Review Article

Non-intubated video-assisted thoracoscopic surgery anatomical resections: a new perspective for treatment of lung cancer

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Abstract: The lung isolation under general anaesthesia with double lumen tubes has become an indispensable part of video-assisted thoracoscopic surgery (VATS) for lung cancer. However, with an attempt to avoid the residual effects of muscle relaxants and the systemic complications due to tracheal intubation, anesthesia without tracheal intubation has also been applied in VATS surgeries for lung cancer. Currently, non-intubated anesthesia under spontaneous breathing has been widely applied in VATS, contributing to more stable anesthesia and lower rate of switching to intubated anesthesia. It can be applied in most VATS procedures including anatomical pulmonary lobectomy, anatomical segmentectomy, and radical resection for lung cancer. In the selected lung cancer patients, non-intubated anesthesia under spontaneous breathing makes the VATS procedures safer and more feasible. With an equal chance for surgery as the intubated anesthesia, this technique lowers the incidences of peri-operative complications and speeds up post-operative recovery. As a novel surgical option, the anatomic VATS under non-intubated anesthesia under spontaneous breathing have shown to be promising. Nevertheless, the long-term outcomes require further evaluation in more multi-center prospective clinical trials with larger sample sizes.

Keywords: Lung cancer; non-intubated anesthesia; spontaneous breathing; switching to intubated anesthesia; anatomical lobectomy; anatomical segmentectomy

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Authors' introduction:

Professor Jianxing He (*Figure 1*) is the Director and Professor of the Thoracic Surgery Department, First Affiliated Hospital of Guangzhou Medical University, Guangzhou Institute of Respiratory Diseases (GIRD), as well as the President of the First Affiliated Hospital of Guangzhou Medical University, China. He has the world-largest clinical experience in video-assisted thoracic surgery and non-intubation minimally invasive thoracic surgery. *Figure 2* is a photo of his surgical team. Dr. Jun Liu is a chief physician who specializes in minimal thoracic invasive surgery. His research interests presently focus on clinical

Figure 1 Professor Jianxing He.

Figure 2 Surgical team.

and experimental study on Non-intubated VATS under spontaneous breathing.

Introduction

While the past decades have witnessed the increase in incidence of non-small cell lung cancer (NSCLC), lobectomy plus systematic lymph node dissection remains the standard radical treatment for this aggressive disease The use of video-assisted thoracoscopic surgery (VATS) lobectomy for the treatment of lung cancer was first reported in 1992 (1). Since then, VATS has become increasingly sophisticated and widely applied, with its feasibility and safety in the radical treatment being widely recognized. VATS has been included in the US National Comprehensive Cancer Network (NCCN) Guidelines since its 2006 edition; in the 2014 edition, the Guidelines further emphasizes that "VATS or other minimally invasive resection of lung is strongly recommended in early NSCLC patients without anatomic or surgical contraindications, in case that such procedure does not violate the tumor treatment criteria and/or chest surgery principles". Therefore, VATS has become a mainstream technique for early NSCLC.

The current minimally invasive procedures such as VATS lobectomy and VATS segmentectomy have become quite sophisticated and can benefit most surgical patients. However, how to develop an "overall minimally invasive" surgery (including anesthetic micro-injury), beginning from the apparently minimally invasive incisions, has become a hot research topic in the field of minimally invasive thoracic surgery.

Anesthesia for VATS should not only ensure an adequate depth of anesthesia but also properly control the negative intrathoracic pressure and the lung expansion during the surgery. In 1940, Zavod proposed anesthesia with double-lumen endobronchial tube intubation, which not only ensures the intra-operative lung ventilation and good lung isolation but also provides a sufficiently large and quiet surgical field for the operators (2). However, the systemic complications due to the use of muscle relaxants and endotracheal intubation during anesthesia as well as various post-operative discomforts such as sore throat and cough due to intubation trauma bring pain to patients and delay the post-operative recovery (3,4). The non-intubated anesthesia, in contrast, can satisfactorily avoid these problems. In 2004, Pompeo first reported the successful application of non-intubated anesthesia (thoracic epidural block in their cases) under spontaneous breathing in VATS wedge resection of lung masses (5). The non-intubated anesthesia techniques have their unique advantages: (I) the spontaneous breathing can be maintained; (II) only simple intravenous drug use, local infiltration anesthesia, intercostal nerve block, or epidural block is needed for anesthesia and analgesia. The one-lung ventilation can meet the needs during VATS by using the artificial pneumothorax. Thus, this technique can avoid the shortcomings of the intubated anesthesia. Currently, non-intubated anesthesia under spontaneous breathing has been widely applied in VATS. It can be applied in most VATS procedures including lobectomy, segmentectomy, and radical resection for lung cancer. Some experienced surgeons can even perform

highly challenging surgeries (e.g., bronchoplasty) under spontaneous breathing (6-13). Furthermore, the intravenous anesthesia under spontaneous breathing can avoid the residual effects of muscle relaxants, lower the incidences of systemic complications, and thus achieve faster recovery of respiratory muscle function (11).

Advances in anesthetic techniques and intra-operative management

Anesthetic methods

The non-intubated anesthesia for VATS has developed from the single thoracic epidural anesthesia to more diversified combined anesthesia under spontaneous breathing in the past 10 years. Initially the non-intubated anesthesia was is only applied in some simple VATS procedures such as pleural biopsy, resection of pulmonary bullae, and removal of peripheral nodules but not in more complicated surgeries such as lobectomy. One of the reasons was is cough reflex; in fact, the pulling of the pulmonary hilum during the surgery may stimulate the vagus nerve and thus cause the swinging of the mediastinum and the uplifting of the diaphragm, which severely affect the surgical operations (14). Vischnevski had applied cervical vagus nerve block to reduce the cough reflex due to the traction of lung hilum (15). In 2011, Chen *et al*. reported that the blockage of thoracic vagus nerve with bupivacaine dramatically reduced cough reflex within a certain period of time. This technique provides a relatively quiet field for VATS, facilitates the dissociation/dissection of vessels and bronchus at the lung hilum, and thus makes the non-intubated anatomical lobectomy possible. This innovative technique payed the way for the advances in non-intubated VATS (6). In our center, the non-intubated anesthesia further develops into the tailored combination of various anesthetic modes including intravenous anesthesia, epidural anesthesia, local anesthesia, intercostal nerve block, intra-operative vagus nerve block, and pleural surface infiltration anesthesia, depending on the patients' specific conditions and the surgical procedures. Such a strategy can both ensure the intra-operative stability and facilitate post-operative recovery.

Tracheal intubation during surgery

An anesthesiologist must be able to timely and properly manage complicated situations (e.g., hypoxemia and hypercapnia) during non-intubated anesthesia. In addition, a qualified anesthesiologist must also be able to switch the anesthesia mode during the surgery and perform tracheal intubation when the patient is in a lateral position. If hypoxemia and hypercapnia occurs during the surgery and can not be resolved after non-invasive management, the single-lumen tube should be inserted under the guidance of fiber optic bronchoscope when the patient is in a lateral position, and a blocker can be used to achieve lung isolation. The rate of switching to intubated anesthesia is directly related with the surgical procedures and skills (15). For instance, it reached 10% in 30 patients who had received lobectomy but was only 4.9% in 285 patients who had undergone different surgical procedures (16). In one of our previous reports enrolling 174 patients undergoing VATS under non-intubated anesthesia, 7 patients (4%) were switched to intubated anesthesia. Among 156 patients undergoing radical treatment for lung cancer, 9 (5.8%) were switched to intubated anesthesia due to various reasons. This percentage was significantly higher than the overall rate (2.2%, 21/938) in our center (under review). Notably, the final case of the switching of anesthetic mode (No. 57, VATS radical treatment for lung cancer under intravenous combined anesthesia under spontaneous breathing) occurred on July 24, 2013; no such case has been recorded since then (till 2015). This may be explained by the following reasons: (I) the anesthesiologist have improved capabilities in dealing with various complicated conditions such as hypoxemia and hypercapnia during the surgeries; (II) with accumulated experiences, the operators are more self-confident and will not easily switch the anesthetic mode when facing problems such as extensive pleural adhesions, small tumors (<6 cm in diameter), and invasion of bronchus, which used to be the contraindications of VATS; (III) the surgical maneuvers are more reasonable. Pulling and traction are the main maneuvers, and tough actions such as lifting and compression are avoided; by doing so, the operation has less stimulation on the lung hilum and thus reduces the swinging of mediastinum; and (IV) the medical team is adapted to the surgical operation under spontaneous breathing, making the whole operation process much smoother.

Various VATS procedures under non-intubated anesthesia for lung cancer

Anatomical lobectomy

For patients with early NSCLC, lobectomy plus systematic

lymph node dissection remains the first-choice treatment for most surgeons. In the earlier years, when the VATS under non-intubated anesthesia was applied for treating lung cancer, if peripheral pulmonary nodules were confirmed by frozen pathology during the surgery, the surgeons often had to switched to intubated anesthesia for lobectomy due to technical limitations (5). Along with advances in non-intubated VATS, lobectomy plus systematic lymph node dissection under spontaneous breathing has become possible for selected patients (6,11). Comparison of the non-intubated and intubated VATS lobectomy in two centers showed that the intra-operative indicators (e.g., surgical duration and intra-operative hemorrhage) were not significantly different between these two groups and the incidences of some complications were significantly decreased in the non-intubated group, which demonstrated the safety and feasibility of this technique; meanwhile, the non-intubated group had significantly better results in terms of post-operative rehabilitation indicators including antibiotic use, post-operative feeding time, thoracic drainage volume, and post-operative hospital stay.

Anatomical segmentectomy

In recent years, many centers have reported the application of anatomical segmentectomy for treating early NSCLC. Compared with lobectomy, this technique had statistically similar prognosis (17-20) and maximized the post-operative lung protection (21,22). The role of segmentectomy for selected lung cancers have increasingly been recognized. These include: *in situ* or microinvasive adenocarcinoma; stage Ia invasive adenocarcinoma less than 2 cm in diameter; synchronous or metachronous multiple primary ground-glass opacity (GGO)/small nodules; NSCLC patients who cannot tolerate lobectomy (17,23,24). Since 2010, the NCCN Guidelines have has clearly stated that segmentectomy can be applied for NSCLC treatment in selected patients. In 2013, Hung *et al*. reported 13 patients with primary lung cancer underwent non-intubated segmentectomy, four patients because they could not tolerate lobectomy and the remaining nine patients because had early lung cancer sized <2 cm (25). In 2014, our center reported ten patients who had undergone non-intubated VATS segmentectomy for early lung adenocarcinoma (12). After the segmentectomy, the patients had smaller incidences of post-operative complications and shorter post-operative hospital stay, which enabled them to recover rapidly. When the tumor was radically removed, the post-operative quality of life was also improved.

Lymph node dissection

Meanwhile, we also evaluated the quality of lymph node dissection (including the number and stations of the dissected lymph nodes), another key indicator of the completeness of the VATS under spontaneous breathing for lung cancer. In 2011, Chen *et al*. performed radical treatment in 30 patients with lung cancer and found that the number of the dissected lymph nodes was (13.8±6.0) in non-intubated group and (14.0±6.0) in intubated group (P=0.915). In 2013, the same group enrolled 36 lung cancer patients aged 65 years or above and found that the number of the dissected lymph nodes was (13.1±7.7) in the non-intubated group and (15.5±8.1) in the intubated group (P=0.133) (26); in contrast, the number of sampled lymph nodes was (6.5±5.9) in patients who had undergone segmentectomy for lung cancer (25). In one of our studies (under review), the number of the dissected lymph nodes in patients who had undergone lobectomy was (17.1±9.0) in the non-intubated group and (16.5±9.4) in the intubated group, with no significant intergroup difference; Among patients who had received segmentectomy, the number of the dissected lymph nodes was (9.5±6.2) *vs*. (6.6±4.7), respectively in these two groups, and the number of the sampled lymph nodes was (3.5±1.0) *vs*. (2.7±3.5). Both comparisons were not significantly different. These findings demonstrated that intravenous combined anesthesia under spontaneous breathing did not negatively affect the completeness of lymph node dissection as compared to intubated anesthesia.

Other surgical procedures

In our center, we performed non-intubated right lower lobe sleeve resection for a male patient with lung cancer. The surgery lasted 165 minutes, with an intra-operative blood loss of about 120 mL. The patient began to eat 4 hours after the surgery, and the chest tube was withdrawn on the third post-operative day. He was discharged on the 6th post-operative day. The lesion was confirmed to be a squamous cell carcinoma by pathology. The bronchial stump was negative. Also, 18 lymph nodes from six stations were found to be negative (13). This was the first report on the application of the non-intubated lung lobe sleeve resection, which represented a breakthrough

in surgical treatment and also marked the maturation of non-intubated VATS as a suitable option for complex lung resections.

Conclusions

Every innovation faces a range of challenges from its very beginning; meanwhile, such challenges drives the innovators to constantly update and vitalize their products. For selected patients with lung cancer, the feasibility, safety, and effectiveness of anatomical VATS under non-intubated anesthesia under spontaneous breathing have been well documented. It is a promising technique with certain socioeconomic values due to its superiorities (e.g., faster post-operative recovery) over intubated anesthesia. Along with the adoption of non-intubated VATS in more centers, the improvements in anesthetic techniques and surgical skills, and the expansion of surgical indications, more lung cancer patients will benefit from this technique. Nevertheless, establishing a complete and systematic assessment system and standards of practices will ensure the safety of these surgeries. Meanwhile, the long-term outcomes require further evaluation in more multi-center prospective clinical trials with larger sample sizes.

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