection including segmental, hilar and mediastinal lymph nodes is undertaken, as is performed during lobectomy (16). The patients were followed up at 1- or 3-month intervals for five years or more. The 5-year disease-free survival (DFS) rate was 91.8%. Postoperative loss of lung function was 11.3% in forced vital capacity (FVC) and 13.4% in forced expiratory volume in one second (FEV1). The authors concluded that extended segmentectomy is viable as a standard operation for patients with small peripheral lung tumors, and causes minimal loss of lung function.

More recently, Nomori *et al*. (17) also examined the outcomes of 179 patients who underwent intentional open radical segmentectomy with systematic lymph node dissection for peripheral cT1N0M0 NSCLC between 2005 and 2009 at a single institution. All analyzed patients had intraoperative frozen section to demonstrate surgical margins of at least 2 cm. Of these 179 patients, 134 (75%) had tumors ≤2 cm, and 45 (25%) had tumors 2.1 to 3 cm. The 5-year DFS was 95% for patients with tumors ≤2 cm and 79% for those who had tumors 2.1 to 3 cm. Postoperative pulmonary function (measured at least six months after surgery) was preserved at 90%±12% of preoperative levels.

The importance of lymph node dissection during segmentectomy has been demonstrated. The frequency of lymph node metastasis in patient with cT1N0M0 NSCLC is approximately 10% (18). A theoretical disadvantage of segmentectomy versus lobectomy is the potential presence of metastatic disease in level 13 lymph nodes in the preserved adjacent segments. Nomori *et al*. (19) investigated the distribution of subsegmental lymph nodes in resected and preserved segments during segmentectomy. Out of 94 patients with cT1N0M0 NSCLC treated with segmentectomy, segmental nodes at both the resected and nonresected segments could be dissected in 42 of the 94 patients. The authors concluded that segmental lymph nodes should be dissected at both the resected and nonresected segments during segmentectomy, especially for tumors in the anteriorly located segment.

Another factor that appears to play an important role in recurrence after segmentectomy is the surgical margin. Schuchert and colleagues (20) performed a retrospective review of 182 consecutive patients undergoing anatomic segmentectomy for stage I NSCLC from 2002 to 2006. The average surgical margin for segmentectomy was 18.2 mm. There were 32 recurrences after segmentectomy (17.6%) at a mean of 14.3 months (14 locoregional, 18 distant), and 89% of recurrences were seen when tumor margins were 2 cm or less. Margin/tumor diameter ratios exceeding 1 were associated with a significant reduction in recurrence rates, compared with ratios of less than 1 (25% versus 6.2%, P=0.0014).

Segmentectomy versus lobectomy for cT1N0M0 NSCLC ≤2 cm

In order to elucidate factors associated with survival, Okumura *et al.* (12) analyzed 144 patients who underwent segmentectomy and 1,241 who underwent lobectomy. The authors concluded that a favorable outcome would be obtained by a segmentectomy in patients with a maximum diameter of the tumor smaller than 2 cm, no nodal involvement, and non-large cell carcinoma. Five- and 10-year overall survival (OS) in patients who met those criteria were both 83%, which was significantly higher than that for those who did not (41%) (P<0.0001). In comparison, 5- and 10-year OS in patients who underwent lobectomy meeting the same criteria (non-large cell carcinoma at stage IA ≤2 cm) was 81% and 64% respectively (P=0.66). There were no 5-year survivors among the six patients with large cell carcinoma who underwent a segmentectomy. In contrast, there was no difference in survival among different histologic types when a lobectomy was performed. The authors concluded that lobectomy, but not a segmentectomy, is recommended for large cell carcinomas, even when the tumor diameter is 2 cm or smaller.

In another retrospective study, Yamato and colleagues (21) reviewed 523 cases of cT1N0M0 peripheral adenocarcinomas ≤2 cm between 1991 and 2004. The surgical procedure was a lobectomy in 277 patients, segmentectomy in 153 patients and wedge resection in 93 patients. The limited resection was intentional in 140 cases, and it was performed for compromised patients in 106 cases. The 5-year survival rate of the patients who underwent a wedge resection was 70.6%, which was significantly worse than the 87.5% after a segmentectomy and the 85.5% after a lobectomy.

A multicenter nonrandomized study comparing lobectomy to sublobar resection was conducted by Okada *et al.* (22) from 1992 to 2001 for patients with a first peripheral cT1N0M0 NSCLC ≤2 cm who were able to tolerate a lobectomy. During the operation, the tumor status was confirmed to be T1N0 on the basis of frozen-section analysis of sampled segmental, lobar, hilar, and mediastinal lymph nodes. For segmentectomy, a margin of at least 2 cm of healthy lung tissue was required. It was specified that when the surgical margin was less than 2 cm or a lymph node was positive, lobectomy had to be performed instead. Of the 567 patients enrolled, 214 patients underwent curative segmentectomy, 30 underwent wedge resection and 236 had lobectomy. DFS and OS were similar in all groups. Five-year DFS was 92.2% after segmentectomy and 91.5% after lobectomy (P=0.64). Five-year OS was 93.9% after segmentectomy and 95.3% after lobectomy (P=0.43).

More recently, Carr and coworkers (11) performed a retrospective review of 429 patients undergoing resection of pathologically confirmed stage IA NSCLC via lobectomy (251 patients) or anatomic segmentectomy (178 patients) from 2002 to 2009. Video-assisted thoracoscopic surgery (VATS) was the approach utilized in 59% of segmentectomies and 39.4% of lobectomies during the study period. The margin:tumor ratio was similar whether performing an anatomic segmentectomy or lobectomy for T1a or T1b tumors. There was no difference in mortality, recurrence rates (14% segmentectomy *vs.* 14.7% lobectomy, P=1.00), or 5-year cancer-specific survival (CSS) for T1a tumors (90% *vs.* 91%, P=0.984) when comparing segmentectomy and lobectomy. The authors concluded that anatomic segmentectomy may achieve equivalent recurrence and survival compared with lobectomy for patients with stage IA NSCLC.

A criticism of the literature comparing the efficacy of segmentectomy and lobectomy since 1995 is that the majority of publications have been limited to single-institution retrospective reviews. However, more recently some investigators have used the Surveillance Epidemiology and End Results (SEER) database to compare survival after lobectomy and limited resection in patients with stage IA NSCLC. Whitson *et al.* (23) analyzed the SEER database for stage I adenocarcinoma or squamous cell carcinoma in patients 40 years and older from 1998 through 2007. The analysis included 13,892 patients who underwent lobectomy and 581 who underwent segmentectomy. Even after stratifying by tumor size, the authors found that lobectomy was associated with more favorable 5-year OS (P=0.0002) and CSS (P=0.0047) rates for tumors ≤2 cm.

Yendamuri and coworkers (13) also used the SEER database to identify surgically treated patients with stage I NSCLC ≤2 cm in size from 1988 to 2008. The cohort included 2,161 patients undergoing sublobar resection and 6,636 patients undergoing lobectomy or greater resection. They grouped these patients into three temporal cohorts:

the first included patients from 1988 to 1997 (early), the second was from 1998 to 2004 (intermediate) and the third was from 2005 to 2008 (late). In the early group, sublobar resection was associated with worse outcome. In the intermediate group, wedge resection but not segmentectomy was associated with a worse outcome compared with lobectomy. The association between extent of resection and OS completely disappeared in the late subgroup, in which neither wedge resection nor segmentectomy had an outcome worse than did lobectomy. The authors concluded that the survival advantage offered by lobectomy over sublobar resection in NSCLC patients with tumor size ≤2 cm has incrementally decreased over the past two decades.

A recent meta-analysis (24) included 24 studies (11,360 patients) published from 1990 to 2010 to compare OS and CSS of stage I NSCLC after sublobectomy or lobectomy. In stage IA patients with tumor ≤2 cm, there were no differences in OS between lobectomy and sublobectomy (HR 0.81; 95% CI, 0.39-1.71; P=0.58). For the comparison between lobectomy and segmentectomy, there was no significant difference on OS (HR 1.09; 95% CI, 0.85-1.40; P=0.45) and CSS (HR 0.99; 95% CI, 0.72-1.38; P=0.97) in stage I NSCLC.

Several studies have specifically limited their objective to compare outcomes between lobectomy and segmentectomy for NSCLC ≤2 cm, excluding larger tumors or wedge resections. Mattioli *et al*. (25) performed a retrospective investigation to compare anatomical segmentectomy and lobectomy for peripheral cT1N0M0 NSCLC ≤2 cm on preoperative CT scan, with regard to the number/station of lymph nodes resected, as well as survival. In this case-matched study, 46 intentional segmentectomy patients were matched with 46 lobectomy patients for age, anatomical segment, and size of the tumor. All patients were able to tolerate a lobectomy as evaluated by cardiopulmonary functional tests. Starting in January 2001, the authors offered anatomical segmentectomy as an alternative to lobectomy to patients affected by a peripheral cT1aN0M0 NSCLC. The cases in which lobectomy was performed within the same time period were retrospectively retrieved from the institutional electronic medical record system database. The approach for the resection was an axillary muscle-sparing thoracotomy. Radical dissection of lymph node stations 4, 5, 6 and 7 was identical in segmentectomies and lobectomies. Node stations 10, 11, 12 and the segmental 13 were also dissected carefully during segmentectomy and in the pathology laboratory after lobectomy. The median number of total dissected lymph nodes was 12 in anatomical segmentectomy compared with 13 in lobectomy (P=0.68), with the number of N1 nodes being 6 and 7, respectively (P=0.43), and N2 nodes 5.5 and 5 (P=0.88). No perioperative mortality was observed. Complications occurred in 13% of segmentectomies and in 15% of lobectomies (P=0.76). The median follow-up was 25 months for the segmentectomy group and 32 months for the lobectomy group. Freedom from recurrence at 36 months was 100% for anatomical segmentectomy and 93.5% for lobectomy (P=0.33)

Thoracoscopic segmentectomy *vs.* lobectomy

The vast majority of the evidence described above involves open procedures. However, a few recent studies have compared the outcomes of thoracoscopic segmentectomy and thoracoscopic lobectomy for small-sized stage IA lung cancer. Shapiro *et al*. (6) analyzed patients between January 2002 and February 2008. Indications for segmentectomy were tumor smaller than 3 cm, limited pulmonary reserve, comorbidities, and peripheral tumor location. Thirty-one patients underwent a segmentectomy and 113 had a lobectomy. Patients undergoing a segmentectomy had worse mean FEV1 than those having a lobectomy (83% *vs*. 92%, P=0.04). There were no differences in mean number of nodes (10) and nodal stations (5) resected. The mean follow-up was 21 months. There were 5 (17.2%) recurrences after segmentectomy and 23 (20.4%) after lobectomy (P=0.71), with locoregional recurrences rates of 3.5% and 3.6%, respectively. OS and DFS were similar between the groups. Zhong and colleagues (26) also compared outcomes between thoracoscopic segmentectomy and thoracoscopic lobectomy. Their inclusion criterion was limited to stage IA NSCLC ≤2 cm. The study period was between March 2006 and August 2011. A total of 39 segmentectomies and 81 lobectomies were analyzed. The two groups had a similar incidence of postoperative complications. The median follow-up was 26.5 months. Local recurrence rates were similar after segmentectomy (5.1%) and lobectomy (4.9%). No significant difference was observed in 5-year OS (79.9% *vs*. 81%) or DFS (59.4% *vs*. 64.2%).

Segmentectomy for clinical T1N0M0 ≤2 cm and ≥50% ground glass opacity component (GGO-dominant)

Tumor characteristics may also play an important role in deciding the extent of surgical resection. Tsutani *et al*. (27)

evaluated 239 patients with GGO-dominant clinical stage IA lung adenocarcinoma from four institutions between August 2005 and June 2010. All patients underwent HRCT and FDG-PET/CT followed by curative R0 resection. The inclusion criteria were absence of >1 cm enlargement in mediastinal or hilar lymph nodes and an absence of >1.5 accumulation for maximum standardized uptake values (SUVmax) in these lymph nodes. Sublobar resection was allowed for a peripheral cT1N0M0 intraoperatively assessed as N0, using frozen section evaluation of enlarged lymph nodes or by ensuring that there was no obvious enlargement of lymph nodes in the thoracic cavity. Systematic lymph node dissection was performed during segmentectomy, but not during wedge resection. Follow-up included a chest CT every six months for the first two years postoperatively, and every year thereafter. Median follow-up period after surgery was 42.2 months. Lobectomy was performed in 90 patients, segmentectomy in 56, and wedge resection in 93. A total of 155 tumors were classified as T1a and 84 as T1b. There was no significant difference in 3-year DFS among patients with GGO-dominant tumors who underwent lobectomy (96.4%), segmentectomy (96.1%), and wedge resection (98.7%; P=0.44). A multivariate Cox proportional hazards model for DFS included variables of age, gender, clinical T descriptor, solid tumor size, SUVmax, and surgical procedure. However, none of these variables were independent prognostic factors.

Pulmonary function tests

With regards to the functional advantage of a limited resection, Harada *et al*. (28) analyzed PFT preoperatively and at two and six months after radical segmentectomy in 38 patients and lobectomy in 45 patients. Both groups were able to tolerate a lobectomy and had cT1N0M0 NSCLC ≤2 cm. The anatomic segmentectomy was made through video-assisted approach with minithoracotomy. They performed segmentectomy if the patient consented to the sublobar resection, and lobectomy if the patient did not. During the postoperative course, statistically significant differences were observed between the two groups in the ratio of postoperative to preoperative FVC (P=0.0006) and FEV1 (P=0.0007), whereas a marginal difference was seen in the ratio of postoperative to preoperative anaerobic threshold (P=0.616). Keenan and colleagues (29) retrospectively analyzed patients undergoing lobectomy (n=147) or segmentectomy (n=54) for stage I NSCLC between March 1996 and June 2001. From the pathologic analysis, there were 126 stage IA and 21 stage IB patients in the lobectomy group, and 47 stage IA and 7 stage IB patients in the segmentectomy group. PFT was obtained preoperatively and at one year. At one year, lobectomy patients experienced significant declines in FVC (85.5% to 81.1%), FEV1 (75.1% to 66.7%), and diffusing capacity (79.3% to 69.6%). In contrast, a decline in diffusing capacity was the only significant change seen after segmental resection. Actuarial survival in both groups was similar (P=0.406), with a 1-year survival of 95% for lobectomy and 92% for segmentectomy. Four-year survivals were 67% and 62%, respectively. Overall, the risk of any recurrence, whether local, regional, or systemic, was identical in the two groups (20.4% segmentectomy, 19% lobectomy). The authors concluded that for patients with stage I NSCLC, segmental resection offers preservation of pulmonary function compared with lobectomy and does not compromise survival.

Ongoing prospective RCTs

The controversy about the optimal extent of surgical resection for peripheral NSCLC ≤2 cm has led to several multicenter prospective RCTs. The JCOG0802/WJOG4607L trial (30) began in August 2009 in Japan to evaluate the non-inferiority in OS of segmentectomy compared with lobectomy in patients with peripheral NSCLC ≤2 cm. A total of 1,100 will be accrued from 71 institutions within three years. The inclusion criteria include age 20-79 years old, sufficient organ function, single tumor, ≤2 cm in maximum diameter, proportion of maximum diameter to consolidation >25%, center of tumor located in the outer third of the lung field, tumor not located at middle lobe, and no lymph node metastasis. The secondary endpoints include postoperative respiratory function, relapse-free survival, and proportion of local recurrence. The distance from the dissection margin to the tumor edge must be evaluated intra-operatively. If the distance is less than 2 cm, the absence of cancer cells in the resection margin must be histologically or cytologically confirmed before finishing surgery. When lymph node metastasis is present or resection margin is not cancer-free, the surgical procedure must be converted to a lobectomy. All randomized patients will be followed for at least five years. Tumor markers, CXR and chest CT is evaluated at least every six months during the first two years and at least every 12 months for the duration of follow-up.

Similarly, the CALGB 140503 study (31) aims to determine whether DFS after sublobar resection (segmentectomy or wedge) is non-inferior to that after lobectomy in patients with NSCLC ≤2 cm. A total of 692 patients will be accrued to the study and randomized intra-operatively to either lobectomy or limited resection. Prior to registration, patients must have a lung nodule measuring ≤2 cm on CT scan, presumed to be lung cancer and located in the outer third of the lung. Intraoperative histological confirmation of NSCLC must be obtained (if not done preoperatively), as well as confirmation of N0 status by frozen examination of levels 4, 7, and 10 on the right side and 5 or 6, 7 and 10 on the left side, either at the time of surgery or pre-operatively by mediastinoscopy within six weeks of the definitive procedure. Patients must also have a performance status of 0-2. Exclusion criteria include prior malignancy within five years, prior chemotherapy or radiation, and age <18 years.

Conclusions

The increasing use of CT scans and improvement in CT resolution has been associated with earlier detection of NSCLC with smaller tumor size. Also, the location and type of lung cancer has evolved over time such that smaller, peripheral adenocarcinomas are now among the most common presentation. An extensive body of literature mainly composed of retrospective studies supports the use of radical anatomical segmentectomy for peripheral cT1N0M0 NSCLC ≤2 cm, certainly for older patients with limited cardiopulmonary function. However, caution should be taken to promote a widespread indication for intentional segmentectomy in young good surgical candidates until the results of the ongoing RCTs become available. When expertise exists, the surgeon should use a minimally invasive approach to realize perioperative and functional patient benefits.

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Treatment of stage I lung cancer in high-risk and inoperable patients: SBRT *vs*. RFA *vs*. sublobar resection

Matthew J. Bott, Traves Crabtree

Division of Thoracic Surgery, Washington University School of Medicine, St. Louis, Missouri, USA

Correspondence to: Traves Crabtree. Division of Thoracic Surgery, Washington University School of Medicine, St. Louis, Missouri, USA. Email: crabtreet@wudosis.wustl.edu.

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Background

Although surgical resection for early stage lung cancer is the mainstay of treatment, many patients are inoperable at the time of presentation due to either disseminated disease or medical comorbidities (1). Novel strategies are currently being developed to treat early-stage non-small cell lung cancer (NSCLC) in this expanding population of high-risk and inoperable patients. Stereotactic body radiotherapy (SBRT) modifies traditional radiation techniques to provide a high-dose per fraction of radiation to the tumor which is administered over a few fractions. This allows for effective tumor ablation with preservation of the surrounding tissue due to steep dose gradients. Radiofrequency ablation (RFA) utilizes CT-guided placement of a radiofrequency-emitting probe. As frictional heat energy from the probe is transferred to the tumor, cancer cells undergo coagulation necrosis.

In an effort to expand the population of operable patients, many groups are currently exploring the use of sublobar resection to treat early stage tumors. Early evidence suggests that sublobar resection may provide satisfactory oncologic outcomes while avoiding the morbidity of standard lobectomy in patients with poor pulmonary reserve (2). Three major clinical trials have been developed to investigate the use of these different modalities to treat early stage lung cancer in inoperable or high-risk patients. A recently published trial, RTOG 0236, is a North American phase II trial of SBRT in patients with stage I NSCLC deemed inoperable by a surgeon or a pulmonologist. The study showed a local control rate of 90.6% at three years, and disease-free survival and overall survival at three years were 48.3% and 55.8%, respectively (3). ACOSOG Z4032 is a phase III randomized controlled trial that compared sublobar resection to sublobar resection with brachytherapy for the treatment of stage I NSCLC. Thirty- and 90-day outcomes from this study have recently been published (4). In addition, three-year results were presented at the 2013 American Society of Clinical Oncology (ASCO) meeting, showing a similar rate of local recurrence for those treated with sublobar resection (12.8%) versus sublobar resection with brachytherapy (12.5%) (5). Overall survival was comparable between the groups (sublobar resection =71%, sublobar resection with brachytherapy =72%). Lastly, ACOSOG Z4033 is a phase II prospective nonrandomized study examining high-risk patients with stage I NSCLC treated with RFA. This study has completed accrual, but survival and recurrence data have not yet matured. We conducted a comparison of selection criteria and short-term outcomes for these three studies.

Patients and setting

Patients

This study focuses on patients with stage I lung cancer that are high risk for surgical intervention due to medical co-morbidities.

Intervention(s)

We explore the selection criteria and short-term outcomes in high risk patients treated with three different treatment modalities: SBRT, sublobar resection, and RFA.

Objective(s)

We sought to compile data from three major North

Table 1 Pre-treatment demographics and comorbidity profiles for RTOG 0236, ACOSOG Z4032, and ACOSOG Z4033

Pre-treatment characteristics	RTOG 0236 (SBRT)	ACOSOG Z4032 (sublobar resection)	ACOSOG Z4033 (RFA)	P value
N	55	211	51	
Age (mean)	72.5±8.8	70.2±8.5	75.6±7.5	0.0003[1]
Age >75	21 (38.9%)	79 (37.4%)	30 (58.8%)	0.02[2]
Female	34 (61.8%)	117 (55.5%)	28 (54.9%)	0.7
ECOG 1-2	43 (78.1%)	169 (80.1%)	42 (82.4%)	0.86
Race (white)	51 (92.7%)	199 (94.3%)	44 (86.3%)	0.02[3]
Clinical stage IA	44 (80%)	208 (98.6%)	51 (100%)	<0.0001[4]
Pulmonary hypertension	NR	5 (2.4%)	1 (2.0%)	0.86
Poor LV function	NR	12 (5.7%)	6 (11.8%)	0.12
MMRC dyspnea score	NR	46 (21.8%)	12 (23.5%)	0.79
pO_2 ≤55 mmHg or SpO_2 ≤88%	2 (3.7%)	10 (4.7%)	1 (2.0%)	0.66
pCO_2 >45 mmHg	8 (14.8%)	6 (2.8%)	0	0.0002[5]
DLCO%	61.6±30.2	46.4±15.6	43.7±18.0	0.001[6]
FEV1%	61.3±33.4	53.8±19.6	48.8±20.3	0.15
FVC%	79.8±23.2	74.8±17	NR	0.4

Values are mean ± SD or n (%) as appropriate. P values are from Chi-square or Kruskall-Wallis test. NR, not reported; [1], P<0.0001 Z4032 *vs*. Z4033; [2], P=0.04 RTOG 0236 *vs*. Z4033, P=0.005 Z4032 *vs*. Z4033; [3], P=0.04 RTOG 0236 *vs*. Z4032; [4], P<0.0001 RTOG *vs*. Z4032, P=0.0007 RTOG 0236 *vs*. Z4033; [5], P=0.0004 RTOG 0236 *vs*. Z4032, P=0.004 RTOG 0236 *vs*. Z4033; [6], P=0.0008 RTOG0236 *vs*. Z4032, P=0.001 RTOG 0236 *vs*. Z4033. ECOG, Eastern Cooperative Oncology Group; DLCO%, diffusing capacity of the lung; FEV1%, forced expiratory volume in one second.

American trials in order to compare the selection of patients for these three treatment options, and to provide some insight into the short-term morbidity and mortality associated with each.

Methodology

The study was a retrospective secondary analysis of prospectively collected data from three multicenter trials (RTOG trial 0236, ACOSOG trial Z4032, and ACOSOG Z4033). The data were formally requested from the RTOG and ACOSOG, and the analysis was approved by both organizations. We compared entry criteria and short-term outcomes using raw data from all three trials. Categorical data were compared using chi-square test and continuous data using the Kruskal-Wallis test. We then performed a propensity-matched analysis of patients treated with SBRT and sublobar resection (RTOG 0236 and ACOSOG Z4032). Variables including age, Eastern Cooperative Oncology Group (ECOG) performance status, percentage of predicted forced expiratory volume in one second (FEV1%), and percentage of predicted carbon monoxide diffusing capacity of the lung (DLCO%) were used to build a propensity score for patients with clinical stage IA NSCLC. These scores were developed to estimate the adjusted risks of short-term outcomes associated with the choice of treatment (SBRT or surgery).

Primary outcomes

Main results

There were 55 patients available for analysis from RTOG 0236 (SBRT), 211 from ACOSOG Z4032 (sublobar resection), and 51 from ACOSOG Z4033 (RFA). RFA patients were older than those undergoing sublobar resection or SBRT (mean age in years =75.6, 70.2, 72.5 respectively, P=0.02) (*Table 1*). Despite having been identified as medically inoperable according to study criteria, SBRT patients had superior DLCO% (61.6%) compared with sublobar resection (46.4%) and RFA (43.7%) (P=0.001). All patients had either T1 or T2 tumors. Twenty percent of patients treated with SBRT had T2 disease (n=11), compared with 1.4% of those treated with sublobar resection (n=3). All patients treated with RFA had T1 tumors. SBRT patients received an average of 60 Gy of radiation. In patients undergoing surgical resection for clinical stage IA disease, 29.3% ultimately had a higher stage on final pathology (pIB in 25%, pIIA in 0.5%, pIIB in 1.6%, pIIIA in 1.1%, pIIIB in 0.5%, and IV in 1.1%).

Thirty- and 90-day outcomes are shown in *Table 1*. For RFA, only mortality data were available. There was no significant difference in 30-day, 90-day, or treatment-related mortality amongst the three modalities. There was, however, a higher incidence of grade 3+ events at 30 days in patients undergoing sublobar resection (28.0%) compared with SBRT (9.1%) (P=0.004). The incidence was equivalent at 90 days (33.2% for sublobar resection, and 21.8% for SBRT, P=0.24). A propensity-matched score was then used to compare SBRT (n=44) and sublobar resection (n=208) in patients with T1 lesions. In the propensity-matched analysis, there was no difference in 30- or 90-day grade 3+ adverse events between these two modalities. An additional analysis was performed examining pre- and post-treatment DLCO% and FEV1% in patients treated with SBRT and sublobar resection. After adjusting for pre-treatment values, there was no difference in DLCO%. However, post-treatment FEV1% was 6.4% greater in patients undergoing sublobar resection compared with those treated with SBRT.

Study limitations

Although each of the trials was designed to evaluate patients with early stage lung cancer, subtle underlying differences in the patient populations exist. Similarly, as long-term data has not yet matured, we cannot comment on the oncologic efficacy of the treatments. In addition, our propensity matched comparison may be underpowered to detect differences in morbidity and mortality. The current analysis was meant to provide preliminary insight and definite conclusions will best be made using specifically designed, randomized controlled data comparing the modalities directly.

Applicability to other populations

These trials were designed to evaluate treatment of early stage lung cancer in high-risk or non-operable patients. The data are not necessarily applicable to patients with more advanced disease or to those who are satisfactory operative candidates.

Conclusions

Variability in patient populations in these three studies underscores the need for more reliable, objective criteria to identify the inoperable patient, the high risk but potentially operable patient, and the very high risk patient that may have a relatively better risk/benefit ratio from non-operative therapy *vs.* operative therapy. Our propensity-matched analysis of high-risk or inoperable patients with clinical stage I lung cancer shows no difference in 30- or 90-day mortality and morbidity between SBRT and sublobar resection. These results emphasize the need for specifically designed randomized trials to compare these treatment modalities and further stratify patients considered high risk.

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Comparison of Different Surgical Methods

Comparative study of systematic thoracoscopic lymphadenectomy and conventional thoracotomy in resectable non-small cell lung cancer

Wei Wang[1,2]*, Weiqiang Yin[1,2]*, Wenlong Shao[1,2]*, Gening Jiang[3], Qun Wang[4], Lunxu Liu[5], Deruo Liu[6], Zheng Wang[7], Zhihua Zhu[8], Hanzhang Chen[1,2], Jianxing He[1,2]

[1]Department of Cardiothoracic Surgery, the First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; [2]Guangzhou Institute of Respiratory Disease & China State Key Laboratory of Respiratory Disease, Guangzhou 510120, China; [3]Department of Thoracic Surgery, Shanghai Pulmonary Hospital of Tongji University, Shanghai 200433, China; [4]Department of Thoracic Surgery, Shanghai Zhongshan Hospital of Fudan University, Shanghai 200032, China; [5]Department of Cardiovascular and Thoracic Surgery, West China Hospital, Sichuan University, Chengdu 610041, China; [6]Department of Thoracic Surgery, China and Japan Friendship Hospital, Beijing 100029, China; [7]Department of Thoracic Surgery, Shenzhen People's Hospital, Shenzhen 518020, China; [8]Department of Thoracic Oncology, Cancer Center of Sun Yat-Sen University, Guangzhou 510060, China

*These authors contributed equally in this study.

Correspondence to: Jianxing He, MD, PhD, FACS. Department of Cardiothoracic Surgery, the First Affiliated Hospital of Guangzhou Medical University. No. 151, Yanjiang Rd, Guangzhou 510120, PR China. Email: drjianxing.he@gmail.com.

Objective: To assess the feasibility and safety of the video-assisted thoracoscopy surgery (VATS) systematic lymph node dissection in resectable non-small cell lung cancer (NSCLC).

Methods: The clinical data of patients with NSCLC who underwent VATS or thoracotomy combined with lobectomy and systematic lymphadenectomy from January 2001 to January 2008 were retrospectively analyzed to identify their demographic parameters, number of dissected lymph nodes and postoperative complications.

Results: A total of 5,620 patients were enrolled in this study, with 2,703 in the VATS group, including 1,742 men (64.4%), and 961 women (35.6%), aged 59.5±10.9 years; and 2,917 in the thoracotomy group, including 2,163 men (74.2%), and 754 women (25.8%), aged 58.5±10.4 years. Comparing the VATS with the thoracotomy groups, the mean operative time was 146 *vs*. 157 min, with a significant difference ($P<0.001$); and the average blood loss was 162 *vs*. 267 mL, with a significant difference ($P<0.001$). Comparing the two groups of patients data, the number of lymph node dissection: 18.03 in the VATS group and 15.07 in the thoracotomy group on average, with a significant difference ($P<0.001$); postoperative drainage time: 4.5 days in the VATS group and 6.37 days in the thoracotomy group on average, with a significant difference ($P<0.001$); postoperative hospital stay: 6.5 days in the VATS group and 8.37 days in the thoracotomy group on average, with a significant difference ($P<0.001$); proportion of postoperative chylothorax: 0.2% (4/2,579) in the VATS group and 0.4% (10/2,799) in the thoracotomy group, without significant difference ($P>0.05$).

Conclusions: For patients with resectable NSCLC, VATS systematic lymph node dissection is safe and effective with fewer postoperative complications, and significantly faster postoperative recovery compared with traditional open chest surgery.

Keywords: Non-small cell lung cancer (NSCLC); video-assisted thoracoscopy surgery (VATS); systematic lymph node dissection

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Introduction

Lung cancer is a serious hazard to human health and life, with a significant rising trend in terms of morbidity and mortality around the world in recent years. This condition has become the leading cause of morbidity and mortality worldwide, both for developed and developing countries (1). Although there are many methods for treating lung cancer at present, the recognized option of choice for the treatment of early- and mid-stage non-small cell lung cancer (NSCLC) is surgical excision, and the standard surgical method is lobectomy combined with systematic lymph node dissection. As early as in 1983, Martini *et al*. (2) first reported the use of lobectomy and mediastinal lymph node dissection for the treatment of primary lung cancer.

With the wide application of minimally invasive techniques in the surgical field, the use of video-assisted thoracoscopy surgery (VATS) in the treatment of NSCLC has been increasingly valued by thoracic surgeons. With the greatest advantage of minimal invasiveness, reduced postoperative pain and less damage to the respiratory muscle and pulmonary function, the VATS technique has been applied in the lobectomy of lung cancer as early as in 1992 (3). In 1995, McKenna *et al*. (4) first reported the use of VATS lobectomy combined with mediastinal lymph node dissection in the treatment of primary lung cancer.

Thorough lymph node dissection is one of the keys for successful comprehensive treatment of lung cancer, as it provides definite staging and guidance for the prognosis and the next treatment, and can improve the local remission rate and prolong disease-free survival time. According to the guidelines issued by the European-Society of Thoracic Surgeons (ESTS), systematic lymph node dissection is required for resectable NSCLC regardless of VATS or thoracotomy (5). Whether VATS allows thorough mediastinal lymph node dissection and can achieve comparable effects to thoracotomy has been controversial. At present, the reported results varied in different studies on the use of VATS for lobectomy combined with lymphadenectomy of resectable NSCLC compared with thoracotomy (6-14). So far, however, the number of studies comparing the two techniques is not large enough for a comprehensive assessment of the effectiveness and safety of systematic lymphadenectomy using VATS versus thoracotomy. This study aims to determine the effectiveness and safety of VATS-based systematic lymphadenectomy by retrospectively analyzing the related multi-center, large-scale clinical data.

Materials and methods

Clinical data

The clinical data of patients with NSCLC who underwent VATS or thoracotomy combined with lobectomy and systematic lymphadenectomy in eight hospitals in China from January 2001 to January 2008 were retrospectively analyzed, and 5,620 patients were included in this study. Upon enrollment, all participants were engaged in a series of preparation before surgery, including quitting smoking, respiratory function exercise, administration of phlegm drugs and chest physiotherapy.

Preoperative examination and surgical methods

Before surgery, all participants received physical examination, routine blood tests, ECG, cardiac color Doppler ultrasound and lower extremity deep venous color Doppler ultrasound. Respiratory function tests included pulmonary ventilation-dispersion function tests. Coronary artery CT or treadmill activity tests were performed in patients with suspected coronary heart disease over the age of 60, as well as coronary interventional examination, if necessary.

Preoperative tumor staging was based mainly on chest CT, head and abdominal MRI, whole body bone scan, and bronchoscopy. PET/CT scans were recommended for patients considered to be stage II or above.

All participants underwent VATS or open chest lobectomy and hilar and mediastinal lymph node dissection, of which the specific surgical techniques were already reported in our previous study (15).

Thoracotomy group: a standard posterolateral incision of about 10-20 cm was made for placement of intercostal distraction to carry out the thoracotomy under direct vision. The operation included anatomic lobectomy plus systematic mediastinal lymph node dissection.

Systematic mediastinal lymph node dissection was common in both procedures, instead of lymph node sampling, involving at least three groups of mediastinal and intrapulmonary lymph nodes (including subcarinal lymph nodes). The surrounding fat tissue was be resected together with the lymph nodes en bloc. The resected lymph node specimens were independently examined and interpreted by two or more senior pathologists.

Data collection and follow-up

The demographic data, operative time, blood loss, number

Table 1 Characteristics of included patients

	VATS (%)	Open (%)	P
Numbers	2,703	2,917	
Sex			<0.001
Male	1,742 (64.4)	2,163 (74.2)	
Female	961 (35.6)	754 (25.8)	
Age (mean ± SD), years	59.5±10.9	58.5±10.4	0.002
Histology			<0.001
Squamous carcinoma	675 (25.0)	1,081 (37.1)	
Adenocarcinoma	1,663 (61.5)	1,326 (45.5)	
Adenosquamous carcinoma	126 (4.7)	168 (5.8)	
Large cell carcinoma	62 (2.3)		
BAC	75 (2.8)	198 (6.8)	
Others	102 (3.8)	101 (3.5)	
TNM stage			<0.001
Stage I	1,415 (52.3)	1,246 (42.7)	
Stage II	657 (24.3)	794 (27.2)	
Stage III (A)	631 (23.3)	877 (30.1)	

Abbreviations: VATS, video-assisted thoracoscopy surgery; BAC, bronchioloalveolar carcinoma.

of dissected lymph nodes, postoperative hospital stay, postoperative chest tube duration, postoperative tumor type, stage, and occurrence of postoperative chylothorax were collected for all patients.

Statistical analysis

Measurement data were expressed as mean ± standard deviation ($\bar{x}\pm s$). The statistical analysis was completed in SPSS 13, with P<0.05 indicating a statistically significant difference.

Results

Clinical data

A total of 5,620 patients were finally included in the retrospective study, with 2,703 in the VATS group, including 1,742 men (64.4%) and 961 women (35.6%), aged 59.5±10.9 years; and 2,917 in the thoracotomy group, including 2,163 men (74.2%), and 754 women (25.8%), aged 58.5±10.4 years (*Table 1*).

All patients underwent VATS or open chest lobectomy plus systematic lymphadenectomy. Comparing the VATS with the thoracotomy groups, the mean operative time was 146 *vs.* 157 min, with a significant difference (P<0.001); and the average blood loss was 162 *vs.* 267 mL, with a significant difference (P<0.001) (*Table 2*). The postoperative pathological test showed 1,663 patients with adenocarcinoma (61.5%), 675 patients with squamous cell carcinoma (25.0%), 126 patients with adenosquamous carcinoma (4.7%), and 239 patients with other types of tumors (8.9%) in the VATS group; and 1,326 patients with adenocarcinoma (45.5%), 1,081 patients with squamous cell carcinoma (37.1%), 168 patients with adenosquamous carcinoma (5.8%), and 342 patients with other types of tumors (11.8%) in the thoracotomy group (*Table 1*). According to the 2009 International Association for the Study of Lung Cancer (IASLC) staging criteria (16), all patients were subject to clinical pathological staging classification. There were 1,415 patients at stage I (52.3%), 657 patients at stage II (24.3%), and 631 patients at stage IIIA (23.3%) in the VATS group; and 1,246 patients at stage I (42.7%), 794 patients at stage II (27.2%), and 877 patients at stage IIIA (30.1%) in the thoracotomy group (*Table 2*).

Postoperative conditions (*Table 2*)

Comparing the two groups of patients data, the number of lymph node dissection (*Figure 1*): 18.03 in the VATS

Table 2 Comparisons of numbers of sampled lymphnodes and operation duration between VATS and open surgery for resectable stage NSCLC

Mean (SD)	VATS (N=2,703)	Open (N=2,917)	P
No. of sampled LNs			
Total	18.03 (10.14)	15.07 (8.55)	<0.001
Stage I	17.26 (9.29)	14.32 (7.98)	<0.001
Stage II	18.53 (11.20)	15.38 (8.91)	<0.001
Stage IIIA	19.27 (10.68)	15.86 (8.90)	<0.001
Operation length/minutes			
Total	145.71 (13.03)	156.72 (17.03)	<0.001
Stage I	145.75 (12.95)	156.09 (17.06)	<0.001
Stage II	145.40 (12.51)	157.63 (16.95)	<0.001
Stage IIIA	145.96 (13.71)	156.80 (17.04)	<0.001
Blood loss/mL	162.20 (142.56)	267.34 (220.31)	<0.001
Drainage days	4.50 (1.84)	6.37 (3.45)	<0.001
Length of hospitalization/days	6.50 (1.84)	8.37 (3.45)	<0.001
Chylothorax	4/2,579 (0.2%)	10/2,799 (0.4%)	0.117

Abbreviations: NSCLC, Non-small cell lung cancer; VATS, video-assisted thoracoscopy surgery; LNs, lymph nodes; Total, all stages (stage I-III).

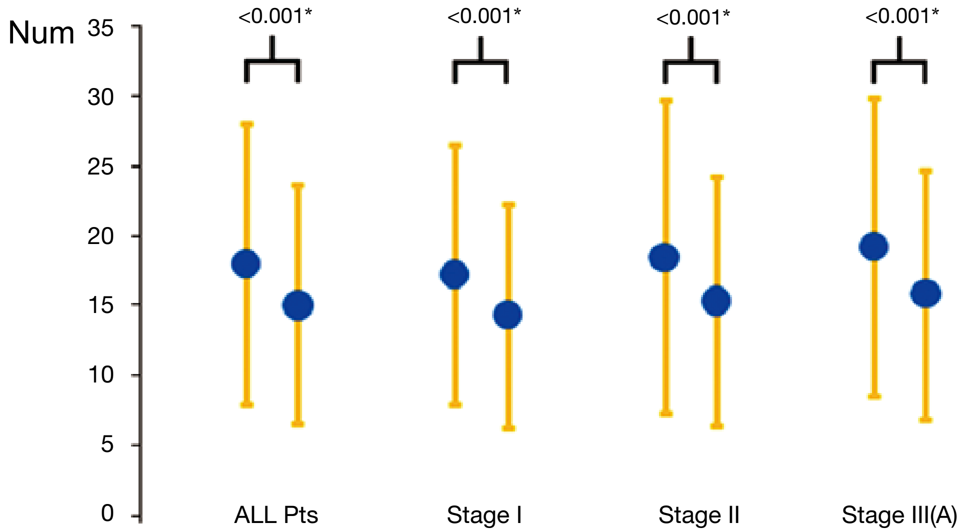

Figure 1 Comparisons of numbers of sampled lymph nodes between VATS and open surgery for resectable stage NSCLC. Abbreviations: NSCLC, Non-small cell lung cancer; VATS, video-assisted thoracoscopy surgery. *, With a significant difference.

group and 15.07 in the thoracotomy group on average, with a significant difference (P<0.001); blood loss: 162.2 mL in the VATS group and 267.34 mL in the thoracotomy group on average, with a significant difference (P<0.001); postoperative drainage time: 4.5 days in the VATS group and 6.37 days in the thoracotomy group on average, with a significant difference (P<0.001); postoperative hospital stay: 6.5 days in the VATS group and 8.37 days in the thoracotomy group on average, with a significant difference (P<0.001); proportion of postoperative chylothorax: 0.2% (4/2,579) in the VATS group and 0.4% (10/2,799) in the thoracotomy group, without significant difference (P>0.05).

Discussion

Lymph node metastasis is an important way of local and distant metastases in malignant cancer, as well as in NSCLC. It has a very important role in the prognostic determination and development of therapeutic strategies. Thus, for resectable NSCLC, the standard surgical method is lobectomy in combination with systematic lymph node dissection, which can improve the local control rate and prolong disease-free survival time.

Although it remains unconfirmed whether systematic lymphadenectomy can benefit patients with NSCLC oncologically, accurate lymph node staging still plays an important role in determining the need of postoperative adjuvant therapy and prognosis. Studies have shown that systematic lymphadenectomy is significantly superior to lymph node sampling in accurate staging. Investigators have found 4% patients at N2 stage with systematic lymph node dissection from 524 stage I patients who were identified with negative lymph nodes based on the sampling (17).

In the past, standard posterior lateral open chest lobectomy and lymph node dissection was mostly used for early and mid-stage resectable NSCLC. However, it is associated with a surgical incision often larger than 10 cm, extensive injury, slower postoperative recovery and higher incidence of postoperative complications. Since the early 1990s, VATS has been rapidly developed and widely applied in the world, involving almost all areas of general thoracic surgery. Compared with thoracotomy, VATS enables a smaller incision without removing or stretching the ribs open, sparing respiratory muscles from injures and thus minimizing the loss of lung function. Moreover, with a smaller incision, patients will suffer less pain postoperatively and expectorate more easily, reducing the incidence of postoperative pulmonary infection and complications as well.

The safety and effectiveness of VATS lobectomy combined with lymph node dissection for the treatment of early NSCLC has been confirmed, more and more studies have shown that this technique has comparable long-term oncological outcomes as a radical option to traditional open thoracic surgery (18,19). Moreover, National Comprehensive Cancer Network (NCCN) treatment guidelines for NSCLC has also clarified that VATS is a viable option for treating resectable lung cancer, particularly for those who can not tolerate standard thoracotomy due to physical conditions. This means that VATS treatment of NSCLC has covered most internationally recognized indications for surgical treatment of lung cancer.

As we all know, a thorough lymph node dissection is essential for the prognosis of patients with NSCLC, but it remains controversial whether this can be achieved with thoracoscopic systematic lymphadenectomy for NSCLC. In contrast to the thoracic surgery, many surgeons suspect the feasibility and thoroughness of thoracoscopic lymph node dissection. The primary concern is residual lymph nodes. In this regard, many studies have confirmed that after VATS lymph node dissection, the residual lymph node rate is very low. Hoksch *et al*. (20) did VATS lymphadenectomy in corpses followed by standard lateral open chest exploration, and the results showed no significant residual hilar and mediastinal lymph nodes. Sagawa *et al*. (21) performed VATS lymph node dissection in 29 NSCLC stage I patients followed by open chest exploration, and confirmed that there were only 2-3% of residues.

Since it has been applied in lymph node dissection, VATS has witnessed numerous controversies about whether it is superior or inferior to thoracotomy in this regard. Retrospective or prospective clinical studies yielded varying results as well (6-14,22). Ramos *et al*. (11) conducted a retrospective study to compare the number of dissected lymph nodes and stations with the two approaches by collecting the clinical and pathological data from patients with stage I non-small cell lung cancer patients. The results showed that an average dissection number of 5.1 stations in the VATS group, which was more than 4.5 stations in the open chest group, with a significant difference. However, the average number of 22.6 dissected nodes in the VATS group was far fewer than 25.4 nodes in the open chest group, with a significant difference. Lee *et al*. (23) analyzed 141 VATS patients and 115 cases of thoracic surgery for resectable NSCLC, finding that VATS yielded fewer dissected nodes compared with the open chest group (11.3±6.4 *vs*. 14.3±8.8, P=0.001), and the total number of dissected stations (3.1±1.1 *vs*. 3.8±1.2, P<0.001). Further analysis revealed that both differences came mainly from the dissection of mediastinal lymph nodes. On the other hand, some studies have confirmed that there is no difference in the number of either dissected nodes or dissected stations between the two approaches. Yang *et al*. (22) compared 62 patients with resectable NSCLC, which 31 cases in each of the VATS and thoracotomy groups, and found no significant difference in the number of either node or station dissected. In the present study, we found through statistical analysis that there was a mean number of dissected nodes of 18.03 in the VATS group and 15.07 in the thoracotomy group, with a significant difference (P<0.001)

Table 3 Comparisons between VATS and open surgery for resectable stage NSCLC

References	No. of patients		No. of sampled LNs		Hospital stay/days		Drainage days		Chylothorax	
	VATS	Open	VATS	Open	VATS	Open	VATS	Open	VATS	Open
Merritt RE, *et al*. 2013 (12)	60	69	9.9	14.7	4.5	5.1				
Ramos R, *et al*. 2012 (11)	96	200	22.6	25.4	7	10.3	4	5.7	2	3
Denlinger CE, *et al*. 2010 (13)	79	464	7.4	8.9	5.1	7.3				
Scott WJ, *et al*. 2010 (10)	66	686	15	19	5	7			0	7
Yang H, *et al*. 2013 (22)	31	31	28.2	29.8	10.6	12.4	6.3	8.3	0	1
Our study	2,703	2,917	18.03	15.07	6.5	8.37	4.5	6.37	4	10

Abbreviations: NSCLC, Non-small cell lung cancer; VATS, video-assisted thoracoscopy surgery; LNs, lymph nodes.

between the two groups, which is inconsistent with previous reports. We believe that the thoracoscopic vision has almost zero dead angles during intrathoracic operations. It can provide a good surgical field and has a visual zoom effect to magnify the surgical field, with which the hilar structures and mediastinal lymph node stations can be more clearly identified and exposed. In this way, we are able to clean out more mediastinal lymph node, reducing the incidence of residual lymph nodes.

The safety of VATS lobectomy in combination with systematic lymphadenectomy for resectable NSCLC is another concern. We have found through literature review and comparison (*Table 3*) that the majority of studies suggest that VATS has great advantages in terms of postoperative complications, postoperative chest tube drainage duration and postoperative hospital stay compared with thoracotomy. This study also confirms this conclusion. We believe that the smaller surgical wound and more clearly exposed blood vessels, lymph nodes and lymph vessels during VATS have made it possible to accurately dissect target tissue during dissection without damaging small blood vessels and lymph nodes, thus reducing lymphatic drainage and the occurrence of postoperative chylothorax, allowing earlier postoperative extubation and reduced postoperative hospital stay.

However, there are several limitations in this study due to its retrospective nature. Although this study has involved the most cases in comparison of VATS and open chest lymph node dissection, the origination of data from several studies with surgeons of varying thoracoscopic technical levels may have contributed to certain data deviation. Secondly, this study only analyzes two surgical procedures only in terms of the number of lymph node dissection and related postoperative complications, without comparing the differences in the prognosis. Therefore, a more comprehensive prospective study will be needed to further determine the safety and effectiveness of VATS lymph node dissection.

In conclusion, for patients with resectable NSCLC, VATS systematic lymph node dissection is safe and effective with acceptably low incidences of postoperative complications, and significantly faster postoperative recovery compared with traditional open chest surgery.

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Contraindications of video-assisted thoracoscopic surgical lobectomy and determinants of conversion to open

Jennifer M. Hanna, Mark F. Berry, Thomas A. D'Amico

Department of Surgery, Duke University Medical Center, Durham, NC 27710, USA

Correspondence to: Thomas A. D'Amico, MD, Professor and Vice Chair of Surgery. Duke University Medical Center, DUMC Box 3496, Duke South White Zone 3589, Durham, NC 27710, USA. Email: thomas.damico@dm.duke.edu.

Abstract: Since the introduction of anatomic lung resection by video-assisted thoracoscopic surgery (VATS) was introduced 20 years ago, VATS has experienced major advances in both equipment and technique, introducing a technical challenge in the surgical treatment of both benign and malignant lung disease. The demonstrated safety, decreased morbidity, and equivalent efficacy of this minimally invasive technique has led to the acceptance of VATS as a standard surgical modality for early-stage lung cancer and increasing application to more advanced disease. However, only a minority of lobectomies are performed using the VATS technique, likely owing to concern for intraoperative complications. Optimal operative planning, including obtaining baseline pulmonary function tests with diffusion measurements, positron emission tomography and/or computed tomography scans, bronchoscopy, and endobronchial ultrasound or mediastinoscopy, can be used to anticipate and potentially prevent the occurrence of complications. With increasing focus on operative planning, as well as comfort and experience with the VATS technique, the indications for which this technique is used has grown. As such, the absolute contraindications have narrowed to inability to tolerate single lung ventilation, inability to achieve complete resection with lobectomy, T3 or T4 tumors, and N2 or N3 disease. However, as VATS lobectomy has been applied to more advanced stage disease, the rate of conversion to open thoracotomy has increased, particularly early in the surgeon's learning curve. Causes of conversion are generally classified into four categories: intraoperative complications, technical problems, anatomical problems, and oncological conditions. Though it is difficult to anticipate which patients may require conversion, it appears that these patients do not suffer from increased morbidity or mortality as a result of conversion to open thoracotomy. Therefore, with a focus on a safe and complete resection, conversion should be regarded as a means of completing resections in a traditional manner rather than as a surgical failure.

Keywords: Video-assisted thoracoscopic surgery (VATS); lobectomy; contraindications; positron emission tomography (PET)

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Introduction

Since the introduction of anatomic lung resection or lobectomy for lung cancer by video-assisted thoracoscopic surgery (VATS) in the 1990s, VATS has experienced major advances in both equipment and technique and has subsequently been demonstrated to be safe and effective for the treatment of early-stage lung cancer (1-5). It is associated with decreased morbidity and length of stay and offers equivalence in terms of survival and recurrence rates (6,7). As such, VATS lobectomy is now accepted as a standard surgical modality for early-stage lung cancer and has been gradually applied to more advanced disease (8). However, only a minority of lobectomies are performed using the VATS technique, as only approximately 45% of lobectomies registered in the Society of Thoracic

Surgeons database are performed thoracoscopically (9). Its adoption has been variable, likely due to perceived technical challenges when compared to an open approach and the concern for intraoperative complications, especially during a surgeon's learning curve, discouraging smaller centers from adopting VATS lobectomy (10).

Operative planning

As with most surgical procedures, the optimal strategy for managing complications of VATS pulmonary resections is to prevent their occurrence. VATS represents a new approach and not a new procedure. Therefore, the preoperative evaluation and indications for VATS major resections remains the same as for conventional resection. Avoiding complications is dependent on appropriate preoperative workup and patient selection. Planning for as safe a VATS resection as possible involves consideration of patient characteristics, the radiographic appearance of the area of lung to be removed, and the anticipated technical aspects of the case.

All patients have a preoperative examination with a positron emission tomography (PET), computed tomography (CT) scan, bronchoscopy, and endobronchial ultrasound/mediastinoscopy for preoperative staging (unless it is benign lung disease or a peripherally-located T1 tumor on PET) (11). Additionally, preoperative evaluation and staging for thoracoscopic resection should include pulmonary function tests (PFTs) with diffusion measurements. The performance of thoracoscopic procedures is usually dependent on the ability to achieve and maintain single-lung ventilation, which involves careful consideration of the patient's contralateral lung status. Obtaining quantitative ventilation-perfusion scans can help in determining the ability of a patient with marginal functional status to tolerate pulmonary resection. The lowest limits in lung function parameters that would still be considered acceptable for VATS lobectomy have not been scientifically studied (12), but this would depend upon, among other factors, the surgeon's judgment, experience, and technique; the contribution of the excised lobe to overall lung function; and the exact location of the pathology. Additionally, VATS resections have been shown to be able to be accomplished in patients with lung function who have typically been thought to be too poor to undergo more conventional resection via thoracotomy (13,14). We have performed lobectomies on selected patients whose forced expiratory volume in 1 second (FEV_1) was less than 30% predicted with excellent outcomes (15). In fact, one major advantage of VATS resection is that it allows recruitment of older and sicker patients with multiple comorbidities who would otherwise not be suitable candidates for resection through a conventional thoracotomy approach (13,16). Moreover, aggressive preoperative pulmonary rehabilitation can be considered in patients initially considered not to be candidates for resection owing to poor PFTs (17). Finally, patients who are not candidates for an anatomical resection could still be considered for VATS wedge resection (18). In all such cases, it is imperative to consider that conversion to thoracotomy is possible for all patients for whom VATS resection is planned.

Contraindications to VATS lobectomy

Since major lung resection by VATS was first introduced in the early 1990s, the indications and contraindications of these procedures have changed over time. Thus, whereas initially a history of prior surgery, endobronchial lesion, or even the administration of induction chemotherapy were regarded as contraindications, the experience that has since been gained, together with improvements in instrumentation and thoracoscopic imaging, have now changed this situation in most hospitals with experience in VATS. As such, recent studies have shown that lobectomy by VATS in cases of bronchogenic carcinoma with prior chemotherapy can be carried out safely and effectively without an increase in the rate of complications (19). And although endobronchial lesions were previously considered a contraindication for VATS, some authors do not consider this issue a contraindication at present (20). Furthermore, there are publications reporting on thoracoscopic sleeve resections (21).

Nevertheless, in addition to the general contraindications, such as recent myocardial infarction and severe coagulopathy, there remain a few absolute contraindications that are specifically applicable to VATS major resections. Apart from the inability to tolerate single lung ventilation, which is relatively uncommon, absolute contraindications to thoracoscopic lobectomy include the inability to achieve complete resection with lobectomy, lobectomy, T4 tumors, and N3 disease (22). Absolute tumor size criteria that would preclude VATS resections have not been defined, though large specimens (tumors greater than 6 cm in diameter) may not be amenable to removal without rib spreading; this tends to negate the benefit of minimal access surgery. Despite these previously cited absolute contraindications, the ideal patient for thoracoscopic lobectomy, particularly early in a surgeon's experience performing the operation, is one with a peripheral T1 or T2 lesion without nodal disease.

It remains controversial as to whether VATS lobectomy is justified for lung cancer patients with lymph node metastasis (23). It was generally considered that patients with lymph node metastasis were not suitable candidates for VATS lobectomy (8,24). Additionally, it has been suggested that if a suspicious looking mediastinal lymph node is detected, it should be biopsied and a frozen section examination performed; confirmation of N2 disease mandates conversion to open surgery for complete mediastinal lymphadenectomy or induction chemotherapy depending on the exact circumstances (25). These guidelines have stemmed from a concern over incomplete lymph node dissection during VATS lobectomy. However, Watanabe *et al*. reported that the outcomes of VATS lobectomy were comparable to those of thoracotomy in clinical N0 but postoperative pathological N2 patients (26). Additionally, previous studies have compared the efficacy of a lymph node dissection of a VATS lobectomy with standard thoracotomy and have demonstrated that the results are similar (23,27,28). Nevertheless, it remains that in some institutions, preoperative or intraoperative lymph node metastasis is a contraindication for a VATS lobectomy and mandates conversion if discovered intraoperatively (29).

True pleural symphysis that leads to abandonment of the VATS approach is uncommon in our experience, but it may represent a contraindication for surgeons without extensive experience. Once a space is created when the correct plane in the pleural space is entered, endoscopic adhesiolysis can proceed quickly and safely using a combination of sharp and blunt dissection under videoscopic vision. VATS has the advantage over conventional thoracotomy in visualizing, with high resolution for details, the apex and base of the hemithorax.

Relative contraindications include tumors that are visible at bronchoscopy and the presence of hilar lymphadenopathy that would complicate vascular dissection (benign or malignant). Tumors visible in the bronchus by bronchoscopy within 2 cm of the origin of the lobe to be resected and where a possible sleeve resection might be needed are likely not amenable to a VATS approach. Calcified hilar adenopathy, such as with histoplasmosis, can likewise complicate vascular dissection (30).

The use of prior thoracic irradiation and induction therapy have previously been considered relative contraindications, but thoracoscopic lobectomy has been shown to be both safe and effective for patients who received induction therapy for non-small cell lung cancer (NSCLC) (19,31). Prior thoracic surgery, incomplete or absent fissures, and benign mediastinal adenopathy should not be considered contraindications. Redo-VATS surgery has been reported, and prior surgery is no longer considered an absolute contraindication to VATS resection (32). Though fused fissures present a technical challenge to VATS lobectomy, with experience and proper operative planning, successful lobectomy can be accomplished—the fused fissure should be divided last following the pulmonary vasculature and the bronchus. Finally, though chest wall involvement requires thoracotomy for resection, VATS can be used to perform the lung portion of the surgery and allow placement of the incision better situated for the area of the chest wall to be removed.

It is important to note that with improving surgeon experience and comfort with VATS lobectomy, just as several indications have been modified and expanded, the number of contraindications has been reduced. However, there remains some institutional variability in contraindications for this same reason. In a high-volume tertiary care institution experienced in the technique of VATS lobectomy such as our own, contraindications evolved to include a narrow patient population. Other institutions cite chest wall invasion, tumor infiltration beyond the fissure, invasion of the pericardium or diaphragm, centrally placed tumors in the hilum and adherent to vessels, as well as induction radiotherapy or chemotherapy as contraindications (11,33). Nevertheless, we do not consider these absolute contraindications. Additionally, evidence from our institution has shown VATS lobectomy to be safe and technically viable in patients receiving induction chemotherapy (19,31). As such, these additional institutional contraindications likely represent surgeon comfort and experience with VATS techniques rather than those deemed necessary for patient safety, anatomical reasons, and complete oncological resection.

Conversion to open thoracotomy

Conversion rates for thoracoscopic lobectomy to open thoracotomy have been reported to range from 2% to as high as 23%, with these higher rates stemming from patients with more advanced NSCLC (34-40). Krasna *et al*. reported an 8% conversion rate in 321 patients undergoing VATS procedures for various indications (41). Most commonly the conversion to thoracotomy was deemed necessary because of oncological reasons, such as centrally located tumors requiring vascular control or sleeve resection, or unexpected T3-T4 tumors that infiltrate to the chest wall, diaphragm, or superior vena cava. These authors concluded that abnormal hilar nodes with granulomatous or metastatic disease adherent to the superior pulmonary vein may be better evaluated and more safely resected with thoracotomy. However, about 30% of thoracotomy conversions in this series were for non-oncological reasons, such as pleural adhesions (41). In the series of the Memorial Sloan-Kettering Cancer Center Thoracic Service, conversion to open thoracotomy because VATS was not "technically adequate" occurred in 44/410 patients (11%) (42). In a recent institutional study, our conversion rate was 4% (36/916) when patients had an attempted VATS lobectomy for lung cancer, with patients with clinically node-positive disease (N1-N3) having statistically significantly higher conversion rates than clinical N0 patients (43).

Overall, causes of conversion can generally be classified into four categories: intraoperative complications (e.g., bleeding from vascular injury, usually to branches of the pulmonary artery and occasionally injury to the pulmonary vein; bronchus injury by the endotracheal tube), technical problems (e.g., equipment or stapler malfunction, failure to progress, poor visualization), anatomical problems (e.g., absent or thick fissure, calcified peri-arterial lymph nodes, diffuse pleural adhesions, chest wall invasion, tumor size precluding removal through the utility incision, need for sleeve resection), and oncological conditions (e.g., intraoperative discovery of N2 tumors, invasion of the artery, invasion of the parietal pleura, positive margins that need to be extended). However, the ability to predict which patients are more likely to require conversion to thoracotomy has not been thoroughly addressed to date. Given that studies have demonstrated that emergent conversion to open thoracotomy has been found to be significantly correlated with VATS-associated complications during the first 30 postoperative days (44), the ability to anticipate patients that may be high-risk for conversion may prevent this unexpected eventuality and its associated morbidity.

One of the most dreaded complications for surgeons is massive bleeding from pulmonary vessels. Dense adhesive disease often increases the risk of vascular injury, necessitating conversion to an open procedure. It is important to note that even in such cases, dissection of vessels can generally be difficult, and risk of vessel injury and bleeding can be high even by thoracotomy. Both Craig *et al.* and Yim *et al.* have reported mechanical failure of the staplers that resulted in massive bleeding (45,46). In these cases, bleeding was controlled by pressing on the bleeder with a sponge stick and conversion to thoracotomy. It should be pointed out that these are anecdotal cases, and the mechanical staplers available now are generally very reliable, and while stapler malfunction may occur, it is relatively rare. Certain avoidable conditions have been incorrectly associated with the stapler. For example, the use of metal clips in the hilar dissection is discouraged, as the stapler will not function if a clip is included in the stapler's jaw. Additionally, attention to the amount of tension when retracting during the stapling of pulmonary artery branches is essential. If excess retraction is applied during the stapling process, the arterial branch may tear before the completion of the stapling when the linear strength of the artery is reduced with the initiation of this process. Additionally, several technical developments have avoided the bleeding problems and consequent conversion to thoracotomy that are pitfalls of VATS techniques (46). These include us of visceral pleura to buttress staple lines, routine use of vertically apposed staplers, and expertise in extracorporeal and intracorporeal knot tying with fine suture.

Nevertheless, these results highlight the fact that even in the event of significant bleeding from a major pulmonary vein or artery branch injury that cannot be repaired thoracoscopically, the source of bleeding can usually be identified and controlled with a thoracoscopic instrument to allow controlled and stable conversion to thoracotomy. However, these injuries are usually managed successfully without conversion by the experienced thoracoscopic surgeon. With advanced skill and experience in endoscopic suturing, in the event of minor to moderate bleeding from the pulmonary vasculature, conversion can often be avoided.

Video equipment malfunctions are unique to VATS compared with open thoracotomy. The surgeon must be prepared when video equipment failures occur to prevent complications from taking place as a result. The operating room team must have someone familiar with the set-up of the camera, light source, and monitors present at all times as well as the ability to obtain back-up equipment or contact an expert in the event of equipment failure. Additionally, the surgeon and the entire operative team must always be prepared with the instruments needed to convert to thoracotomy in the event of patient instability or nonrecoverable video equipment problems.

An additionally described cause of conversion to open lobectomy is particular to areas in which histoplasmosis is endemic, specifically states bordering the Ohio River valley and the lower Mississippi River, making the hilar dissection challenging (30). In a recent study by Samson *et al.*, patients with evidence of calcifications specifically involving the hilum of resection had a 37% risk of conversion, and those with evidence of calcifications along the bronchial tree, but not along the hilum of resection had an intermediate rate of conversion at 25% (47). In fact, calcification score was the only predictor of conversion to open thoracotomy in multivariable modeling including lobe resection, race, gender, reoperation status, age, body mass index, tumor size, baseline PFTs, and time since first VATS lobectomy case to factor in the possible learning curve effect. In another study examining unplanned conversion for VATS lobectomy by Park and colleagues, 41% of conversions were due to hilar nodal anthracofibrosis and hilar adhesions, and were associated with increased operative time and length of stay (48). When the authors retrospectively reviewed the CT scans, hilar calcifications were seen in 71% of these patients. In these cases, careful review of the preoperative chest CT scan is essential, focusing on calcifications in the hilum, especially at the origin of the lobar bronchus that is to be divided. To date, however, there are few studies evaluating the role of imaging studies in selecting the surgical approach for lobectomy, and those that do are limited to the size and location of the tumor. Mason and colleagues evaluated the role of imaging studies in predicting complications associated with VATS and demonstrated that pleural thickening and calcifications on CT or chest X-ray predicted difficulties (49). However, this study included all VATS procedures with only a small number of lobectomies.

Samson and colleagues additionally demonstrated, not surprisingly, that when compared with completed VATS, converted VATS operations were significantly more likely to result in postoperative atrial fibrillation, increased length of stay, increased duration of chest tube drainage, longer surgery time, and increase in estimated blood loss (47). Interestingly, on comparison of converted VATS to planned open thoracotomy, VATS conversion was only an independent predictor of longer length of stay, and combined mortality and morbidity were similar. In fact, several studies have examined the implications of unplanned conversion from VATS to thoracotomy. One study evaluated the outcomes in 26 patients who underwent a converted VATS procedure and compared them with the outcomes of 52 patients who underwent a planned thoracotomy. There were no significant differences between the groups in perioperative (30-day) or long-term outcomes (50). Sawada and colleagues found that VATS conversion was associated with increased blood loss, perioperative complications, and length of surgery compared with completed VATS, similar to the recent data of Samson and colleagues (47,51). Nevertheless, these authors concluded that patients with evidence of calcifications involving the hilum of resection can undergo attempted VATS lobectomy, but perhaps this should not be attempted during the learning curve or by surgeons who are not as experienced with open pulmonary resection in these patients.

The number of patients undergoing VATS lobectomy as opposed to an open procedure has significantly increased over recent years but conversion rates have fallen (52). The anticipated learning curve for an advanced minimally invasive procedure can be clearly tracked. Cause of conversion initially was for a variety of reasons, but with experience and as confidence levels increased, reason for conversion for anatomical reasons has also increased, possibly reflecting bolder patient selection or discomfort with a perceived anatomical problem, such as chest wall adhesions. In addition, there are oncological reasons a decision to convert may be taken, with tumor size and location and extranodal invasion by a metastatic node being obvious markers. However, apart from the latter case, the decision of conversion depends solely on the surgeon's preference. Several reports have supported the use of VATS for complete lymph node dissection and showed no significant differences in survival or recurrence between VATS and thoracotomy (8,53-55). Thus, in cases of gross lymph node metastasis, the decision to convert must be carefully weighed.

But as programs developed, despite increasing numbers of VATS resections, conversions for anatomical reasons have tended to fall as have conversions for vascular injury (53). This is explained by the experience gained in vascular dissection and in the management of the fissure, particularly in complex cases, post-chemotherapy patients and even reoperations. The nature of the conversion and whether conversion is controlled is important both for the obvious safety aspects of the patient but also for how smoothly the minimally invasive approach is perceived amongst colleagues as well as the confidence of the surgeons performing the VATS lobectomy.

Generally, high conversion rates have declined as surgeons became more familiar with advanced thoracoscopic lobectomy, an operation with a challenging learning curve. This trend has been demonstrated previously, with a decreasing proportion of conversions as an increasing number of thoracoscopic lobectomies were performed for advanced-stage disease (35). And although conversion to thoracotomy should always be considered as a tool available to manage any unexpected situation, conversion rates have been shown to be as low as 1.6% to 2.5% in large series by experienced thoracoscopic surgeons (35,56). Further, though it is clear that the accumulation of experience has improved the surgical team's skill, allowing them to avoid and/or manage problems, resulting in a reduced conversion rate, these results also suggest that there remains a patient population in which VATS lobectomy is difficult to perform. It is generally accepted that dense hilar lymphadenopathy, pleural symphysis and fused fissure make VATS lobectomy difficult, and increase the likelihood of conversion to an open procedure. Specifically, persistent air leak beyond seven days was the most common morbidity seen in earlier experience and almost certainly related to hilar dissection when the fissures were incomplete (57).

Ultimately, the decision for conversion is left to each surgeon's skills and patience. It is difficult to establish any guideline for the conversion; however, our approximate timing of the decision for conversion is as follows: in cases with bleeding, as previously described, a sponge stick is first applied in order to tamponade the bleeding. Once the bleeding is controlled, a decision about whether or not the repair can be performed under VATS is made. When the bleeding cannot be controlled or repair seems to be difficult under VATS, conversion to thoracotomy is considered. In cases with a fused fissure or dense hilar lymphadenopathy, if the pulmonary artery cannot be isolated, conversion is considered.

Finally, although it may ultimately be difficult to predict who will require conversion from VATS to open surgery, there are a few important considerations regarding this matter. First, one of the advantages of VATS lobectomy is the magnified visualization it affords, which is useful for dissecting vessels or identifying small bleeders and makes this technique useful even in cases where conversion to an open procedure may be considered likely preoperatively. Secondly, after the surgeon's learning curve with advanced VATS techniques is surpassed and the conversion rate presumable reaches its nadir, attempts at decreasing conversion rates may only serve to delay the timing of conversion and increase the risks. The first objective of the operation is to perform a safe and complete resection. Once problems arise, repair takes a longer time, and the risks are increased. It is important not only to plan safe maneuvers to avoid problems, but also to have the courage to convert if there is any sense of discomfort experienced by the surgeon with VATS. Finally, long-term outcome is an important parameter to evaluate the safety and feasibility of converted VATs lobectomy. Jones *et al.* reported that the long-term outcome of converted VATS lobectomy for lung cancer was equivalent to that of successful VATS lobectomy (50). Therefore, it is reasonable to conclude that VATSs lobectomy is feasible for lung cancer surgery even from the viewpoint of the safety rate of converted VATS.

Conclusions

VATS was introduced nearly 20 years ago. Since then, VATS has experienced major advances in both equipment and technique, especially for the treatment of benign lung disease (58). With the accumulation of experience for the treatment of benign diseases, VATS has gradually begun to be employed for radical resection of lung cancer (3,4). VATS lobectomy is now considered standard in thoracic surgery, with acceptable safety and efficacy for both lung cancer and benign lung diseases (59,60). Several investigators have reported that the outcomes of VATS lobectomy for lung cancer are comparable to those of thoracotomy (35,38,61,62). While no large, controlled studies have been conducted to compare VATS with thoracotomy, it is now generally accepted that the outcomes of VATS are not inferior to those of thoracotomy. However, another concern is the safety of VATS lobectomy. Subsequent to VATS lobectomy, perioperative complications and mortality have been reported to occur at rates of approximately 5-32% and 0-7%, respectively; these rates are also generally accepted to be comparable to those reported for thoracotomy (35,38,63,64).

However, VATS lobectomy sometimes requires, for a variety of reasons, emergency conversion to thoracotomy. There are difficulties with the procedure, including a narrow view angle, complicating conditions such as pleural adhesions and dense hilar lymphadenopathy, oncologic problems if the disease is lung cancer, and the surgeon's discomfort with VATS instruments. As such, even though the technical safety of VATS lobectomy is widely accepted, there remains a range of situations that can result in unplanned conversion to open thoracotomy during the procedure, especially during a surgeon's training period (30).

The most important concern with unplanned conversions is the possible increased risk of mortality, morbidity, and cancer recurrence. Patients who undergo unplanned conversion to open thoracotomy most likely experience a longer operating time, extra lung manipulation, increased risk of injury to adjacent tissue, and increased blood loss, which may all adversely affect the outcome. And although the safety and efficacy of successful VATS lobectomy has been documented by many authors, there are fewer data regarding failed VATS lobectomy. The few studies regarding this problem report no significant increase in mortality or morbidity (50,51). Apart from vascular and bronchial injuries, which result from technical problems, the other causes of conversion may be predictable preoperatively. For example, in light of clear hilar calcifications on preoperative CT, conversions due to anthracofibrosis may be able to be anticipated. Certain vascular anomalies resulting in conversion are often visible on preoperative enhanced CT. Finally, preoperative PET scans can show a high probability of lymphatic metastasis in cases converted because of gross metastasis of these lymph nodes. Although unexpected conversion to thoracotomy during VATS does not appear to compromise prognosis, the decision to convert must be made promptly to reduce the operating time, blood loss, and possible complications. Accordingly, when attempting a VATS procedure, access ports must be placed to facilitate immediate conversion to open thoracotomy and to support instrument manipulation and anatomic accessibility of the stapler to close vessels and the bronchus. And in the context of narrowing contraindications for VATS lobectomy and surgeons overcoming the learning curve associated with increasingly complex resections, conversion should not be regarded as a surgical failure but rather as a way to safely complete resections in a traditional manner.

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A meta-analysis of unmatched and matched patients comparing video-assisted thoracoscopic lobectomy and conventional open lobectomy

Christopher Cao[1,2,3], Con Manganas[3], Su C. Ang[3], Tristan D. Yan[1,2]

[1]The Systematic Review Unit, The Collaborative Research (CORE) Group, Sydney, Australia; [2]The Baird Institute for Applied Heart and Lung Surgical Research, Sydney, NSW, Australia; [3]Department of Cardiothoracic Surgery, St. George Hospital, Sydney, NSW, Australia

Correspondence to: Christopher Cao. The Systematic Review Unit, The Collaborative Research (CORE) Group, Sydney, Australia. Tel: +61291131111; Fax: +61291133393. Email: drchriscao@gmail.com; Tristan D. Yan, The Systematic Review Unit, The Collaborative Research (CORE) Group, Sydney, Australia. Email: tristanyan@annalscts.com.

Background: Video-assisted thoracic surgery (VATS) for patients with early-stage non-small cell lung cancer (NSCLC) has been established as a safe and feasible alternative to open thoracotomy. This meta-analysis aims to assess the potential difference between unmatched and propensity score-matched cohorts who underwent VATS versus open thoracotomy in the current literature.

Methods: Three relevant studies with unmatched and propensity score-matched patients were identified from six electronic databases to examine perioperative outcomes after VATS lobectomy versus open thoracotomy for patients with early-stage NSCLC. Endpoints included perioperative mortality and morbidity, individual postoperative complications and duration of hospitalization.

Results: Results indicate that perioperative mortality was significantly lower for VATS compared to open thoracotomy in unmatched patients but no significant difference was detected amongst propensity score-matched patients. Similarly, the incidences of prolonged air leak and sepsis were significantly lower for VATS in the unmatched cohort, but not identified in the propensity score-matched cohort. In both the unmatched and matched groups, patients who underwent VATS were found to have a significantly lower overall perioperative morbidity rate, incidences of pneumonia and atrial arrhythmias, and a shorter duration of hospitalization in comparison to patients who underwent open thoracotomy.

Conclusions: The present meta-analysis indicates that VATS lobectomy has superior perioperative outcomes compared to open thoracotomy in both matched and unmatched cohorts. However, the extent of the superiority may have been overestimated in the unmatched patients when compared to propensity score-matched patients. Due to the limited number of studies with available data included in the present meta-analysis, these results are only of observational interest and should be interpreted with caution.

Keywords: Video-assisted thoracic surgery; thoracotomy; non-small cell lung cancer; propensity score analysis; meta-analysis

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Introduction

Similar to the introduction of laparoscopic appendicectomy in the 1980s, video-assisted thoracic surgery (VATS) for patients with non-small cell lung cancer (NSCLC) was pioneered in the early 1990s with great anticipation and enthusiasm. The benefits of this minimally invasive surgical technique has since shown encouraging perioperative outcomes in the form of reduced incidences of pneumonia (1), cardiac arrhythmias (2) and pain (3) compared to open thoracotomy. A recent meta-analysis suggests improved outcomes for VATS in terms of systemic recurrence and

5-year overall survival when compared to open thoracotomy for selected patients with early stage NSCLC (4).

Despite the multitude of reported superior short- and long-term outcomes in retrospective observational studies, the acceptance of VATS within the thoracic community has been slow. Currently, only a small fraction of pulmonary resections are performed by VATS globally. There is a paucity of robust clinical data in the form of large randomized controlled trials to compare VATS to open thoracotomy, and publication bias in the vast majority of retrospective studies in the existing literature cannot be excluded. Critics of VATS argue that the non-randomized patient selection process in retrospective studies may provide a 'false positive' finding of superior outcomes for VATS when more favorable patients are selected for this novel technique. Indeed, no randomized controlled trial has ever been completed to compare conventional VATS according to the current accepted Cancer and Leukemia Group B (CALGB) definition with open thoracotomy (5-7). To assess the potential patient selection bias for VATS in the current literature, we compared perioperative outcomes in unmatched patients with propensity score-matched patients to identify any significant differences between these two study cohorts.

Methods

Literature search strategy

Electronic searches were performed using PubMed, Ovid Medline, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ACP Journal Club, and Database of Abstracts of Review of Effectiveness from their date of inception to April 2012. We combined the terms "video-assisted thoracic surgery" or "VATS" or "thoracoscopic surgery" with "propensity*" or "propensity score" or "propensity match" as key words or MeSH terms. The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies. Eligible comparative studies for the present meta-analysis included those in which perioperative data were available for unmatched and propensity score-matched patients with NSCLC who underwent VATS or open thoracotomy.

All data were extracted from article texts, tables and figures. Two investigators (C.C. and S.A.) independently reviewed each retrieved article. Discrepancies between the two reviewers were resolved by discussion and consensus. The final results were reviewed by the senior investigators (C.M. and T.D.Y.).

Statistical analysis

The propensity score is the conditional probability of assignment to a particular treatment given a vector of observed covariates (8). This statistical method aims to minimize bias in retrospective observational studies by matching the individual's measured covariates between two treatment groups, so that differences in the measured outcome can be more directly attributed to the treatment rather than the individual's observed covariates (9). Propensity score matching is considered to significantly strengthen observational studies (8-10). Studies included in the present meta-analysis provided comparative data on perioperative outcomes for unmatched and propensity score-matched patients who underwent VATS or open thoracotomy. Meta-analysis was performed by combining the results of reported incidences of postoperative mortality, postoperative morbidity, individual postoperative complications and duration of hospitalization for unmatched patients. The same process was then performed for the propensity score-matched patients.

The relative risk (RR) was used as a summary statistic. In the present study, the random effect models were tested, where it was assumed that there were variations between studies and the calculated ratios thus had a more conservative value (11). X^2 tests were used to study heterogeneity between trials. I^2 statistic was used to estimate the percentage of total variation across studies, due to heterogeneity rather than chance. I^2 can be calculated as: $I^2=100\%\times(Q-df)/Q$, with Q defined as Cochrane's heterogeneity statistics and df defined as degree of freedom (12). In the present meta-analysis, the results using the random-effects model were presented to take into account the possible clinical diversity and methodological variation amongst studies. All P values were 2-sided. All statistical analysis was conducted with Review Manager Version 5.1.2 (Cochrane Collaboration, Software Update, Oxford, United Kingdom).

Results

Quantity and quality of trials

Nineteen potentially relevant references were identified through the six electronic database searches. After exclusion of duplicate or irrelevant references, 7 potentially relevant articles were retrieved for more detailed evaluation (13-19). After applying the selection criteria, three comparative studies remained for assessment (13-15). Manual search of the reference lists did not identify any additional relevant studies. All 3 studies included for final analysis in the present meta-analysis were from retrospective observational studies. In these 3 studies, 7,730 unmatched patients with NSCLC were compared, including 5,636 patients who underwent open thoracotomy and 2,094 patients who underwent VATS. After propensity score-matching, these same 3 studies reported perioperative outcomes on 1,681 patients who underwent open thoracotomy with 1,681 patients who underwent VATS.

Assessment of perioperative mortality and morbidity

From the three selected studies, the overall perioperative mortality rate of unmatched patients was significantly lower in patients who underwent VATS compared to patients who underwent open thoracotomy (1.4% *vs*. 1.7%; RR, 0.54; 95% confidence interval [CI], 0.32-0.92; P=0.02; I^2=30%). In comparison, propensity score-matched patients from the same studies reported a statistically non-significant difference in mortality rate between the two treatment groups (1.4% *vs*. 1.9%; RR, 0.72; 95% CI, 0.42-1.23; P=0.23; I^2=0%). These results are summarized in *Figure 1*.

Overall perioperative morbidity rates were consistently reported to be significantly lower after VATS compared to open thoracotomy in both unmatched patients (26.7% *vs*. 36.1%; RR, 0.64; 95% CI, 0.52-0.79; P<0.0001; I^2=74%) and propensity score-matched patients (25.9% *vs*. 36.5%; RR, 0.65; 95% CI, 0.52-0.83; P=0.0004; I^2=65%). These results are summarized in *Figure 2*.

Assessment of postoperative complications

A number of postoperative complication rates were comparable between the three selected studies for both unmatched and propensity score-matched patients. These included prolonged air leak, pneumonia, pulmonary embolism, atrial arrhythmias, significant bleeding, empyema and sepsis. Patients who underwent VATS were found to have significantly lower incidences of pneumonia and atrial arrhythmias in both the unmatched and propensity score-matched cohorts.

In the unmatched cohort, patients who underwent VATS were reported to have a statistically significantly lower incidence of prolonged air leak (8.5% *vs*. 9.9%; RR, 0.68; 95% CI, 0.51-0.91; P=0.009; I^2=50%) and sepsis (0.5% *vs*. 1.0%; RR, 0.40; 95% CI, 0.21-0.77; P=0.006; I^2=0%) compared to patients who underwent thoracotomy. However, these outcomes were not statistically significant when propensity score-matched patients were compared in the same studies. These results are summarized in *Figures 3 and 4*, respectively.

Assessment of length of hospitalization

Comparable data for the duration of hospitalization was reported in two studies (13,15). VATS was found to be associated with a significantly shorter period of hospitalization for both unmatched patients (standardized mean difference –0.35; 95% CI –0.48- –0.21; P<0.00001; I^2=42%) and propensity score-matched patients (standardized mean difference -0.33; 95% CI –0.49- –0.17; P<0.0001; I^2=42%). These results are summarized in *Figure 5* and an overall summary of perioperative outcomes for unmatched and propensity score-matched patients who underwent VATS versus open thoracotomy is presented in *Table 1*.

Discussion

To date, the highest level of clinical evidence comparing VATS with open thoracotomy have been from retrospective observational studies. Two small randomized controlled trials compared patients with NSCLC who underwent VATS lobectomy versus open thoracotomy (6-7). However, it should be acknowledged that rib-spreading was performed in both reports and thus these studies no longer conform to the current definition of 'true' VATS lobectomies (5-7). The study conducted by Kirby *et al*. in 1995 randomized 61 patients with clinical stage I NSCLC to undergo VATS lobectomy or open thoracotomy (6). This study reported that VATS was associated with significantly fewer postoperative complications but not a significant decrease in blood loss, duration of chest tube drainage, length of hospital stay, or postoperative pain. A second study by Sugi and colleagues randomized 100 patients with clinical stage IA NSCLC to undergo VATS lobectomy or open lobectomy(7). This trial found no significant differences in recurrence or survival rates between the two treatment groups. It is important to note that patients randomized to the VATS arm in both studies were not analyzed according to an intention-to-treat approach, and patients intended for VATS but converted to open thoracotomy were included in

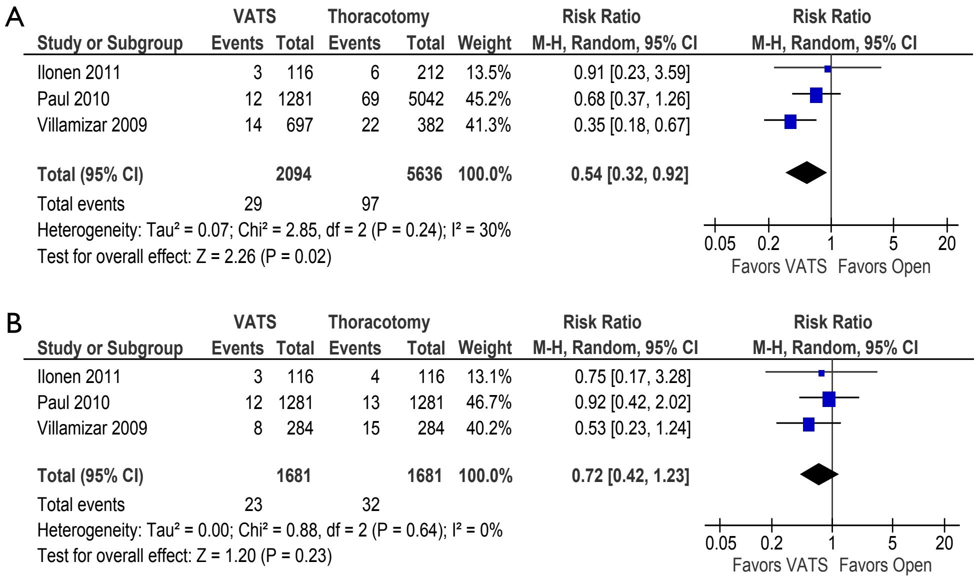

Figure 1 Forest plots of the relative risk (RR) of all-cause perioperative mortality after video-assisted thoracic surgery (VATS) versus open thoracotomy for patients with non-small cell lung cancer (NSCLC) in unmatched (A) and propensity score-matched (B) patients. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

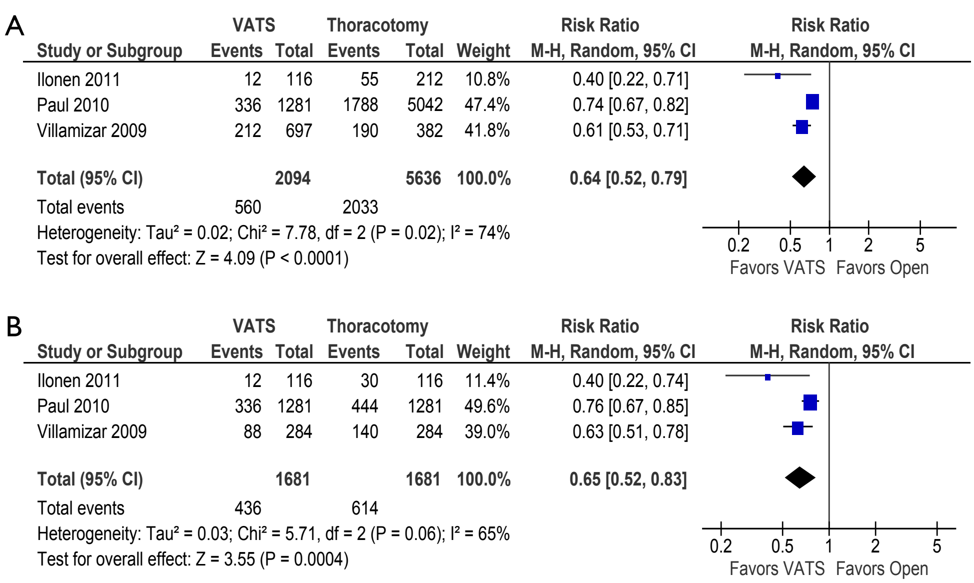

Figure 2 Forest plots of the relative risk (RR) of perioperative morbidity after video-assisted thoracic surgery (VATS) versus open thoracotomy for patients with non-small cell lung cancer (NSCLC) in unmatched (A) and propensity score-matched (B) patients. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

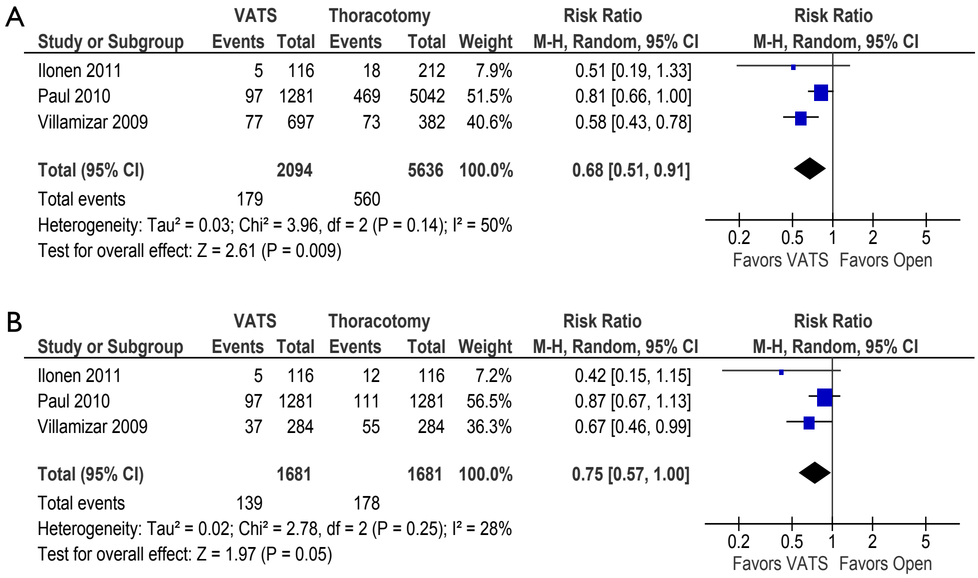

Figure 3 Forest plots of the relative risk (RR) of prolonged air leak after video-assisted thoracic surgery (VATS) versus open thoracotomy for patients with non-small cell lung cancer (NSCLC) in unmatched (A) and propensity score-matched (B) patients. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

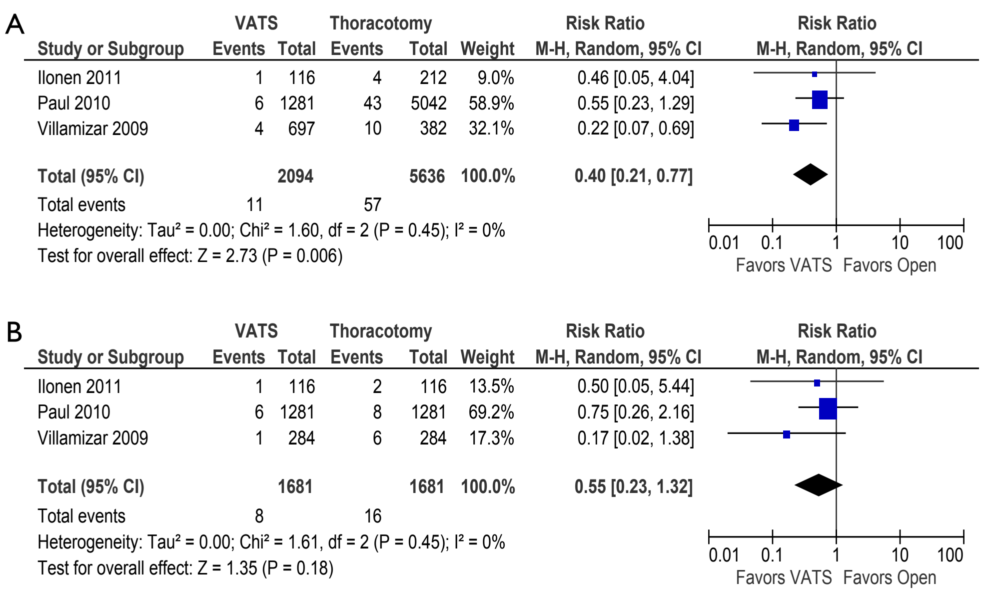

Figure 4 Forest plots of the relative risk (RR) of sepsis after video-assisted thoracic surgery (VATS) versus open thoracotomy for patients with non-small cell lung cancer (NSCLC) in unmatched (A) and propensity score-matched (B) patients. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

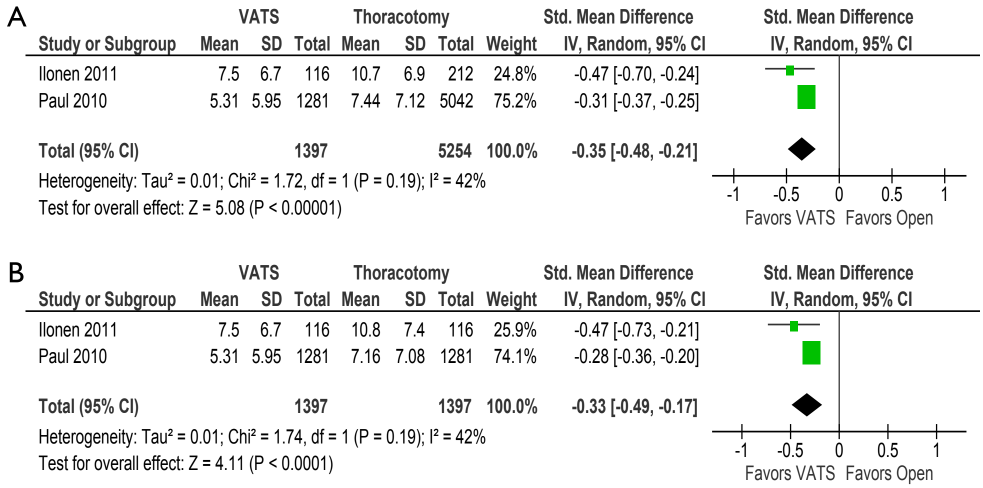

Figure 5 Forest plots of the standardized mean difference (SMD) of duration of hospitalization after video-assisted thoracic surgery (VATS) versus open thoracotomy for patients with non-small cell lung cancer (NSCLC) in unmatched (A) and propensity score-matched (B) patients. The estimate of the SMD of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). For each subgroup, the sum of the statistics, along with the summary SMD, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

Table 1 Summary of perioperative outcomes of unmatched and propensity score-matched patients who underwent video-assisted thoracic surgery (VATS) versus open thoracotomy for non-small cell lung cancer in three selected studies

Measured outcome	Unmatched patients		Matched patients	
	VATS n=2,094	Open n=5,636	VATS n=1,681	Open n=1,681
Perioperative mortality	VATS < Open		NS	
Perioperative morbidity	VATS < Open		VATS < Open	
Prolonged air leak	VATS < Open		NS	
Pneumonia	VATS < Open		VATS < Open	
Pulmonary embolism	NS		NS	
Atrial arrhythmias	VATS < Open		VATS < Open	
Bleeding	NS		NS	
Empyema	NS		NS	
Sepsis	VATS < Open		NS	
Length of stay	VATS < Open		VATS < Open	

'<' indicates statistically lower rate or duration according to meta-analysis; NS, not significant.

the open thoracotomy group or excluded altogether from statistical analysis (20).

In recent years, a number of retrospective studies have utilized propensity score-matching as a statistical tool to minimize patient selection bias between VATS and open thoracotomy treatment groups (13-19). Flores and colleagues compared 313 propensity score-matched patients who underwent VATS lobectomy or open thoracotomy, and reported a similar 5-year overall survival, but significantly fewer postoperative complications and a shorter duration of hospitalization for VATS patients when compared to open thoracotomy. Unfortunately, detailed data were not available to be included in the present meta-analysis. Scott *et al.* reported two studies which used propensity score to compare patients undergoing VATS versus open thoracotomy (18-19). However, individuals were categorized into propensity score groups rather than being case-matched according to a 1:1 ratio, with 'outlier' patients who underwent thoracotomy being excluded from analysis (18). Park *et al*. recently published a study that provided data on 136 propensity score-matched patients and found VATS to be associated with a significantly shorter duration of hospitalization (16). However, no data was presented for unmatched patients in their cohort so this study was also excluded from the present meta-analysis.

Within the current literature, three studies were found to provide data on perioperative outcomes for both unmatched and propensity score-matched patients who underwent VATS versus open thoracotomy. Results from the present meta-analysis indicate that unmatched patients from these studies were likely to report more significant benefits after VATS compared to open thoracotomy. Specifically, unmatched patients who underwent VATS were found to have superior overall perioperative mortality and morbidity rates, as well as lower incidences of prolonged air leak, pneumonia, atrial arrhythmias and sepsis. In addition, the duration of hospitalization was significantly shorter after VATS compared to open surgery. In comparison, patients who were matched according to propensity score analysis in the same 3 studies did not show statistically significant difference in overall postoperative mortality and incidences of prolonged air leak and sepsis. These results may suggest that unmatched patients in the three included retrospective observational studies have overestimated the potential perioperative benefits of VATS compared to open thoracotomy. However, it should be acknowledged that the propensity score-matching process invariably reduces the number of patients included in the data analysis, which may decrease the statistical power of the comparative studies. In addition, due to the small number of the studies included in the present analysis, these results can only be regarded as an interesting observation, and should be interpreted with care.

There is growing evidence to suggest that VATS lobectomy is a safe and feasible operation associated with improved perioperative outcomes compared to conventional open thoracotomy (4,13,20). VATS lobectomy may be superior to open lobectomy in terms of oncologic efficacy based on advantages seen in surgical outcomes after thoracoscopic resections, and the delivery of adjuvant chemotherapy (21). As a result of these findings, the VATS lobectomy technique has become an addition to the armamentarium of many modern thoracic surgeons. However, it is necessary to appreciate that there are currently no randomized controlled trials comparing 'true' VATS lobectomy as defined by the CALGB criteria versus the open technique (5). Due to a lack of clinical equipoise and widely reported benefits of the minimally invasive approach, we may have missed the opportunity to conduct such randomized controlled trials. Despite the large number of retrospective comparative studies over the past two decades, the favored surgical approach for early-stage NSCLC remains controversial. From a different perspective, attention should perhaps be directed at the patient selection process to identify the most appropriate patients who will gain the maximal benefit from a minimally invasive approach. More emphasis should also be placed on the use of standardized, objective and reproducible outcome measures to provide a more reliable estimate of how much benefit can be offered to patients undergoing VATS. This may consolidate the role of VATS in lung cancer management, and may raise the standards of outcome measurement in thoracic surgery as a whole.

The present meta-analysis indicates that VATS lobectomy has superior perioperative outcomes compared to open thoracotomy in both matched and unmatched cohorts. However, the extent of these reported superior outcomes may be overestimated in the unmatched patients when compared with propensity score-matched patients.

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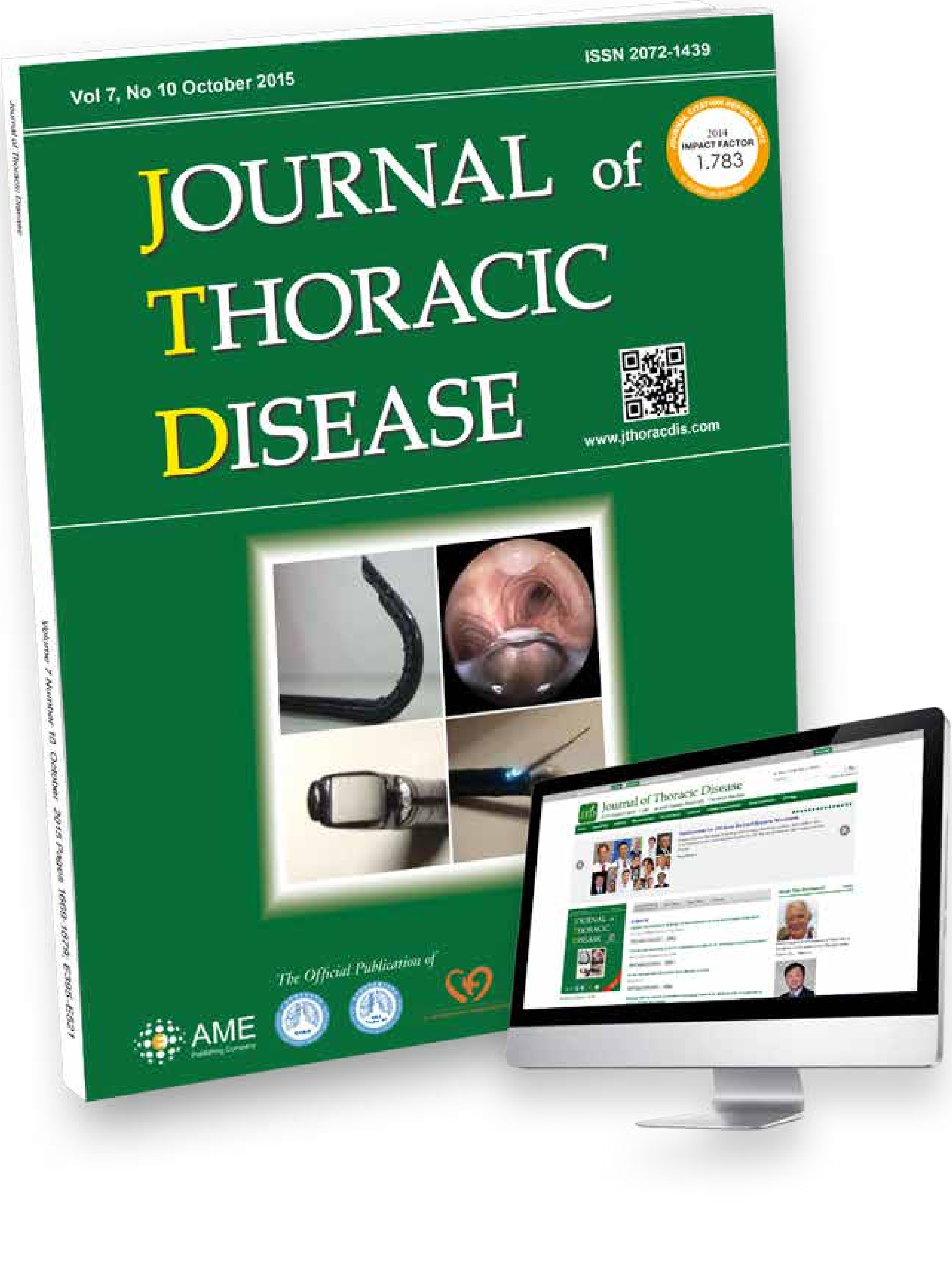
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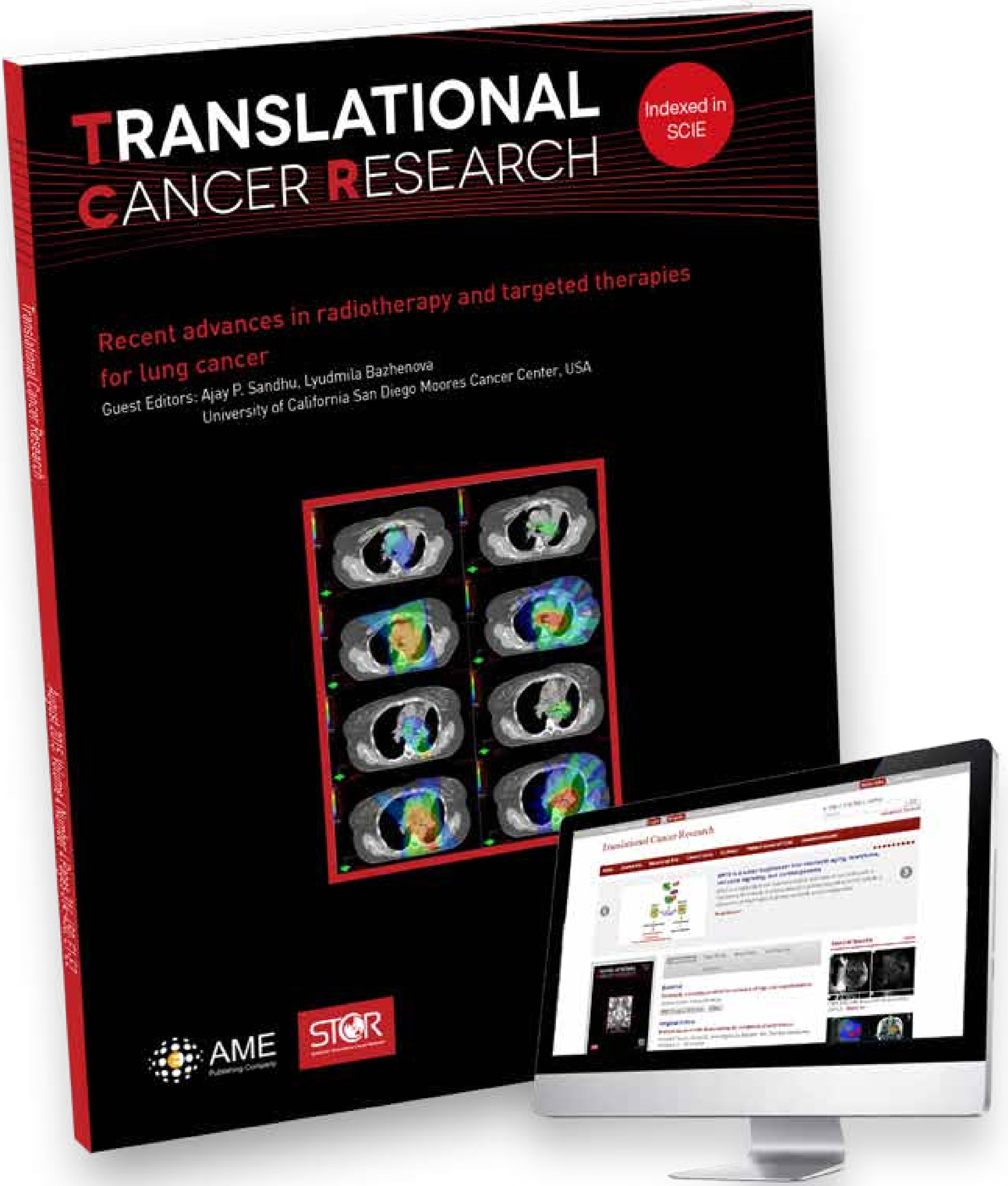

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