

## Non-intubated video-assisted thoracoscopy : a narrative review

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### Abstract

**Non-intubated video-assisted thoracoscopic surgery (NIVATS) is an emerging technique in thoracic surgery that avoids the use of general anaesthesia and mechanical ventilation. The evolution from traditional VATS to NIVATS has shown significant potential in reducing postoperative complications, shortening hospital stays, and improving patient satisfaction. By allowing spontaneous breathing, NIVATS minimizes the invasiveness of thoracic procedures and reduces the risks associated with tracheal intubation and general anaesthesia. A comprehensive literature search was conducted across multiple databases, including the Cochrane Library, Embase, Medline (Ovid), PubMed, and Scopus, focusing on studies published between 2013 and 2023. Keywords included terms related to NIVATS, spontaneous breathing, and one-lung ventilation. The search yielded 56 relevant studies selected for inclusion in our review.**

**This narrative review explores the physiological aspects and clinical implications induced by the respiratory management in thoracoscopic surgery. It also examines equipment and techniques for lung isolation, emphasizing the importance of optimizing perioperative management.**

**In conclusion, both VATS and NIVATS offer significant advantages over traditional open thoracotomy. NIVATS, in particular, shows promise in enhancing patient outcomes through reduced complications and faster recovery. We present our current protocol for NIVATS at the University Hospitals in Leuven, although further studies are needed to confirm these benefits and refine protocols for broader clinical adoption.**

### Introduction

One-Lung Ventilation (OLV) is a pivotal technique in thoracic surgery, enabling complex procedures such as lobectomy, pneumonectomy, thoracic aorta aneurysm repair, and oesophageal resection. This technique is crucial for providing an optimal surgical field and protecting the contralateral lung from contamination during surgeries involving extensive bleeding or pus. Efficient gas exchange, relying on the precise matching of ventilation and perfusion, is essential for the success of OLV. However, OLV poses several physiological challenges, including ventilation-perfusion mismatch, hypoxemia, and hypercapnia, which require careful management to optimize patient outcomes. Moreover, the technique and equipment used for lung isolation, such as double-lumen tubes (DLTs) and bronchial blockers (BBs), significantly impact patient outcomes.

Proper management of these devices is critical to avoid complications such as mispositioning, airway trauma, and severe hypoxic events.

This narrative review aims to provide an overview of the physiology of unipulmonary respiration, focusing on the challenges and management strategies associated with OLV. It explores the implications of OLV on gas exchange, the role of HPV, and the impact of various anaesthetic drugs. Additionally, the review briefly discusses the stress response to tracheal intubation and its modulation through pharmacological interventions, highlighting the importance of optimizing perioperative management to improve patient outcomes in thoracic surgery.

Video-assisted thoracoscopic surgery (VATS) has revolutionized thoracic surgery by offering a minimally invasive alternative to traditional open surgery. Recently, non-intubated VATS (NIVATS) has emerged as a promising technique,

potentially offering further benefits by avoiding general anaesthesia and mechanical ventilation. We highlight the significance of unipulmonary respiration in thoracic surgery and the transition from conventional VATS to NIVATS, and also compare the benefits and challenges of VATS and NIVATS, provided on recent research findings.

## Methods

A comprehensive literature search was conducted in the Cochrane Library, Embase, Medline (Ovid), PubMed, and Scopus databases. Keywords included: NIVATS, nonintubated, non-intubated, spontaneously breathing, awake VATS, tubeless, thoracoscopy, unipolar, VATS, one lung ventilation, hypoxemia, permissive hypercapnia, hyperoxia, and stress response intubation. The search was limited to articles published from January 1, 2013, to January 1, 2023. Studies included involved adults undergoing thoracic surgery. Exclusion criteria were paediatric populations, ARDS, COVID-19, critically ill patients, transplantation surgery, animal studies, and non-English language publications.

The initial search yielded 1348 articles. After removing 344 duplicates, 1004 articles were screened by title and abstract, excluding those not focused on VATS, NIVATS, or OLV. A total of 136 articles were assessed for eligibility through a detailed full-text review, resulting in the selection of 40 articles. Additionally, references from these articles were checked, resulting in the inclusion of 16 additional articles. We utilized a total of 56 articles for our review.

Our current protocol for NIVATS in the University Hospitals in Leuven has also been included.

### *Physiology of unipulmonary respiration*

#### *One-lung ventilation*

One-Lung Ventilation (OLV) is a critical manoeuvre in thoracic surgery and can be achieved through either lung separation or lung isolation techniques. Lung separation enables an optimal surgical field view, essential for performing complex procedures such as lobectomy, pneumonectomy, thoracic aorta aneurysm repair, and oesophageal resection. Lung isolation serves as a method to protect the contralateral lung from contamination caused by extensive bleeding or pus. In patients with conditions like cystic fibrosis or pulmonary alveolar proteinosis, lung isolation is crucial to prevent contamination of the contralateral lung. Additionally, lung isolation is utilized to provide a low-resistance pathway (e.g. bronchial fistula),

particularly during positive pressure ventilation. This approach helps mitigate risks and improve outcomes in complex surgical procedures<sup>1-3</sup>.

Efficient gas exchange is a critical aspect of OLV physiology, relying on an optimal match between ventilation and perfusion. When implementing OLV in the lateral decubitus position, there is uneven distribution of cardiac output (60% to dependent lung, 40% nondependent lung). However, the implementation of OLV can lead to ventilation-perfusion mismatch<sup>10</sup>. The ventilated, dependent lung typically exhibits better perfusion, while the nondependent lung, once excluded from the ventilator circuit, experiences residual absorption of oxygen from the unventilated alveoli. This absorption triggers complete resorption, leading to atelectasis. Furthermore, the nondependent lung may create a transpulmonary shunt while atelectasis develops in the dependent lung due to the impact of muscle relaxants. The situation further exacerbates the shunt fraction, resulting in hypoxemia.

The lateral position during OLV has been found to effectively reduce shunt flow to the nondependent lung due to the influence of gravity. Conversely, procedures performed in a supine position have been known to cause desaturation in patients due to high shunt flow in nondependent lung areas. Reduction in blood flow to the nondependent lung is achieved through passive and active mechanisms, including surgical manipulation, lateral positioning, gravity, pre-existing disease and hypoxic pulmonary vasoconstriction (HPV)<sup>4</sup>.

Hypoxic pulmonary vasoconstriction (HPV) serves as a protective reflex, redistributing blood flow from low-oxygen areas to improve gas exchange and ventilation-perfusion matching. HPV is reversible and primarily triggered by hypoxia or atelectasis-induced hypoxia, with its severity correlating with hypoxia levels. It is primarily influenced by alveolar oxygen tension (PAO<sub>2</sub>) and mixed venous oxygen tension (PvO<sub>2</sub>). HPV consists of two phases: an initial vasoconstriction that occurs within seconds and can last up to several hours depending on the duration of hypoxemia<sup>5</sup>.

Several factors inhibit HPV, including haemodilution, hypothermia, and increased left atrial pressure, which can reduce the shunt flow through the nondependent lung to approximately 40%. Various drugs also interact with HPV. Antihypertensive agents (e.g., phosphodiesterase inhibitors, nitric oxide donors, calcium antagonists, angiotensin-converting enzyme inhibitors, or angiotensin II receptor blockers) and inotropes (e.g., epinephrine, dobutamine, dopamine) negatively affect HPV by increasing pulmonary vasodilation and shunting<sup>5,6</sup>.

Conversely, catecholamines, particularly phenylephrine as a pure  $\alpha 1$  agonist, enhances HPV and have shown to improve oxygenation in several studies<sup>5</sup>. Almitrine also induces increased vasoconstriction of pulmonary arteries over systemic arteries, potentially improving oxygenation<sup>5</sup>. A recent systematic review focused on the effects of various anaesthetic drugs in one-lung ventilation (OLV) reported better oxygenation and less shunting with continuous low-dose almitrine infusion, especially in combination with intravenous propofol, inhaled nitric oxide, and sevoflurane. However, compared to inhalational agents alone, its efficiency was reported as equivalent<sup>5-7</sup>.

Volatile anaesthetics partially inhibit HPV due to dose-dependent cardio depressive effects, leading to an increased intrapulmonary shunt fraction and worse oxygenation compared to intravenous anaesthesia. Despite this, volatile anaesthesia offers benefits, including convenient management of anaesthesia depth, potentiation of neuromuscular blocking agents, bronchodilatory effects, and reduced inflammatory and oxidative stress responses, resulting in fewer postoperative pulmonary adverse events<sup>6</sup>.

Intravenous propofol infusion, compared to sevoflurane, improves shunt fraction and oxygenation, although sevoflurane has been reported to reduce inflammatory response and preserve epithelial integrity during ischemia, induced by reperfusion in OLV<sup>7,8</sup>. Additionally, intravenous dexmedetomidine as an adjuvant has favourable effects on shunt fraction and oxygenation during OLV. It lowers the demand for propofol or inhaled anaesthetics, which in turn reduces negative interference with HPV and oxygenation. Dexmedetomidine also contributes to vasoconstriction in HPV through its agonistic effect on alpha-2B receptors in pulmonary vascular smooth muscle<sup>7,9,10</sup>.

Thoracic epidural anaesthesia can also affect HPV, depending on the cardio depressant effects related to the dosage of local anaesthetics used in combination with the general anaesthesia regimen. When combined with total intravenous anaesthesia, HPV is less affected due to the lesser cardio depressive effects of total intravenous anaesthesia<sup>6</sup>.

#### *Hypoxemia in OLV*

Hypoxemia, defined as a decrease in arterial oxygen saturation (SaO<sub>2</sub>) below 90%, occurs in 1% to 24% of the minimally invasive thoracic surgeries<sup>11</sup>. Preventing tissue hypoxia by avoiding significant hypoxemia is essential during one-lung ventilation. Hypoxemia during OLV primarily results from an increased shunt fraction, leading to impaired

oxygenation. Factors influencing the occurrence of hypoxemia include lung function, the distribution of perfusion between the lungs, and the position of the patient (supine or lateral decubitus)<sup>12</sup>.

Effective management of hypoxemia during OLV involves several strategies. Apnoeic oxygen insufflation (AOI) has been shown to decrease the incidence of hypoxemia and improve arterial oxygenation during OLV for both open and thoracoscopic surgeries. In a randomized controlled trial, the incidence of hypoxemia was significantly lower in the AOI group compared to the non-AOI group (0% vs. 18%, respectively)<sup>11</sup>. This technique provides oxygen without applying pressure, thus not interrupting the surgery.

CPAP is a standard therapy for managing hypoxemia during OLV. However, it can interfere with surgical exposure, making it less ideal for thoracoscopic procedures<sup>13</sup>.

Other treatment options include increasing the inspired fraction of oxygen, ventilating the non-ventilated lung, correcting the position of the double-lumen tube, and optimizing cardiac output. Clearing the main bronchi of the ventilated lung from secretions and improving the ventilation strategy are also crucial steps in managing hypoxemia<sup>3</sup>.

#### *Hypercapnia in OLV*

Hypercapnia is an inevitable consequence of OLV. However, excessive hypercapnia can lead to adverse effects, including increased intracranial pressure, pulmonary hypertension, depressed cardiac contractility, arrhythmias, reduced renal blood flow, and production of endogenous catecholamines<sup>14</sup>. Patients with uncontrolled hypercapnia, especially those with underlying lung disease, are at high risk of acute respiratory or cardiac failure. In such cases, inotropic agents may be required to improve cardiac function, particularly in patients with concurrent cardiac pathology.

Conversely, mild permissive hypercapnia has demonstrated benefits by enhancing arterial oxygenation, improving hemodynamics, optimizing ventilation-perfusion matching, and protecting against inflammatory responses. OLV can induce local and systemic inflammatory responses, contributing to lung injury. Permissive hypercapnia has been shown to attenuate these inflammatory responses and improve postoperative respiratory function. Patients with elevated CO<sub>2</sub> levels during OLV exhibited lower concentrations of pro-inflammatory cytokines and better lung compliance<sup>15</sup>.

Overall, permissive hypercapnia, reduces inflammatory responses and enhances respiratory function without severe complications. It can

also improve arterial oxygenation and pulmonary mechanics, suggesting its potential as a valuable strategy for managing oxygenation during OLV<sup>16</sup>.

### *Harmful effects of hyperoxia*

While molecular oxygen is the most common drug in medicine, intended primarily to ensure availability for aerobic metabolism, hyperoxia increases the production of toxic reactive oxygen species (ROS) by mitochondria, leading to vasoconstriction and paradoxically resulting in hypoxemia<sup>18,19</sup>.

Although perioperative hyperoxia has been employed to prevent wound infection in elective surgeries, it has not shown a general benefit for wound healing<sup>19</sup>.

The literature highlights that the human lung is susceptible to high oxygen levels, which can cause absorption atelectasis due to nitrogen escape from the alveoli, resulting in increased shunt fraction and decreased oxygenation<sup>17</sup>.

Traditional treatment for one-lung ventilation (OLV) often involves administering 100% oxygen to prevent or manage oxygen desaturation. However, studies indicate that high oxygen concentrations can be detrimental. Acute hyperoxia-induced vasoconstriction reduces cerebral, coronary, and skeletal muscle perfusion. Prolonged exposure to hyperoxia can suppress the function of peripheral chemoreceptors and reduce sympathetic activity, which may result in hypotension, and can cause cellular death, including apoptosis and necrosis. Evidence indicates that hyperoxia reduces cardiac output by approximately 10% and increases systemic vascular resistance by 11-25%<sup>20</sup>.

Excessive supplemental oxygen in the perioperative period can result in absorption atelectasis and direct alveolar damage from ROS, impairing gas exchange and potentially causing tracheobronchitis. In patients with COPD, it can reduce hypoxic respiratory drive and cause hypercarbia upon returning to spontaneous breathing<sup>21</sup>. Reducing the Fraction of Inspired Oxygen (FiO<sub>2</sub>) mitigates the risks associated with hyperoxia. FiO<sub>2</sub> levels of 0.3-0.35 are generally considered safe<sup>18</sup>. However, a study comparing 5000 patients with FiO<sub>2</sub> levels of 80% and 40% found no difference in the rate of postoperative respiratory complications, suggesting no definitive evidence that perioperative hyperoxia leads to respiratory complications and poor outcomes<sup>22</sup>.

### *Equipment and techniques for unilateral pulmonary ventilation*

#### *Accoutrements for OLV*

There are two commonly used methods to achieve OLV: the double lumen tube (DLT) or

the bronchial blocker (BB). In emergencies, a standard single lumen tube can be also inserted into the main bronchus, resulting in the spontaneous collapse of the contralateral lung due to absorption atelectasis, though this technique is primarily used in paediatric cases.

The choice of intubation or perioperative airway management technique, particularly between DLTs and BBs, significantly impacts patient outcomes, as well as the efficiency and cost-effectiveness of healthcare delivery.

There are several types of double lumen tubes, all similar in design and made of polyvinyl chloride. The Robertshaw endotracheal tube is widely used in thoracic surgery. While the Carlens tube encounters more difficulties when passing through the larynx compared to the Robertshaw tube, both tubes show no significant difference in complications during one-lung ventilation<sup>3,23</sup>.

The most common issues, arising from the use of DLT are linked to mispositioning and airway trauma. Mispositioning results in the collapse of the dependent lung, causing gas-trapping during positive pressure ventilation, and contamination of the nondependent lung. This, in turn, can lead to various intraoperative ventilatory problems such as hypoxemia, severe respiratory complications, and postoperative pneumonia. Notably, dislocation of DLT is reported more frequently after positioning patients in the lateral position and during surgical manoeuvres of the bronchus. Tracheal or bronchial iatrogenic injury is another potential risk following double-lumen tube intubation and extubation, especially during extension and flexion of the neck. Maintaining consistent confirmation and utilizing fiberoptic visualization to ensure accurate position of DLT is crucial<sup>24</sup>.

Tracheobronchial damage resulting from rupture or lacerations after intubation of DLT is a rare but serious airway trauma. The primary cause of the injury is the overinflation of tracheal but mostly brachial cuffs. The utilization of an inappropriate lumen size with the DLT can lead to iatrogenic airway trauma, resulting in severe bleeding, air leaks, and subcutaneous emphysema. Undersized DLT can migrate distally, causing laceration or injury of the membranous portion of the trachea or bronchus<sup>1,2,25</sup>. Furthermore, intubating with a DLT in individuals with difficult airway necessitates an experienced and skilled anaesthesiologist<sup>3</sup>.

Endobronchial blockers (BB) are an alternative to DLTs for lung separation, particularly useful in cases of predictable difficult intubation, rapid sequence induction (RSI), and when postoperative ventilation is needed, as they avoid the need for tube replacement. These devices can also be displaced

by surgical manipulations and are difficult to reposition. Severe hypoxic complications can arise if the inflated BB balloon dislodges into the trachea, potentially causing complete airway obstruction or significant gas trapping, leading to cardiovascular collapse<sup>2</sup>.

While DLTs offer quicker and more reliable placement, BBs are associated with fewer postoperative complications and adverse events. Both techniques provide comparable quality of lung collapse. Consequently, from a pharmacoeconomic perspective, BBs may be more advantageous due to their lower incidence of complications, potentially reducing overall healthcare costs and improving patient outcomes.

### *Stress response to tracheal intubation*

Direct laryngoscopy with tracheal intubation is known to elicit significant cardiovascular and neuroendocrine stress responses. This manoeuvre triggers a sympathetic response due to stimulation in the supraglottic region by the laryngoscope blade, tracheal tube placement, and cuff insufflation. The increase of adrenaline and noradrenaline levels is associated with marked alterations in arterial blood pressure and heart rate.

This intubation-induced stress response can also elevate intracranial pressure, intraocular pressure, and induce vasoconstriction, thereby increasing myocardial oxygen demand and potentially leading to myocardial infarction and arrhythmias. Patients with pre-existing cardiovascular conditions are at risk, because this stress response can lead to severe morbidity<sup>26</sup>.

Recent studies indicate that the insertion of a laryngeal mask airway (LMA) compared to direct laryngoscopy results in a more stable hemodynamic profile, reduced inflammatory and oxidative responses, and a smoother recovery<sup>27</sup>. Additionally, the use of video laryngoscopes provides superior hemodynamic stability and ease of intubation compared to conventional Macintosh laryngoscopes in patients with ischemic heart disease<sup>28</sup>.

Pharmacological interventions can modulate the stress response to tracheal intubation. Current studies highlight that dexmedetomidine and sufentanil demonstrate superior efficacy in providing hemodynamic stability during tracheal intubation, particularly in high-risk patient populations<sup>29,30</sup>.

### *The role of PEEP*

Mechanical ventilation is crucial in anaesthesia care due to its significant role in mitigating postoperative pulmonary complications (PPCs), which impact morbidity and mortality. PPCs, including both

minor and major pulmonary events, typically arise within seven days post-surgery, with a 30-day mortality rate reported up to 20%<sup>22,31</sup>. Thoracic surgery exhibits the highest PPC incidence (19-59%), followed by upper-abdominal surgery (16-17%) and lower-abdominal surgery (0-5%)<sup>32</sup>.

The perioperative ventilation regimen can be guided by various patient characteristics and surgical factors, as outlined in the ARISCAT Risk Index and the ASA physical status index, to predict the high-risk population for developing PPCs after thoracic surgery<sup>32</sup>.

Recent international expert panel-based consensus recommends protective ventilation strategies, utilizing lower tidal volumes (6-8 ml/kg of ideal body weight) with an initial positive end-expiratory pressure (PEEP) of 5 cm H<sub>2</sub>O and the focus on minimizing ventilator driving pressure<sup>33</sup>. However, employing low tidal volumes can lead to increased dead space ventilation and oxygenation challenges, especially with low PEEP. Excessive PEEP, on the other hand, can reduce preload and cardiac output, worsening oxygenation<sup>31</sup>. Whilst, the use of zero end-expiratory pressure (ZEEP) may lead to reduced end-expiratory lung volume and contributes to increased formation of atelectasis. Atelectasis in turn decreases the respiratory compliance and thereby increasing the risk of overinflation, known as volutrauma<sup>31</sup>. Careful PEEP implementation is pivotal for maintaining open alveoli, enhancing gas exchange, and preserving surfactant functionality<sup>3,34</sup>.

Recruitment manoeuvres and the judicious use of PEEP can further improve oxygenation and prevent atelectasis, though these interventions must be carefully managed to avoid hemodynamic compromise. The strategic application of extrinsic PEEP during one-lung ventilation can enhance compliance, functional residual capacity (FRC), and oxygenation<sup>34</sup>. Although the optimal tidal volume and PEEP levels during intraoperative ventilation remain debated, protective strategies are essential for reducing inflammation, improving oxygenation, and minimizing lung-related complications<sup>35</sup>. The choice of ventilation mode and settings should be tailored to the patient's condition and surgical requirements. PCV-VG (volume guaranteed) mode, combining the benefits of PCV and VCV, maintains consistent tidal volumes while minimizing peak inspiratory pressures<sup>35</sup>.

### *Complication and risks*

#### *Acute lung injury after one lung ventilation*

A significant cause of mortality following thoracic surgery is the development of acute lung injury (ALI). ALI can affect up to 4% of patients

undergoing one-lung ventilation, with mortality rates reaching up to 70%<sup>36</sup>.

ALI manifests in two clinical patterns based on different pathogenic triggers. The primary form occurs within 3 days post-surgery, while the delayed form, typically is observed between days 3 and 10 post-surgery. It arises from postoperative complications such as broncho aspiration, pneumonia, or bronchopleural fistulas<sup>37</sup>.

The risk factors contributing to the development of ALI can be categorized into two groups: patient-related and surgery-related factors. Patient-related risk factors include an inability to predict postoperative lung function, previous lung injuries such as trauma or chemotherapy, female gender, and alcohol abuse. Genetic predisposition may also play a role.

Surgery-related risk factors include lung transplantation, lobectomy, transfusion, high-stretch ventilation, oxidative stress, surgical-induced inflammation, and excessive fluid infusion<sup>37,38</sup>.

Employing protective ventilation strategies and a goal-directed fluid approach can reduce the number of ventilator days and improve outcomes. Prophylactic treatment with inhaled  $\beta$ 2-adrenergic agonists, smoking cessation, and recruitment manoeuvres may help manage ALI, although their impact on mortality is not well-established<sup>38</sup>.

## *Surgical Approaches*

### *Comparison VATS and NIVATS*

Video-Assisted Thoracoscopic Surgery (VATS) has revolutionized thoracic surgery by providing a minimally invasive approach that reduces chest wall trauma, recovery time, pain, and complications compared to traditional open thoracotomy<sup>39,40</sup>. Since the inaugural VATS procedure in 1992, surgeons have continually enhanced their surgical skills and techniques to address increasingly complex procedures. Concurrently, they have broadened the indications for VATS, facilitating its application to a wider array of surgical scenarios and in patients with significant comorbidities<sup>40-42</sup>.

Intubated VATS offers several significant advantages, particularly for patients with compromised lung function or those undergoing complex surgical procedures. The use of general anaesthesia and mechanical ventilation during intubated VATS allows for precise control of ventilation, which is essential for maintaining optimal oxygenation and carbon dioxide levels. This precise control is crucial for ensuring the patient's stability throughout the procedure. Furthermore, general anaesthesia and mechanical ventilation provide a more stable and controlled

surgical field, thereby reducing the risk of intraoperative complications<sup>43</sup>.

Conventional VATS is associated with higher rates of postoperative complications, including respiratory issues and infections<sup>44,45</sup>. Common complications of VATS include air leak, bleeding, and pneumonia, which can be exacerbated by pre-existing lung tissue pathology and corticosteroid use. Less common complications may include atelectasis, arrhythmias, prolonged dependence on mechanical ventilation, empyema, wound infection, deep vein thrombosis, and conversion to thoracotomy<sup>45</sup>. Additionally, surgical separation, stress responses, pulmonary ischemia-reperfusion, and anaesthetics during VATS can activate immune inflammation, leading to the release of inflammatory factors and subsequent impairment of postoperative pulmonary function which may negatively affect recovery. Patients undergoing intubated VATS often experience extended hospital stays and slower postoperative recovery compared to non-intubated approach<sup>46</sup>.

To mitigate the adverse effects associated with tracheal intubation and general anaesthesia, the non-intubated VATS technique has been developed and implemented, further minimizing the invasiveness of thoracic procedures. NIVATS allows patients to breathe spontaneously, with or without the use of a laryngeal mask airway (LMA), thereby reducing the impact of anaesthesia<sup>33</sup>. NIVATS is typically performed to treat conditions such as primary spontaneous pneumothorax, pleurodesis, secondary pneumothorax in patients with emphysema, resection of solitary pulmonary nodules, lung volume reduction surgery, palliative thoracic surgery (e.g., treatment of pericardial and pleural effusion), and empyema. This minimally invasive approach has also been successfully applied to patients with myasthenia gravis undergoing thymectomy, as avoiding volatile anaesthetics and muscle relaxants can prevent respiratory insufficiency and prolonged ventilation in this particular patient population. (see Table I)<sup>42,44,46-48</sup>.

However, non-intubated VATS presents challenges for surgeons due to diaphragm movement and mediastinal shifting, complicating the procedure. These movements require adaptation to respiratory motions for optimal exposure and may force the surgeon to temporarily halt operations during coughing or muscle contractions. Common surgical reasons for conversion include severe adhesions, major bleeding, and significant mediastinal and diaphragmatic movements. Paradoxical breathing in the non-dependent lung also limits success, although these are technical hurdles rather than absolute conversion

**Table I.** — Procedures performed using non-ventilated video-assisted thoracic surgery.

Diagnostic procedures	biopsy of pleura, lung and mediastinum, pleural effusions drainage
Therapeutic interventions	empyema drainage, haemothorax evacuation, treatment of chylothorax, treatment of pneumothorax, pleural decortication, wedge resection, segmentectomy, lobectomy, bullectomy, lung volume reduction, bronchial and tracheal resection, resection of mediastinal tumours and thymomas, sympathectomy for palmar hyperhidrosis
High-risk patients	high risk for general anaesthesia due underlying cardiovascular or pulmonary comorbidity

indications<sup>42,49</sup>. Contraindications for non-intubated video-assisted thoracoscopy can be classified as patient-related, anaesthesia-related, and surgery-related. These contraindications are outlined in Table II<sup>39,42</sup>.

A crucial aspect of spontaneous breathing anaesthesia is managing hypercapnia during surgery. Common anaesthesiologic reasons for conversion to tracheal intubation include excessive hypercapnia, hypoxia, airway spasm, and persistent cough, with conversion rates ranging between 2% and 12%, influenced by the team’s experience<sup>49</sup>. Intubating a patient in the lateral decubitus position during VATS procedures is technically challenging for anaesthesiologists. While direct laryngoscopy can be attempted, reliable alternatives include fiberoptic bronchoscopy, video-assisted laryngoscopy, and the use of a laryngeal mask airway (LMA).

Patients undergoing non-intubated video-assisted thoracic surgery (NIVATS) exhibit significantly lower rates of overall complications compared to those undergoing intubated VATS. The odds ratio (OR) for overall complications in NIVATS patients is 0.41, indicating a substantial reduction

in risk. Additionally, specific complications such as air leaks (OR 0.45), pharyngeal discomfort (OR 0.08), hoarseness (OR 0.06), and gastrointestinal reactions (OR 0.23) are markedly reduced in the NIVATS group<sup>50</sup>. The perioperative mortality rate is significantly lower in NIVATS patients, with an OR of 0.13, suggesting a notable decrease in the risk of death during the perioperative period. Moreover, NIVATS is associated with a shorter hospital stay, with a mean difference (MD) in the length of hospital stay between NIVATS and IVATS patients of -1.41 days, indicating earlier discharge for NIVATS patients<sup>50</sup>. Another study corroborates this finding with a weighted mean difference (WMD) of -1.35 days<sup>44</sup>. Patients undergoing NIVATS report less postoperative pain, with the visual analogue scale (VAS) showing a mean difference of -0.34, indicating less pain in the NIVATS group. Another study reports less chest pain with a WMD of -1.31<sup>44</sup>. Anaesthesia satisfaction scores are significantly higher in the NIVATS group, with a mean difference of 0.50, reflecting better overall patient comfort and satisfaction<sup>49</sup>. There is no statistically significant difference in the length of operation

**Table II.** — Contraindications for non-ventilated video-assisted thoracic surgery.

Patient related contraindications	Anaesthesia (when using epidural) related contraindications	Surgery related contraindications	Absolute contraindications
<ul style="list-style-type: none"> <li>• Morbid obesity</li> <li>• Patients with obstructive sleep apnoea syndrome (OSAS)</li> <li>• Patients with altered airway anatomy or fascial trauma                             <ul style="list-style-type: none"> <li>• High risk aspiration</li> </ul> </li> <li>• Certain Respiratory conditions, like COPD with high risk of air trapping</li> <li>• Persistent cough or clinically significant sputum production                             <ul style="list-style-type: none"> <li>• Resting hypoxemia and hypercapnia</li> </ul> </li> <li>• Contralateral phrenic nerve palsy                             <ul style="list-style-type: none"> <li>• Severe haemodynamic instability</li> </ul> </li> <li>• Neurological conditions</li> </ul>	<ul style="list-style-type: none"> <li>• Allergic reaction to local anaesthesia, medication or sedation                             <ul style="list-style-type: none"> <li>• Coagulopathy</li> </ul> </li> <li>• Skin infection at the site of puncture thoracic epidural</li> </ul>	<ul style="list-style-type: none"> <li>• Previous thoracic surgery                             <ul style="list-style-type: none"> <li>• Pleural adhesion</li> <li>• Previous pleurodesis</li> </ul> </li> <li>• Complex surgery: Sleeve lobectomy, large centrally located tumour.</li> <li>• Prior radiation therapy</li> </ul>	<ul style="list-style-type: none"> <li>• Uncooperative or unconscious patient                             <ul style="list-style-type: none"> <li>• Patient refusal</li> <li>• Difficult airway management</li> </ul> </li> <li>• Inexperienced team</li> </ul>

time between NIVATS and IVATS patients, with a mean difference of 0.90 hours<sup>49</sup>. However, another study reports a shorter global in-operating time for NIVATS with a WMD of -35.96 minutes. Additionally, NIVATS is associated with a shorter anaesthesia time, with a WMD of -7.29 minutes<sup>44</sup>.

### *Perioperative anaesthetic management VATS and NIVATS*

The goal of analgesia is to eliminate discomfort during surgical procedures. Initially, the placement of VATS ports induces pain from the skin to the parietal pleura. Once the ports are in position, further manipulation of the lung and traction on intrathoracic structures can irritate the visceral pleura<sup>43</sup>. Several approaches have been developed to provide analgesia during VATS and NIVATS. Due to the significant postoperative pain associated with thoracic surgery, current guidelines recommend the use of regional analgesia in conjunction with multimodal analgesia<sup>50</sup>.

Thoracic epidural analgesia (TEA), although effective, is less advocated in the guidelines published by the Enhanced Recovery after Surgery Society and PROSPECT guidelines for VATS. This is primarily due to the side effects associated with TEA, including postoperative nausea and vomiting, bladder dysfunction, immobilization due to muscle weakness, hemodynamic implications, and respiratory depression from opioid use. Additionally, adverse events such as block failure, postdural puncture headache, infection, epidural hematomas, and spinal anaesthesia further limit the recommendation for TEA in current practice<sup>51,52</sup>.

Several locoregional techniques have been used in VATS surgery as an alternative to TEA.

Paravertebral block (PVB) has been demonstrated to be as effective as thoracic epidural analgesia (TEA) in VATS, with fewer side effects. The PROSPECT guidelines do not specify a preferred technique for PVB placement; however, surgical catheter placement under direct vision is often easily performed<sup>50</sup>. In the context of NIVATS, PVB is favored due to its efficacy and reduced side effect profile. Commonly reported adverse events associated with PVB include block failure, intercostal block, pneumothorax, vascular damage, and potential epidural or spinal displacement of local anaesthetics. These risks can be minimized through ultrasound-guided placement<sup>51</sup>.

Another recommendation is the use of an erector spinae plane (ESP) block, particularly when parietal pleural damage is anticipated, with a preference for catheter placement over a single shot. Studies have demonstrated that ESP is non-inferior to PVB for VATS procedures<sup>50</sup>. Additionally, ESP blocks offer the advantage of potentially aiding in the treatment of neuropathic pain following thoracic surgery<sup>51</sup>.

Postoperative neuropathic pain is a common problem observed in VATS patients, affecting approximately 25,9% of individuals and persisting for up to a year for some cases<sup>53</sup>. This unexpected pain not only diminishes patient satisfaction but also prolongs hospital stays and may contribute to the development of persistent postoperative opioid misuse. The complex innervation of the thoracic cage (see figure 1) highlights the importance of carefully selecting postoperative analgesia techniques.

Several studies have suggested that dexmedetomidine, beyond its sedative and analgesic properties, may play a crucial role in managing

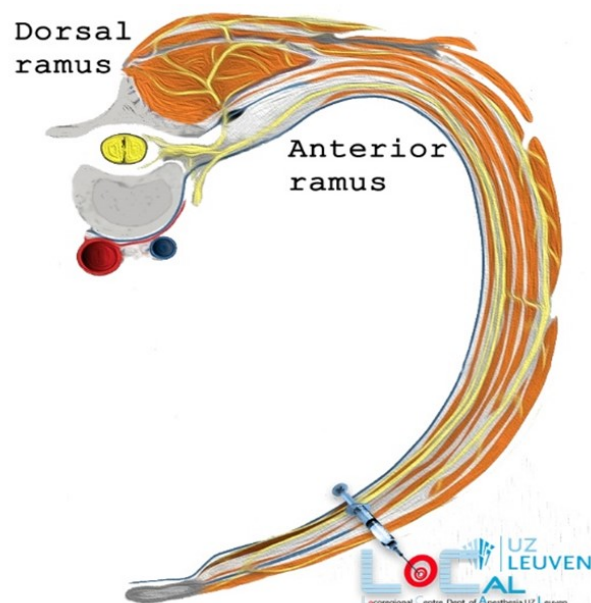


Fig. 1



neuropathic pain and reducing inflammation, providing potential therapeutic benefits in clinical settings<sup>54</sup>.

Another easily performed block, which can also be applied under direct surgical vision, is the intercostal nerve block (ICNB). This technique is particularly advantageous in uniportal NIVATS, where only a single intercostal space is involved, making ICNB a viable alternative to TEA<sup>51</sup>. A systematic review with an exploratory meta-analysis found that unilateral ICNB resulted in better average pain scores compared to TEA, attributing the superior scores to the continuous infusion of opioids. The authors recommended using ICNB in conjunction with multimodal analgesia as an alternative to TEA during VATS<sup>52</sup>.

The locoregional techniques mentioned earlier can also be applied for NIVATS. There have also been significant advancements in perioperative anaesthetic management. Historically, awake VATS began under thoracic epidural anaesthesia (TEA), using locoregional anaesthesia and an oxygen facemask for minor thoracic surgeries by researchers in Europe. Over time, with increased experience, this anaesthetic method was expanded to major VATS procedures. This expansion included the introduction of bispectral index (BIS)-controlled sedation combined with intercostal nerve block (ICNB) instead of TEA. For demanding perioperative procedures in thoracic surgery, such as re-insufflation, bronchoscopy, or thoracotomy, the management of periprocedural anaesthesia evolved to using a supraglottic airway device alongside BIS-guided target-controlled propofol anaesthesia<sup>43</sup>. This approach maintains BIS readings between 40 and 60 and incorporates a surgically placed ICNB to enhance aesthetic efficacy<sup>39</sup>.

Another perioperative anaesthesia management technique adopted in Asia involves using BIS-guided target-controlled propofol infusion alongside ICNB and airway management with a transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) system, suitable for paediatric and geriatric patients<sup>39</sup>.

More recently, a novel method involving spontaneous breathing through a double-lumen tube (DLT) has been introduced, demonstrating feasibility and safety in thoracic surgery<sup>55</sup>.

To reduce the cough reflex during awake and non-intubated VATS, lidocaine was initially administered as an aerosol. Presently, a surgical ICNB, along with additional vagal nerve blocks, is used to prevent the cough reflex. Blocking the ipsilateral stellate ganglion is another method to dampen the cough reflex<sup>39,56</sup>. Additionally,

infusions of dexmedetomidine or remifentanyl, and inhalational sevoflurane, have shown efficacy as antitussives<sup>51</sup>.

### *NIVATS Protocol University Hospitals Leuven*

To date, we have successfully treated ten patients in UZ Leuven who underwent unipolar NIVATS to obtain biopsies of their left upper and lower lobes.

Preprocedural routine preoperative evaluation is mandatory.

The patients were given detailed explanations of the upcoming procedure, ensuring they fully understood what would be involved and any potential risks or benefits. After providing this information, informed consent was obtained from each patient. Perioperative anaesthesia was administered under standard monitoring, including electrocardiography (ECG), pulse oximetry, capnography, arterial line for arterial blood gas (ABG) sampling every 15 minutes, Bispectral Index (BIS) monitoring, and Near-infrared spectroscopy (NIRS) monitoring. Additionally, patients received an epidural catheter for pain management and were consciously sedated while maintaining spontaneous breathing throughout the surgery.

The thoracic epidural anaesthesia was performed at either T4-5 or T5-6 levels, aiming to achieve a sensory block ranging from T10/12 to T3. Initially, a bolus of 0.1 – 0.15 ml/kg of levobupivacaine 0.5% was administered, and sensory levels were confirmed ten minutes later. If the block was insufficient, a second bolus of 0.05 ml/kg of levobupivacaine 0.5% was given, followed by retesting of the sensory block level ten minutes later. Once the target block level was achieved, a patient-controlled epidural analgesia (PCEA) regimen was initiated, providing a continuous infusion of 5-7ml/hr with 5 ml boluses every 20 minutes, up to a maximum of 24 hours. This approach aimed to ensure safe and effective pain management while minimizing the risk of adverse events.

For sedation, dexmedetomidine was administered at a dosage of 1µg/kg/hr for 10 – 15 minutes after intravenous access placement. A maintenance dosage of 0.5 µg/kg/hr was then continued throughout the procedure to sustain sedation. In cases of heightened anxiety, a bolus of 1 µg/kg of dexmedetomidine or low-dose propofol (0.1-0.3 µg) via Target-controlled infusion (TCI) was administered as needed. Additionally, all patients received 5 – 6 L oxygen via an oxygen mask to ensure proper oxygenation. The necessary equipment for urgent intubation and safe airway management in the lateral position was obviously readily available.

Patients were positioned in a lateral decubitus position (see figure 2), and measures were taken to ensure disinfection and sterile covering. All uniportal procedures received 1% lidocaine (5-10ml) if needed for skin incision followed by careful steps to open the subcutis. Another dose of lidocaine 1% (not exceeding 10 ml) was administered in the m. serratus anterior, intercostal and pleural areas.

The incision diameter is limited 4-5 cm to minimize pain from instrument friction. An Alexis wound retractor (XS) was inserted, and a 5 mm camera was used for visualization during lung biopsy. Verbal communication with the patient was maintained throughout the procedure to ensure their comfort. After completing the biopsy, a small chest drain was placed, and the incision was closed. Both the chest drain, and epidural catheter were removed 24 hours after the procedure.

Thus far, we have performed procedures on only 10 patients. Our preliminary data is currently insufficient to formulate any definitive recommendations. Further patient inclusion is necessary to reach conclusive findings.

In conclusion, both VATS and NIVATS offer significant advantages over traditional open thoracotomy, with VATS providing a minimally invasive approach and NIVATS further minimizing invasiveness by eliminating the need for general anaesthesia. Intubated VATS remains a versatile and reliable option, especially for more complex procedures and patients with significant comorbidities. Although OLV presents several physiological challenges, including hypoxia,

hypercapnia, and the modulation HPV, as well as issues associated with techniques to achieve lung isolation. Understanding these mechanisms and employing practical strategies, such as optimized ventilatory modes, pharmacological interventions, and appropriate positioning, can significantly improve patient outcomes in thoracic surgery.

NIVATS, in particular, shows promise in reducing postoperative complications. It reduces stress and inflammatory responses, along with the potential side effects of mechanical ventilation, while enhancing cellular immune function<sup>42,46</sup>. Another aim is to decrease the incidence of respiratory complications associated with neuromuscular blocking agents and positive pressure ventilation, lowering morbidity rates. Additionally, NIVATS can lead to less postoperative pain, which plays a crucial role in pain management, faster mobilization, and participation in respiratory and coughing exercises, which shortens hospital stays, and facilitating faster recovery and ultimately increasing patient satisfaction.

The choice between VATS and NIVATS should be guided by the specific clinical scenario, patient factors, and the surgeon's expertise. While VATS remains the standard for a wide range of thoracic procedures, NIVATS represents a promising alternative for selected patients, particularly those at high risk for general anaesthesia. Identifying suitable patients for NIVATS through preoperative assessments is essential for improving postoperative outcomes to achieve rapid patient mobilization, minimize hospital stay and potentially reduce costs while maintaining physiological muscular,

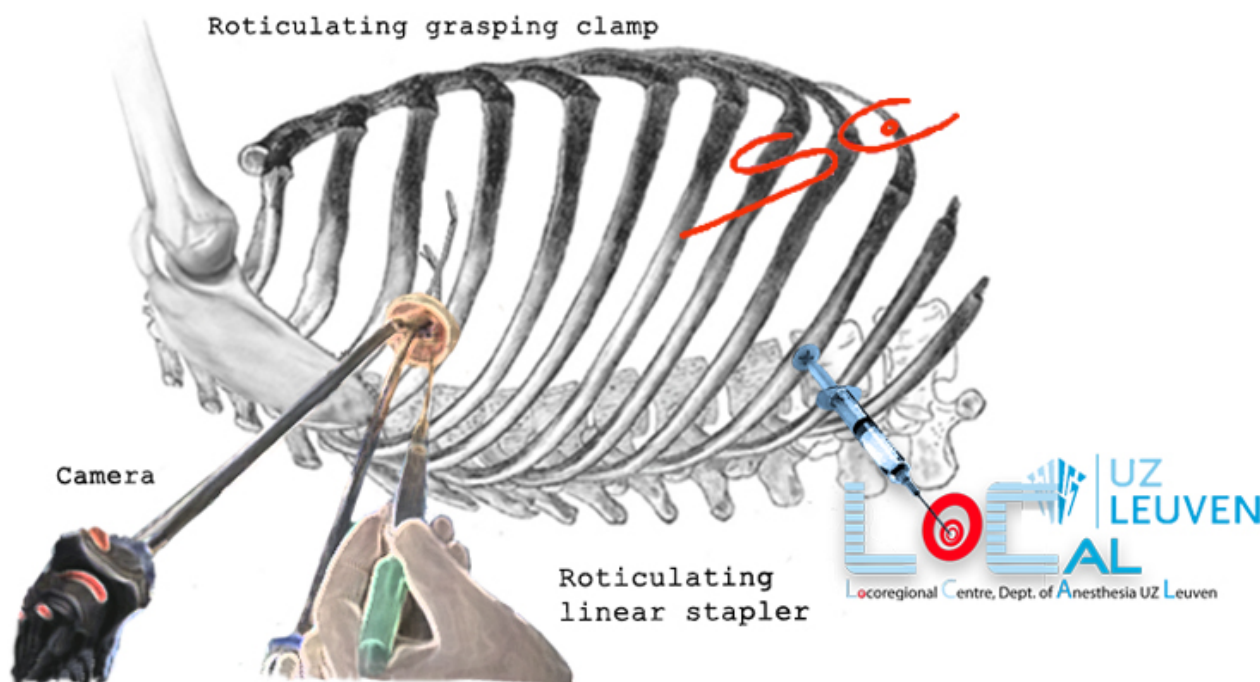


Fig. 2

neurological, and cardiopulmonary status for faster recovery<sup>40,42,44</sup>

Further research and patient inclusion are necessary to solidify these findings and provide more comprehensive recommendations for the use of NIVATS in clinical practice.

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