Non-intubated video-assisted thoracoscopic lung resections: the future of thoracic surgery?

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Summary

Thanks to the experience gained through the improvement of video-assisted thoracoscopic surgery (VATS) technique, and the enhancement of surgical instruments and high-definition cameras, most pulmonary resections can now be performed by minimally invasive surgery. The future of the thoracic surgery should be associated with a combination of surgical and anaesthetic evolution and improvements to reduce the trauma to the patient. Traditionally, intubated general anaesthesia with one-lung ventilation was considered necessary for thoracoscopic major pulmonary resections. However, thanks to the advances in minimally invasive techniques, the non-intubated thoracoscopic approach has been adapted even for use with major lung resections. An adequate analgesia obtained from regional anaesthesia techniques allows VATS to be performed in sedated patients and the potential adverse effects related to general anaesthesia and selective ventilation can be avoided. The non-intubated procedures try to minimize the adverse effects of tracheal intubation and general anaesthesia, such as intubation-related airway trauma, ventilation-induced lung injury, residual neuromuscular blockade, and postoperative nausea and vomiting. Anaesthesiologists should be acquainted with the procedure to be performed. Furthermore, patients may also benefit from the efficient contraction of the dependent hemidiaphragm and preserved hypoxic pulmonary vasoconstriction during surgically induced pneumothorax in spontaneous ventilation. However, the surgical team must be aware of the potential problems and have the judgement to convert regional anaesthesia to intubated general anaesthesia in enforced circumstances. The non-intubated anaesthesia combined with the uniportal approach represents another step forward in the minimally invasive strategies of treatment, and can be reliably offered in the near future to an increasing number of patients. Therefore, educating and training programmes in VATS with non-intubated patients may be needed. Surgical techniques and various regional anaesthesia techniques as well as indications, contraindications, criteria to conversion of sedation to general anaesthesia in non-intubated patients are reviewed and discussed.

Keywords: Non-intubated patient • Awake surgery • Lobectomy • Spontaneous ventilation • Local anaesthesia • Uniportal

‘Only the people who study the past can define the future’—Confucius

INTRODUCTION

During the last decade, there have been huge developments of new minimally invasive surgical techniques for major pulmonary resections [1, 2]. Advances in anaesthesiology include thoracic operations performed without the employment of general anaesthesia, through maintaining spontaneous ventilation and with minimally sedated patients. One-lung spontaneous ventilation is more physiological and has more advantages than mechanical ventilation. However, open pneumothorax in a non-intubated patient may compromise ventilation and oxygenation. Movements of the patient during surgery, coughing, mediastinal shift and diaphragmatic displacement can make surgical manoeuvres in video-assisted thoracoscopic surgery (VATS) more technically demanding [3].

Non-intubated minor and major thoracic surgery can be performed safely by VATS through regional anaesthesia and sedation in spontaneously breathing patients [4, 5]. Non-intubated thoracic surgery for major procedures is not risk free, and the ideal standard management in daily practice still needs to be better elucidated.

A BRIEF HISTORICAL PERSPECTIVE OF ANAESTHESIA IN NON-INTUBATED THORACIC SURGERY

Before 1930, the performance of thoracic surgery through a thoracotomy in a slightly anaesthetized patient with spontaneous...
ventilation was very daring and the results on patients’ survival were disappointing. In 1928, Guedel introduced the endotracheal tube and 3 years later, Gale and Waters [6] put this tube in the bronchus of the healthy lung to achieve one-lung ventilation (OLV). However, up until the 1960’s, mechanical ventilation was not introduced. Ventilation was either spontaneous or manually assisted, diaphragm activity was preserved, and lung mobility was present until the surgeon managed iatrogenic pneumothorax. In 1956, Vischnevski developed a multimodal technique with blocking of the phrenic and vagus nerves in the neck, adding an extensive intercostal blockade, and finally by administering novocaine in the lung hilum after opening the hemithorax. Through this technique, Vischnevski [7] performed more than 600 major lung procedures. In 1960, Ossipov [8] published a series of more than 3000 operations performed with a similar technique.

After 1960, the introduction of mechanical ventilation and new improvements for OLV allowed the further development of thoracic surgery. Moreover, the development of endoscopic surgery with minimal surgical trauma led surgeons to reconsider those techniques and to evaluate their real advantages over the standard thoracic surgery.

In 2004, Pompeo et al. [9] proved it was possible, through the use of epidural anesthesia, to perform thoracic surgery in the awake patient. However, in patients requiring lobectomies, the procedure was done under general anesthesia.

Reviewing the anaesthesia in endoscopic thoracic surgery, we can find some differences between the operations performed in non-intubated patients. Those performed with the patient awake or minimally sedated are mainly wedge or peripheral nodule resections [4, 9–15], and the others performed with deeper sedation include major lung surgery (segmentectomy or lobectomy) [5, 16].

In 2007, Al-Abdullatief et al. [17] showed the possibility of performing some cases of major thoracic surgery, even thoracotomy for lung resection, with the patient awake or minimally sedated.

Nowadays, the evolution of video-assisted thoracic surgery to less invasive techniques, such as uniportal VATS (with only one incision of 3 cm and involving only one intercostal space) allows us to consider the possibility of avoiding intubated general anesthesia [18].

ADVERSE EFFECTS OF INTUBATED GENERAL ANAESTHESIA

The main advantage of non-intubation surgery is to avoid the perioperative morbidity derived from the deleterious effect of general anesthesia and OLV, in addition to the beneficial effects of spontaneous ventilation in a non-intubated patient.

The beneficial effects of the use of loco-regional techniques are often highlighted in non-intubated surgery. However, as often shown in publications, it is wrong to attribute the beneficial effects mainly to the loco-regional techniques. These techniques (such as paravertebral block, epidural and intercostal block) are frequently used intraoperatively in thoracic surgery along with general anesthesia [19].

Mechanical ventilation has a series of potential side-effects such as airway pressure-induced injury, damage caused by lung overdistension, shear stress of repetitive opening, closing of alveoli and the release of a variety of pro-inflammatory mediators. Atelectasis in the dependent lung is frequent during OLV with muscle paralysis [20, 21]. The formation of atelectasis in the non-operative lung is highly undesirable during OLV because it worsens the already high shunt fraction, increasing the probability of hypoxemia. It can also increase the risk of postoperative pulmonary complications. In the dependent lung, OLV induces ventilation-to-perfusion mismatch, and promotes further inflammatory changes (low V/Q regions increased in the ventilated lung or signs of alveolar damage), suggesting that OLV has more damaging consequences than a period of complete lung collapse and surgical manipulation. Ventilator-related lung injury occurs in about 4% of major lung resections and carries a mortality rate as high as 25%. However, subclinical lung injury leading to minor respiratory impairment is more frequent and related to postoperative complications. Protective ventilation with low tidal volume ventilation, positive end-expiratory pressure, lower FiO2, lower ventilation pressures, permissive hypercapnia and recruitment manoeuvres are all mandatory in mechanical ventilation in thoracic surgery to minimize lung injury [22].

High-frequency jet ventilation may be an alternative way of ventilation in thoracic surgery, with lower peak inspiratory pressure and shunt fraction but we need general anaesthesia and orotracheal intubation [23].

Orotracheal and bronchial intubation can also have potential local complications, including throat pain, mucosal ulceration and laryngeal or tracheal injuries. Tracheobronchial rupture may carry a mortality rate as high as 22% [24].

General anesthesia also has deleterious systemic side-effects that do not occur in regional anaesthetic techniques in awake patients or those minimally sedated. Deep anaesthesia used in thoracic surgery has been related to a higher mortality, morbidity and cognitive dysfunction postoperatively [25].

The use of muscle relaxants has been known to produce diaphragmatic dysfunctions, particularly in the hemithorax, where the lung is collapsed, therefore producing associated complications as a result of residual muscle block [26]. The intravenous analgesics during general anaesthesia, primarily opioids, are associated with important postoperative complications such as hyperalgesia, vomiting and/or nausea and ventilatory depression. These can reduce the patient’s comfort and increase the need for postoperative analgesics and prolong the postoperative stay [27].

Patients with spontaneous ventilation avoid these complications, proving that spontaneous ventilation has a series of beneficial effects. The resulting ventilation/perfusion mismatch increases the risk of hypoxemia, but is preserved in awake patients using spontaneous ventilation. This is due to a more efficient contraction of the dependent hemidiaphragm and the increase in the alveolar pressure with mechanical ventilation attenuates the efficiency of the hypoxic pulmonary vasoconstriction (HPV) [28].

Hypercapnia is a central component in non-intubated thoracic surgery related to hypventilation. However, ‘permissive hypercapnia’ is frequently used in ventilatory strategies for patients under OLV. It has been suggested that permissive hypercapnia may improve haemodynamics and the ventilation/perfusion match and protective effects in inflammatory response [29].

Hypercapnia should be avoided in patients with elevated pulmonary pressures, major cardiac rhythm disturbances or increased intracranial pressure. Patients awake or sedated, with normal right ventricular function and PaCO2 levels up to 70 mmHg are likely to tolerate it well [30].

Moreover, the perioperative surgical stress response could be attenuated in non-intubated patients undergoing VATS as a result of the reduced postoperative stress hormones and pro-inflammatory mediators related to mechanical ventilation [31, 32]. Spontaneous
ventilation is less aggressive than mechanical ventilation and only reductions of tidal volume and subsequently decreased peak airway pressures have significant effects on alveolar tumor necrosis factor, soluble intercellular adhesion molecule 1 and IL-10 concentrations after OLV and in the postoperative course [20]. In the non-intubated patient, a regional anaesthetic technique is mandatory. Thoracic epidural anaesthesia, paravertebral block and intercostal block all improve postoperatively respiratory function, absence of diaphragmatic relaxation and mechanical irritation of the airways ensuring better ventilation than with general anaesthesia. Regional anaesthesia attenuates immunosuppression and neuroendocrine stress with potential improvement of survival and cancer recurrence [33]. However, regional anaesthetic techniques are used in general anaesthesia and these beneficial effects are not exclusive to non-intubated surgery.

PATHOPHYSIOLOGY OF SURGICAL PNEUMOTHORAX IN NON-INTEUBATED PATIENTS

In an anaesthetized patient, OLV in a lateral decubitus position produces a ventilation/perfusion mismatch and the non-dependent lung increases its compliance while the dependent lung receives better perfusion as a result of gravity, increasing the risk of hypoxaemia. Nevertheless, the match of ventilation/perfusion is preserved in non-intubated spontaneous ventilation due to a more efficient contraction of the dependent hemidiaphragm; consequently ventilation and perfusion is better maintained in the dependent lung [34].

In the anaesthetized patient, the non-dependent lung receives zero ventilation and perfusion decreases due to HPV, gravity, surgical interference and pre-existing disease. However, hypoxaemia is frequent due to the collapsed lung as it continues to be perfused without being ventilated, which may lead to a large right-to-left intrapulmonary shunt. The lung volume can have deleterious effects on HPV. If the delivered tidal volume and the total positive end-expiratory result in overdistension of the ventilated alveoli, blood flow may be diverted to the atelectatic or hypoxic alveoli, attenuating the HPV response and worsening V/Q mismatch. Volatile anaesthetics have been reported to inhibit HPV and may promote hypoxaemia during OLV [35].

In non-intubated patients, once the incision is opened, the negative pressure is lost and paradoxical respiration occurs. On expiration, gas flow may enter the lung in the open hemithorax and on inspiration the reversal phenomenon occurs. The continuous atmospheric pressure environment in the open hemithorax leads to mediastinal movement towards the dependent hemithorax during inspiration. However, the modified pattern of ventilation induced by the open pneumothorax is well tolerated.

The perfusion to the dependent ventilated lung is better in non-intubated surgery because of the low or negative pressure in this lung. Respiratory efficiency and lung recruitment is increased by the maintained diaphragmatic function. Intrapulmonary shunt and hypoxaemia is reduced compared with OLV-intubated patients.

There is a risk of experiencing hypercapnia rebreathing effect from the initial paradoxical respiration and hypventilation due to collapse of the operated lung and sedation. However, it is rare to need support ventilation, and this is only needed in patients with severe restrictive or obstructive ventilatory defect. Ventilatory obstruction and hyperinflation in dependent ventilated lung produce intrinsic positive end-expiratory pressure, decrease mediastinal shift, increasing functional residual capacity and decreasing atelectasis and thus the risk of hypoxaemia is reduced contrary to the restrictive ventilatory defect [3].

ANAESTHESIA TECHNIQUES IN NON-INTEUBATED THORACIC SURGERY

The realization of non-intubated thoracic surgery requires the implementation of a protocol including description of indications-contraindications, exclusion criteria, patient consent, the most appropriate anaesthetic technique for the surgical procedure and criteria for conversion to general anaesthesia. Moreover, the acceptance and knowledge of this method by surgeons with extensive experience in VATS is required.

The criteria for non-intubated VATS in minor or pleural procedures are different from those in major pulmonary resections and recommendations have been established in patients with increased risk, using general anaesthesia. Inclusion criteria included all selected patients in whom the avoidance of morbidity of conventional thoracotomy and the risk of intubated general anaesthesia could be reduced [3, 36–39].

Patient exclusion criteria are given in Table 1 (according to our experience and the experience from other major research groups).

Non-intubated VATS entails thoracoscopic procedures performed under regional anaesthetic techniques in spontaneously breathing patients. The regional anaesthetic techniques consist of local anaesthesia, intercostal nerve blocks, interpleural block, paravertebral blocks or thoracic epidural anaesthesia [12, 40–42]. The anaesthetic technique used is what will determine whether there is a need for sedation. In uniportal surgery, a single intercostal space block is usually sufficient to control the afferent nerves. These local anaesthetic techniques are insufficient to control the pleural surface, other level handling intercostal spaces, hilar and bronchi, so additional sedation and analgesia is required [12, 18, 41, 42]. Our preliminary results with uniportal VATS suggest that a good management is obtained with an infiltration of a single intercostal space under thoracoscopic view and topic anaesthesia on the surface of the lung and the hilum. Oxygen (6–9 l/min) is

Table 1: Exclusion criteria in non-intubated VATS major pulmonary resections

| Patients with expected difficult airway management evaluated by the anaesthesiologists |
| Haemodynamically unstable patients |
| Obesity (body mass index >30) |
| Inexperienced and poorly cooperative surgical team |
| Coagulopathy (international normalized ratio >1.5) |
| Persistent cough or high airway secretion |
| Patient with elevated risk of regurgitation |
| Neurological disorders: risk of seizure, unable to cooperate, intracranial mass or brain oedema |
| Extensive pleural adhesions or previous pulmonary resections (related to surgeons’ skills) |
| Hypoxaemia (PaO₂ <60) or hypercarbia (PCO₂ >50) |
| Central hypoventilation syndrome |
| Any contraindications for use of regional anaesthesia technique specifically selected |
| Procedures requiring lung isolation to protect the contralateral lung from contamination |
supplied via facial mask. Standard monitoring must include electrocardiogram, non-invasive blood pressure, pulse oximetry and respiratory rate, along with an approximation of the end-tidal carbon dioxide with a catheter placed in one nostril. The pharmacological management is based on a target-controlled infusion of remifentanil and propofol, with a premedication of midazolam (0.15–0.25 mg/kg) and atropine (0.01 mg/kg) 15 min before anaesthesia, adjusting real-time rate of infusion with the aggressiveness of each period during the surgery. The use of a nebulization of 5 ml of lidocaine 2% 30 min before helps to avoid coughing that could be troublesome when performing lung traction and intense hilar manipulation during surgery [18].

A greater extension of the regional block in thoracic surgery is achieved by paravertebral blocking. Using this technique with a single administration of local anaesthetic level T3–T5, a block of several intercostal spaces is achieved in order to avoid any reaction of the patient due to the surgical incision.

None of these techniques are able to achieve an analgesic block and allow the performance of thoracic surgery without sedation. Hypnotic doses administered are similar to general anaesthesia, in this case using more than light sedation or anxiolysis, we use the term monitored anaesthesia care (MAC). This term also includes the possibility of using anaesthetics and opioids for sedation and the use of supraglottic devices to improve ventilation and prevent obstruction of the airway [18, 37–42].

The majority of the reported techniques in thoracic surgery with non-intubated and spontaneously breathing patients include epidural anaesthesia in their strategies. This technique allows to achieve a more extensive and deeper blockade, and depending on the placement level (usually T3–T5), the dosage and the volume of the anaesthetic administered can be adjusted [13–15]. The epidural anaesthesia has allowed surgeons to perform numerous procedures in thoracic surgery with patients awake and with minimal sedation. However, major pulmonary resections (lobectomy or pneumonectomy) are not possible without a MAC protocol [37, 43]. The combination of hypnotic drugs (mainly propofol) and ultra-short action opioids (remifentanil) in a continuous perfusion is indispensable because the epidural anaesthesia does not block the phrenic nerve nor the vagus nerve, which are the main nerves responsible for the cough reflex [42]. The peripheral manipulation of the lung tissue does not produce a high degree of stimulation to the vagus nerve, and for this reason, the peripheral resections of small nodules or other minor resection are susceptible to be performed in the patients awake. However, the bronchi and the trachea can highly stimulate this nerve and their manipulation can generate haemodynamic effects and coughing, which can impede the realization of the surgery. Apart from a deep sedation, the different groups that perform VATS lobectomies try to control the cough reflex, either through intrathoracic vagus nerve infiltration or pre-emptive inhalation of nebulization of lidocaine 2% for 30 min before surgery. In shorter procedures, an incremental intravenous remifentanil is applied in place of vagal block for the sake of decreasing cough suppression duration. However, intrathoracic vagal block is easily performed and comes with minimal side effects [3, 36–38]. Spontaneous ventilation in non-intubated patients can be done with oxygen support through the use of a facial mask. With deeper sedation, supraglottic devices are well tolerated and useful, as nasopharyngeal tube or Guedel cannula, to prevent positive pressure in the airway during the expiration and to avoid the insufflation of the collapsed lung. Laryngeal mask can be useful in selected patients. It can be a good alternative to facial mask in case of deeper sedation, because it guarantees a permeable airway before reaching the glottis. It allows spontaneous ventilation with monitoring ventilator pressure and volumes, therefore reducing the risk of bronchoaspiration. Moreover, in case of hypoxaemia or hypercapnia due to hypoventilation, we can introduce ventilation with support pressure. A positive pressure of 5–8 mmHg is sufficient to improve the lung volumes in the lung with spontaneous ventilation and non-intubated patient. It even allows for the introduction of a bronchoscopy-guided endobronchial blockade in the operated lung while administering positive pressure with OLV and without intubation [44].

We can conclude that, to perform a major pulmonary resection in non-intubated patients, MAC is mandatory, due to the absence of the phrenic and vagus nerve blockade. However, we do not know if a minimal sedation in combination with epidural anaesthesia and the phrenic and vagus nerves blockade is enough. This anaesthetic technique could provide a stress-free surgery, due to the existence of a complete sensitive blockade of the whole innervation of the thorax [45].

Nowadays, our team is introducing a new anaesthetic protocol while aiming to perform a totally awake major thoracic surgery, using epidural anaesthesia (level T3–T4, sensitive blockade T2–T10) in combination with vagus and phrenic nerve blockades under ultrasound control at the neck. In Table 2, we show the different anaesthetic possibilities in non-intubated thoracic surgery both from our point of view and through other published studies.

### CONVERSION TO INTUBATED GENERAL ANAESTHESIA

To ensure patient safety, a clearly defined protocol for elective or urgent intubation must be determined prior to the operation.

**Table 2:** Anaesthesia techniques for VATS minor and major pulmonary resections

<table>
<thead>
<tr>
<th>Anaesthesia technique</th>
<th>Minor resection procedures</th>
<th>Multiportal VATS lobectomy</th>
<th>Uniportal VATS lobectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local infiltration – intercostal block</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sedation</td>
<td>++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>MAC</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Paravertebral blockade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sedation</td>
<td>++</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>MAC</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Epidural blockade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sedation</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>MAC</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Epidural + nerve vagus blockade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td>N</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sedation</td>
<td>N</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>MAC</td>
<td>N</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Epidural + phrenic + vagus nerve blockade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td>N</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Sedation</td>
<td>N</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>MAC</td>
<td>N</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

Not recommended (–), possible (+), technical feasibility (++), recommended (+++), not proved (?), not necessary (N)
MAC: monitored anaesthesia care.
Sometimes, intraoperative conversion to general anaesthesia is inevitable and the surgical team must have a plan to minimize the risk to the patient (Table 3). Intubation in the lateral decubitus position is a technical challenge to anaesthesiologists. The anaesthesiologist must be skilled in placing a double-lumen tube, laryngeal mask, fibreoptic bronchoscopic intubation, video-assisted system management and endobronchial blocker in order to securely choose the most appropriate device depending on the patient’s airway, the position of the patient, time of completion of the procedure and the causes that have led to the conversion to general anaesthesia.

In any case, continuous and effective communication between surgical and anaesthetic teams is paramount.

### FROM AWAKE MINOR PROCEDURES TO NON-INTUBATED UNIPORTAL LOBECTOMIES

Awake or non-intubated surgical procedures must be divided in minor procedures such as pleural, lung or mediastinal biopsies, resections of peripheral nodules, thymectomies, lung volume reduction surgery and major anatomical pulmonary resections. A summary of anaesthetic protocols employed in both awake and non-intubated procedures as well as postoperative results from different groups are given in Table 4.

#### Minor procedures

The most common thoracoscopic procedures reported in the literature performed under local anaesthesia or sedation have been for the management of pleural effusions [60] or talc pleurodesis [46].

The first series of thoracoscopic pulmonary resections under local anaesthesia were published in 1997, showing a low rate of complications and shorter hospital stay [47]. Mukaida et al. [48] reported several cases of VATS for pneumothorax under local and epidural anaesthesia in 1998 in high-risk patients contraindicated for general anaesthesia. In this publication, patients experienced well-managed pain and cough reflex and well-maintained breathing during the surgery.

Pompeo and Mineo have been the most active team in awake surgery for non-anatomic pulmonary resections. They showed the superiority of the awake thoracoscopic surgery in the treatment of pleural effusion [61], pulmonary biopsies [54], mediastinal biopsies [14], metastatic tumours [15], spontaneous pneumothorax [62], empyema thoraci [51] and emphysematous bulla including lung volume reduction surgery [63].

In 2007, in a small randomized trial [50], these authors compared VATS bullectomy and pleural abrasion performed in awake patients with spontaneous pneumothorax and epidural anaesthesia versus patients under general anaesthesia with OLV. Results of this study have suggested that awake VATS bullectomy with pleural abrasion was feasible and resulted in shorter hospital stay as well as reduced procedure-related costs equal to procedures performed under general anaesthesia.

Other non-intubated minor VATS procedures were also reported by other authors to manage pericardial effusion [64] and hyperhidrosis [65].

### Resection of pulmonary nodules

Mineo and Pompeo published exhaustive reviews describing the state-of-the-art awake surgery for nodule resection and other minor procedures [4, 66, 67]. In these reviews, quicker recovery, less morbidity and the possibility of offering surgery to very high-risk patients for general anaesthesia are all shown. They also highlight the potential impact of attenuation of the immune response and the decreasing levels of hormones released by stress that could lead to future oncological perspectives. They emphasize the use of this technique when considering the development of fast-track programmes and outpatient thoracic surgery.

In a randomized study performed by Pompeo et al. [9], 60 patients with pulmonary nodules were randomized to undergo wedge resection through either non-intubation with epidural or general anaesthesia with double-lumen intubation with epidural. They concluded that the awake thoracoscopic approach was superior in terms of the global in-operating theatre time, postoperative recovery, need for nursing care and overall hospital stay in comparison with the conventional thoracoscopic approach under general anaesthesia. In the awake group, 47% of the patients were discharged within the second postoperative day compared with 17% of the patients in the general anaesthesia group.

Bilateral surgery can also be performed without intubation. Tsai and Chen [68], reported a case of bilateral resection with a non-intubated thoracoscopic technique. It is logical to think that prolonged sequential single-lung breathing could lead to excessive hypoxia and hypercapnia when major pulmonary resections are needed, being feasible and well tolerated when performing a bilateral wedge resection.

Other small series of patients show advantages of the non-intubated procedures over conventional anaesthesia [53, 69].

#### Table 3: Reasons for conversion to general anaesthesia

- Surgical complications: major bleeding, strong pleural adhesions, large tumours, lack of progress during the intervention related to the surgeon’s thoracoscopic experience
- Severe hypoxaemia (PaO2 <60%), hypercapnia (PaCO2 >80) and acidosis (pH <7.1)
- Haemodynamic instability: severe hypotension, cardiac index decreased, intractable arrhythmias and right ventricular failure
- Persistent cough that creates difficulty or prevents performing surgery
- Excessive movement of the diaphragm or mediastinum, causing unsafe surgery
- Failure of regional block where MAC is insufficient and decreases the safety of the procedure
- Inability to collapse the lung: paradoxically maintained ventilation, Positive end-expiratory pressure intrinsic, dynamic hyperinflation ...

#### Thymectomy in myasthenic patients

In patients with myasthenia gravis, muscle relaxants are associated with prolonged mechanical ventilation or reintubation. In addition, risks of intubated general anaesthesia could be increased when an anterior mediastinal mass compresses the airway after the muscle relaxation. Several authors reported the feasibility and satisfactory results with awake VATS thymectomy, using thoracic epidural anaesthesia and avoiding muscle relaxants [10, 17, 49].
<table>
<thead>
<tr>
<th>Name of author</th>
<th>Year of publication</th>
<th>Number of patients</th>
<th>Anaesthetic technique</th>
<th>Epidural</th>
<th>Other blockades</th>
<th>Oxygen supplement</th>
<th>Surgical procedure</th>
<th>% conversion to general anaesthesia</th>
<th>Days of HOS (mean)</th>
<th>Main outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tschopp [46]</td>
<td>1997</td>
<td>89</td>
<td>Local anaesthesia</td>
<td>No</td>
<td>Not reported</td>
<td>Spontaneous pneumothorax (talc insufflation)</td>
<td>0</td>
<td>5.2</td>
<td>9 redo procedures reported No mortality Minor morbidity: 3 patients (10%) No mortality No major complications No mortality</td>
<td></td>
</tr>
<tr>
<td>Nezu [47]</td>
<td>1997</td>
<td>34</td>
<td>Local anaesthesia + sedation</td>
<td>No</td>
<td>Nasal cannula</td>
<td>Spontaneous pneumothorax (bleb resection)</td>
<td>0</td>
<td>4.5</td>
<td>No mortality</td>
<td></td>
</tr>
<tr>
<td>Smit [81]</td>
<td>1998</td>
<td>45</td>
<td>Local anaesthesia</td>
<td>No</td>
<td>Nasal cannula</td>
<td>Pleural diseases</td>
<td>0</td>
<td>4.1</td>
<td>No mortality</td>
<td></td>
</tr>
<tr>
<td>Mukaida [48]</td>
<td>1998</td>
<td>4</td>
<td>Awake</td>
<td>Yes</td>
<td>Local anaesthesia</td>
<td>Facial mask</td>
<td>Secondary pneumothorax surgery (only one bleb resection)</td>
<td>0</td>
<td>Not reported</td>
<td>No significant postoperative complications No mortality No postoperative complications No mortality No mortality</td>
</tr>
<tr>
<td>Tsunezuka [49]</td>
<td>2004</td>
<td>3</td>
<td>Awake</td>
<td>Yes</td>
<td>Local anaesthesia (occasionally)</td>
<td>Room air or naso-oral oxygen</td>
<td>Extended thymectomy</td>
<td>0</td>
<td>Not reported</td>
<td>No mortality</td>
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<tr>
<td>Pompeo [9]</td>
<td>2004</td>
<td>30</td>
<td>Awake</td>
<td>Yes</td>
<td>Local anaesthesia (occasionally)</td>
<td>Ventimask</td>
<td>Wedge resections</td>
<td>6.7 (n = 2)</td>
<td>2</td>
<td>No mortality</td>
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<td>Sakuraba [82]</td>
<td>2006</td>
<td>32</td>
<td>Local anaesthesia</td>
<td>No</td>
<td>Not reported</td>
<td>Tubercular effusions</td>
<td>0</td>
<td>Not reported</td>
<td>No major complications No mortality</td>
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<td>Mineo [13]</td>
<td>2006</td>
<td>12</td>
<td>Awake</td>
<td>Yes</td>
<td>Venturimask/face</td>
<td>Non-resectional lung volume reduction surgery</td>
<td>8.3 (n = 1)</td>
<td>7.8</td>
<td>No mortality</td>
<td></td>
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<tr>
<td>Pompeo [15]</td>
<td>2007</td>
<td>14</td>
<td>Awake</td>
<td>Yes</td>
<td>Local anaesthesia (occasionally)</td>
<td>Ventimask</td>
<td>Thoracoscopic metastasectomy</td>
<td>0</td>
<td>2.5</td>
<td>No major morbidity No mortality No significant complications No mortality No mortality 2% hospital mortality No operative mortality Morbidity: 3% No mortality</td>
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<td>Pompeo [50]</td>
<td>2007</td>
<td>21</td>
<td>Awake</td>
<td>Yes</td>
<td>Local anaesthesia (occasionally)</td>
<td>Not reported</td>
<td>Spontaneous pneumothorax</td>
<td>0</td>
<td>2</td>
<td>No major morbidity No mortality No significant complications No mortality No mortality 2% hospital mortality No operative mortality Morbidity: 3% No mortality</td>
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<td>Al-Abdullatief [17]</td>
<td>2007</td>
<td>79</td>
<td>Awake</td>
<td>Yes</td>
<td>Stellate ganglion (occasionally)</td>
<td>Facemask</td>
<td>Major and minor resections</td>
<td>11 (n = 9)</td>
<td>1.5</td>
<td>No major morbidity No mortality No significant complications No mortality No mortality 2% hospital mortality No operative mortality Morbidity: 3% No mortality</td>
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<td>Katlic [83]</td>
<td>2010</td>
<td>353</td>
<td>Local anaesthesia + sedation</td>
<td>No</td>
<td>Facemask</td>
<td>Minor thoracoscopic procedures (including lung biopsy and pleural diseases)</td>
<td>0</td>
<td>Not reported</td>
<td>No major morbidity No mortality No significant complications No mortality No mortality 2% hospital mortality No operative mortality Morbidity: 3% No mortality</td>
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<td>Tacconi [51]</td>
<td>2010</td>
<td>19</td>
<td>Awake</td>
<td>Yes (15) No (4)</td>
<td>Paravertebral block (4)</td>
<td>Ventimask</td>
<td>Decortication for empyema thoracis</td>
<td>0</td>
<td>6</td>
<td>No major morbidity No mortality</td>
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<td>Macchiarini [11]</td>
<td>2010</td>
<td>20</td>
<td>Awake</td>
<td>Yes</td>
<td>Automized local anaesthesia</td>
<td>Facemask</td>
<td>Tracheal resections</td>
<td>5 (n = 1)</td>
<td>3.1</td>
<td>No early complications Minor morbidity: 20% No mortality</td>
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<td>Pompeo [52]</td>
<td>2011</td>
<td>41</td>
<td>Awake</td>
<td>Yes</td>
<td>Local anaesthesia (2)</td>
<td>Venturi mask face</td>
<td>Non-resectional lung volume reduction surgery</td>
<td>4.9 (n = 2)</td>
<td>6</td>
<td>No mortality</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>Number</td>
<td>Anesthesia Type</td>
<td>Vagal Blockade</td>
<td>Ventilation Mask</td>
<td>Procedure Description</td>
<td>Mortality</td>
<td>Complications</td>
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<tr>
<td>Chen [16]</td>
<td>2011</td>
<td>30</td>
<td>Regional anaesthesia + targeted sedation</td>
<td>Yes</td>
<td>Vagal blockade</td>
<td>Thoracoscopic lobectomies VTG wedge resections</td>
<td>10.0 (n = 3)</td>
<td>5.9</td>
<td></td>
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<td>Dong [53]</td>
<td>2012</td>
<td>22</td>
<td>Regional anaesthesia + targeted sedation</td>
<td>Yes</td>
<td>Vagal blockade</td>
<td>Nasopharyngeal airway and face maskVTG wedge resections</td>
<td>0</td>
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<td>Tseng [84]</td>
<td>2012</td>
<td>46</td>
<td>Regional anaesthesia + targeted sedation</td>
<td>Yes</td>
<td>Vagal blockade</td>
<td>Needleoscopic VTG for lung nodule surgery (wedge resections)</td>
<td>4.3 (n = 2)</td>
<td>2.7</td>
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<td>2012</td>
<td>15</td>
<td>Awake</td>
<td>Yes</td>
<td>Local anaesthesia</td>
<td>Secondary spontaneous pneumothorax (bleb resection and abrasion)</td>
<td>0</td>
<td>2.6</td>
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<td>2012</td>
<td>285</td>
<td>Regional anaesthesia + targeted sedation</td>
<td>Yes</td>
<td>Vagal blockade</td>
<td>Major and minor procedures</td>
<td>4.9 (n = 14)</td>
<td>Not reported</td>
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<td>2013</td>
<td>30</td>
<td>Awake</td>
<td>Yes (20)</td>
<td>Intercostal blockade (10)</td>
<td>Thoracoscopic lung biopsy of interstitial lung disease</td>
<td>0</td>
<td>1.4</td>
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<td>2013</td>
<td>36</td>
<td>Regional anaesthesia + targeted sedation</td>
<td>Yes</td>
<td>Vagal blockade</td>
<td>VATS lobectomies in geriatric patients</td>
<td>2.8 (n = 1)</td>
<td>6.7</td>
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<td>Chen [56]</td>
<td>2014</td>
<td>446</td>
<td>Regional anaesthesia + targeted sedation</td>
<td>Yes (290)</td>
<td>Vagal blockade</td>
<td>Major and minor procedures</td>
<td>3.6 (n = 16)</td>
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<td>Vagal blockade</td>
<td>Minor and major (1 lobectomy)</td>
<td>3 (n = 1)</td>
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<td>2014</td>
<td>15</td>
<td>Regional anaesthesia + sedation</td>
<td>Yes</td>
<td>Vagal blockade</td>
<td>Anatomic segmentectomies</td>
<td>0</td>
<td>5</td>
<td></td>
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<td>Ambrogi [59]</td>
<td>2014</td>
<td>40</td>
<td>Awake</td>
<td>Yes (20)</td>
<td>Intercostal blockade (20)</td>
<td>VATS biopsy of interstitial lung disease (wedge resections)</td>
<td>5 (n = 1)</td>
<td>3.7</td>
<td></td>
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<td>Gonzalez-Rivas unpublished</td>
<td>2014</td>
<td>30</td>
<td>Regional or local anaesthesia + targeted sedation</td>
<td>No</td>
<td>Intercostal blockade</td>
<td>Major pulmonary resections</td>
<td>2 (6.6%)</td>
<td>3</td>
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</table>
Emphysema and lung volume reduction surgery

Lung volume reduction surgery carries a high rate of complications. The use of lung resection techniques for emphysematous patients under spontaneous ventilation is controversial. In 2006, Mineo et al. [13] published a novel technique to perform lung volume reduction surgery in awake patients under thoracic epidural anaesthesia. Their further studies included a randomized trial showing that awake non-resectional lung volume reduction surgery caused significantly more functional improvement, including an increase in several parameters of pulmonary function tests. In comparison with conventional intubated general anaesthesia, durations of postoperative air leak and hospital stay were significantly shorter in awake technique, while 3-year survival was comparable [52, 70].

Major anatomic pulmonary resections by conventional video-assisted thoracoscopic surgery

There is an important difference between the performance of minor procedures and anatomical resections in non-intubated patients. The risk of a surgical complication during a wedge or lung biopsy cannot be compared with the potential risk of major bleeding in the pulmonary hilum during a lobectomy in a patient with spontaneous ventilation. The performance of a lobectomy with mediastinal lymph node dissection by VATS is usually associated with longer operative time, frequent lung traction and hilar manipulation, which can trigger cough reflex in awake patients. Rates of conversion to intubated general anaesthesia were reported between 2.3 and 10.0%, depending on the type of procedure and the experience of the team. Previous experience in VATS lobectomy and minor awake thoracoscopic procedures is crucial.

To date, only four groups have reported results of major pulmonary resections. Al-abdullatief et al. reported a series of 79 patients operated on with no intubation and epidural catheter, with blockade of stellate ganglion. This series includes open procedures such as thoracotomies and sternotomies, VATS lobectomies, thymectomies and even pneumonectomies but these authors do not clearly describe which cases were performed by VATS. They reported no negligible intraoperative complications such as cardiac arrest or right ventricle opening and an 11% rate of conversion to general anaesthesia. Only 5 patients went to the intensive care unit and they conclude that this is a feasible and safe technique reducing hospitalization and minimizing costs [17].

Chen et al. reported their initial experience with non-intubated major resections in 2011. They used a three-port VATS technique and epidural pain control and ipsilateral intrathoracic vagal block to control the cough reflex [16]. They concluded that non-intubated VATS lobectomy and segmentectomy with mediastinal lymphadenectomy for early stage non-small-cell lung cancer could be safely performed [5].

The same group published the largest series of non-intubated surgery, which included 446 patients within a period of 4 years [56]. A total of 290 of the patients were controlled with epidural and the rest with intercostal block. The median induction time was 30 min with epidural and 10 min with intercostal block. Reasons for conversion to general anaesthesia (3.6%) were excessive mediastinal movement (7 patients), persistent hypoxaemia (2 patients), severe adhesions (2 patients), ineffective epidural (3 patients), bleeding (2 patients) and tachypnoea (1 patient). This group also published several reviews about non-intubated major and minor pulmonary resections [43].

In the study of Wu et al., the feasibility of non-intubated major procedures in geriatric patients was studied. They compared 36 non-intubated cases with 48 patients under tracheal intubation. Stridor was noted in 3 patients and delirium in 4 in the intubated group, but none occurred in the non-intubated group. Surgical operative time and hospital stay showed similar results [55].

Recently, Liu et al. conducted a randomized trial with 354 patients, comparing the results of awake thoracoscopic surgery, minor resections and lobectomy, versus those of a control group treated under general anaesthesia with single-lung ventilation. In their study, 174 patients underwent the awake approach, while the remaining 180 patients served as a control group. Seven (4%) of the 174 subjects in the awake group required conversion to general anaesthesia with single-lung ventilation. The authors demonstrated that concentration of tumour necrosis factor-α level in the bronchoalveolar lavage fluid was lower and fasting time and duration of postoperative antibiotics were shorter in a non-intubated group. The rates of postoperative complications in the awake group were significantly lower than those of the control group [71].

Several authors published their experience with the non-intubated technique for anatomical segmentectomy with good postoperative results [58, 72]. Most of the cases were early stage tumours and the median hospital stay was 5 days.

Non-intubated uniportal video-assisted thoracoscopic surgery

In recent years, VATS has evolved from a multiport to a single incision approach, representing the least invasive way to operate on lung pathologies. Uniportal or single incision VATS has been shown to reduce postoperative pain, residual paresthesia and hospital stay compared with conventional multiport VATS [73, 74].

The choice of a single incision technique combined with the avoidance of general anaesthesia could minimize even more the invasiveness of the procedure. There are several case reports published showing that non-intubated uniportal wedge resection can be performed in an awake patient. Rocco et al. described the awake technique of nodule resection, under mild sedation and giving a single-shot epidural regional anaesthesia. Under guidance provided by a bronchoscope, a Fogarty balloon was positioned to occlude the lobar bronchus to facilitate collapse of the targeted parenchyma [75]. Another case report published by the same author includes a young patient operated on for pneumothorax, using a similar technique, and noting that the patient could be discharged on the first postoperative day [41].

Galvez et al. [76] describe a case of uniportal awake wedge resection under epidural anaesthesia in a patient with a previous contralateral lobectomy with the aim to prevent mechanical ventilation in the remaining lobe in the contralateral side.

Our group published the first non-intubated single port VATS lobectomy in a patient with lung cancer, discharging the patient 36 h after the operation with excellent postoperative recovery. For this first case, we used a laryngeal mask and sevoflurane but now we manage the patients by using a facial mask, propofol and remifentanil [18] [Fig. 1; Video 1].

These non-intubated major pulmonary resections must only be performed by very experienced uniportal thoracoscopic surgeons, preferably skilled and experienced with complex or advanced...
cases and bleeding control through uniportal VATS [77, 78]. We consider it very important to reduce the surgical and anaesthetic trauma in high-risk patients for general intubated anaesthesia such as elderly patients or those with poor pulmonary function [79].

When performing a uniportal approach, we can easily apply blockade of the single intercostal space under thoracoscopic view. The importance of avoiding epidural thoracic blockade is obvious: if we are able to control postoperative pain without opioids, it will result in faster recovery and return to daily activities.

Recently, Ambrogi et al. compared interstitial biopsies under uniportal VATS with intercostal block versus three-port VATS technique with epidural. They concluded that uniportal VATS biopsies under intercostal block provide better intraoperative and postoperative outcomes [59].

Hung et al. reported a series of 32 patients with peripheral nodules operated by uniportal VATS with no epidural, using a combination of intercostal nerve block and intrathoracic vagal block with bupivacaine. Within this group of patients, there was only one major pulmonary resection attempted by single port, but it was converted to a multiport VATS. Conversion to intubated general anaesthesia was necessary in 1 patient (vigorous diaphragmatic and mediastinal movement). Postoperative pain intensity was evaluated, using a numeric pain intensity scale showing little pain [57].

The same group also published an anatomical uniportal VATS anterior segmentectomy in a patient with lung cancer. They used intercostal and vagus blockade, a single incision and a wound protector, 5 mm 30° scope and endoscopic instruments [80].

Our initial experience with uniportal VATS major pulmonary resections is promising (Table 4). Most of the cases were lobectomies for lung cancer (Video 2). The mean surgical time was 90.8 ± 22.3 min. Only 2 patients were converted to traditional intubated surgery (6.6%): one because of bleeding controlled by uniportal VATS, and the other because of excessive movement of the diaphragm. These 2 cases were finished by uniportal VATS and postoperative outcomes were satisfactory.

CONCLUSIONS

According to the literature and based on our experience, non-intubated VATS major and minor resections are safe procedures, technically feasible and successfully managed with facial mask, regional anaesthesia and sedation. Patients remain stable intraoperatively, without severe hypoxemia or hypercapnia, coughing or a decreased mediastinal shift throughout the operation.

Although the long-term benefits remain unclear, we suggest that it can potentially be an attractive alternative of intubated one-lung ventilated thoracoscopic surgery, especially for patients with high risk for intubation. In a modern era of minimally invasive thoracoscopic procedures, adequate training of awake or non-intubated VATS surgery will be essential. Uniportal VATS and non-intubated spontaneous breathing represent a less invasive approach to consider. This surgical and anaesthetic combination is on the fast track to becoming an indispensable and fully reliable tool within thoracic surgery programmes.

Conflict of interest: none declared.

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