Review Article

Minimally invasive thoracic surgery: beyond surgical access

Max K. H. Wong, Alva K. Y. Sit, Timmy W. K. Au

Department of Cardiothoracic Surgery, Queen Mary Hospital, Hong Kong, China

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Correspondence to: Dr. Max K. H. Wong. Department of Cardiothoracic Surgery, Room 308, 3/F New Clinical Building, Queen Mary Hospital, 102 Pok Fu Lam Road, Hong Kong, China. Email: maxkhwong@gmail.com.

Abstract: Thoracic surgery has evolved throughout the decades. The difficulty of accessing the intrathoracic organs through the bony rib-cage has been a challenge for thoracic surgeons. In the past, large incisions stretching across the chest, such as posterolateral thoracotomies with rib spreading was the standard approach to access the lungs. These methods cause large amounts of trauma to the patient, with high rates of mortality and morbidity. However, with the advances in technology and the improvements in surgical technique, thoracic surgery has progressed to minimise trauma to the patient while still maintaining oncological and surgical principles. State-of-the-art technology, combined with wide variety of old and new surgical techniques give the thoracic surgeon a formidable armamentarium. Although there has been a focus on reducing the number and size of surgical wounds, considerations other than surgical approach can reduce the trauma suffered by the patient. Preservation of pulmonary function via organ preservation and anaesthetic techniques to further minimise the systemic inflammation such as non-intubated anaesthesia have also been shown to improve patient outcomes. This article aims to review the recent advances in minimally invasive thoracic surgery.

Keywords: Minimally invasive thoracoscopic surgery; single port video-assisted thoracic surgery (SPVATS); segmentectomy; non-intubated thoracoscopic surgery

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Introduction

The advancements in thoracic surgery have been rapidly evolving through the decades. The benefits of minimally invasive surgery (MIS) have become more and more apparent with the passing of time and the general acceptance of these techniques by surgeons and patients alike. One of the aims of MIS is to minimize the overall surgical trauma suffered by the patient. There has been much focus on the minimization of number and size of incisions as it is the most externally apparent. However, the scope of MIS also ranges from organ preservation by reduction of lung parenchyma resection, to the reduction in the systemic inflammation caused by general anaesthesia and intubation. Lung cancer behaviour has also evolved over time, with a shift from large central tumours to smaller nodules in incidental findings, and the increasing genetic components in tumour formation, thoracic surgeons must adapt to the new challenges these tumours represent. Newer bodies of evidence suggest that early stage non-small cell lung carcinoma (NSCLC) can be treated with new minimally invasive techniques with good oncological outcome. This article aims to summarize the recent advances in MIS via surgical approach, organ preservation and systemic inflammation.

Surgical approach

Due to the limitations of the bony ribcage, access to the lung and mediastinal structures traditionally relied on large posterolateral thoracotomy incisions and rib spreading. This results in large amounts of surgical trauma with associated morbidity. The damage that occurred anteriorly to the cartilaginous junction of the ribs, posteriorly to the costovertebral joint and associated rib fractures was also notoriously painful: the pain could last for years and even decades. Increasing interest to reduce the associated complications gave rise to the muscle sparing thoracotomy and its many variations, which were shown to reduce the postoperative pain and improve muscle strength as compared to standard posterolateral thoracotomy (1).

With the introduction of keyhole surgery in the 1980s, MIS was quickly adopted and adapted for surgery in the thoracic cavity (2). Progress has been swift, with the establishment of video-assisted thoracic surgery (VATS) as the standard procedure of choice in Asia. VATS has been proven to reduce postoperative wound pain, minimize intraoperative blood loss, shorter hospital stays, and improve postoperative quality of life compared to open thoracotomy (3-5,6). Some critics of VATS argue that due to the limitation of instrumentation through the small, fixed ports, the ability of the surgeon to perform extensive lymph node dissection is sacrificed in VATS. Although there is a lack of large randomized controlled trials comparing oncological outcomes in VATS to open thoracotomy, retrospective data has shown that locoregional recurrence, systemic recurrence and survival rate at 5 years are non-inferior when comparing VATS with open lobectomy for early stage NSCLC (5-8).

There are many different variations of port placement and incision number amongst different centres around the world. An example of a "conventional" VATS approach would be 3-port VATS, with a 10 mm port for camera placement, a posterior port for retraction, one larger utility port (usually less than 7 cm), and without the presence of rib spreading. However, despite the reduction in wound size, long term disability with chronic pain and paraesthesia is still seen in up to a third of patients after VATS surgery (9). Prevention of injury to the intercostal nerve during manipulation of instruments has been postulated to minimize the morbidity associated with surgery. With this in mind, surgical access to the thoracic cavity has progressed with the evolution of medical devices and equipment. The developments of fine instruments, 3 to 5 mm, have allowed needlescopic VATS procedures for procedures such as sympathectomy for hyperhidrosis (10) and pleurodesis for pneumothorax (11). The fine instruments with subsequently smaller incisions can further decrease the trauma associated with surgical wound, improve cosmesis and minimise postoperative pain compared to conventional 3-port VATS (12).

The development of single port VATS (SPVATS) at the turn of the century further exemplified the surgeon's drive for fewer incisions and to minimize the surgical trauma associated with surgical access. SPVATS for wedge resection was described by Dr. Rocco in 2004 (13) and more recently, has been shown to be applicable for major lung resection (14,15). The technique has been shown to be feasible and safe: Gonzalez-Rivas *et al.* reported a series of 102 patients who underwent single port VATS lobectomy with low rates of conversion to thoracotomy, low rates of complication and no mortalities (16). The benefits of SPVATS have been reproducible in multiple centres, with reports coming from different parts of Asia (17-19). Postoperative analgesic requirement and chronic pain are further reduced in SPVATS compared to conventional VATS (20). A meta-analysis on multiple retrospective Asian studies demonstrated statistically favourable outcomes (regarding perioperative mortality and morbidity, operative time, length of hospital stay, perioperative blood loss, duration of postoperative drainage and rates of conversion to open thoracotomy) for SPVATS lobectomy in the treatment of lung cancer compared to the conventional multiport approach (21). The authors noted however, that the benefits may be marginal in the clinical setting and further randomized control trials and long-term data are needed to prove the oncological benefits of SPVATS. Critics of SPVATS claimed that lymph node dissection may be inferior in SPVATS compared to conventional 3-ports VATS, due to the limitations of the fixed port placement. However, there are series of data showing that the number of lymph nodes sampled in SPVATS is similar or even higher (15,22). As the experience with SPVATS increases, more technically demanding operations such as segmentectomy (15), sleeve resections with bronchoplasty, arterioplasty and resection of complex mediastinal tumours can be performed (23). SPVATS is now a well-established surgical approach for the management of lung and mediastinal diseases.

Robotic technology has also progressed throughout the years; there has been case series on resection of mediastinal tumours and lung resection (24,25). Robot-assisted thoracoscopic surgery (RATS) usually requires three to four incisions as conventional VATS, with the added benefit of 3-dimensional vision and wristed instruments, allowing for 360-degree dexterity. This hypothetically increases the ability of the surgeon to operate on technically more complicated and demanding cases. The safety profile has been similar to conventional VATS with a Japanese series showing low complication rate and no conversion to open and no mortality (26). However, there are several barriers to entry to the general acceptance of RATS: the largest being availability of the Robotic system and its high maintenance costs. The lack of tactile feedback, limited training centres and easily available alternative approaches also discourage thoracic surgeons from RATS. SPVATS can be performed with the same instruments available in conventional VATS, without having to purchase additional expensive equipment and with fewer incisions. If the barriers to entry and costs of the Robotic systems decrease, RATS may have a more important role to play in the future.

The goal to avoid the intercostal bundle completely has given rise to alternate approaches to the thoracic cavity. The trans xiphoid approach for bilateral lung metastasectomy was initially described in 1999 using a 7 cm incision (27). Due to the large incision and the need for intercostal port access, the benefit of avoiding the intercostal bundle was negated. Recently, the subxiphoid approach has been refreshed and described by Taiwanese and Japanese surgeons for surgical resections of the lung and mediastinum (28,29). Using a 3 cm abdominal incision, Suda *et al.* has shown that the subxiphoid approach can access bilateral lung cavities to perform bilateral wedge resections, avoiding the intercostal bundle completely and minimizing postoperative neuralgia (30). The benefit of the subxiphoid approach has been promising with further reduction in postoperative pain, intraoperative blood loss when compared to conventional VATS in thymectomy (31). However, further studies are required to fully evaluate this approach in the future.

Organ preservation

The history of lung cancer surgery is a story of continuous adaptation and evolution: the first described radical resection of lung cancer was a left pneumonectomy performed by Dr. Evarts Graham in 1933 (32). At that time, lobectomies were performed usually for benign diseases as it was deemed unsuitable for lung cancer surgery. Interest began in more lung preserving approaches to avoid the high morbidity and mortality associated with pneumonectomy. After Cahan introduced the concept of “radical lobectomy” in the 1960s, comprising of lobectomy plus lymph node dissection (33), Jensik *et al.* described the concept of segmentectomy, suggesting that a lesser resection would be adequate for oncological clearance in early stage lung cancer (34). With the advancement in medical technology and increasing public awareness, there now is a trend to early detection, diagnosis and subsequently smaller tumours. The interest of sublobar resection for early stage lung cancer has been re-ignited. Lung parenchymal preservation is associated with reduced surgical trauma and improved perioperative morbidity and mortality, increased potential for second resection in subsequent primary tumours and improved postoperative lung function (35). Sublobar resection, in the form of segmentectomy or wedge resection, is another form of MIS by reducing internal organ injury.

In the 1980s, the Lung Cancer Study Group (LCSG) trial aimed to prove lesser resection would have similar disease-free survival and similar local recurrence. They conducted a randomized control trial, comparing open lobectomy to sublobar resection in patients with tumours less than 30 mm in size and without lymph node involvement (36). On the contrary to their aims, they found that compared with lobectomy, limited resection patients had higher local recurrence rate, lower 5-year survival rate and with minimal improvement in postoperative pulmonary function. Thus, lobectomy has been the standard treatment for early stage lung cancer since the 1990s. Critics of the paper noted that there was a high rate of non-anatomical wedge resections, large tumours up to 3 cm, and no regular CT surveillance as part of the study protocol. These factors may have negatively impacted survival in the sublobar resection group.

Subsequent studies have been performed in order to address the limitations of the LCSG trial: Okada *et al.* showed that tumour size larger than 20 mm is an independent and significant prognostic factor in a retrospective study of 1,272 patients, concluding that lobectomy should be performed in tumour size larger than 30 mm, segmentectomy is acceptable in tumours sized 20 mm or less without nodal involvement, and tumours sized 21–30 mm required further studies (37). These results were consistent with other studies evaluating tumour size as an independent predictor of survival and locoregional recurrence (38,39). A systematic review and meta-analysis comparing overall survival in segmentectomy *vs.* lobectomy showed that there was no statistical difference in survival for stage I NSCLC (40). However, the results must be interpreted with caution as 24 of the 27 studies analysed were retrospective in nature, some reviews involved analysis of summary data, staging was not differentiated between clinical or pathological and there was considerable heterogeneity amongst studies. Another systematic review had similar findings, establishing several favourable factors that improve survival in sublobar resection: small tumours less than 2 cm, pure ground glass opacity (GGO) appearance on CT, less invasive histology, peripheral ⅓ located tumour, adequate surgical margins of more than 2 cm, good cardiopulmonary status and presence of mediastinal lymph node dissection (35).

With the increasing use in CT scan as a diagnostic modality, more studies are being undertaken to determine if surgical outcomes can be predicted by CT findings. The postulation is that pure GGO seen on CT scans may be more suggestive of a less invasive disease such as adenocarcinoma *in situ*. The less invasive tumour histology is associated with 100% 5-year survival rate (41). A Chinese study showed that less invasive histological types (adenocarcinoma *in situ* and minimally invasive adenocarcinoma) seen on frozen section intraoperatively have a low risk of lymph node metastasis and sublobar resection would have adequate oncological clearance (42). Other studies suggest those with pure or mixed GGO lesions have better survival compared to solid nodules, even postulating mediastinal lymph node dissection may not be necessary (43,44). Sugi *et al.* highlighted the importance of favourable CT appearance with high GGO ratio more than 75% (higher likelihood of adenocarcinoma *in situ*), size of lesion less than 2 cm and adequate resection margins to achieve similar survival between wedge resection, segmentectomy and lobectomy in stage IA NSCLC in Japan (45). With cancer surgery, adequate surgical margin is required regardless of the procedure performed. Thus, anatomical segmentectomy is preferable over wedge resection as it is more likely to achieve at least 2 cm margins, decreasing the risk of local recurrence and improving disease-free survival (46,47).

Unfortunately, the majority of evidence available for analysis is retrospective and there is a lack of good quality data to support limited resection for early stage NSCLC. Two randomized prospective, multi-centre phase III trials are being conducted by the Cancer and Leukaemia Group B (CALGB 140503) and the Japan Clinical Oncology Group (JCOG 0802) comparing overall survival in NSCLC less than 2 cm without pure GGO/non-invasive cancer on CT scan. The results will provide guidance in the management of such tumours in the future.

Systemic inflammation

Another approach to MIS and reducing trauma suffered by the patient is to reduce systemic response induced by surgical stress. Traditionally, lung resection surgery has been performed under general anaesthesia with single lung ventilation. These techniques can occasionally cause complications and have adverse effects: ventilation induced lung injury, residual neuromuscular blockade and other complications of muscle relaxants, such as impaired cardiac function. The aforementioned complications can increase the pulmonary and systemic inflammatory response and subsequently impair outcomes and patient recovery. There are also considerable risks involved with isolation of the lung, with potential damage during placement of the bronchial blocker or double lumen tubes (48). To avoid these risks, the development of newer, less invasive techniques has become a subject of further interest.

In 2004, Pompeo first reported a case of non-intubated thoracoscopic surgery, spontaneous ventilation with thoracic epidural block in a case of VATS wedge resection (49). Subsequently, different techniques have been described. Pain control can be managed by combining local and regional anaesthesia with local wound infiltration, intercostal nerve block, serratus anterior plane block or paravertebral block (50). Continuous sedation and analgesia throughout the procedure via intravenous access can be administered to achieve adequate sedation while allowing spontaneous ventilation and avoiding patient hyperactivity. Non-intubated anaesthesia is also technically more challenging: there is a risk of hypercapnia and hypoventilation during the operation, which requires the anaesthetic team to be constantly alert to the possibility of conversion to intubated single lung ventilation while the patient is already in lateral position with surgical drapes. This can be done with fibre optic bronchoscope guidance and bronchial blocker. Communication between the surgical and anaesthetic teams is critical to success (51).

Patient selection for non-intubated thoracic surgery requires a holistic approach: the surgical team must bear in mind the appropriate anaesthetic considerations for the indicated disease. Relative contraindications to non-intubated thoracoscopic surgery include: difficult airway, obesity, hemodynamic instability, contraindication to regional anaesthesia, difficulty in cooperation/neurological disorders, hypoxaemia/hypercarbia and patients with high risk of regurgitation (51). There are also different variations in the anaesthesia between centres, tailored to the operation needs (52): surgical procedures can be performed under sedation or monitored anaesthesia care (MAC), epidural or paravertebral block for regional anaesthesia. Spontaneous ventilation can be assisted with high flow oxygen masks, nasopharyngeal tubes, oropharyngeal tubes, or laryngeal masks. Iatrogenic pneumothorax is created upon entry to the thoracic cavity. Major pulmonary resections can be performed under non-intubated anaesthesia with the aid of vagal block and/or phrenic block to reduce reactions to vagal stimulation during lung manipulation.

Initial experience with non-intubated thoracoscopic surgery performed for pneumothorax showed shorter hospital stay and quicker recovery time compared to general anaesthesia and single lung ventilation (53). Further randomised control trials comparing wedge resection under general anaesthesia with single lung ventilation *vs.* non-intubated anaesthesia with epidural block showed reduced morbidity, improvement in postoperative recovery, reduced pain, shorter in operating theatre time and overall hospital stay in the non-intubated group (54). Other procedures such as sympathectomy, mediastinal biopsies and thymectomy in myasthenia patients have been shown to be feasible and safe (55). There are also biochemical parameters that suggest non-intubated thoracoscopic surgery reduces systemic inflammatory response: postoperative TNF-alpha and hs-CRP are significantly lower in non-intubated anaesthesia *vs.* general anaesthesia in a randomized control trial conducted by Liu *et al.* (56).

Major anatomic lung resection brings about different potential risks during non-intubated thoracoscopic surgery. The potential consequences of injury caused by coughing during manipulation of the lung to the pulmonary vasculature or mediastinal lymph node dissection can be disastrous. High volume VATS centres with experience in non-intubated procedures are essential and there are only a few studies showing the benefit of non-intubated anaesthesia in major lung resection. A retrospective propensity score matching analysis of 339 patients undergoing lobectomy and segmentectomy was conducted, comparing non-intubated anaesthesia with spontaneous ventilation *vs.* intubated anaesthesia with single lung ventilation (57). The authors demonstrated statistically significant shorter postoperative fasting time, reduced chest drainage volume and shorter hospital stay in the non-intubated anaesthesia group, while showing no difference in intraoperative blood loss, surgical duration, postoperative complications or lymph nodes dissected. There was a high conversion rate of 7% to intubated single lung ventilation, in which the authors attributed to the learning curve. Further retrospective analysis of 285 patients described by Chen *et al.* (58) was conducted, using 3 port VATS, non-intubated spontaneous ventilation, epidural, vagal nerve block for lung resection (including lobectomy, wedge resection and segmentectomy). The analysis showed that there was a 4.9% conversion rate due to mediastinal movement, persistent hypoxemia, dense pleural adhesions, ineffective epidural anaesthesia, bleeding, and tachypnea, complication rate of 3.9% and no mortality. The authors concluded that non-intubated thoracoscopic lung resection is safe and feasible, acknowledging that it was a single centre review with possible selection bias. It was suggested that Asian patients with shorter body habitus, female, and shorter trachea may benefit from non-intubated spontaneous ventilation techniques due to the difficulty in intubation.

To further minimize the invasiveness of surgery, non-intubated techniques can be combined with SPVATS. Rocco *et al.* reported a case of SPVATS non-intubated wedge resection (59) and subsequently published a series of non-intubated SPVATS lobectomies (60). Experience with both SPVATS techniques and troubleshooting ability in non-intubated techniques is a prerequisite in order to fully utilize the minimally invasive techniques available. More complicated procedures such as bronchial sleeve resection (61) and carinal reconstruction surgery (62) have been reported with early success. Key considerations to success include a well-defined inclusion and exclusion criteria for patient selection, an experienced team with gradual progression from minor procedures to major lung resection, awareness of potential risks of hypoxia, coughing and bleeding as well as crisis training and defined conversion criteria (63). Although current studies show that non-intubated anaesthesia techniques can be safely performed, further studies are required to determine the long-term benefit as current data fails to show an overwhelming benefit over current practises. Non-intubated techniques have the potential to further reduce surgical trauma in minimally invasive thoracic surgery.

Conclusions

Increasing demand for less invasive techniques has given rise to the continuous evolution of minimally invasive thoracic surgery. While there is an assortment of techniques to cater to each individual patient, basic oncological principles should still remain a priority for lung cancer surgery and no minimally invasive approach should compromise patient survival in the search of reducing patient trauma. There has been a focus on the size and number of surgical wounds in recent years. However, there may be a limit to the benefits gained from continuously reducing incisional trauma. There are other approaches that may soon see breakthroughs, such as the randomised control trials in Japan and America studying the benefits of limited resection for early stage NSCLC. There is a growing body of evidence to support the trend of minimally invasive approaches, with reduction in wound size and number to SPVATS, organ preservation with limited lung resection and non-intubated techniques. These analyses open the road to further studies and advances.

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Footnote

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