Anesthesia in Thoracic Surgery

Changes of Paradigms

Manuel Granell Gil
Mert Şentürk
Editors

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Contents

Introduction

This book presents the new paradigms and objectives that have been raised during the last decades in all aspects of thoracic anesthesia. Thus, the objectives and protocols related to airway management, mechanical ventilation, and analgesia have changed a lot, but also the new monitoring methods such as ultrasound, hemodynamic, and NIRS. Some new aspects of perioperative management in thoracic surgery are also reviewed, such as the pharmacology of neuromuscular relaxants, anticoagulants, platelet antiaggregants, as well as the prevention and treatment of infections.

In addition, this book includes new preoperative approaches that consist of Fastrack, Prehabilitation, and evaluation of perioperative risks. Finally, the most frequent thoracic surgical procedures that range from a classic approach to the most modern robotic surgery are reviewed.

Part I

Introduction

Pulmonary Resection: From Classical Approaches to Robotic Surgery

1

Ricardo Guijarro Jorge and Alper Toker

1.1 The Thoracic Surgery in Antiquity

Today pulmonary resections and other intrathoracic procedures are performed in many hospitals around the world, but only 50 years ago opening the thorax in an operating room was a risky venture that very few people did because it caused a pneumothorax. For many patients it meant death. Because there was no endotracheal intubation and ventilation with endotracheal pressure, once pneumothorax occurred, and a severe cardiorespiratory failure appeared.

Celso, practicing vivisection in criminals, something fashionable in Alexandria 300 years before Christ, said: *You can open the abdomen with the subject alive, but as soon as the knife opens the thorax, a kind of membrane that separates the inside from the outside , the individual loses his life immediately* ... [1].

Intimately related to the evolution of thoracic surgery has gone the development of breathing concepts and open pneumothorax. The findings in pulmonary physiology allowed surgeons to operate a chest safely.

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Acute empyema was undoubtedly the first of thoracic diseases to be surgically treated successfully in the history of mankind and the Hippocratic texts masterfully describe the procedure [2]:

> *When the purulent collection protrudes externally, you should make an incision in the most protuberant site, evacuate the pus and make washes with warm wine and oil through an inserted metallic stem. Each day you will repeat the washing until on the twelfth day when you will remove the metal stem and insert a strip of linen, until the wound closes.*

When the purulent effusion did not kill the patient and became chronic, with the corresponding fibrin deposit that trapped the lung, thoracic adhesions developed, in that moment thoracic openings could be made and thus doesn't developed open pneumothorax without the disastrous consequences previously exposed.

Until the last part of the nineteenth century, draining empyema was the only disease treatable in thoracic surgery, lung resection surgery simply was not possible, nevertheless Vesalius already in 1543 in the last chapter of his De Humanis Corporis Factory said that the lungs could be insufflated in the animals if the trachea was intubated by a cane, thus giving the solution to the problem of open pneumothorax [3]. However, this concept was not used in the operating rooms until 350 years later.

The first successful attempt to open a thorax with a certain control of the consequences of the open pneumothorax was not made until 1904, when Ferdinand Sauerbruch, von Mikulicz's assistant in Breslau, built a room (bunker) of negative pressure to make the intervention [4]. In this operating room where the patient's head was outside isolated from the wall with rubber rings, which allowed the surgical team to work under the atmospheric pressure so avoided lung collapse, with the deleterious consequences.

Rudolph Nissen from Berlin is considered to be the first surgeon to successfully perform a pneumonectomy in 1931. The patient was a 12-year-old girl with bronchiectasis of a whole lung [5].

On April 5, 1933 Evarts A. Graham of St. Louis performed this operation for the first time treating lung cancer. His patient, a colleague gynecologist, survived even the longer than the surgeon himself.

The era of pulmonary lobectomies began with Harold Brunn, who in 1929 published his first experiences with six cases of bronchiectasis, using chest tubes as an innovation in the postoperative period.

In the last century, lung cancer was a rarity and the entire panorama of lung diseases was dominated by tuberculosis, an important infectious-contagious illness that killed one young person every 17 in Europe.

The classic approach for lung resection surgery is the posterolateral thoracotomy [6], an incision that follows the superior ridge of the sixth rib and it is equidistant from the apex and the base, allowing a suitable exposure of the intrathoracic organs. This is the preferred approach by a large majority of current thoracic surgeons.

A variant of the posterolateral thoracotomy is the thoracotomy without muscular division, in which the muscles of thoracic wall are widely exposed and are not sectioned, they are simply separated to access the interior of the thorax. This variant is widely used in lung resection surgery.

1.2 Classical Thoracoscopy

The beginning of thoracoscopy can be fixed in 1910 [7], just over 100 years ago, the Swedish Hans Christian Jacobeus published his experiences in the diagnosis and treatment of pleural effusions and lysis of adhesions in tuberculous patients to achieve lung collapse in the therapeutic pneumothorax, the fashionable intervention practiced in that time to achieve the collapse of the lung caverns that originated in this terrible pandemic. To do this, he inserted a cystoscope into the thorax and with a galvanocautery he performed the section of pleural adhesions.

The development of light transmission by optical fiber, the improvements in cold light illumination, and the progress of video cameras with increasingly powerful chips allowed the expansion of endoscopic surgery after the 1990s and today thoracoscopy has become a basic and very important surgical tool for the thoracic surgeon.

The structure of a traditional thoracoscope is similar to a laparoscope. It is a tube with a working channel and a cold light at its end. It therefore allows obtaining biopsies directed at specific lesions and therefore rarely gives a false positive when biopsied macroscopically visible lesions. It allowed blind pleural biopsies (that failed 80% of the time), became almost infallible procedures. In addition, when it comes to effusions of malignant origin, the cell weight itself causes the implants to be found in the diaphragms and cardio and costophrenic sinuses, places forbidden to blind biopsies.

However, this instrumentation had important limitations, mainly that only the surgeon who looked through the eyepiece could see what he made, the rest of the staff present in the operating room were not aware of the findings and therefore was difficult to teach, another limitation is that the visual field and the power of light was limited, since it is a telescope, without the possibility of zooming or of increasing the image digitally.

1.3 Tracheal Surgery

Despite the historical development of the tracheostomy, trachea was the last organ in the development cardiothoracic surgery field. After the improvements of endotracheal anesthesia, pulmonary surgery evolved a lot in the 1930s. In the 1960s tracheal surgery advanced a lot. In the article published at 1990. It has been demonstrated that technical capabilities increased the resection rates of the tracheal tumors to 63% for squamous cell carcinoma, to 75% for adenoid cystic carcinoma, and to 90% for other tumors [8].

Repair of the bronchus after a chest trauma demonstrated the feasibility of airway reconstruction. In 1949, Griffith [9] operated on a strictured bronchus and resected the stenotic part and anastomosed the bronchus 3 months after the bronchial rupture. Treatment of other delayed bronchial rupture repairs followed this operation [9]. The developing technic helped in the surgery for low-grade tumors and eventually to carcinoma, as sleeve lobectomy evolved [10]. At this time of

surgical development one of the major difficulties was the maintenance of safe, continuous, stable ventilation during the procedure, especially during surgery for intrathoracic trachea.

Surgical technical developments in tracheal surgery took a long time during its evolution. Dermal grafts, polyethylene tubes or patches were used to repair the tracheal defects. The replacement of the trachea has been described very recently, although there has not been much developments despite all efforts [11]. Grillo performed autopsy studies in humans, and demonstrated that more than half of the adult trachea can be resected safely and reconstruction of the defect is possible by full mobilization of structures limiting its movement [12]. He claimed that the mobilization could be possible through right hilar dissection and division of the right pulmonary ligament; division of the left main bronchus; and freeing pulmonary vessels from the pericardium. Tracheal mobilization by keeping the anatomic principles intact—pretracheal mobilization, cervical flexion, hilar dissection and intrapericardial freeing, and even with the mobility of detached main bronchi—aggressive approaches possible. By using these principles, surgeons developed themselves with series of resections and reconstructions.

In 1957 Barclay resected 5 cm of trachea and carina to treat recurrent adenoid cystic carcinoma [13]. Authors claimed that by the pulmonary ligament division, anastomosis of the trachea to the right main bronchus became possible. Later the left main bronchus was anastomosed end-to-side to the bronchus intermedius. During the operation intermittent ventilation provided enough support for the second anastomosis.

Carinal pneumonectomy for bronchogenic carcinoma became further established with significant series reported by Jensik [14]. The initial high operative mortality of a form of adult respiratory distress syndrome, *postpneumonectomy pulmonary edema*, of noncardiogenic origin, caused nearly 30% mortality rate. It has been claimed that the condition could be treated with prompt nitric oxide and believed to be the result of barotrauma. This complication became less frequent with close cooperation of anesthesiologist an surgeons and mortality decreased to 10%. Barclay's anesthesiology team developed the use of cross-field ventilation with the endotracheal intubation. They used intermittent ventilation during the implantation of the left main bronchus into the bronchus intermedius. They later recognized that the preceding development of one-lung anesthesia provided the groundwork for carinal anesthesia. Baumann and Forster are the first to describe systematic approaches to anesthesia for tracheal surgery. These included intubation through distal tracheostomy and operative field ventilation. Cross-table ventilation strategies were fully developed by Grillo [15]. The use of cardiopulmonary bypass for tracheal and especially carinal resections has been performed in the earlier experiences. With the developments of the surgical techniques and extensive experience in the tracheal surgery, leaders in the field such as Eschapasse, Grillo, Pearson, and Perelman found bypass to be unnecessary.

1.4 Lung Transplantation

Hardy was the first surgeon to dare lung transplantation in human in 1963. Fifty-eight year old life sentence in prisoner who had lung cancer in the left main airway and obstructing distal airways. Operation was uncomplicated and the recipient began spontaneous ventilation. Chest X-rays and an angiogram confirmed that the transplanted lung was very well ventilated and perfused [16]. The surgery was demonstrated to be doable however, immunosuppressive regimen was consisted of azathioprine, prednisone, and cobalt radiation to the mediastinum and thymus. The first experience did not have a good outcome probably mostly due to inadequate infection control.

The patient developed kidney failure and died on postoperative day eighteen. An autopsy showed no evidence of rejection. Over the next ten years, 36 lung transplants were performed worldwide and only two recipients survived more than a month. The major cause of death was problems at the healing of the bronchial anastomosis, which sometimes caused bronchosvascular fistula by causing infection on the adjacent vessels anastomosis.

In 1981, Shumway and Reitz from Stanford University performed two successful heart-lung transplants and the recipients were still alive 1 year after operation [17]. Shumway claimed that the success was the result of refinement of surgical techniques and the development of cyclosporine. Cyclosporine caused a reduction in the amount of necessary steroids and the negative impact of steroids on anastomotic healing disappeared.

In 1983, the Toronto Lung Transplant Group performed the first successful lung transplantation [18]. Cooper provided the standardization of lung transplantation in the clinical practice. Candidates under age 50, with disabling disease of the lung, and have a life expectancy of less than 6 months were selected as first transplant patients. The first transplant patient survived for another 4 years. This success was remarkably encouraging but the early rejection noticed in that particular patient was the first sign of future obstacles and limitations. First bilateral lung transplantation was also performed at Toronto General Hospital in 1986. Later in 1988 cystic fibrosis patients were recruited and transplanted again at the same center. In the meantime, in Europe, active lung transplant programs were being developed.

By 1990, more than 400 lung transplants were performed around the world. Lung transplant operations increased in mid 1990s and the number of annual transplants became around 1400 per year. In recent years, the number of transplants per year has increased to 2200. Outcomes also have improved due to refinement of surgical techniques, donor and recipient selection criteria, and medical therapies. The median survival of patients who had lung transplant between 2000 and 2006 was 5.5 years compared to 4 years transplanted between 1988 and 1994. However, outcomes in the modern era remain far from ideal as chronic rejection has emerged as the leading obstacle to better long-term.

1.5 The Video Assisted Thoracic Surgery (VATS)

The introduction of digital technology changed all this, since the instruments allowed to amplify the image, to show it on monitors, with which everyone present in the operating room participated, the lenses allowed different angulations and even interventions for teaching could be recorded. The optical industry allowed to reduce the diameter of the instruments and even make them flexible like the fiber-optic bronchoscope. The modern camcorders are based on CCD technology (charged coupled device), which allows converting the analog signal into digital one, the use of three different chips achieves the chromatic agreement that is needed in these cases. There were also advances in lighting systems and thus could be obtained "cold light" at 300 W, which allowed to see even in very bloody fields, because when there is blood in the operating field, it absorbs 50% of the light.

Many authors point out laparoscopic cholecystectomy, carried out for the first time in 1985 by Muhe in West Germany, as the event that defines the growth of Minimally Invasive Surgery, it is from the 1980s when this type of surgery lives its true development and begins its expansion. In less than a decade, in 1993, In United States minimally invasive cholecystectomies reached a percentage of 67% of all cholecystectomy procedures. Never before had there been such a revolution in the field of surgery, nor had a new technique achieved such rapid universal acceptance.

The clear advantages of this surgery could be summarized as: reduction of the systemic inflammatory response, reduction of postoperative pain, minor complications of the surgical wound and shorter hospital stay have made it rapidly spread, because it reduces hospital costs, decreases nosocomial infections and also the waiting lists.

It also has disadvantages such as: difficulty in spatial perception (interventions are controlled through monitors), loss of binocular vision, although with robotics three-dimensional perception is achieved, inability to palpate (it is necessary to learn to feel through the instruments), debatable oncological management and in case of major bleeding, its difficult control by these means.

Minimally Invasive Surgery is not of exclusive use in the digestive system, although it is where it has developed most, today it is used by all surgical specialties, including ours.

VATS (video assisted thoracic surgery), also called CVT (videothoracoscopic surgery), has been used widely in the diagnosis of pleural diseases, interstitial diseases and in the evaluation of the solitary pulmonary nodule. That is, minor thoracic procedures. Its use in parenchymal diseases of the type of lung cancer, however, is much more controversial, from a philosophical and also technical point of view. Today its use is not widespread, 40% of surgeons use posterolateral thoracotomy in more than 50% of their cases and less than 30% of thoracic surgeons (mainly young) use VATS in less than 5% of their total of cases, therefore we are far from affirming that VATS becomes a standard procedure in thoracic surgery.

In classic thoracoscopy or diagnostic pleuroscopy, access is usually made by the sixth or seventh intercostal space, anterior axillary line, and can be modified

depending on the location of the pathology. It can be done with local anesthesia assisted by anesthesiologist.

VATS surgery involves the use of two or three ports and a minithoracotomy (also called utility thoracotomy) for the extraction of the piece, general anesthesia and selective intubation. No costal retractors are used, this is the main difference with classic thoracotomy approaches. All dissection is done by visualizing the monitor not under direct vision. In the classic three port video-assisted thoracoscopic approach, described by Landrenau, these are placed in the middle, anterior and posterior axillary line. The orientation of the instruments and the thoracoscope is key to the success of the intervention. The trocars and the endoscope should be located away from the lesion to have a panoramic view and provide space to manipulate the tissue.

The definition of VATS lobectomy is ambiguous, even today. The technique varies in terms of the number of incisions (from 1 to 5), length of the utility thoracotomy (the largest wound through which the resected piece is removed) of 4–10 cm and the degree of separation of the ribs and if even if separator is used (Finocchietto) or not. A technical advance of VATS is to use it through a single incision (VATS uni or monoportal) [19].

The first publications on lobectomies using VATS are from the 1990s, since then the technique of major resections by video-assisted thoracoscopy has found strong resistance to its implantation by most of the thoracic surgeons, all derived from two unknowns: the radicalism as regards to cancer surgery and patient safety. Few data have been published that directly compare VATS lobectomy with that performed by posterolateral thoracotomy and even less compared with those performed by robotic surgery [20].

In 2008, a meta-analysis was carried out by the Society of Minimally Invasive Cardiothoracic Surgery, collecting all randomized and non-randomized studies, comparing the results of VATS with conventional open surgery for lung resection surgery in lung cancer. These were the results presented as follows [21]:

1. The prognosis was better when VATS was compared to conventional open surgery if these series were compared in non-randomized studies, but not in randomized studies.
2. Postoperative complications were significantly lower in the VATS group, when compared with conventional surgery in randomized and non-randomized studies.
3. Blood loss was lower with VATS, but there was no difference in the incidence of cases of excessive blood loss or in the number of redo interventions due to bleeding.
4. The postoperative pain was much lower in the group operated by VATS and as a consequence a significant decrease in the use of analgesics.
5. The postoperative vital capacity improved dramatically in the VATS group, this beneficial effect was maintained until after the first year after surgery. However, comparing vital capacity after 3 years with classic approaches, there were no significant differences.

6. The hospital stay was shorter in the VATS group (although the operating time was longer than conventional classic approaches).
7. The duration of postoperative stay in hospital after surgery was significantly lower in the VATS group.
8. Adjuvant chemotherapy could be administered in the VATS group safely and earlier, although there were no differences in recurrence rates compared to classical approaches.
9. There were also no differences in mortality rates if both approaches were compared.

It is clear after reading these conclusions that there is an evident benefit for minimally invasive approaches in lung cancer and that this needs adequate technological support.

There is a great variability in the use of VATS in lung resection. According to the aforementioned meta-analysis, less than 5% of all lung resections are performed with this technique, mainly by novice surgeons. Senior surgeons widely prefer classic approaches for safety reasons and also oncological resectability. However, it is fair to recognize that technological advances are increasingly driving the extension of VATS surgery in lung resection.

Perhaps one point to develop more and better in the future is studies that show the advantages of VATS in high-risk patients demonstrating that they better tolerate pulmonary resection. At a time when chemo-radiotherapy is getting more and more progress with tumor reductions that allow for rescue surgeries, showing that in these patients resection is feasible with fewer complications would be a breakthrough.

1.6 Robotic Surgery

Video-assisted thoracoscopic (VATS) lobectomy has proved itself, even through single port approach and became the shining star surgical technique during the last decade. VATS is a videoscopic surgery directed by the surgeon on the table who is controlling and manipulating the tissue. As opposed to open surgery, surgeon performs the operation by looking at a monitor, without placing a rib spreader, via one to three ports in the chest wall. Robotic surgery is a different type of minimally invasive surgery. In robotic surgery, the surgeon is at the console outside the sterile operating area. Surgeon at the console is still the director of the team and he/she is performing the operation by controlling two or more robotic arms and a camera. However, this is an indirect control of the operation. “Robot assisted thoracoscopic surgery” (RATS) has become an accepted term. The term RATS basically means the transportation of the surgeon’s ability inside a patient through “remote telemanipulators.” A sterile surgeon or physician assistant helps at the table. He/she fires the staplers, remove lymph nodes or other tissues for pathologic examinations, and help to carry out the manipulations performed by the console surgeon. Robotic surgery could be defined as a surgical procedure that a computer technology is involved in the transportation of tasks between a surgeon and a patient. In this part of the chapter, robotic surgery use in lung cancer patients, mediastinal pathologies, and for other conditions will be discussed (Table 1.1).

Table 1.1 VATS utility in different thoracic illnesses, anaesthetic management, use of drains and data for patient hospitalization

Intrathoracic conditions, suggested anesthetic management, chest drain policy, and operative settings for uniportal VATS					
Condition	Uniportal VATS	Anesthetic modality	Drain	Setting	Notes
Pleural effusion	Diagnostic	Local	Yes	Outpatient	—
		Locoregional			
Trauma	Diagnostic	General	Yes	In hospital	Hemodynamic stability
Pericardial effusion	Operative (window)	Locoregional	Yes	In hospital	Hemodynamic stability
		General			
Stage I/II empyema	Diagnostic/operative (loculations)	Local	Yes	In hospital	—
		Locoregional			
Interstitial lung disease	Operative (wedge)	Locoregional	No	Outpatient	—
Sympathectomy	Operative	Locoregional	No	Outpatient	Bilateral
Nodal biopsy	Diagnostic	General	No	In hospital	—
		Locoregional			
Lymphadenectomy	Operative	General	Yes	In hospital	—
Primary pneumothorax	Operative (pleurectomy/abrasion)	Locoregional	Yes	In hospital	—
				Outpatient	
Peripheral subpleural nodule	Operative	Locoregional	No	In hospital	Intraoperative ultrasound
				Outpatient	
Peripheral nodule (outer third of the lung)	Operative	General	No	In hospital	Intraoperative ultrasound
				Outpatient	
		Locoregional			
Chest wall lesion	Operative	General	Yes	In hospital	—

From: Rocco G. One-port (uniportal) video-assisted thoracic surgical resections. A clear advance. J Thor Cardiovasc Surg 2012; 144: 27–31
VATS video-assisted thoracic surgery

1.6.1 Concerns and Disadvantages of VATS and Why There Is a Potential to be Replaced by RATS

Lymph node dissection should be a standard technique in surgery for lung cancer however, concerns remain about the systematic approach to nodal dissection with VATS. Some studies showed that there exists no difference in the number of dissected lymph nodes and lymph node stations, when VATS is compared to thoracotomy [22, 23]. Other surgeons claimed that the dissection of the lymph nodes with VATS might be unsatisfactory [24]. Although It has been established knowledge that the extent of the dissection was not related to the oncologic outcomes; surgeons still believe that lymph node dissection is important for the proper staging and planning of the adjuvant treatment. Less experienced VATS surgeons may not demonstrate similar capabilities in lymph node dissection as thoracotomy [25].

The Cancer and Leukemia Group B study clearly demonstrated that in 15% of the patients no lymph node removed, and in more than 50% of the patients only two stations were evaluated during VATS lobectomies [26]. For a complete lung cancer surgery the number of removed or sampled lymph nodes is an important quality measure. VATS technique still needs standardization in lymph node dissection, although the instrumentation, optical systems, and teaching platforms developed efficiently. Adoption of VATS is still limited and unequivocal. The perioperative mortality, duration of hospital stay, and costs were similar between VATS and open surgeries [27]. Experienced centers and surgeons may exhibit different results for the benefit of VATS. Currently, VATS has been presented as the "standard-of-care" for the stage 1 and 2 lung cancer, but the findings do not show so. In developing countries, the most of the lung cancer operations are performed via thoracotomy. Experienced thoracic surgeons may feel difficulty in adoption of the VATS platform. Surgeons with oncological surgical expertise, knowledge, analytic minds, and capabilities to solve catastrophic and very important prognostic intraoperative events may have difficulty in adopting VATS techniques. Also, the catastrophic intraoperative complications may pose important medicolegal problem if they occur during education period of a surgeon. These complications occur frequently but they are rarely reported. Flores [28] published these rare catastrophes (13 major intraoperative complications in 633 VATS lobectomies). A catastrophic complication could be defined as causing an unplanned major surgical procedural change. These catastrophic complications included vascular injury or stapling of main pulmonary artery or bronchus instead of a lobar one. Learning curve for VATS has been studied extensively and 100–200 operations are reported to be required to achieve a level of efficiency, and for consistency more experience may be needed [29].

Duration of the postoperative stay, and morbidity may be related to surgeon's volume. That is why better outcomes are generally provided by high-volume surgeons and centers, but this could not be generalized. In general (1) difficulties in adoption, and becoming efficient, and consistent; (2) Open surgeons have no advantage in learning VATS but, their experience is highly valuable for the treatment of catastrophic intraoperative problems; and (3) the unequivocal nodal dissections. Because of above mentioned characteristics, another platform is required for minimally invasive surgery (Table 1.2).

Table 1.2 Number of operations considered necessary to acquire the skills with VATS or robotic surgery

Study, year	Lung operation	No. of operations required
Melfi and Mussi 2008	Robotic lobectomy	20
Gharagozloo et al.2009	Robotic lobectomy	20
Veronesi et al.2010	Robotic lobectomy	20
Jang et al.2011	Robotic lobectomy	6
Lee et al.2009	VATS lobectomy	30–50
Belgers et al.2010	VATS lobectomy	25–30
Petersen and Hansen 2010	VATS lobectomy	50

From: Veronesi G. Robotic lobectomy and segmentectomy for lung cancer: results and operating technique. J Thor Dis 2015; 7: 122–130

1.6.2 Robotic Lobectomy

Robotic surgeons theorized that the three-dimensional optics and the high capabilities of the robotic instrumentations could increase the capabilities of the minimally invasive surgery. They claimed that the less blood loss, less conversions to open, less catastrophes, and more radical oncological resections could be performed. At the beginning, RATS studies compared robotic lobectomies with open or muscle-sparing lobectomies [30]. Superior early outcomes with prolonged duration of operations are demonstrated. The adoption of RATS occurred unequivocally and only case series were presented to prove feasibility. The presented data suggest that robotic lobectomy may offers similar advantages as with VATS. A study comparing 106 RATS patients to 318 muscle-sparing lobectomy patients [30]. Robotic surgery patients exhibited better results in terms of postoperative morbidity (27% vs. 38%), mental quality of life, chest tube duration (1.5 vs. 3 days), and hospital stay [30]. Three different eminent RATS centers presented their experience on 325 patients with a median length of stay of 5 days, with a perioperative morbidity rate of 25%, a mortality rate of 0.3%, and a conversion rate of 8% [31]. The long-term outcomes and survival were similar at similar stages. Open surgeons welcome robotic surgery and believed that in their hands, reproducible results and similar outcomes could be produced. Yet, all the published documents demonstrate that, anatomic lung resections, including segmentectomy operations via the robotic platform are feasible and safe [32, 33]. Some studies reported superiority in the number of the mediastinal lymph nodes dissected [34–40]. Robotic surgery has been demonstrated to be feasible and safe, and morbidity and mortality to that of open surgery and VATS are comparable [41]. The miniaturized instruments with the capabilities of a surgeon wrist and help of the high-definition, three-dimensional camera, certainly increase the transportation of the surgeon's fundamental surgical abilities into the thoracic cavity. The robotic platform's exposure in a narrow operative space, with abilities to act precisely around vital organs and vessels create the difference. One of the most important series without any mortality was presented by Dylewsky. It is the earliest experience demonstrating that locally advanced disease, and complex cases, requiring pneumonectomy, chest wall resection, and sleeve resection, can be managed using RATS [42]. One important advantage of the robotic platform is the alternative

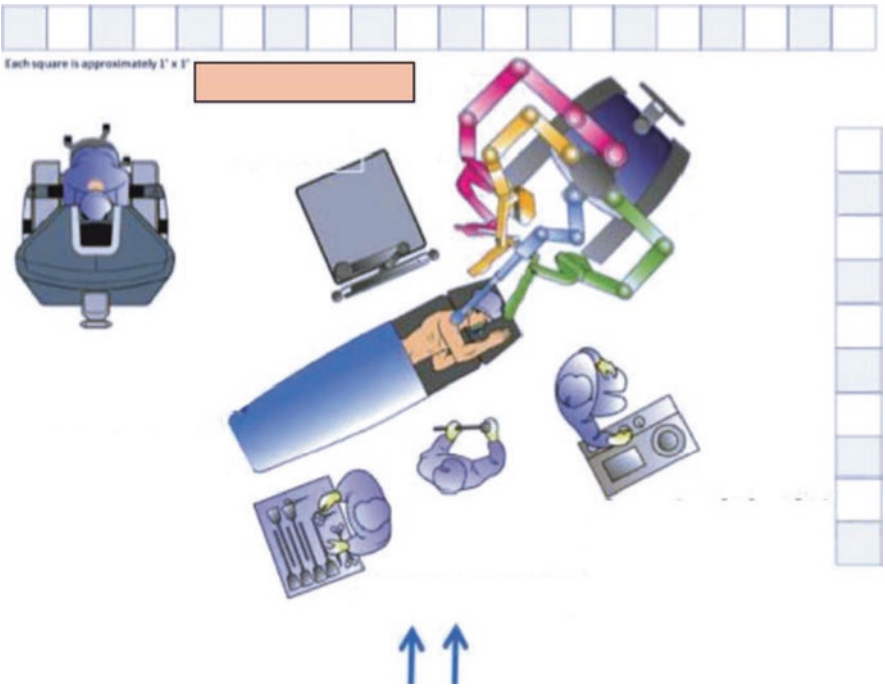

Fig. 1.1 Robotic position in right lobectomies. (From: Veronesi G. Robotic lobectomy and segmentectomy for lung cancer: results and operating technique. J Thor Dis 2015; 7: 122–130)

options when dissection is difficult or dangerous through an anterior approach. The surgeon has alternative options as in open lobectomy. For example in a right open lobectomy case, surgeon can perform the surgery through anterior approach, fissure approach, posterior approach, or superior approach. During a robotic surgery, the surgeon can shift from one approach to another during the dissection if a difficulty persists. However, only the anterior approach is possible with current VATS techniques (Fig. 1.1).

Nodal upstaging is one of the quality markers in the thoracic surgery. Most of the time, during a robotic surgery, lymph nodes are completely removed without rupturing their capsule, unlike VATS. In our study, we compared open, video-assisted and robotic-assisted thoracoscopic surgical techniques in the dissection of N1- and N2-level lymph nodes during surgery for lung cancer [43]. In this study three techniques exhibited similar results. RATS provided more lymph nodes in total and in the N1-level nodes. With all techniques similar number of mediastinal lymph nodes were removed, but only robotic-assisted thoracic surgery (RATS) provided the dissection of more station #11 and #12 lymph nodes.

The evidence suggesting better perioperative outcomes with minimally invasive thoracic surgery is becoming concrete when compared to the outcomes provided by open thoracotomy. Complications like pneumonia, pain, arrhythmia, and inflammatory markers has been shown to be reduced [15–18]. Adverse events, hospital costs,

surgery time, and length of stay were studied in the United States to compare the VATS ad RATS [44].

RATS was calculated to have higher average hospital costs per patient when compared to open and VATS. RATS took longer operative times when compared to VATS lobectomy (4.49 vs. 4.23 h). The duration of postoperative stay was similar, Cost analyses may be different in different countries mainly due to the cost of hospital stay.

1.7 Conclusions

In summary, we will expose the positive factors that help the growth of these modalities of Minimally Invasive Surgery:

- The choice of surgical method must be tailored to the patient and the surgeon, prioritizing the resolution of the problem and the patient's safety above all.
- The modern surgeon must have knowledge of all the possible procedures to be used in each situation, since his decision on the surgical technique or method is fundamental for the optimal result of the intervention.
- Virtual surgical simulators will allow surgeon training in minimally invasive surgical techniques, helping to complete and reduce the period of experimental and clinical learning.
- Digital visualization in three dimensions of the area to be intervened will be generalized, obtained by computerized axial tomography, ultrasound, magnetic resonance, etc. And it will be useful for the personalized surgical planning of each patient before his intervention.
- A greater investment of companies and hospitals in education, awareness of the group of surgeons and patient awareness, will revert in an increase in the use of all modalities of Minimally Invasive Thoracic Surgery.
- Immersive virtual surgery systems will allow obtaining a real model of the patient's pathology, taking into account the functional nature of the organs. These systems will be used as a training tool for the intervention before the operation, implying a reduction in the associated risk for them.
- It will change the current design of the implants (which will be customized and many manufactured in 3D printers) and the instruments to adapt them to Minimally Invasive Surgery techniques.
- Improve all the ergonomic aspects that surround Minimally Invasive Surgery (instruments, equipment, postural conditions, etc.).

Not all factors are positive, in terms of *negative factors* that are slowing down the rapid implementation of these procedures are:

- Budgetary pressures of hospitals, reluctant to implement new procedures that require heavy investments in properly trained time and personnel.
- The learning curve of these techniques is very slow and therefore the surgeon requires a great investment in time and effort in learning them.

- Lack of documented and documented evidence on cost-benefit studies that demonstrate the effectiveness of these procedures.
- Lack of training in Minimally Invasive Surgery procedures in the current educational system and lack of training courses to acquire an adequate level of experience.
- Conservationism of the surgeons, which feels comfortable with traditional techniques.
- Immature technologies that are still undergoing rapid evolution.
- Political measures that restrict the number of new procedures adopted.

References

1. Herbsman H. Early history of pulmonary surgery. J Hist Med. 1958;13:329–48.
2. Lindskog GE. A history of pulmonary resection. Yale J Biol Med. 1957;30:187–200.
3. He J. History and current status of mini-invasive thoracic surgery. J Thor Dis. 2011;3:115–21.
4. Logan A. The beginning of thoracic surgery. S Afr J Surg. 1986;24:136–8.
5. D'Abreu AL. Obituary. En: lives of the fellows of the Royal College of Surgeons of England. The history of cardiothoracic surgery from early times. London 1996. Edit Parth. 1996;30:468–79.
6. Sevilla S, Vaquero M, Menal P, Jiménez R. Incisiones y vías de abordaje. Arch Bronconeumol. 2011;47:21–5.
7. Jacobeus HC. Ueber die Moglichkeit die Zystoskopie bei Untersuchung seroser Honlungen anzuwenden. Munchen Med Wxhenschr, 190: 57: 2090–2092. Robotic Surgery. Squeezing into tight places. N Engl J Med. 2006;354:2099–101.
8. Grillo HC, Mathisen DJ. Primary tracheal tumors: treatment and results. Ann Thorac Surg. 1990;49:69–77.
9. Griffith JL. Fracture of the bronchus. Thorax. 1949;4:105–9.
10. Paulson DL, Shaw RR. Bronchial anastomosis and bronchoplastic procedures in the interest of preservation of lung tissue. J Thorac Surg. 1955;29:238–59.
11. Grillo HC. Tracheal replacement: a critical review. Ann Thorac Surg. 2002;73:1995–2004.
12. Grillo HC, Dignan EF, Miura T. Extensive resection and reconstruction of mediastinal trachea without prosthesis or graft: an anatomical study in man. J Thorac Cardiovasc Surg. 1964;48:741–9.
13. Barclay RS, McSwan N, Welsh TM. Tracheal reconstruction without the use of grafts. Thorax. 1957;12:177–80.
14. Jensik RJ, Faber LP, Milloy FJ, Goldin MD. Tracheal sleeve pneumonectomy for advanced carcinoma of the lung. Surg Gynecol Obstet. 1972;134:231–6.
15. Grillo HC. Circumferential resection and reconstruction of mediastinal and cervical trachea. Ann Surg. 1965;162:374–88.
16. Hachem R. *Lung transplant association of St. Louis. Second Wing. The history of lung transplantation*. https://secondwindstl.org/who-we-are/articles-by-dr-hacheem/thehistory-of-lung-transplantation/
17. Reitz B. The first successful combined heart-lung transplantation. J Thorac Cardiovasc Surg. 2011;141:867–9. https://doi.org/10.1016/j.jtcvs.2010.12.014.
18. Toronto Lung Transplant Group. Unilateral lung transplantation for pulmonary fibrosis. N Engl J Med. 1986;314:1140–5.
19. Ch C, Hsu P. Global development and current evidence of uniportal thoracoscopic surgery. J Thorac Dis. 2016;8:308–18.
20. Flores R, Alam N. Video-assisted thoracic surgery lobectomy (VATS), open thoracotomy, and the robot for lung cancer. Ann Thorac Surg. 2008;85:710–5.

21. García Berro M, Toribio C. El futuro de la Cirugía Mínimamente Invasiva. Fundaciones OPTI y FENIN. Madrid: Ed. Cyan, proyectos y producciones editoriales S.A; 2004.
22. Sagawa M, Sato M, Sakurada A, Matsumura Y, Chiaki C, Handa M, et al. A prospective trial systematic nodal dissection for lung cancer by video-assisted thoracic surgery: can it be perfect? Ann Thorac Surg. 2002;73:900–4.
23. Ramosa R, Girarda P, Masueta C, Validireb P, Gossot D. Mediastinal lymph node dissection in early-stage non-small cell lung cancer: totally thoracoscopic vs. thoracotomy. Eur J Cardiothorac Surg. 2012;41(6):1342–8.
24. Yamamoto K, Ohsumi A, Kojima F, Imanishi N, Matsuoka K, Ueda M, et al. Long-term survival after video-assisted thoracic surgery lobectomy for primary lung cancer. Ann Thorac Surg. 2010;89:353–9.
25. Bofa DJ, Dosinski AS, Paul S. Lymph node evaluation by open or video-assisted approaches in 11500 anatomic lung cancer resections. Ann Thorac Surg. 2012;94:347–53.
26. Swanson S, Herndon J, D'Amico T, Demmy T, McKenna R, Green M, et al. Video-assisted thoracic surgery lobectomy: report of CALGB 39802 – a prospective, multi-institution feasibility study. J Clin Oncol. 2007;25:4993–7.
27. Gopaldas RR, Bakaeen FG, Dao TK, et al. Video-assisted thoracoscopic versus open thoracotomy lobectomy in a cohort of 13,619 patients. Ann Thorac Surg. 2010;89:1563–70.
28. Flores RJ, Ihekweazu U, Dycoco J, et al. Video-assisted thoracoscopic surgery (VATS) lobectomy: catastrophic intraoperative complications. J Thorac Cardiovasc Surg. 2011;142:1412–7.
29. Li X, Wang J, Ferguson M. Competency versus mastery: the time course for developing proficiency in video-assisted thoracoscopic lobectomy. J Thorac Cardiovasc Surg. 2014;147:1150–4.
30. Cerfolio RJ, Brayn AS, Skylizard L, et al. Initial consecutive experience of completely portal robotic pulmonary resection with 4 arms. J Thorac Cardiovasc Surg. 2011;142:740–6.
31. Park BJ, Melfi F, Mussi A, et al. Robotic lobectomy for non small cell lung cancer (NSCLC): long term oncologic results. J Thorac Cardiovasc Surg. 2012;143:383–9.
32. Pardolesi A, Park B, Petrella F, et al. Robotic anatomic segmentectomy of the lung: technical aspects and initial results. Ann Thorac Surg. 2012;94:929–34. 4-29.
33. Toker A, Ayalp K, Uyumaz E, Kaba E, Demirhan O¨, Erus S. Robotic lung segmentectomy for malignant and benign lesions. J Thorac Dis. 2014;6(7):937–42.
34. Dylewski MR, Ohaeto AC, Pereira JF. Pulmonary resection using a total endoscopic robotic video-assisted approach. Semin Thorac Cardiovasc Surg. 2011;36–42(31):23.
35. Park BJ, Flores RM, Rusch VW. Robotic assistance for video-assisted thoracic surgical lobectomy: technique and initial results. J Thorac Cardiovasc Surg. 2006;131(1):54–9. 32.
36. Gharagozloo F, Margolis M, Tempesta B. Robot-assisted thoracoscopic lobectomy for early-stage lung cancer. Ann Thorac Surg. 2008;85(6):1880–5; discussion 1885–6.
37. Veronesi G, Galetta D, Maisonneuve P, Melfi F, Schmid RA, Borri A, et al. Four-arm robotic lobectomy for the treatment of early-stage lung cancer. J Thorac Cardiovasc Surg. 2010;140(1):19–25. 34.
38. Cerfolio RJ, Bryant AS, Skylizard L, Minnich DJ. Initial consecutive experience of completely portal robotic pulmonary resection with 4 arms. J Thorac Cardiovasc Surg. 2011;142(4):740–6. 35.
39. Louie BE, Farivar AS, Aye RW, Vallie'res E. Early experience with robotic lung resection results in similar operative outcomes and morbidity when compared with matched video-assisted thoracoscopic surgery cases. Ann Thorac Surg. 2012;93(5):1598–605. 36.
40. Jang HJ, Lee HS, Park SY, Zo JI. Comparison of the early robot-assisted lobectomy experience to video-assisted thoracic surgery lobectomy for lung cancer. Innovations. 2011;6(5):305–10.
41. Cao C, Manganas C, Ang SC, et al. A meta-analysis of unmatched and matched patients comparing video-assisted thoracoscopic lobectomy and conventional open lobectomy. Ann Cardiothorac Surg. 2012;1:16–23.
42. Dylewski MR, Ohaeto AC, Pereira JF. Pulmonary resection using a total endoscopic robotic video-assisted approach. Semin Thorac Cardiovasc Surg. 2011;23:36–42.

43. Toker A, Ozyurtkan O, Demirhan O, Ayalp K, Kaba E, Uyumaz E. Lymph node dissection in surgery for lung cancer: comparison of open vs. video-assisted vs. robotic-assisted approaches. Ann Thorac Cardiovasc Surg. 2008. doi:https://doi.org/10.5761/atcs.oa.16-00087.
44. Swanson S, Miller DL, McKenna JR Jr, et al. Comparing robotassisted thoracic surgical lobectomy with conventional video-assisted thoracic surgical lobectomy and wedge resection: results from a multihospital database (Premier). J Thorac Cardiovasc Surg. 2014;147:929–37.

2 Preoperative Evaluation: Frailty Parameters, Preoperative Neoadjuvant Therapy—Indications for Postoperative Care Unit

P. Cruz, F. De la Gala, I. Garutti, and G. Sanchez Pedrosa

2.1 Introduction

Due to the world-wide evidence of a raise of life expectancy, patients of advanced age are increasingly considered as candidates for thoracic surgery. Consistent with this demographic shift, more than 50% of patients with lung cancer are over 70. Additionally, in the elderly, less aggressive squamous cell cancer, presenting as a local disease is more frequent than in younger patients, making elderly patients candidates for curative resection. In spite of that, these patients are less likely to be proposed for surgical treatment. Assessment for thoracic surgery in frail elderly patients requires careful evaluation to individualize the morbidity and mortality risk for each patient. Surgery implies an inflammatory response and stress, which may trigger different fluctuations of homeostasis in elderly patients. In this context, it is essential a meticulous approach that identifies modifiable conditions that can be optimized to improve the outcomes of high-risk patients.

2.2 Concept of Frailty

There is a growing demand to determine frailty in surgical patients, as it can be an under-recognized key factor far beyond single comorbidities and able to predict postoperative complications and mortality. Additionally, frailty patients are at greater risk of readmission to hospital, lower quality of life after surgery and generate higher overall costs in relation to health care.

Frailty is defined as a multidimensional syndrome of physiological decline characterized by a state of increased vulnerability to physiologic stressors. Frailty patients are less able to adapt to stressors such as acute illness or trauma than

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younger patients and other older adults in non-frail condition. Importantly, advanced age by itself does not define frailty. Frailty patients often have a higher burden of disease, medical complexity and reduced tolerance for medical interventions. However, frailty patients may present with lung function and cardiac risk factors within normal range.

Frailty is even more common in surgical patients and correlates with postoperative complications and mortality. Identifying frailty in elderly patients could change the surgical treatment choice, give rise to preoperative interventions for presurgical optimization, modify their chances of surviving to surgery and improve the global outcomes. Increasing frailty in older surgical patients can predict postoperative complications (Clavien-Dindo grade > 3), reintubation, ventilator dependence, return to the operating room and 30-day mortality, and is among the most robust predictors of outcomes [1].

2.3 How Do We Assess Frailty?

Although there is no gold standard to detect frailty in elderly adults, multiple tools for frailty screening have been developed for risk assessment and epidemiological studies. Several frailty scales have proven useful predicting surgical and chemotherapy outcomes. The *Comprehensive Geriatric Assessment (CGA), Fatigue Inventory, Geriatric Depression Screen, Eastern Co-Operative Oncology Group (ECOG) Performance scale, Mini Mental State Examination and Instrumental Activities of Daily Living* have been used as methods of determining preoperative frailty. These tools have been used mainly to identify patients at high risk of suffering adverse results in different clinical contexts.

The *Modified Frailty Index* (mFI), which includes variables regarding cardiac, respiratory, metabolic and neurologic state, has been identified retrospectively as an independent risk factor of morbidity and mortality in a cohort of patients submitted to thoracic surgery [2]. It has been established as a consistent predictor of postoperative outcomes in the elderly surgical patients.

In the surgical context, the *Fried Phenotypic Frailty Criteria* (Table 2.1) and *Frailty Index (FI)* have been widely used. The first one (Frailty Phenotype), has

Table 2.1 Frailty phenotype

Frailty phenotype
• Exhaustion
• Unintentional weight loss
• Low activity (kcal)
• Slow walk (s)
• Weakness—grip strength (kg)
0 points: not frail 1–2 points: pre-frail 3–5 points: frail

been shown to anticipate increased surgical complications, length of hospital stay, and institutionalization after discharge. It is based on five predefined criteria of the presence of some signs or symptoms, it can be applied easily en the preoperative consultation without a clinical assessment. Oppositely, FI consists of a long checklist of diseases and clinical conditions (70 items) that requires a complete clinical evaluation, but consequently makes it more sensitive to changes, and has demonstrated to be more accurate to predict death or poor recovery than Frailty Phenotype after surgery in older patients. The ease of use of the Frailty Phenotype makes it a good option to start the implementation of frailty assessment in clinical practice, it offers a friendly tool to detect the frail patient who need different care or interventions. The selection of the frailty tool may depend on the feasibility and intended use in each case.

2.4 Frailty and Thoracic Surgery

Nowadays, there is limited evidence about the exact usefulness and signification of a specific frailty score for risk stratification previous to thoracic surgery. A retrospective review including more than 4000 thoracic surgeries established a significant relationship between frailty, according to mFI, and postoperative complications and death [3]. Beckert et al. performed an investigation on frailty screening in thoracic surgical patients, almost 70% were categorized as Frail or Pre-Frail according to Frailty Phenotype. Exhaustion was the most common frailty criterion, it may be related to cancer due to hypermetabolic state or depression [4]. This proportion of high-risk patients reflects a potential capacity for nutritional or exercise interventions to modify their frailty status in order to improve the outcomes. This approach should be parallel to any other preoperative optimization of concomitant clinical conditions (ischemic heart disease, congestive heart failure, renal function…). These susceptible patients may also benefit of intensive monitoring and integrated supervised care after surgery (early mobilization, optimized pain control, opioid-free analgesia or respiratory physiotherapy).

The intervention prior to an operation to optimize patient's frailty status and physiologic reserve is feasible. The ability to improve physical performance in a short-time period is especially crucial in the design of preoperative therapies. The concept of Prehabilitation has gained popularity in many surgical procedures as a part of Enhanced Recovery After Surgery (ERAS) programs, it implies preoperative exercise to reduce morbidity and mortality. In thoracic surgery this exercise programmes significantly enhances pulmonary function, and with nutritional interventions that target protein deficiency and sarcopenia have proven useful. Pulmonary rehabilitation programs of 3 weeks can improve maximum oxygen uptake and pulmonary function prior to surgery, that are the best independent factors to predict complications after thoracic surgery. However, despite the high feasibility and acceptability, the body of evidence is still poor to conclude that preoperative interventions on frailty patients submitted to thoracic surgery reduce the poor postoperative outcomes associated with frailty condition [5].

Probably, screening of frailty in thoracic surgery will become a standard of care in the short-term future. A large proportion of elderly patients submitted to thoracic surgery have risk factors related to frailty. Identifying these patients can be useful to modify the postoperative course, broaden treatment alternatives, give patients more accurate information about potential personal risks for shared decision making and to concern them to participate in prehabilitation activities, setting goals to achieve in order to improve their frailty status.

2.4.1 Implications of Neoadjuvant Therapy in Preoperative Evaluation

The treatment of patients with non-small cell lung cancer (stage IIIA [N2]) is one of the most controversial issues in thoracic oncology [6].

Surgery may be indicated as a component of treatment in some patients with locally advanced lung cancer. It usually involves extensive pulmonary resection (frequently pneumonectomy), which may include adjacent tissues or structures (e.g., chest wall, and blood vessels), and extensive lymphadenectomies or complex reconstructions of the airway, thus increasingly complexity and the risk of postoperative complications. Consequently, functional evaluation of patients before surgery is of fundamental importance in order to determine the risk of surgery and to decide whether or not surgery is a viable option. In summary, we must find a balance between the postoperative risks and benefits of surgery [7].

The preoperative algorithm proposed by the American Collage of Chest Physicians in the assessment of patients with locally advanced lung cancer who may be candidates for lung resection surgery does not differ from that used for patients with earlier stage disease [8].

An important issue to be taken into account in patients with locally advanced lung cancer is that many of them have received chemotherapy and/or radiotherapy prior to surgery as part of their multimodal treatment. Such treatment is called neoadjuvant therapy or induced therapy [9].

Neoadjuvant therapy with chemotherapy or the combination of chemotherapy and radiotherapy is used to downstage locally advanced lung cancer in order to enable as complete a tumor resection as possible [10].

The benefit of multimodal treatment regimens in terms of survival is clear [11, 12]. A meta-analysis of 12 randomized studies demonstrated that neoadjuvant chemotherapy before surgery improves survival in these patients [13]. Of all the chemotherapy regimens that can be used, platinum-based neoadjuvant options have the best rate of response. However, the question of whether preoperative use of neoadjuvant chemotherapy increases postoperative surgical risk remains controversial. While some studies conclude that this therapy is not associated with an increase in postoperative complications or death [14], other studies report that neoadjuvant therapy is associated with an increase of up to 30% in surgery-related complications and mortality, specifically when this treatment is followed by pneumonectomy, mainly right pneumonectomy [15, 16]. However, this increase in respiratory

complications and mortality is not found in more limited lung resections, such as lobectomy [17].

The increase in postoperative risk has been related not only to the type of surgery, but also to the use of neoadjuvant therapy.

Lung impairment due to chemotherapy can range from acute toxicity to subclinical modifications. Acute toxicity is a rare event (<1%) after chemotherapy and is more frequent in older patients with previous lung disease or smokers. Functional impairment is more frequently an asymptomatic event (80%) that is only detected based on a decrease in the diffusing capacity of the lung for carbon monoxide (DLCO) [18].

The chemotherapy drugs usually administered in neoadjuvant therapy have been associated with a decrease of 10–20% in DLCO values, although the spirometric values improve or remain unchanged [19].

The decrease in DLCO values after neoadjuvant chemotherapy has been associated with the potential damage to lung tissue produced by chemotherapy [20, 21]. Decreased DLCO values have been associated with an increase in postoperative respiratory complications [22, 23].

Although the mechanism of action underlying this decrease is unclear, it is believed that an inflammatory response in the lung leads to a pulmonary infiltrate that often develops within days of administration of chemotherapy. This pulmonary infiltrate is caused by a delayed-type hypersensitivity reaction that is thought to involve T lymphocytes. Furthermore, combination of these agents with radiation causes lymphocytopenia, which may in turn lead to interstitial infiltrates from opportunistic pulmonary infections, and, while the forced expiratory volume in 1 s (FEV_1) may increase, the DLCO is often reduced.

The decrease in DLCO and increase in FEV_1 after neoadjuvant therapy are due to impaired gaseous exchange in the alveoli that is not accompanied by acute changes in lung volume [24].

Radiotherapy without chemotherapy prior to surgery can also induce lung damage in patients with locally advanced lung cancer. Pneumonitis and pulmonary fibrosis caused by radiotherapy administered to the lungs in the months after this treatment are common.

Predictors of increased risk after neoadjuvant therapy include performance status, pulmonary function test results, age, underlying comorbidities, desire and determination to undergo surgery, and cardiac function. However, other than the few studies reported above, few authors have examined specific changes to pulmonary function that may predict a greater risk of pulmonary resection after neoadjuvant therapy [21].

Patients with locally advanced lung cancer whose treatment includes induced therapy (chemotherapy and/or radiotherapy) and subsequent lung resection surgery (most frequently pneumonectomy) should undergo a cardiopulmonary exercise test in addition to determination of DLCO and FEV_1 during the first step of the preoperative lung resection algorithm. Cardiopulmonary exercise testing makes it possible to detect underlying coronary artery disease, pulmonary hypertension, and ventilatory inefficiency [19].

Surgery should be delayed by 3–4 weeks in patients with decreased DLCO values after neoadjuvant therapy. This time is necessary for the pneumonitis caused by the neoadjuvant therapy to resolve and, therefore, for DLCO values to improve. The interval should not exceed 3 months, which is sufficient time for the harmful effects of fibrosis induced by radiotherapy to begin to manifest [6, 21].

2.5 Indications for Postoperative Care Unit

Lung resection surgery is increasing in recent years due to the increase of the number of patients presenting for such surgery; probably because of identify early stage lesions with potential resection rates in the order of 95%. However; populations age and comorbidities in those presenting for surgery increase in number and complexity of this surgery.

Postoperative management of thoracic surgical patients has been the subject of many debates. Thoracic surgery is one of the specialties that use Intensive Care Units (ICUs) resources more often, electively, for routine recovery and monitoring patients in the postoperative period for surveillance purposes; or emergently for postoperative major cardiorespiratory complications. In the past, postoperative care was often accomplished only in the ICU, largely due to the relatively high incidence of complications; however, a significant increase in the number of patients presenting for surgical resection of their lesions and the tendency to "over-admit" patients to the ICU may result in important implications for ICU resource utilization (inappropriate bed occupation), raising hospital costs, workload, delay in surgery if UCI beds are unavailable, delaying patient's mobilization and increasing risk of nosocomial infections. Today postoperative care may now be possible for many cases without ICU admission. In addition, there is no agreement on the need for postoperative admission to an ICU after major lung resection and there are considerable differences among institutions in this respect. These decisions are probably based on current routine, availability of ICU beds, availability of trained personnel and on-call specialized physicians. Financial considerations may also play an important role because of the increased costs of intensive care.

This test is focused on two points: determine the risk factors to select the patients who should be admitted to ICU and to explain the different types of postoperative care units.

2.5.1 Postoperative Care Units: Intermediate Care vs. Intensive Care

Due to restricted availability and high cost of ICU beds, ***Intermediate-Level Care Units (IMCU)*** has become an attractive alternative for patients who do not need full ICU support. So, depending upon patients' comorbidities and the

complexity of surgery, decisions regarding postoperative care should be made well in advance. The characteristics, type, and amount of services provided depend on factors such as resource availability, institutional infrastructure, and the overall health care system. These IMCU are logistically situated between the Intensive Care Unit (ICU) and the General Ward and are named: Progressive Care Unit (PCU), High Dependency Unit (HDU), Postanesthesia Care Unit (PACU) or Dedicated-Intermediate/step down unit (SDU). The American College of Critical Care Medicine issued guidelines regarding selection criteria of patients admitted to HDUs and ICUs. Admission to the HDU should be considered for *patients who, after major surgery, are hemodynamically stable, but may require fluid resuscitation and transfusion due to major fluid shifts* and *who require close nurse monitoring during the first 24 h.* Admission to the ICU is restricted for a minority of patients requiring *hemodynamic monitoring/ventilatory support or extensive nursing care*; so these concepts could be applied in thoracic surgery.

Two distinct patterns of clinical pathways have been reported in thoracic surgery:

1. Routine ICU admission of operated patients providing precautionary cardiopulmonary monitoring and assistance by highly qualified healthcare personnel
2. Selective ICU admission only for ventilatory support and/or on an emergency basis, due to major peri-operative complications, while the majority of patients are transferred to the surgical ward either after a short 2–4 h stay in the PACU (for uncomplicated cases and low-risk patients) or after a 12–36 h stay in a HDU; for higher risk cases.

So, during first 24 postoperative hours after thoracic surgery patients could be managed in three different kinds of postoperative care units, depending risk factor and kind of surgery (Table 2.2):

2.5.1.1 Postanesthesia Care Unit (PACU)

Diagnostic and staging procedures such as bronchoscopy, pleurodesis, pleural or lung biopsies, cervical mediastinoscopy, pneumothorax surgery just need to be a few hours in these units. Some patients after lobectomy or wedge resection by VATS, in absence of other major risk factors for postoperative complications can be admitted to the PACU for a limited time (less than 24 h) for monitoring and recovery from anesthesia and then be discharged to unmonitored beds afterwards without any increase in morbidity and mortality.

2.5.1.2 Dedicated Intermediate Care/Step Down Unit (SDU) or High Dependency Unit (HDU)

They are more specialized areas, offers a higher level of care than in the ward and they can provide longer care with a better balance between patient needs, staffing and monitoring (i.e. physical therapy, early ambulation, nutrition consults). The

association of Anesthetists of Great Britain and Ireland define HDU as *an area for patients who require more intensive observation, treatment and nursing care than can be provided on a general Ward*. Their general characteristics are [25]:

- These beds may be collocated within ICUs, in a stand-alone unit, or in an enhanced care area on a specialist ward. In general, it is recommended to be adjacent to the ICU.
- Monitored beds: ECG pulse-oxymeter, temperature, systemic blood pressure, oxygen and aspiration points, pumps or syringes for infusion administration of medication.
- Drug hemodynamic support.
- Non invasive ventilation modalities (CPAP, VMNI, high flow oxygen therapy).
- Trained nurses during 24 h a day, 365 days a year. It is recommended a ratio nurse/patient of 1:2–1:4.

The provision of dedicated thoracic HDUs would probably optimize the outcome and the resource utilization.

Table 2.2 Characteristics of postoperative care units

	PACU	HDU/SDU	ICU
Type of patients	Short-term critical care	Critically ill patients who do not need full ICU resources or active ICU treatment Patients with moderate to high risk of complications	Patients who need specialized organ support, or prolonged care; or for unstable patients
Location	Adjacent to the OR	Adjacent to the ICU or as part of the ICU	Independent Area
Equipment	Ventilators, CPAP, continuous monitoring (ECG, pulse-oxymeter, systemic blood pressure…). Every bed has oxygen and aspiration points	Ventilators, CPAP, invasive ventilation, continuous monitoring haemodynamic (ECG, pulse-oxymeter, systemic blood pressure…) haemodynamic support Every bed has oxygen and aspiration points	Ventilators, CPAP, invasive ventilation, continuous monitoring, specialized organ support: renal replacement, vasoactive medication use
Nurse/patient ratio	1:3	1:2	1:1
Time spent in the unit	Generally <24 h	>24 h	>24 h
Cost	Moderate	Moderate	Expensive
Staff	Critical care-trained nurses, anesthesiologist or surgeon (one resident with or without a staff)	Specially trained nurses, one resident (for eight patients) with at least one staff always present	Critical care nurses, intensivist or anesthesiologist (ratio 1:5 during the day, ratio 1:10 during de night)

ICU intensive care unit, *HDU* high dependency unit, *SDU* step/down unit, *PACU* postanesthesia care unit

2.5.1.3 ICU

Mandatory admission to ICU is based on presence of patients who require prolonged mechanical ventilation after the first 24 h or reintubation, unstable respiratory or hemodynamic patients, requiring hemodynamic and/or respiratory support. Patients with unstable condition (severe or very severe COPD or restrictive lung disease) or multiple organ dysfunction still will require management in the ICU environment. Patients undergoing high-risk thoracic surgical procedure like pneumonectomy, extended lung resection or tracheal-bronchial resection must be admitted to ICU.

It has been documented that 6–18% of patients undergoing lung resection require unplanned admission to ICUs because of **a postoperative complication**. Within the first 5 postoperative days, cardiopulmonary complications occur in as many as 15–40% of patients and markedly prolong the hospital stay. The most common reason for ICU readmission was pulmonary complication, which affected 70% patients, and the most common pulmonary complication was acute respiratory distress syndrome. The second-most common cause for ICU readmission was cardiovascular complication, which affected (12.7%). The most common cardiovascular complication was atrial fibrillation. The ICU readmission is believed to be associated with increase in hospital mortality and may predict poor outcomes.

These IMCU well equipped have proven their effectiveness in the management of high-risk thoracic surgical [25]. It provides excellent pain control facilities, detects complications early and avoids unnecessary ICU admissions. Brunelli et al. in 2005, in a single study compared outcome in a center where patients were transferred to a dedicated general thoracic surgery ward, resorting to ICU only for the management of complications requiring invasive mechanical ventilation; with other center who transferred patients to the UCI immediately after the surgery. Although, there is a reduction in total morbidity (23% vs. 35%) they observed longer postoperative hospital stay (11.5 vs. 9.7 days) and higher costs in patients admitted electively to the ICU; and the mortality did not differ. Another studies that compare elective care in the ICU, PACU, or SDU showed a decreasing trend in total morbidity (mainly cardiac and pulmonary) with ICU admission, but no change in mortality rate; however, the overall hospital costs were markedly increased [26], with the daily cost being the highest during the first 3 days in the ICU. Also, Schweizer et al. reported that effective PACU care followed by general thoracic surgery unit care could reduce the utilization of ICU from 57% to 4%; and they are not an option that compromises the health of the patient.

So, the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS) in 2009 recommended:

- Do not recommend systematic ICU admission after thoracotomy.
- Very high risk patients, patients with complications or those patients requiring support for organ failure (i.e. ventilatory mechanical assistance) should be admitted to ICU.
- Moderate to high-risk patients or patients with reduced cardiopulmonary reserve undergoing complex resection should be admitted to HDU.
- Patients who are estimated to be at low risk for complications should be referred to a PACU.

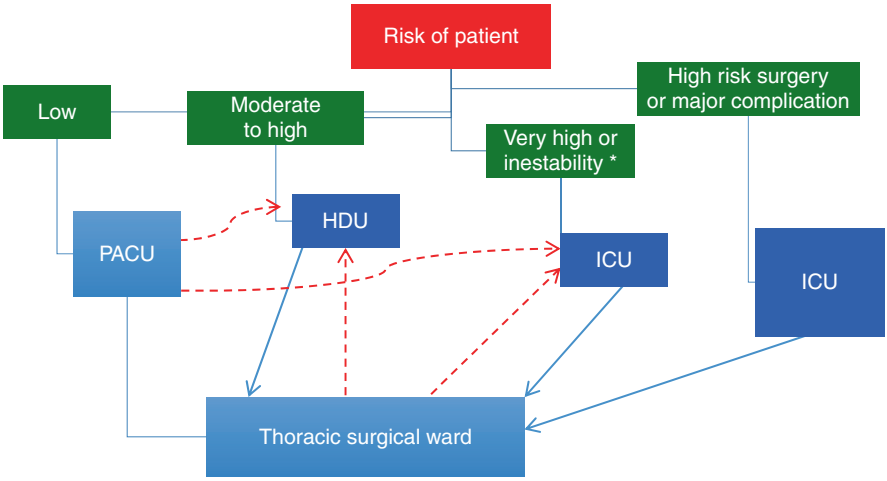

Fig. 2.1 A model of postoperative care. *PACU* postanesthesia care unit, *ICU* intensive care unit, *HDU* high dependency unit

- Then, all patients have to be sent to a dedicated thoracic unit surgery and not to general surgery ward.

A model of postoperative care are presented in Fig. 2.1.

2.5.2 Routine Admission to Intensive Care After Lung Resection? Risk Factors ICU Admission

ICU resources are limited and expensive, thus identification of which patients are most likely to benefit from ICU admission is a major issue for those involved in delivering perioperative care. The need to identify high-risk patients, develop strategies for appropriate post- operative placement, either in an ICU or suitable alternative is vital.

There are centers that all their patients are attended to an IMCU or HDU for a 24 to 48-h period with well trained personnel and the availability of noninvasive continuous monitoring, reserving ICU mainly for patients likely to develop complications needing invasive assisted ventilation or invasive monitoring; whereas in other centers, in the absence of a dedicated ward or an HDU, 'over-admit' patients to ICUs because all their patients spent the first postoperative night in the ICU and were then transferred to the thoracic surgery ward if no complication occurred.

This policy not only causes inappropriate ICU bed occupation, increasing the hospital costs. Therefore, it appears logical to try and identify the predictors of an appropriate admission to an ICU in order to rationalize intensive care management. Anticipating, and preferably predicting, which patients undergoing thoracic surgery will require intensive care postoperatively assumes considerable clinical significance and has implications for resource provision and utilization and for costs.

Few studies have bothered to determine prognostic factors associated with the need for ICU admission, and in the literature there is no consensus regarding indications for ICU. Two larges studies [27, 28] have attempted to model predictive factors for poor outcome and in-hospital death. Factors significantly associated with the occurrence of in hospital death were: age (older than 70 years old), ASA score (≥3), dyspnea score, sex (male), performance status classification, priority of surgery, extent of procedure (pneumonectomy versus lobectomy), comorbid disease (scores and cardiovascular risk assessment, mainly), diagnostic group (malignant). Some of these factors have been associated with need for admission to ICU in different studies.

- Pieretti et al. 2006 used a set of pre-established criteria for predicting the need for ICU admission and obtained satisfactory results. Multivariate analysis identified ASA score, predictive postoperative diffusion capacity of the lung for carbon monoxide (ppoDL_{CO}), and predictive postoperative product (PPP) (was obtained by multiplying the predicted postoperative percent of predicted FEV_1 by the predicted postoperative percent-of-predicted single-breath diffusing capacity of the lung for carbon monoxide) as independent predictors of a need for admission to an ICU [29].
- **Brunelli 2008**: developed and validated the first risk score for predicting the need for ICU admission after major pulmonary resection, principally for patients with lung cancer. It incorporates five preoperative adverse prognostic indicators. The risk factors were age older than 65 years (1 point), pneumonectomy (2 points), ppoFEV_1 of less than 65% (1 point), ppoDLCO of less than 50% (1 point), and cardiac comorbidity (1 point). Up to 73% of patients with a score >3 exceeded 20% ICU admission rate. This system may help in assessing and planning the need for additional postoperative resources and in modifying indicators used to determine the appropriateness of the initial transfer of postoperative patients from ICU [30].
- **Okiror 2012**: performed external validation of the scale developed and concluded that the scale of Brunelli had a moderate discriminatory power for predicting the need for ICU admission [31].
- **Pinheiro 2015**, choose the presence of one or more risk criteria: (pneumonectomy; severe/very severe COPD; severe restrictive lung disease; FEV_1 or DLCO predicted to be <40% postoperatively; SpO_2 on room air at rest <90%; need for cardiac monitoring; American Society of Anesthesiologists physical status ≥3) or postoperative characteristics (maintenance of mechanical ventilation or reintubation; acute respiratory failure or need for noninvasive ventilation; hemodynamic instability or shock; intraoperative or immediate postoperative complications). These criteria showed good accuracy, higher than 80%, for predicting ICU admission [32].

The **validated multivariate model Thoracoscore** of 2007 [27] is a scoring system to evaluate the risk of in-hospital death among adult patients after general thoracic surgery and was developed with national data. Uses only nine variables and

has good performance characteristics. It appears to be a valid clinical tool for predicting the risk of death and could also help to decided which patients must been admitted to ICU. Although not previously reported as important in determining the need for ICU care, it would seem intuitive that those patients at higher risk of mortality would be at higher risk of unplanned ICU admission.

In conclusion, the use of composite measures for predicting the need for ICU admission after pulmonary resection is feasible and accurate, uses clinical variables that do not require high technology. Accurate identification of patients at risk of postoperative ICU admission can facilitate appropriate (elective) planning in the expectation that this would lead to better postoperative monitoring and support and hence improve the outcomes of surgery in patients at risk.

In conclusion, after elective lung resection, the majority of patients can initially recover in PACU, where alternative resources and specialized teams are readily available, even in the presence of low risk factors for postoperative complications. If they are relatively stable but continued monitoring or specialized care is necessary, admission to a IMCU (SDU or HDU) is justified and cost-effective. The elective postoperative ICU management did not clearly improve the early outcome after major lung resection. Therefore, this policy should be limited to highly selected patients (through the development of risk-adjusted models and after optimization of their clinical and functional status) in order to correctly utilize the available resources in the most efficient manner. No randomized controlled trials have compared the outcome and treatment costs in similar thoracic surgical patients admitted either to the ICU, HDU, PACU or surgical wards. However, observational studies have demonstrated the appropriateness and advantages of the HDU as reflected by low mortality and morbidity rates (2–3% and 10–20%, respectively). The provision of dedicated thoracic-HDUs would probably optimize the outcome and the resource utilization and these areas should be implemented to optimize the postoperative management.

Increasing use of specialist HDUs, PACUs or similar may allow delivery of some of the important elements of ICU after thoracic elective surgery while avoiding some of its undesirable effects.

The trend for moving thoracic surgical postoperative care from the ICU towards HDUs or PACUs depends on the patient, procedure-related risk factors and on local specificities.

References

1. Congiusta DV, Palvannan P, Merchant AM. The impact of frailty on morbidity and mortality following open emergent colectomies. Biomed Res Int. 2017;2017:5126452.
2. Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. J Surg Res. 2013;183(1):104–10.
3. Dunne MJ, Abah U, Scarci M. Frailty assessment in thoracic surgery. Interact Cardiovasc Thorac Surg. 2014;18(5):667–70.
4. Beckert AK, Huisingh-Scheetz M, Thompson K, Celauro AD, Williams J, Pachwicewicz P, Ferguson MK. Screening for frailty in thoracic surgical patients. Ann Thorac Surg. 2017;103(3):956–61.

5. Sanchez-Lorente D, Navarro-Ripoll R, Guzman R, Moises J, Gimeno E, Boada M, Molins L. Prehabilitation in thoracic surgery. J Thorac Dis. 2018;10(Suppl 22):S2593–600.
6. Lewis J, Gillaspie EA, Osmundson EC, et al. Before or after: evolving neoadjuvant approaches to locally advanced non-small cell lung cancer. Front Oncol. 2018;8:5.
7. Choi H, Mazzone P. Preoperative evaluation of the patient with lung cancer being considered for lung resection. Curr Opin Anesthesiol. 2015;28:18–25.
8. Brunelli A, Kim AW, Berger KI, et al. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: diagnosis and management of lung cancer, 3rd edn: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143:e166S–90S.
9. Tong S, Qin Z, Wan M, et al. Induction chemoradiotherapy versus induction chemotherapy for potentially resectable stage IIIA (N2) non-small cell lung cancer: a systematic review and meta-analysis. J Thorac Dis. 2018;10(4):2428–36.
10. Stamatis G, Djuric D, Eberhardt W, et al. Postoperative morbidity and mortality after induction chemoradiotherapy for locally advanced lung cancer: an analysis of 350 operated patients. Eur J Cardiothorac Surg. 2002;22:292–7.
11. Ettinger DS, Akerley W, Bepler G, et al. Non-small cell lung cancer. J Natl Compr Cancer Netw. 2010;8:740–801.
12. Rosell R, Gomez-Codina J, Camps C, et al. A randomized trial comparing preoperative chemotherapy plus surgery with surgery alone in patients with non-small-cell lung cancer. N Engl J Med. 1994;330:153–8.
13. Cerfolio RJ, Bryant AS, Jones VL, et al. Pulmonary resection after concurrent chemotherapy and high dose (60Gy) radiation for non-small cell lung cancer is safe and may provide increased survival. Eur J Cardiothorac Surg. 2009;35:718–23.
14. Evans NR, Li S, Wright CD, et al. The impact of induction therapy on morbidity and operative mortality after resection of primary lung cancer. J Thorac Cardiovasc Surg. 2010;139:991–6.
15. Albain KS, Swann RS, Rusch VW, et al. Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small-cell lung cancer: a phase III randomised controlled trial. Lancet. 2009;374:379–86.
16. Stamatis G. Risks of neoadjuvant chemotherapy and radiation therapy. Thorac Surg Clin. 2008;18:71–80.
17. Brunelli A, Charloux A, Bolliger CT, et al. ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). Eur Respir J. 2009;34:17–41.
18. Bhalla KS, Wilczynski SW, Abushamaa AM, et al. Pulmonary toxicity of induction chemotherapy prior to standard or high dose chemotherapy with autologous hematopoietic support. Am J Respir Crit Care Med. 2000;161:17–25.
19. Brunelli A. Preoperative functional workup for patients with advanced lung cancer. J Thorac Dis. 2016;8(Suppl 11):S840–8.
20. Leo F, Pelosi G, Sonzogni A, et al. Structural lung damage after chemotherapy fact or fiction? Lung Cancer. 2010;67:306–10.
21. Cerfolio RJ, Talati A, Bryant AS. Changes in pulmonary function tests after neoadjuvant therapy predict postoperative complications. Ann Thorac Surg. 2009;88:930–6.
22. Takeda S, Funakoshi Y, Kadota Y, et al. Fall in diffusing capacity associated with induction therapy for lung cancer: a predictor of postoperative complication? Ann Thorac Surg. 2006;82:232–6.
23. Leo F, Solli P, Spaggiari L, et al. Respiratory function changes after chemotherapy: an additional risk for postoperative respiratory complications? Ann Thorac Surg. 2004;77:260–5.
24. Rivera MP, Detterbeck FC, Socinski MA, et al. Impact of preoperative chemotherapy on pulmonary function tests in resectable early-stage non-small cell lung cancer. Chest. 2009;135:1588–95.
25. Ghosh S, Steyn RS, Marzouk JF, Collins FJ, Rajesh PB. The effectiveness of high dependency unit in the management of high risk thoracic surgical cases. Eur J Cardiothorac Surg. 2004;25(1):123–6.

26. Jordan S, Evans TW. Predicting the need for intensive care following lung resection. Thorac Surg Clin. 2008;18(1):61–9.
27. Falcoz PE, Conti M, Brouchet L, et al. The thoracic surgery scoring system (Thoracoscore): risk model for in-hospital death in 15,183 patients requiring thoracic surgery. J Thorac Cardiovasc Surg. 2007;133(2):325–32.
28. Berrisford R, Brunelli A, Rocco G, et al. European thoracic surgery database project: modeling the risk of in hospital death following lung resection. Eur J Cardiothorac Surg. 2005;28:306–11.
29. Pieretti P, Alifano M, Roche N, Vincenzi M, Forti Parri SN, Zackova M, Boaron M, Zanello M. Predictors of an appropriate admission to an ICU after a major pulmonary resection. Respiration. 2006;73(2):157–65.
30. Brunelli A, Ferguson MK, Rocco G, Pieretti P, Vigneswaran WT, Morgan-Hughes NJ, Zanello M, Salati M. A scoring system predicting the risk for intensive care unit admission for complications after major lung resection: a multicenter analysis. Ann Thorac Surg. 2008;86(1):213–8.
31. Okiror L, Patel N, Kho P, Ladas G, Dusmet M, Jordan S, Cordingley J, Lim E. Predicting risk of intensive care unit admission after resection for non-small cell lung cancer: a validation study. Interact Cardiovasc Thorac Surg. 2012;14(1):31–3.
32. Pinheiro L, Santoro IL, Perfeito JA, Izbicki M, Ramos RP, Faresin SM. Preoperative predictive factors for intensive care unit admission after pulmonary resection. J Bras Pneumol. 2015;41(1):31–8.

Prehabilitation in Thoracic Surgery

3

Marc Licker and Ricard Navarro

3.1 Introduction

Currently, only 10–20% of patients diagnosed with lung cancer are eligible for curative surgical resection [1]. Reasons to dismiss surgical treatment are not only related to advanced disease stage or histological type (small cell carcinoma), but also to comorbidities and poor functional capacity and low aerobic capacity [2].

Besides preexisting chronic obstructive lung disease (COPD), ventilatory-induced lung injury, and fluid overload, poor aerobic fitness is an important contributory factor of postoperative pulmonary complications (PPCs) [3]. Insufficient lung expansion due to respiratory muscle weakness results in atelectasis and hypoxemia that favor bacterial proliferation and emergence of pneumonia. A growing body of evidence indicates that patients with PPCs are more likely to die from cancer recurrence after hospital discharge [4]. Local tumor recurrence and reduced life expectancy can be explained by the combined effects of surgery-induced immunosuppression and upregulation of vascular adhesion molecules owing to local bacterial growth.

From the diagnosis of lung cancer to decision to operate, there is a limited time frame to control and stabilize active illnesses such as coronary artery disease, heart failure, COPD and possible infection. Patient physiological condition can also be optimized by correcting anemia and encouraging patient to adopt a healthier life. In this chapter, we review the evolving evidence supporting the implementation of a bundle of interventions aimed to enhance patient functional status and to reduce major complications after thoracic surgery.

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3.2 Nutritional Aspects

Nutrition is a key factor in preoperative optimization and all patients should be screened for malnutrition before lung surgery. Malnutrition is a potentially modifiable risk factor for adverse outcomes after major surgery and perioperative nutritional status optimization may be helpful in decreasing postoperative complications. Malnutrition and loss of muscle mass are frequent in the preoperative period and have a negative effect on clinical outcome as a result of inadequate food intake, low level of physical activity and catabolic derangements associated with chemotherapy.

Currently, nutritional components have been included in the ERAS guidelines (Table 3.1), suggesting that when patients receive such optimized nutritional and metabolic care, the metabolic response to surgery can be minimized [5].

Nutrition assessment should be done routinely before the surgery. In cases where severe malnourishment is present (weight loss >10%, body mass index <18.5 kg/m^2 or serum albumin <30 g/L) a multidisciplinary approach is needed, as patient may benefit from delaying the surgery to supplement nutrition and improve overall status [6, 7]. This decision should be individualized in order to achieve optimal preoperative status without worsening oncologic prognosis.

The MUST (Malnutrition Universal Screening Tool) score is a five-step screening tool to identify adults, who are malnourished, at risk of malnutrition (undernutrition), or obese. It is easy to perform and useful to detect patients at risk who may specially benefit from optimizing its preoperative nutritional status. An algorithm of screening and management according to MUST score is proposed in Fig. 3.1.

Protein intake should be specifically assessed, especially in those patients attending to prehabilitation or pulmonary rehabilitation with exercise training as they have higher dietary demand. An intake of 1.5 mg/kg/day of protein is recommended and high quality protein supplementation such as whey protein isolate supplementation should be considered in those who are unable to reach such amount with dietary counselling alone.

Table 3.1 Recommendations of perioperative nutrition included in the ERAS programme

Preoperative
– Patients should be screened for nutritional status
– Oral supplements should be considered in malnourished patients, including immune-enhancing nutrition
Intraoperative
– Clear fluids should be allowed until 2 h before the surgery
– Oral carbohydrate loading may be useful to decrease insulin resistance
Postoperative
– Oral intake should be restarted as soon as possible

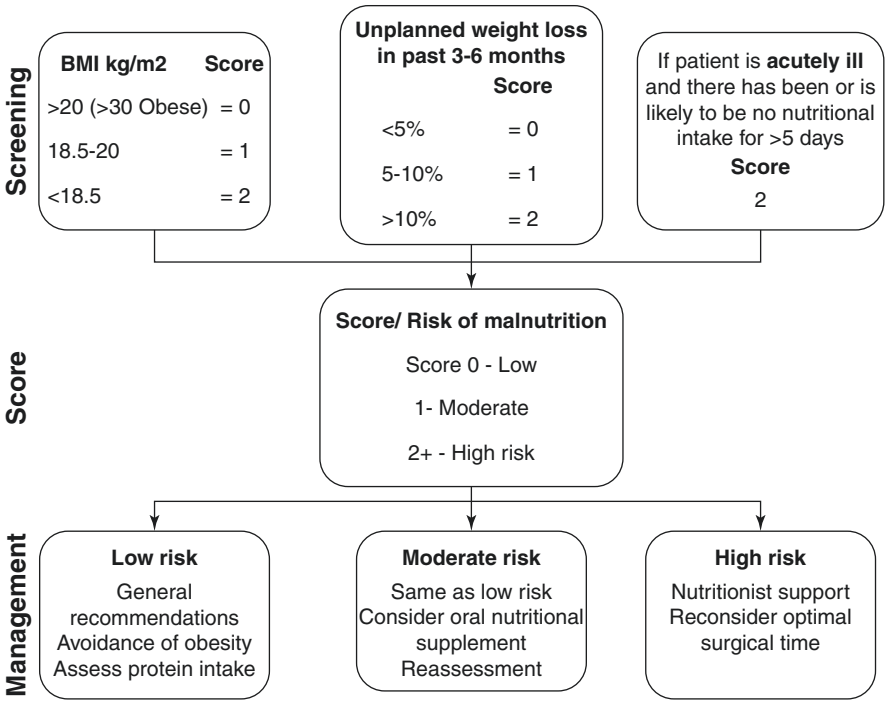

Fig. 3.1 Nutrition flowchart according to MUST (Malnutrition Universal Screening Tool) score

3.3 Education and Counselling

Preoperative counselling is useful to decrease fear, fatigue and pain and facilitate recovery and early discharge. Patient and next of kin should be instructed by dedicated health care professional trained in education therapy. These important messages should be reemphasized at preoperative visit by the surgeon, the anesthesiologist and the physiotherapist. Traditional leaflets describe the perioperative pathway including preoperative medical assessment, general nutritional and life-style recommendations, description of the surgical and anaesthetic procedures and key steps in postoperative care. Even considering that evidence is limited, it seems that patient empowerment through information booklet and diary keeping is useful to improve quality of care regarding postoperative pain [8]. Information and communication technology (ICT) and new portable applications describing the surgical pathway are being developed and may be useful tools to guide patients in the perioperative period and facilitate communication between patient and health care system.

3.4 Smoking Cessation

Smoking is a modifiable risk factor for reducing the risks for postoperative complications, and cessation has long-term health benefits. In lung surgery, smoking may be associated with a higher risk of postoperative complications, especially pulmonary postoperative complications [9]. However, evidence is controversial regarding timing of quitting smoking and some authors have even showed no significant increase in complications in current smokers, specially those who underwent intensive physiotherapy [10]. Moreover, some studies described a paradoxical effect, described as an increase in complications in patients who quit smoking a few weeks before surgery, although other authors were not able to reproduce those findings.

Current guidelines recommend that smoking should ideally be stopped at least 4 weeks before surgery. Pulmonary effects of smoking can be improved within 4 weeks of cessation. However, it is unclear what is the ideal delay between cessation and surgery because postponing the procedure could lead to an upstaging and decreased long-term survival in lung cancer patients.

Indication of surgery due to lung cancer may be a suitable moment for patients to quit smoking. Intensive behavioural support and pharmacological interventions are known to be effective strategies for smoking cessation [11]. Pharmacotherapy (nicotine substitution, varenicline, and bupropion) with behavioural support is indicated in nicotine dependent patients (those smoking within 30 min of waking, >10 cigarettes/day, history of withdrawal symptoms in previous weaning).

Few data support the use of electronic nicotine device systems (ENDS) in smoking cessation. The amount of nicotine they contain is variable and they also contain additives such as propylene glycol and vegetable glycerin, that are added to facilitate nicotine absorption but they have never been used in inhalers before. They contain less carcinogenic substances and less concentrated when compared to conventional cigarette, but concentrations can change according to the voltage and temperature. In fact, exposure to nicotine to in-vitro cells stimulates proliferation, migration, invasion and angiogenesis and it seems that cells exposed to ENDS show similar changes that those exposed to smoke. So far, there is little evidence about the perioperative management of patients who use ENDS [12]. Harm reduction and harm escalation is difficult to assess, considering the risk of toxicity and postoperative pulmonary complications and the potential risk of re-starting conventional cigarettes if withdrawn. Individual assessment considering previous smoking history, nicotine dependence, anxiety and personal predisposition to quit smoking may be helpful when determining the preoperative management of ENDS [13].

3.5 Alcohol Dependency

Apart from the well-known alcohol-induced disorders of the liver, pancreas, and nervous system, heavy drinking results in impaired immune response, nutritional defects and alteration in autonomic nervous control as well as cardiac performances.

Accordingly, alcohol abuse increases the risk of postoperative complication and may decrease long-term survival [14]. Specifically, alcohol abuse has been identified as an independent risk factor for primary acute lung injury after thoracic surgery for lung cancer.

Preoperative abstinence may help to modify at some extent the pathophysiological processes seen among alcohol abusers. Preoperative abstinence has been shown to significantly reduce the incidence of arrhythmia in the postoperative period [15]. Two to four weeks of alcohol abstinence immune control and bleeding time are both improved, and after 8 weeks, delayed hypersensitivity and the neuroendocrine stress response are restored to normal levels. Intensive alcohol cessation interventions include patient empowerment, with detailed information and recommendations regarding prophylaxis/treatment of alcohol withdrawal. Prior to elective surgery, these strategies may help to reduce postoperative complications if started at least 4 weeks before the surgery. The relatively short period of abstinence required to normalize damaged organs and systems among hazardous drinkers may explain the beneficial effects of alcohol cessation interventions on postoperative complication rates. However, there is little evidence regarding the underlying protective mechanisms of these interventions although no effect on hospital length-of-stay and mortality has been reported. Even if optimal timing of preoperative alcohol cessation remains unclear, a 4-weeks period is recommended.

3.6 Oral Hygiene

Patients with cancer—particularly those receiving chemotherapy—are prone to develop periodontitis and odontogenic foci [16]. Indeed, colonization of dental plaque by Gram-negative bacteria has been recognized as an important contributor to the oropharyngeal bacterial pool. In anesthetized patients, infrequent swallowing and lack of spontaneous movement of the tongue and jaws, can result in formation of a biofilm or plaque that constitutes a reservoir of respiratory pathogens as early as 24 h after initiation of mechanical ventilation. Moreover, the potential of recurrent nerve paralysis increases the risk of bronchial aspiration and dissemination of oral bacteria into the upper respiratory tract. Mouth rinses with chlorhexidine or brushing the teeth more than three times a day have been shown to remove and prevent the formation of biofilms [16]. A recent meta-analysis based on six studies supports the view that perioperative decontamination of the nasopharynx and/or oropharynx reduce the number of nosocomial infections in general, and specifically respiratory tract infections and surgical site infections after cardiac surgery [17]. In a recent pilot study including patients undergoing pulmonary resection, close adherence to chlorhexidine toothbrushing protocol was associated with reduced occurrence of postoperative pneumonia. Interestingly, from a nationwide database in Japan focused in major cancer surgery (N = 509,179), preoperative oral care by a dentist was associated with a decreased rate in postoperative pneumonia and all-cause mortality within 30 days of surgery [18].

3.7 Psychological Support

There is good evidence that show how negative feelings and thoughts before surgery affect outcomes after surgery [19]. Negative psychological factors such as anxiety, depression and catastrophizing have been found to predict postoperative pain. Persistent distress, depression, and pain are among the predisposing risk factors for cancer anorexia-cachexia syndrome. Moreover, lung cancer patients have one of the highest malignancy-associated suicide risks.

A wide variety of mechanisms exist by which psychological variables could affect recovery after surgery. Negative emotions can enhance pain sensations, cognitions and emotions influence behaviour (modifying adherence to physiotherapy exercises, medication intake) and are likely to influence pain and return to usual activities. Stress has also an effect on psychoneuroimmunological mechanisms (mechanisms whereby psychology interacts with the nervous and immune systems), there has been shown to be a negative association between stress and wound healing and positive influence of optimism, conscientiousness and emotional stability.

Many mediators and blood cytokine levels may play a role between psychological status and cancer. Levels of interleukin (IL)-10, IL 6, and TNF-α are more elevated in lung tumor patients than in healthy individuals and that they can be positively correlated to the depression scoring index.

It is therefore logical to think that psychological interventions that try to reduce negative emotions such as anxiety, worry about surgery and perceptions of stress, or that change patients' recovery-related behaviour, may help to improve postoperative outcomes [20]. However, there has been a long-standing controversy about whether psychiatric and psychological treatments improve the survival of patients with cancer.

Interventions described to improve psychological status are diverse and include procedural information, sensory information, behavioural instruction, cognitive intervention, relaxation techniques, hypnosis and emotion-focused interventions.

The evidence suggests that psychological preparation may be beneficial for the outcomes postoperative pain, behavioral recovery, negative affect and length of stay, and is unlikely to be harmful. However, at present, the strength of evidence is not enough to reach firm conclusions on the role of psychological preparation for surgery.

Psychological support may play a role in the multimodal prehabilitation of patients who are programmed for lung surgery. Evidence as an isolated preoperative action to improve outcomes may be hard to obtain, as action differ widely and bias is difficult to be ruled out. Nevertheless, psychological support may be useful when combined with other strategies such as exercise training, alcohol and smoking cessation, anaemia and nutrition optimization.

3.8 Physical Fitness

3.8.1 Preoperative Functional Assessment (Table 3.2)

Physical inactivity is highly prevalent in both Western and Emerging countries (31% in men and 34% in women) and has become the fourth leading risk factor for global mortality just behind hypertension, tobacco and diabetes mellitus [21].

Table 3.2 Physical assessment tools

	Cardiopulmonary exercise testing CPET	Stair climbing or other maximal stress test	Shuttle or 6-min walk test	Age-predicted HR test
	Maximal		Submaximal	
Principle	Direct measurements VO_2, VCO_2, power, HR, BP, lactate	Estimated VO_2max from highest workload, HR achieved	Distance (m)	Workload achieved at 70–85% $_{Pred}$HR
Equipment	Cycle ergometer/ treadmill Expired-Inspired gas HR (SpO_2, BP)	Stair climbing (1–6 floors) Cycle ergometer/ treadmill (SpO_2, BP, ECG)	30 m corridor Monitor HR, SpO_2, stop watch	Cycle ergometer/ treadmill Monitor HR, SpO_2, BP (ECG), stop watch
Duration	8–12 min	5–20 min	4–6 min	5–20 min
Operative risk				
Low	peakVO_2 > 20 ml/kg/min	>22 m altitude or six floors	>600 m	
Moderate	peakVO_2 15–20 ml/kg/ min	8–20 m alt. or 3–5 floors		
High	peakVO_2 10–15 ml/kg/ min	3–7 m alt. or 1–2 floors	400 m	
Very high	peakVO_2 < 10 ml/kg/min	<2.4 m alt. or 1 floor		

Approximately 3.2 million deaths are attributable each year to insufficient physical activity. Likewise, assessing physical performance has become a key parameter in preoperative risk stratification since a low level of aerobic fitness is highly predictive of early mortality and morbidity as well as prolonged hospital stay following major surgical procedures [22].

Using self-report questionnaires such as the Duke Activity Status Index or simple instruments (accelerometer, pedometer), physical fitness can be qualitatively rated in *Metabolic Equivalents of Task* (METs), one MET being equivalent to the amount of energy expanded or oxygen consumed (VO_2) at rest (0.8–1 kcal/kg/h, VO_2 2.5–3.5 mL/kg/min) [23]. Physical fitness level is correlated with long term survival regardless of the presence of cardiopulmonary disease and socioeconomic factors, mortality increasing by 13% for every 1 MET decrement in exercise capacity (starting at 8–10 METs).

Cardiopulmonary exercise testing (CPET) on a cycloergometer or a treadmill represents the gold standard test to evaluate aerobic capacity with maximal or peak oxygen consumption (peakVO_2, VO_{2max}) that reflects the integrative functioning of the pulmonary and circulatory systems, blood oxygen carrying content (hemoglobin) and skeletal muscles mechanical performances [24]. Additional parameters—peak heart rate (peakHR), peak workload, respiratory exchange ratio and anaerobic threshold (AT)—have demonstrated great interest in exercise physiology and as prognostic markers in cardio-pulmonary diseases. Noteworthy, the slope (or ratio) of ventilation to carbon dioxide [VE/VCO_2]), has been shown useful in predicting

long term survival in patients with heart failure, pulmonary hypertension and pulmonary fibrosis but also after lung cancer surgery [4, 24].

Alternate testing modalities of aerobic fitness have also been developed such as stair climbing (height of ascent, number of stairs) and the shuttle test or six minute walk test (6MWT) (Table 3.1) [23]. Simple assessment of active mobilisation (e.g., gait speed test, time up and go), the handgrip strength test, continuous recording of all motions throughout the day (with pedometer, accelerometer), the mini-mental test and subjective performance scoring status (e.g., Karnofsky Performance Status), may all provide valuable information particularly in elderly and frail patients [25].

The scientific rationale to assess aerobic capacity and functional status is to identify "unfit" subjects who might not be able to sustain the postoperative physiological impairments and the increased metabolic burden consequent to the surgical-induced neuroendocrine and inflammatory responses. Cut-off values of 15–16 ml/kg/min VO_{2max} (4 METs) and 10–12 ml/kg/min anaerobic threshold (3 METs) have been shown helpful to discriminate patients at low-moderate risk and those at high-(or very high) risk of major postoperative complications [2].

3.8.2 Causes of Poor Physical Fitness

The predicted VO_{2max} or peakVO_2 takes into account patient's age, gender, height and ideal body weight. As genetics accounts for only 20–30% of peakVO_2 values, morphometric characteristics, lifestyle and concomitant diseases are main contributory determinants of human aerobic capacity. Compared with men, VO_{2max} is approximately 15–25% lower in women and decreases on average by 5–15% per decade, the decline being sharper among sedentary persons and after the age of 60 [26].

Poor aerobic physical fitness is primarily dependent on ventilatory limitations (respiratory muscle and gas exchange capacity), cardiovascular limitations (cardiac and vascular components, hemoglobin level) and/or skeletal muscle limitations (muscular deconditioning, joint disorders or neurological deficits).

Associated with the loss of muscular mass, poor aerobic physical fitness result from the combined effects of aging, physical inactivity, metabolic and cardiopulmonary diseases as well as chemotherapy [27]. Muscle wasting (sarcopenia) often coexists with anemia, neural dysautonomia, impaired ventricular function (down-regulation of adrenergic receptors) and increased vascular stiffness (endothelial dysfunction). Systemic inflammatory processes involving the release of reactive oxygen species (ROS) and cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 have been implicated in causing to deregulation of mitochondrial function and degradation of striated muscle proteins via the ubiquitin-proteasome system and overexpression of cathepsin-L and muscle-specific E3 ligases. Interestingly, among all skeletal muscles, the diaphragm is most prone to inactivity- and inflammatory-induced proteolysis. Consequently, diaphragm weakness and atrophy result from the combined effects of ventilator-induced diaphragmatic inactivity, oxidative stress and systemic inflammation.

Following major surgery, the high levels of counterregulatory hormones (e.g., cortisol, catecholamines) lead to decreased uptake/utilization of glucose (insulino-resistance) and increased breakdown of skeletal and visceral proteins into amino acids [28]. Postoperatively, urinary nitrogen excretion increases to 40–100 g/day resulting in early muscle wasting (loss of 2–4 kg skeletal muscles) that takes several weeks for complete recovery [29]. Importantly, the acquired diaphragm dysfunction impairs the ability of the respiratory pump to compensate for an increased workload due to lung injury, fluid overload and pain. Muscle weakness and fatigability when completing minor tasks impede early deambulation, full expansion of chest and therefore promote atelectasis, hypoxemia and later pneumonia [30, 31].

3.8.3 Exercise-Induced Improvement in Muscular and Cardiopulmonary Function

Physical exercise training is currently recognized as the most efficient intervention to improve health in patients with cardiovascular, pulmonary or rheumatic diseases as well as with cancer, obesity or mental disorders [32].

Physical activity fall in four main categories: endurance (aerobic), strength (resistive), balance (stretching) and flexibility. Building up muscular mass is usually achieved by "resistive work" or static (isometric) contraction with little change in muscle length but increasing load [33]. In contrast, improvement in aerobic capacity which speeds up heart rate and breathing, is largely promoted by dynamic (isotonic) concentric and eccentric contractions leading to muscle shortening and lengthening, respectively. Some activities fit into more than one category, for example, many endurance activities also build strength and strength exercises can also help improve balance.

The energy-rich phosphate compound adenosine 6-triphosphate (ATP) is the main fuel used for cross-bridging formation between myosin and for maintenance of trans-membrane ionic gradients. Given the limited storage capacity of muscle ATP and creatinine-phosphate (CP), these high-energy compounds are continuously regenerated through anaerobic (glycolytic) and/or aerobic (oxidative) metabolic pathways. Human skeletal muscles contain at least three types of fibers that are tailored for specific contraction and working conditions: fibers expressing type I Myosin Heavy Chain (MHC) isoforms, type IIa/IIb MHC isoforms and type IIx MHC isoforms [33]. Slow twitch (ST) or type I fibers are strongly associated with endurance activity and contain large amounts of mitochondria. In contrast, fast twitch or type II fibers are involved in power production with high glycolytic activity (FTb) or in fast contractile activity coupled with higher aerobic metabolism (FTa).

3.8.3.1 Mechanisms of Exercise-Induced Improvement in Physical Fitness

In "frail" sarcopenic subjects, resistance exercises (isometric and eccentric contractions) produce hypertrophic changes in skeletal muscles and are particularly effective in restoring muscle mass, with significant improvement in strength and joint

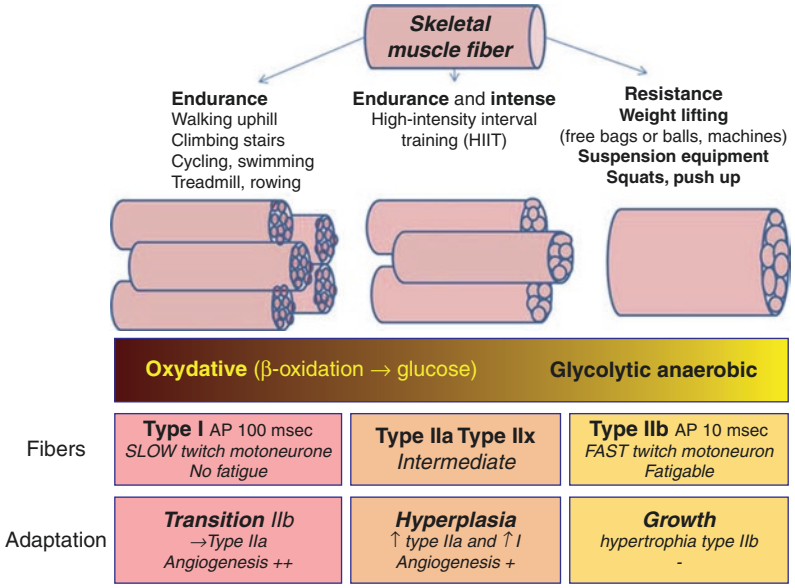

Fig. 3.2 Type of exercise and metabolic pathways muscle fibers (Russell AP, Foletta VC, Snow RJ, Wadley GD: Skeletal muscle mitochondria: a major player in exercise, health and disease. Biochimica et biophysica acta 2014, 1840(4):1276–1284)

mobility [34]. In contrast, aerobic exercises lead to minor increase in muscle mass/strength but mitigate systemic inflammation and transform cardiac and skeletal myocytes into oxidative phenotypes that result in most beneficial health benefits (Fig. 3.2). The mechanisms underlying the aerobic exercise-induced increase in VO_{2max} are multifactorial involving partial reversal of endothelial dysfunction and adrenergic receptor responsiveness, higher capillary density, restoration of insulin sensitivity and enhanced mitochondrial performances owing to tighter coupling between beta-oxidation and the tricarboxylic acid cycle. The enhanced cardiac output, facilitated tissue oxygen diffusion coupled with greater extraction of oxygen extraction by the working muscle all contribute to increase in aerobic capacity after short training periods.

In skeletal muscles, nuclear factors such as the peroxisome proliferator-activated receptor (PPAR) and their co-regulators, sirtuin (SIRT) and adenosine monophosphate activated protein kinase (AMPK) play important roles in sensing energy homeostasis, coordinating metabolic flux and up-regulation of genes involved in fatty acid uptake and oxidation [34]. Endurance exercise and electrical stimulation of ST fibers have been shown to induce PPARβ/δ expression in skeletal muscle and has been associated with muscular hyperplasia, angiogenic response and a shift towards oxidative ST fibers [35]. Likewise, structured exercise interventions have been associated with increased muscular expression of Insulin Growth Factor [IGF-1] and down-regulation of pro-inflammatory mediators such as TNF-α, IL-1β and IL-6. The enhanced IGF-1 activity could promote muscle hypertrophy or prevent muscle atrophy via an Akt- and Foxo-1-dependent signaling pathway and/or down-regulation of MuRF-1.

Table 3.3 Mechanisms of exercise-induced improvement in oxygen transport and utilization components

Oxygen transport component		Long-term (≥4 weeks	Short-term (<4 weeks)
Pulmonary	Respiratory muscles (breathing exercise)	=	=
	Diffusion capacity	=	=
	Airway obstruction, airflow trapping	=	=
	Pulmonary vascular (remodeling)	=	=
Cardiac	Systolic ventricular function (contractility)	↗or =	?
	Diastolic ventricular function (relaxation)	↗or =	?
	Peak stroke volume	↗↗	(↗)
	Peak heart rate	↗↗	↗
	Ventilatory equivalents at ventilatory threshold	↙	?
	Cardiac Output	↗↗↗ (♂>♀)	↗ (♂>♀)
	Tolerance to myocardial ischemia	↗	↗
Vascular	Endothelial function (NO release)	↗	↗
	Arterial stiffness	↙	?
	Anti-inflammatory expression	↗	?
Blood	Hemoglobin concentration	↗	=
	Ventilatory (anaerobic) threshold	↗	?
Skeletal muscle	Arterio-venous oxygen difference	= elderly ♂ ↗elderly ♀	
	Capillary density	↗	?
	Enzymes for oxidative phosphorylation	↗↗	↗
	Mitochondrial density	↗↗	↗
	Myoglobin concentration	↗	?
	Fiber transition to fatigue resistant phenotype (type I to type IIA)	Yes	?
	Muscle mass	↗	(↗)

↗: enhancement ↙: decrement =: no change

In animal models of myocardial ischemia-reperfusion, repeated bouts of intense muscular activity (equivalent to High Intensity Training [HIT]) have been demonstrated to limit the size of myocardial infarct and attenuate ventricular dysfunction [36]. Protective cellular processes are mediated by sarcolemmal and mitochondrial ATP-sensitive potassium channels, generation of antioxidants molecules (superoxide dismutase, catalase), overexpression of heat shock protein (HSP70, HSP27) and up regulation of autophagic responses (Table 3.3). Exercise-induced cardiac mitochondrial adaptations were shown to result in decreased ROS production, increasing the heart ability to tolerate high calcium levels and to sustain subsequent acute ischemic events.

Regarding the risk of ventilation-induced diaphragmatic dysfunction, Sollanek et al. elegantly demonstrated that endurance training (10 days, 60 min treadmill at 70% VO_{2max}) increased both antioxidants and HSP72 capacity while minimizing oxidative damage, protease activation, diaphragm myofiber atrophy and contractile dysfunction induced by 12 h mechanical ventilation [37]. Similar global training programs (running in a wheel) have been shown to protect against lung ischemia-reperfusion injuries, preserving alveolar-capillary permeability by limiting proinflammatory mediators (TNF-α and IL-1) and oxidative stress (superoxide dismutase activity) [38].

3.8.4 Impact of Exercise Training in Thoracic Surgery

So far, rehabilitation training conducted over 6–12 weeks has been shown successful in improving exercise tolerance and quality of life in patients with COPD, heart failure and various neuromuscular disorders [39, 40]. These programs typically entail physical exercise, breathing techniques, psychological support, nutrition counseling and education about nutrition, tobacco and alcohol withdrawal as

well as hospital clinical pathways. The term "prehabilitation" refers to all interventions that are implemented within the limited preoperative time frame with the aim to optimize patient physiological condition and secondarily speed the recovery process. The preoperative period represents a window of "therapeutic opportunity", patients are in better physical condition than in the early postoperative period and more receptive to adopt a "healthy behavior" (diet, tobacco or alcohol cessation, mobilization). Whether patient's poor physical fitness could be "reversed" within a period of 2–4 weeks by implementing structured exercise programs associated with nutritional and psychological support remains questionable [41].

Several systematic reviews have examined the impact of exercise programs in patients undergoing major surgery [42–46]. From a total of 26 RCTs, ten included patients scheduled for thoracic surgery (N = 560) and the effectiveness of respiratory muscle training (deep breathing, vital capacity maneuver, diaphragmatic and abdominal muscle exercise), endurance training (cycloergometer, treadmill) or a combination of both was evaluated compared with usual care. Training sessions varied in duration (from 6 to 45 h) and intensity (continuous or high-intensity interval, 50–90% maximal load) and were applied over 1–4 weeks before surgery. Such patient-centered physical training protocols represent attractive non-pharmacological intervention aimed to maximize preoperative physiological reserve by stimulating mitochondrial aerobic processes, reversing muscle weakness and therefore facilitating functional recovery after surgery.

Altogether, these data support favorable clinical and functional effects of physical prehabilitation as demonstrated by fewer occurrences of PPCs and shorter hospital length of stay that was associated with improved aerobic fitness and increased inspiratory muscle strength. Although perioperative mortality and cardiovascular complications rate were not reduced with prehabilitation, the reduction in early PPCs could result in important health cost savings and increased long-term survival. Minor adverse effects such as transient hypotension, low back pain or exacerbation of shoulder arthritis have been reported anecdotally. However, some patients could not perform the prescribed exercise program due to osteoarthrosis or neuromuscular disorders and others failed to exhibit beneficial effects to prehabilitation. Nonresponse to exercise training can be attributed to genetic factors, physical disabilities, adjunctive chemotherapy, low volume/low intensity or inappropriate training modality.

Despite these encouraging preliminary results, it is currently not possible to establish the optimal exercise protocol in patients requiring curative lung cancer resection given the low number of RCTs and substantial heterogeneity in training modalities and study outcomes.

3.9 Conclusions

Implementation of an effective prehabilitation protocol represents a truly multidisciplinary endeavour where anaesthetists, surgeons, oncologists, pneumologists, physiotherapists, specialist nurses and dieticians all have important roles to play [47].

Particularly in cancer patients, the time scale is often very tight to implement an integrative bundle of care including physical exercise training, nutritional adjustments, counseling on healthier life styles as well as psychological support. Importantly, delivering such evidence-based non-pharmacological interventions to optimize physiological status have the potential to improve clinical outcome by increasing the number of patients deemed suitable for curative lung cancer surgery and by reducing efficiently the occurrence of complications while speeding up the recovery process [48].

References

1. Howington JA, Blum MG, Chang AC, Balekian AA, Murthy SC. Treatment of stage I and II non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143(5 Suppl):e278S–313S.
2. Brunelli A, Charloux A, Bolliger CT, et al. The European Respiratory Society and European Society of Thoracic Surgeons clinical guidelines for evaluating fitness for radical treatment in patients with lung cancer. Eur J Cardiothorac Surg. 2009;36:181–4.
3. Agostini P, Cieslik H, Rathinam S, Bishay E, Kalkat MS, Rajesh PB, Steyn RS, Singh S, Naidu B. Postoperative pulmonary complications following thoracic surgery: are there any modifiable risk factors? Thorax. 2010;65:815–8.
4. Ellenberger C, Garofano N, Reynaud T, Triponez F, Diaper J, Bridevaux PO, Karenovics W, Licker M. Patient and procedural features predicting early and mid-term outcome after radical surgery for non-small cell lung cancer. J Thorac Dis. 2018;10:6020–9.
5. TJP B, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, Gonzalez M, Ljungqvist O, Petersen RH, Popescu WM, Slinger PD, Naidu B. Guidelines for enhanced recovery after lung surgery: recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). Eur J Cardiothorac Surg. 2018;55(1):91–115.
6. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, Fearon K, Hütterer E, Isenring E, Kaasa S, Krznaric Z, Laird B, Larsson M, Laviano A, Mühlebach S, Muscaritoli M, Oldervoll L, Ravasco P, Solheim T, Strasser F, de van der Schueren M, Preiser JC. ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 2017;36:11–48.
7. Nakagawa T, Toyazaki T, Chiba N, Ueda Y, Gotoh M. Prognostic value of body mass index and change in body weight in postoperative outcomes of lung cancer surgery. Interact Cardiovasc Thorac Surg. 2016;23:560–6.
8. Schmidt M, Eckardt R, Scholtz K, Neuner B, von Dossow-Hanfstingl V, Sehouli J, Stief CG, Wernecke KD, Spies CD, PERATECS Group. Patient empowerment improved perioperative quality of care in cancer patients aged ≥ 65 years – a randomized controlled trial. PLoS One. 2015;10:e0137824.
9. Gajdos C, Hawn MT, Campagna EJ, Henderson WG, Singh JA, Houston T. Adverse effects of smoking on postoperative outcomes in cancer patients. Ann Surg Oncol. 2012;19:1430–8.
10. Rodriguez M, Gómez-Hernandez MT, Novoa N, Jiménez MF, Aranda JL, Varela G. Refraining from smoking shortly before lobectomy has no influence on the risk of pulmonary complications: a case-control study on a matched population. Eur J Cardiothorac Surg. 2017;51:498–503.
11. Thomsen T, Villebro N, Møller AM. Interventions for preoperative smoking cessation. Cochrane Database Syst Rev. 2014;3:CD002294.
12. Zwar NA, Mendelsohn CP, Richmond RL. Supporting smoking cessation. BMJ. 2014;348:f7535.
13. Masefield S, Powell P, Jiménez-Ruiz C, Hajek P, Lewis K, Andreas S, Tønnesen P, van Schayck O, Gratziou C, Dautzenberg B, Tonstad S, Hering T, Nardini S, Fletcher M. Recommendations

to improve smoking cessation outcomes from people with lung conditions who smoke. ERJ Open Res. 2016;2:00009-2016.
14. Graf SA, Zeliadt SB, Rise PJ, Backhus LM, Zhou XH, Williams EC. Unhealthy alcohol use is associated with postoperative complications in veterans undergoing lung resection. J Thorac Dis. 2018;10:1648–56.
15. Oppedal K, Møller AM, Pedersen B, Tønnesen H. Preoperative alcohol cessation prior to elective surgery Cochrane. Database Syst Rev. 2012;7:CD008343.
16. Semenkovich TR, Frederiksen C, Hudson JL, Subramanian M, Kollef MH, Patterson GA, Kreisel D, Meyers BF, Kozower BD, Puri V. Postoperative pneumonia prevention in pulmonary resections: a feasibility pilot study. Ann Thorac Surg. 2018;107(1):262–70.
17. Pedersen PU, Larsen P, Håkonsen SJ. The effectiveness of systematic perioperative oral hygiene in reduction of postoperative respiratory tract infections after elective thoracic surgery in adults: a systematic review. JBI Database System Rev Implement Rep. 2016;14:140–73.
18. Ishimaru M, Matsui H, Ono S, Hagiwara Y, Morita K, Yasunaga H. Preoperative oral care and effect on postoperative complications after major cancer surgery. Br J Surg. 2018;105:1688–96.
19. Mulick A, Walker J, Puntis S, Burke K, Symeonides S, Gourley C, Wanat M, Frost C, Sharpe M. Does depression treatment improve the survival of depressed patients with cancer? A long-term follow-up of participants in the SMaRT Oncology-2 and 3 trials. Lancet Psychiatry. 2018;5:321–6.
20. Powell R, Scott NW, Manyande A, Bruce J, Vögele C, Byrne-Davis LM, Unsworth M, Osmer C, Johnston M. Psychological preparation and postoperative outcomes for adults undergoing surgery under general anaesthesia. Cochrane Database Syst Rev. 2016;2016:CD008646.
21. Kerr J, Anderson C, Lippman SM. Physical activity, sedentary behaviour, diet, and cancer: an update and emerging new evidence. Lancet Oncol. 2017;18:e457–71.
22. Dronkers JJ, Chorus AM, van Meeteren NL, Hopman-Rock M. The association of preoperative physical fitness and physical activity with outcome after scheduled major abdominal surgery. Anaesthesia. 2013;68:67–73.
23. Struthers R, Erasmus P, Holmes K, Warman P, Collingwood A, Sneyd JR. Assessing fitness for surgery: a comparison of questionnaire, incremental shuttle walk, and cardiopulmonary exercise testing in general surgical patients. Br J Anaesth. 2008;101:774–80.
24. Guazzi M, Bandera F, Ozemek C, Systrom D, Arena R. Cardiopulmonary exercise testing. what is its value?J Am Coll Cardiol. 2017;70:1618–36.
25. Shem Tov L, Matot I. Frailty and anesthesia. Curr Opin Anaesthesiol. 2017;30:409–17.
26. Ades PA, Toth MJ. Accelerated decline of aerobic fitness with healthy aging: what is the good news? Circulation. 2005;112:624–6.
27. Ali S, Garcia JM. Sarcopenia, cachexia and aging: diagnosis, mechanisms and therapeutic options – a mini-review. Gerontology. 2014;60:294–305.
28. Kohl BA, Deutschman CS. The inflammatory response to surgery and trauma. Cur Opin Crit Care. 2006;12:325–32.
29. Brandi LS, Bertolini R, Janni A, Gioia A, Angeletti CA. Energy metabolism of thoracic surgical patients in the early postoperative period. Effect of posture. Chest. 1996;109:630–7.
30. Beyer I, Njemini R, Bautmans I, Demanet C, Bergmann P, Mets T. Inflammation-related muscle weakness and fatigue in geriatric patients. Exp Gerontol. 2012;47:52–9.
31. Powers SK, Wiggs MP, Sollanek KJ, Smuder AJ. Ventilator-induced diaphragm dysfunction: cause and effect. Am J Physiol Regul Integr Comp Physiol. 2013;305:R464–77.
32. Bishop-Bailey D. Mechanisms governing the health and performance benefits of exercise. Br J Pharmacol. 2013;170:1153–66.
33. Grgic J, Mcllvenna LC, Fyfe JJ, Sabol F, Bishop DJ, Schoenfeld BJ, Pedisic Z. Does aerobic training promote the same skeletal muscle hypertrophy as resistance training? A systematic review and meta-analysis. Sports Med. 2018;49(2):233–54.
34. Drake JC, Wilson RJ, Yan Z. Molecular mechanisms for mitochondrial adaptation to exercise training in skeletal muscle. FASEB J. 2016;30:13–22.
35. Bowen TS, Schuler G, Adams V. Skeletal muscle wasting in cachexia and sarcopenia: molecular pathophysiology and impact of exercise training. J Cachexia Sarcopenia Muscle. 2015;6:197–207.

36. Marongiu E, Crisafulli A. Cardioprotection acquired through exercise: the role of ischemic preconditioning. Curr Cardiol Rev. 2014;10:336–48.
37. Sollanek KJ, Smuder AJ, Wiggs MP, Morton AB, Koch LG, Britton SL, Powers SK. Role of intrinsic aerobic capacity and ventilator-induced diaphragm dysfunction. J Appl Physiol (1985). 2015;118:849–57.
38. Mussi RK, Camargo EA, Ferreira T, De Moraes C, Delbin MA, Toro IF, Brancher S, Landucci EC, Zanesco A, Antunes E. Exercise training reduces pulmonary ischaemia-reperfusion-induced inflammatory responses. Eur Respir J. 2008;31:645–9.
39. Price KJ, Gordon BA, Bird SR, Benson AC. A review of guidelines for cardiac rehabilitation exercise programmes: is there an international consensus? Eur J Prev Cardiol. 2016;23:1715–33.
40. Garvey C, Bayles MP, Hamm LF, Hill K, Holland A, Limberg TM, Spruit MA. Pulmonary rehabilitation exercise prescription in chronic obstructive pulmonary disease: review of selected guidelines. an official statement from the American Association of Cardiovascular and Pulmonary RehabilitationJ Cardiopulm Rehabil Prev. 2016;36:75–83.
41. Templeton R, Greenhalgh D. Preoperative rehabilitation for thoracic surgery. Curr Opin Anaesthesiol. 2018;32(1):23–8.
42. Piraux E, Caty G, Reychler G. Effects of preoperative combined aerobic and resistance exercise training in cancer patients undergoing tumour resection surgery: a systematic review of randomised trials. Surg Oncol. 2018;27(3):584–94.
43. Steffens D, Beckenkamp PR, Hancock M, Solomon M, Young J. Preoperative exercise halves the postoperative complication rate in patients with lung cancer: a systematic review of the effect of exercise on complications, length of stay and quality of life in patients with cancer. Br J Sports Med. 2018;52:344.
44. Cavalheri V, Granger C. Preoperative exercise training for patients with non-small cell lung cancer. Cochrane Database Syst Rev. 2017;6:CD012020.
45. Li J, Guo NN, Jin HR, Yu H, Wang P, Xu GG. Effects of exercise training on patients with lung cancer who underwent lung resection: a meta-analysis. World J Surg Oncol. 2017;15:158.
46. Pouwels S, Fiddelaers J, Teijink JA, Woorst JF, Siebenga J, Smeenk FW. Preoperative exercise therapy in lung surgery patients: a systematic review. Respir Med. 2015;109:1495–504.
47. Minnella EM, Awasthi R, Loiselle SE, Agnihotram RV, Ferri LE, Carli F. Effect of exercise and nutrition prehabilitation on functional capacity in esophagogastric cancer surgery: a randomized clinical trial. JAMA Surg. 2018;153(12):1081–9.
48. Sanchez-Lorente D, Navarro-Ripoll R, Guzman R, Moises J, Gimeno E, Boada M, Molins L. Prehabilitation in thoracic surgery. J Thorac Dis. 2018;10(Suppl 22):S2593–600.

Part II

Airway and Ventilation Management in Thoracic Surgery

Lung Isolation Versus Lung Separation: Double-Lumen Tubes

4

Laszlo L. Szegedi and Marc Licker

4.1 Introduction

First described in anesthetic practice in 1931, selective endobronchial intubation combined with positive pressure ventilation was the long awaited solution to the deadly pneumothorax problem associated with chest opening [1]. Whilst providing positive pressure ventilation, various types of catheters with an inflatable distal balloon (e.g., urinary catheter, Fogarty embolectomy catheter or Swan-Ganz catheter) were inserted within bronchial divisions to exclude the ventilation of the distal lung parenchyma [2]. These techniques were hazardous and the shape of the balloon was not designed for airway blockade.

Over the next decades, different techniques for securing the airways and selectively ventilating the lungs have largely contributed to the development of intrathoracic surgery [3]. With the recent advances in video technology, endoscopic instruments, and mini-invasive approaches, the demand for selective one-lung ventilation (OLV) has increased not only in thoracic surgery but also for various cardiac, orthopedic and neurological procedures [4–7].

Currently, two main techniques are available to achieve selective OLV coupled with the exclusion of the opposite lung: the double-lumen tubes (DLTs) or the endobronchial blockers (BBs). The ultimate choice between DLTs and BBs depending on the clinical settings, the specific properties of these devices and the operator's personal preferences [8]. In emergency conditions and in pediatric patients, a

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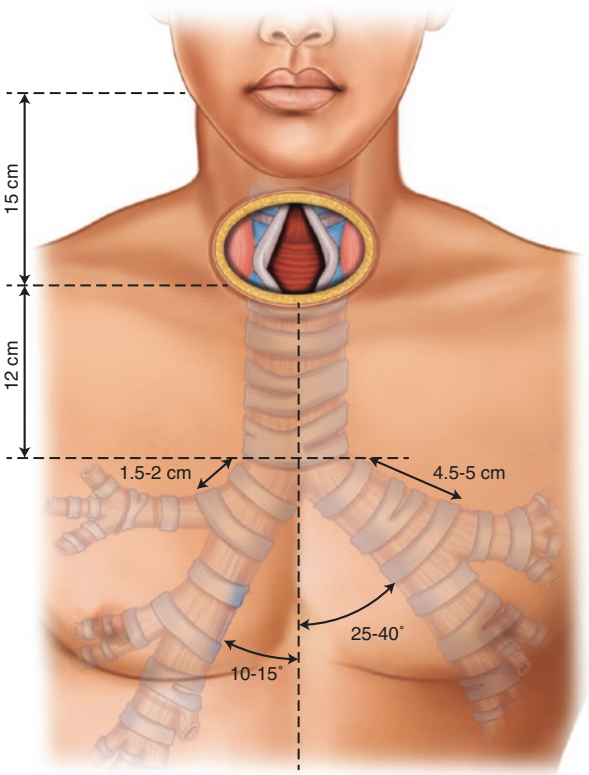

Fig. 4.1 Anatomy of the upper airways, from the mouth to the segmental bronchial divisions (average distances and angles measured in a 170 cm adult)

standard single lumen tube (SLT) can also be advanced into a main bronchus stem or a Fogarty catheter can be inserted along the SLT, to prevent soiling of the ventilated lung and/or to facilitate transient collapse of the lung according with the tracheobronchial anatomy (Fig. 4.1).

According to recent surveys in the United Kingdom, Italy the Middle East and a survey conducted by the European Association of Cardiothoracic Anesthesiologists, DLTs are preferred by a large majority of thoracic anesthesiologists (more than 90%) [9–11]. Interestingly, although most of these experts declare being familiar with BBs, up to 30% acknowledge never using BBs.

A working knowledge of tracheobronchial anatomy, expertise in fiber-optic bronchoscopy (FOB) and familiarity with specific lung isolation devices are essential conditions for successful placement of BBs and DLTs as well as for safe management of OLV [12]. Anesthesiologists with limited exposure to thoracic surgery

should develop basic knowledge and practical skills with anesthesia simulator training, computer-based programs and continuous education via thoracic anesthesia workshops [13–15].

4.2 Indications

Besides ensuring adequate gas exchange, selective lung ventilation techniques have three main purposes: (1) preventing contamination of a healthy lung with pus, blood or other fluids from the contralateral lung, (2) facilitating exposure of intrathoracic anatomic structures for diagnostic and therapeutic procedures, and (3) providing differential ventilation and securing the airways in unilateral thoracic disorders (e.g., bronchopleural fistula, giant bulla, lung contusion) [8].

The purpose of OLV is to provide a good surgical exposure of a collapsed lung while ensuring adequate gas exchange with the other. Currently, DLTs or BBs are used to achieve these goals. The separation of the lungs today means a completed "anatomical" sealing with a DLT, and the isolation of the lung means a "functional" sealing with a BBs [8, 16, 17]. In the first case, there are some absolute indications in which a protective strategy for the contralateral lung is needed, including potentially life-threatening conditions such as: massive pulmonary bleeding, pneumonia with pus, broncho-pleural and broncho-cutaneous fistulae, as well as giant unilateral bullae. Maintenance of adequate gas exchange, prevention of soiling/flooding the other lung with contaminated material/blood and avoidance of barotrauma are best achieved with DLTs in these situations. Some surgical interventions as sleeve pneumonectomy, or bronchopulmonary lavage for alveolar proteinosis or cystic fibrosis require lung separation with a DLT. In all the other situations, in which lung separation is a relative indication, lung isolation could be best considered (Table 4.1) [18–22].

Overall, the DLT remains the gold standard technique in various surgical procedures requiring lung separation/isolation and are favored by most thoracic anesthesiologists [23]. The BBs offer the advantage of being placed through a conventional SLT. In emergency situations, securing the airways is a priority and this is performed easier and faster with an SLT for all anesthesiologists. Moreover, in patients with abnormal airway anatomy (post-laryngeal/pharyngeal surgery, tracheotomy), predicted difficult intubation or at risk of vocal cord injuries (e.g., singers) as well as in children, BBs are most suitable for lung separation as far as the chest wall and lungs compliances are normal. Likewise, if postoperative ventilation is needed, the use of a BB is a good choice, avoiding the (risky) replacement of the DLT by an SLT with an airway exchange catheter [24, 25]. Finally, BBs remains the sole option in children and in patients who have undergone pneumonectomy and those requiring selective lobar exclusion (e.g., severe lung disease).

Table 4.1 Indications for lung isolation technique

		Indications	Main goal	Suggestion
Absolute indications		Unilateral lung abscess or cyst	Contralateral Lung protection	DLT
		Unilateral lung hemorrhage (e.g., thromboembolism, aneurysm)	Contralateral Lung protection	DLT
		Bronchoalveolar lavage with saline to treat alveolar proteinosis	Contralateral Lung protection	DLT
		Bronchopulmonary fistula, trachea-bronchial injury	Secure the airways and gas exchange	DLT
		Severe unilateral disease (giant emphysematous bullae)	Differential lung ventilation	DLT
		Lung transplantation	Secure the airways and differential ventilation	DLT
Relative indications	High priority	Pneumonectomy, sleeve resection on the bronchial mainstem Tumor obstructing the main bronchial stem	Surgical exposure	DLT
		Thoracic aneurysm with cardiopulmonary bypass	Surgical exposure	DLT > BB
		Lobectomy and lesser lung resection (any surgical approach[a])	Surgical exposure	DLT = BB
	Low priority	Interventions on the pleura and mediastinal structures	Surgical exposure	DLT = BB
		Oesophagectomy	Surgical exposure	DLT = BB
		Orthopedic surgery on the chest, thoracic spine surgery	Surgical exposure	DLT = BB
		Minimally invasive cardiac surgery	Surgical exposure	DLT = BB
		Bilateral cervical sympathectomy	Surgical exposure	EBBs > DLT

DLT double lumen tube, *BB* bronchial blocker
[a]Video-assisted thoracoscopy, robotic surgery or open thoracotomy

4.3 Methods for Lung Ventilation (OLV)

In modern practice, endobronchial double-lumen tubes (DLTs) are most widely employed (Figs. 4.2 and 4.3). The DLTs available in the recent years, have a fixed curvature and do not have a carinal hook, in order to avoid tracheal laceration and reduce the likelihood of kinking. Numerous manufacturers produces clear disposable Robertshaw design DLTs, which are available in French sizes from 35 to 41 [26]. Essentially, they all have similar features but modified cuff shape and location. A colored bronchial cuff, commonly blue, permits its easy identification by fiber-optic bronchoscopy. The right endobronchial cuff is donut-shaped, and allows the right upper

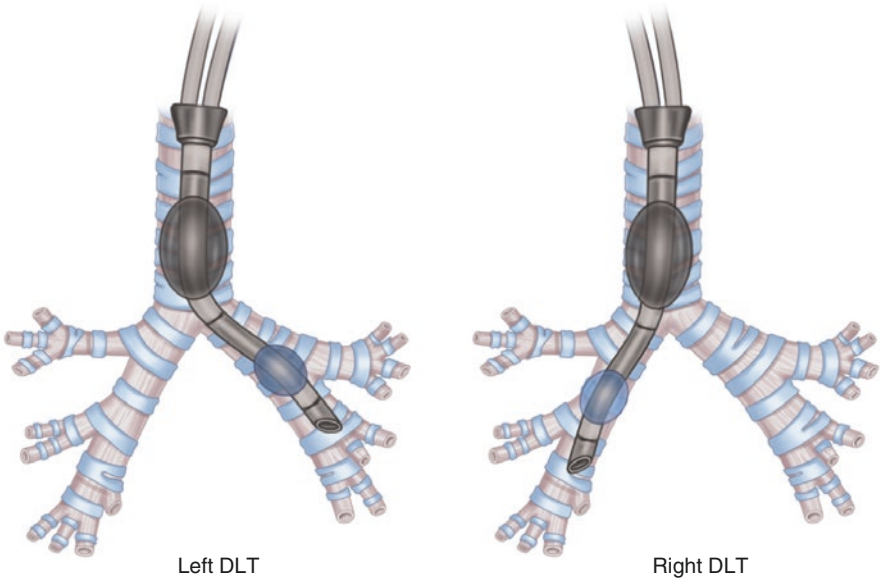

Fig. 4.2 Left and right double lumen tubes (DLTs)

Fig. 4.3 Sizes of bronchoscope reported in mm of external diameter (OD) fit differently from 26 to 41 Fr Double Lumen Tubes (DLTs) with different internal diameters (ID)

	FOB OD mm	>5	4.2-4.7	3.5-3.9	2.8-3.2	1.8-2.5
DLT	41 Ch/Fr ID mm 5-6					
	39 Ch/Fr ID mm 4.8-5.5					
	37 Ch/Fr ID mm 4.5-5.1					
	35 Ch/Fr ID mm 4.2-4.8					
	32 Ch/Fr ID mm 3.4					
	28 Ch/Fr ID mm 3.1-3.8					
	26 Ch/Fr ID mm 3.4					

Impossible Difficult Easy

lobe ventilation slot to ride over the right upper lobe orifice. Most authors refrain from using right-sided DLT simply to avoid potential obstacles. Instead of its extensive use, one of the major challenges for a DLT is the lack of an objective method and guideline for selecting the proper size and its optimal depth. The most accurate method to select a left-sided DLT size is to measure the left bronchus width and the outer diameter of the endobronchial lumen of the DLT, then the largest tube that safely fits that bronchus can be selected [27]. For a right-sided DLT there is no study available that addresses the issue of optimal size for a determined patient. In general a 37 Fr DLT can be used in most of the adult females, while 39 Fr can be used in the average adult male. Keeping in mind that, undersized or oversized DLTs could led to serious airway complications, including tracheo-bronchial rupture. The optimal depth of insertion for a left-sided DLT is strongly correlated to the patient's height. In general, the depth of insertion for a DLT should be between 27 and 29 cm at the marking of the incisors [28, 29]. An inadvertent deep insertion of a DLT could lead to rupture of the left main stem bronchus or unilobar ventilation. Three other sizes (26 and 28 Fr for pediatrics and 32 Fr for small adults) have recently been introduced in the market.

When a conventional laryngoscopy reveals a grade III view (only the epiglottis) or a grade IV view (only the soft palate) in the Cormack-Lehane scale, the airway may be termed difficult [30]. When the separation of the lung is strictly indicated, the use of tubes such as DLT or Univent, that are inherently difficult to insert, cannot be recommended [31–33]. If the patient has a recognized difficult airway, awake intubation with fiber-optic bronchoscopy (FOB) can be attempted using a SLT. The same approach may be used for the patient with an unrecognized difficult airway [34]. However, thoracic anesthesiologists' expertise and propensity with a DLT rather than a BB and vice versa, and their knowledge in fiber-optic tracheobronchial anatomy, plays an important role in that choice. On the other hand, for the occasional thoracic anesthesiologist, DLTs and BBs are difficult to use and none of these devices provides any advantage over the other [35].

In modern clinical practice, this instrument has been replaced by three different types of 9 Fr BBs with a steering mechanism and a patent 1.6 mm lumen to facilitate the collapse of the lung and/or oxygen insufflation through continuous positive airway pressure (CPAP) to the nondependent lung [20]. Of these three devices the Arndt blocker is available in 7 and 5 Fr for small adults and pediatrics; it uses a wire-guided mechanism [21]. The Cohen blocker possesses a rotating wheel that allows it to flex the tip of the blocker [5]. Both blockers use a multiport adapter. The Uniblocker. which has a fixed curve similar to a hockey stick, has been recently introduced in clinical practice. It is essentially the same blocker as the Univent tube which is somewhat bulky, but now available as an independent blocker [22].

4.4 Comparative Performances and Limitations of DLTs and BBs

Several randomized control trials including more than 800 patients have compared DLTs versus BBs [20, 35–46]. The time needed for initial insertion and for lung collapse as well as the success rate for proper position and the quality of surgical exposure have been rated quite similarly with both techniques. The major drawback

was related to more frequent displacements of the EBB when the surgeon manipulates the lung and the difficulties encountered to reposition the blocker with FOB while the patient lies on his side.

Transient symptoms such as sore throat (10–45%), voice hoarseness (15–25%) and irritative cough have been more frequently reported postoperatively with DLTs than with SLTs combined with BBs [38, 44]. Likewise, a higher incidence of mucosal damage and hematoma has been observed within the larynx and the tracheabronchial tree following the utilization of DLTs versus BBs [37, 38]. Anecdotal cases of rupture of the trachea-bronchial membrane have been related to placement of an oversized DLT or keeping the stylet in place whilst attempting to guide the endobronchial tip into the mainstem bronchus [47–49]. In the rare case of tracheal bronchus (prevalence ranging from 0.1% to 1%), the use of a left (or right) sided DLT will fail to achieve satisfactory lung isolation or may result in lobar atelectasis [50, 51]. Successful lung isolation can be achieved by using one (or two simultaneous) BBs. On the other hand, inadvertent resection of the guide-wire and stapling the distal tip of the BB have been reported that required surgical re-exploration. Near-fatal hypoxic complication may also result from dislodgment of the inflated BB balloon into the trachea, leading to complete airway obstruction or severe gas trapping into the lung(s) associated with cardiovascular collapse. Table 4.2 summarizes the advantages and disadvantages of DLTs and BBs.

Table 4.2 Advantages and disadvantages of double lumen tubes and endobronchial blockers

	Double-lumen tubes (DLTs)	Endobronchial blockers (BBs)
Advantages	• Suctioning and drainage of blood, pus, secretions (protection against contralateral lung contamination or flooding with any fluid) • Secure damaged (or operated) airways	• Suitable in patients with difficult airways, abnormal anatomy (e.g., porcine trachea) • In patients/surgeries requiring nasal intubation • Failure to pass a DLT
	• Lesser risk of intraoperative displacement • Easier to correct position under FOB guidance (with patient in lateral position) • Lesser interference with surgical manipulation	• Lesser risk of laryngeal injuries and postoperative sore throat or hoarseness • Lesser risk of tracheal cuff damage (during intubation)
	• Conversion from two- to one-lung ventilation (vice versa), • CPAP to correct intraoperative hypoxemia • Differential lung ventilation (if different lung compliance), re-ventilation of the excluded lung at the end of surgery	• CPAP to correct intraoperative hypoxemia
	• Possibility of “blind” insertion (if FOB not available)	• Postoperative ventilation through the standard single lumen tube (no need to re-intubate the patient)

Table 4.2 (continued)

	Double-lumen tubes (DLTs)	Endobronchial blockers (BBs)
Disadvantages	• Difficulties to place in patients with abnormal airways, after lung surgery (e.g., post-pneumonectomy), in children (< 120 cm)	• Small suction channel does not allow drainage of fluids
	• Laryngeal and trachea-bronchial injuries, sore throat • Difficulties in selecting proper size	• More frequent intraoperative displacement or loss of seal • Difficulties in repositioning
	• Damage to tracheal and/or bronchial cuffs (during intubation)	• No differential lung ventilation
		• Absolute requirement for fiber-optic guidance

4.5 Double-Lumen Tubes: First Step—The Positioning

Following intubation, the tracheal cuff should be inflated first, and then the tube's correct position should be confirmed. To avoid mucosal damage from excessive pressure applied by the bronchial cuff, the cuff is inflated with incremental volumes until air leaks disappear. Inflation of the bronchial cuff seldom requires more than 2 ml of air. If the cuff needs less than 1 ml to obtain a correct seal means that the DLT is too big, if the inflation volume of the bronchial cuff exceeds 3 ml means that the DLT is too small for that patient. Bilateral breath sounds should be re-checked to confirm that the bronchial cuff is not herniating over the carina, impeding the ventilation of the lung. An important step is to verify that the tip of the bronchial lumen is located in the designated bronchus. One simple way to check this is to first clamp the tracheal lumen, then observe and auscultate. Usually, inspection will reveal unilateral ascent of the ventilated hemithorax. Following proper auscultation, the bronchial lumen is clamped to ventilate the tracheal lumen. Each time a right-sided DLT is used, appropriate ventilation of the right upper lobe should be ensured. This can be accomplished by a careful auscultation over the right upper lung field or more accurately by fiber-optic bronchoscope [52–54]. When a left-sided DLT is used, the risk of occluding the left upper lobe bronchus by the bronchial tip advanced too far into the left main bronchus should be always kept in mind. If the peak airway pressure is 20 cmH_2O during two-lung ventilation, for the same tidal volume that pressure should not exceed 40 cmH_2O on OLV.

Two techniques for DLT insertion are currently recommended: (1) a "blind" insertion, associated or not, with fiber-optic control and (2) the fiber-optic-guided approach [55], but there is no consensus about the correct insertion method. Fiber-optic bronchoscopy may reveal a malposition in 20–48% of the DLTs thought to be correctly positioned by inspection and auscultation only. The simplest method to evaluate proper positioning of a left sided DLT is bronchoscopy via the tracheal lumen. The carina is then visualized, while only the proximal edge of the endobronchial cuff is visualized just below the tracheal carina. Herniation of the bronchial

cuff over the carina to partially occlude the ipsilateral main bronchus should be excluded. Bronchoscopy should then be performed via the bronchial lumen to identify the patent left upper lobe orifice [56]. When using a right-sided DLT, the carina is visualized through the tracheal lumen. More importantly, the right upper lobe bronchial orifice must be identified while the bronchoscope is passed through the right upper lobe ventilating slot. This is somewhat complex to accomplish and requires a relatively skilled endoscopist. Moreover, anatomically, the margin of safety for positioning right-sided DLTs is much narrower than left-sided ones, given the distance from the carina to the splitting of upper-lobe bronchus. In the left lung this is about 5 cm, while at the right side just about 2.5 cm, and sometimes the right upper lobe bronchus emerges above the level of the carina, so it's impossible to insert a right-sided DLT.

Several sizes of bronchoscope are available for clinical use: 5.6, 4.9, 3.9 and 2.2 mm of external diameter. The 3.9 mm-diameter bronchoscope can easily pass through a 37 Fr or larger tube, while it is a tight fit through a 35 Fr tube and can not be used for smaller DLTs (Fig. 4.2) [52–56].

4.6 Terminating Surgery and Reintubating the Patient: Tube Exchangers

The vast majority of patients undergoing thoracic surgery are extubated at the end of surgery. However, after complicated or prolonged surgery, some patients require postoperative ventilation. Either the DLT is pulled back with the bronchial tip above the carina and the patient is ventilated via the DLT further, or the DLT is replaced by a SLT. However, after ventilating a patient via a DLT, airway edema may occur and re-intubating the patient may be difficult, so airway guides or exchange catheters should be used for facilitating this procedure. The airway guide may be used for inserting an SLT over a DLT and vice versa, or simply inserting a difficult tube. Several tube exchangers are available. All of these airway guides are commercially made, depth is marked in cm, the tip is atraumatic, are available in a wide range of sizes, and are easily adapted for either oxygen insufflation or jet ventilation. Critical details to keep in mind to maximize benefit and minimize risk of airway injuries are as follows: first, the size of the airway guide and the size of the difficult tube must be determined and should be tested in vitro before the use of the airway guide. Second, the airway guide should never be inserted against a resistance; the clinician must always be aware of the depth of insertion. Two reported perforations of the tracheobronchial tree have occurred [57, 58]. Third, a jet ventilator should be immediately available in case the new tube does not follow the airway guide into the trachea, and the jet ventilator should be preset at 25 psi by the use of an additional in-line regulator [59]. Finally, when passing any tube over an airway guide, a laryngoscope should be used to facilitate the passage of the tube over the airway guide past the supraglottic tissues. Because of the potential injury to the bronchial tree from the stiff tip of the tube exchanger, a new catheter has been designed with a soft tip to reduce the risk of trauma.

4.7 Conclusion

Thoracic anesthesia—still very fascinating—is the world of OLV during anesthesia. The indications for OLV, classified as absolute or relative are more representative of the new concepts in OLV: it includes either the separation or the isolation of the lungs. Modern DLTs are most widely employed worldwide to perform OLV including the concept of one lung separation. Endobronchial blockers are a valid alternative to DLTs, and they are mandatory in the education of lung separation and in case of predicted difficult airways as they are the safest approach (with an awake intubation with a SLT through a FOB). Every general anesthesiologist should know how to insert a left-sided DLT, but he/she should also have in his technical luggage and toolbox, basic knowledge and minimal expertise with BBs, this option being considered a suitable alternative, particularly in emerging situation and/or difficult airways. One should keep in mind that extubation or re-intubation after DLT might be difficult too, and additional intubation tools are necessary for the safety conditions. Protective lung ventilation with a tidal volume less than that used for two lung ventilation (i.e. 4–6 mL/kg) and with the lowest feasible peak/plateau airway pressure, I:E ratio of 1:2, with a rapid respiratory rate are considered the standard of care. Recruitment manoeuvres and PEEP should be used to reduce the amount of atelectasis in the dependent lung. They should be applied with sustained peak pressure of 40 cmH_2O to be effective. Also CPAP and iNO or inhaled epoprostenol could improve oxygenation in selected cases. Fluid administration should be limited during thoracic surgery procedures to avoid fluid overload. Finally, a balanced anesthetic technique with inhalational agents and opioids to reduce the required concentration of potent inhaled agent appears the best choice during OLV.

References

1. Brodsky JB, Lemmens HJ. The history of anesthesia for thoracic surgery. Minerva Anestesiol. 2007;73(10):513e24.
2. Rovenstine E. Anesthesia for intrathoracic surgery: the endotracheal tube and endobronchial techniques. Surg Gynecol Obstet. 1936;63:325e30.
3. Macintosh R, Leatherdale RA. Bronchus tube and bronchus blocker. Br J Anaesth. 1955;27(11):556e7.
4. Pardolesi A, Park B, Petrella F, Borri A, Gasparri R, Veronesi G. Robotic anatomic segmentectomy of the lung: technical aspects and initial results. Ann Thorac Surg. 2012;94(3):929e34.
5. Iwata H. Minimally invasive pulmonary surgery for lung cancer, up to date. Gen Thorac Cardiovasc Surg. 2013;61(8):449e54.
6. Rocco G. One-port (uniportal) video-assisted thoracic surgical resections--a clear advance. J Thorac Cardiovasc Surg. 2012;144(3):S27e31.
7. Steenwyk B, Lyerly R 3rd. Advancements in robotic-assisted thoracic surgery. Anesthesiol Clin. 2012;30(4):699e708.
8. Campos JH. Which device should be considered the best for lung isolation: double-lumen endotracheal tube versus bronchial blockers. Curr Opin Anaesthesiol. 2007;20(1):27e31.
9. Della Rocca G, Langiano N, Baroselli A, Granzotti S, Pravisani C. Survey of thoracic anesthetic practice in Italy. J Cardiothorac Vasc Anesth. 2013;27(6):1321e9.

10. Eldawlatly A, Turkistani A, Shelley B, El-Tahan M, Macfie A, Kinsella J. Anesthesia for thoracic surgery: a survey of middle eastern practice. Saudi J Anaesth. 2012;6(3):192e6.
11. Shelley B, Macfie A, Kinsella J. Anesthesia for thoracic surgery: a survey of UK practice. J Cardiothorac Vasc Anesth. 2011;25(6):1014e7.
12. Campos JH. Update on tracheobronchial anatomy and flexible fiberoptic bronchoscopy in thoracic anesthesia. Curr Opin Anaesthesiol. 2009;22(1):4e10.
13. Campos JH, Hallam EA, Ueda K. Training in placement of the left-sided double-lumen tube among non-thoracic anaesthesiologists: intubation model simulator versus computer-based digital video disc, a randomised controlled trial. Eur J Anaesthesiol. 2011;28(3):169e74.
14. Bustamante S, Bose S, Bishop P, Klatte R, Norris F. Novel application of rapid prototyping for simulation of bronchoscopic anatomy. J Cardiothorac Vasc Anesth. 2013;28(4):1122–5.
15. Failor E, Bowdle A, Jelacic S, Togashi K. High-fidelity simulation of lung isolation with double-lumen endotracheal tubes and bronchial blockers in anesthesiology resident training. J Cardiothorac Vasc Anesth. 2014;28:865–9.
16. Campos JH. Progress in lung separation. Thorac Surg Clin. 2005;15:71–83.
17. Cohen E. Pro: the new bronchial blockers are preferable to double-lumen tubes for lung isolation. J Cardiothorac Vasc Anesth. 2008;22:920–4.
18. Campos JH. An update on bronchial blockers during lung separation techniques in adults. Anesth Analg. 2003;97:1266–74.
19. Cohen E. The Cohen flexitip endobronchial blocker: an alternative to a double lumen tube. Anesth Analg. 2005;101:1877–9.
20. Narayanaswamy M, Lacroix M, Kanellakos G, et al. A clinical comparison of three designs of bronchial blockers with double-lumen tubes for lung isolation. Anesth Analg. 2007;104:123.
21. Prabhu MR, Smith JH. Use of the Arndt wire-guided endobronchial blocker. Anesthesiology. 2002;97:1325.
22. Kamaya H, Krishna PR. New endotracheal tube (univent tube) for selective blockade of one lung. Anesthesiology. 1985;63:342–3.
23. Slinger P. Con: the new bronchial blockers are not preferable to double-lumen tubes for lung isolation. J Cardiothorac Vasc Anesth. 2008;22(6):925e9.
24. Harris K, Chalhoub M, Maroun R, Elsayegh D. Endotracheal tube exchangers: should we look for safer alternatives? Heart Lung J Crit Care. 2012;41(1):67e9.
25. McLean S, Lanam CR, Benedict W, Kirkpatrick N, Kheterpal S, Ramachandran SK. Airway exchange failure and complications with the use of the Cook Airway Exchange Catheter(R): a single center cohort study of 1177 patients. Anesth Analgesia. 2013;117(6):1325e7.
26. Seymour AH, Prasad B, McKenzie RJ. Audit of double-lumen endobronchial intubation. Br J Anaesth. 2004;93:525–7.
27. Brodsky JB, Lemmens HJ. Tracheal width and left double-lumen tube size: a formula to estimate left bronchial width. J Clin Anesth. 2005;17:267–70.
28. Brodsky JB, Benumof JL, Ehrenwerth J, et al. Depth of placement of left double-lumen endobronchial tubes. Anesth Analg. 1991;73:570–2.
29. Bahk JH, Oh YS. Prediction of double-lumen tracheal tube depth. J Cardiothorac Vasc Anesth. 1999;13:370–1.
30. Merli G, Guarino A, Della Rocca G, et al. Recommendations for air way control and difficult air way management in thoracic anesthesia and lung separation procedures. Minerva Anesthesiol. 2009;75:59–96.
31. Cohen E, Benumof JL. Lung separation in the patient with a difficult airway. Curr Opin Anesthesiol. 1999;12:29–35.
32. Arndt GA, Buchika S, Kranner PW, et al. Wire-guided endobronchial blockade in a patient with a limited mouth opening. Can J Anaesth. 1999;46:87–9.
33. Benumof JL. Difficult tubes and difficult airways. J Cardiothorac Vasc Anesth. 1998;12:131–2.
34. Klafta JM, Ovassapian A. Lung separation and the difficult airway. Probl Anesth. 2001;13:69–77.
35. Campos JH, Hallam EA, Van Natta T, Kernstine KH. Devices for lung isolation used by anesthesiologists with limited thoracic experience. Anesthesiology. 2006;104:261–6.

36. Dumans-Nizard V, Liu N, Laloe PA, Fischler M. A comparison of the deflecting-tip bronchial blocker with a wire-guided blocker or left-sided double-lumen tube. J Cardiothorac Vasc Anesth. 2009;23:501–5.
37. Mourisse J, Liesveld J, Verhagen A, van Rooij G, van der Heide S, Schuurbiers-Siebers O, et al. Efficiency, efficacy, and safety of EZ-blocker compared with left-sided double-lumen tube for one-lung ventilation. Anesthesiology. 2013;118:550–61.
38. Knoll H, Ziegeler S, Schreiber JU, Buchinger H, Bialas P, Semyonov K, et al. Airway injuries after one-lung ventilation: a comparison between double-lumen tube and endobronchial blocker: a randomized, prospective, controlled trial. Anesthesiology. 2006;105:471–7.
39. Campos JH, Reasoner DK, Moyers JR. Comparison of a modified double-lumen endotracheal tube with a single-lumen tube with enclosed bronchial blocker. Anesth Analg. 1996;83:1268–72.
40. Campos JH, Massa FC. Is there a better right-sided tube for one-lung ventilation? A comparison of the right-sided double-lumen tube with the single-lumen tube with right-sided enclosed bronchial blocker. Anesth Analg. 1998;86:696–700.
41. Bauer C, Winter C, Hentz JG, Ducrocq X, Steib A, Dupeyron JP. Bronchial blocker compared to double-lumen tube for one-lung ventilation during thoracoscopy. Acta Anaesthesiol Scand. 2001;45:250–4.
42. Grocott HP, Darrow TR, Whiteheart DL, Glower DD, Smith MS. Lung isolation during port-access cardiac surgery: double-lumen endotracheal tube versus single-lumen endotracheal tube with a bronchial blocker. J Cardiothorac Vasc Anesth. 2003;17:725–7.
43. Lehmann A, Zeitler C, Lang J, Isgro F, Kiessling AH, Boldt J. A comparison of the Arndt endobronchial blocker with a double lumen tube in robotic cardiac surgery. Anasthesiol Intensivmed Notfallmed Schmerzther. 2004;39:353–9.
44. Zhong T, Wang W, Chen J, Ran L, Story DA. Sore throat or hoarse voice with bronchial blockers or double-lumen tubes for lung isolation: a randomised, prospective trial. Anaesth Intensive Care. 2009;37:441–6.
45. Campos JH, Hallam EA, Ueda K. Lung isolation in the morbidly obese patient: a comparison of a left-sided double-lumen tracheal tube with the Arndt(R) wire-guided blocker. Br J Anaesth. 2012;109:630–5.
46. Ruetzler K, Grubhofer G, Schmid W, Papp D, Nabecker S, Hutschala D, et al. Randomized clinical trial comparing double-lumen tube and EZ-blocker for single-lung ventilation. Br J Anaesth. 2011;106:896–902.
47. Venkataramanappa V, Boujoukos AJ, Sakai T. The diagnostic challenge of a tracheal tear with a double-lumen endobronchial tube: massive air leak developing from the mouth during mechanical ventilation. J Clin Anesth. 2011;23:66–70.
48. Yuceyar L, Kaynak K, Canturk E, Aykac B. Bronchial rupture with a left-sided polyvinylchloride double-lumen tube. Acta Anaesth Scand. 2003;47:622–5.
49. Sakuragi T, Kumano K, Yasumoto M, Dan K. Rupture of the left main-stem bronchus by the tracheal portion of a double-lumen endobronchial tube. Acta Anaesth Scand. 1997;41:1218–20.
50. Yoshimura T, Ueda K, Kakinuma A, Nakata Y. Difficulty in placement of a left-sided double-lumen tube due to aberrant tracheobronchial anatomy. J Clin Anesth. 2013;25:413–41.
51. Wiser SH, Hartigan PM. Challenging lung isolation secondary to aberrant tracheobronchial anatomy. Anesth Analg. 2011;112:688–92.
52. Klein U, Karzai W, Bloos F, et al. Role of fiberoptic bronchoscopy in conjunction with the use of double-lumen tubes for thoracic anesthesia. Anesthesiology. 1998;88:346–50.
53. Benumof JL. The position of a double lumen-tube should be routinely determined by fiberoptic bronchoscopy. J Cardiothorac Vasc Anesth. 2001;7:513–4.
54. Klein U, Karzai W, Bloos F, et al. Role of fiberoptic bronchoscopy in conjunction with the use of double-lumen tubes for thoracic anesthesia: a prospective study. Anesthesiology. 1998;88:346–50.
55. Brodsky JB. Fiberoptic bronchoscopy need not to be a routine part of double-lumen tube placement. Curr Opin Anesthesiol. 2004;17:7–11.

56. Campos JH. Update on tracheobronchial anatomy and flexible fiberoptic bronchoscopy in thoracic surgery. Curr Opin Anesthesiol. 2009;22:4–10.
57. Benumof JL. Airway exchange catheters: simple concept, potentially great danger. Anesthesiology. 1999;91:342–4.
58. DeLima L, Bishop M. Lung laceration after tracheal extubation over a plastic tube changer. Anesth Analg. 1991;73:350–1.
59. Baraka AS. Tension pneumothorax complicating jet ventilation via Cook airway exchange catheter. Anesthesiology. 1999;91:557–8.

Bronchial Blockers: Applications in Thoracic Surgery

5

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5.1 Introduction

Lung isolation techniques are designed fundamentally to allow for the ventilation of a single lung in patients who are about to undergo cardiac, thoracic, mediastinal, vascular, oesophageal, or orthopaedic interventions that directly implicate the thoracic cavity. Lung isolation is also employed in order to protect the lung from contamination in cases of bronchopleural fistulas, pulmonary haemorrhage or bronchoalveolar cleaning in the contralateral lung. Lung isolation is also useful in lung transplant or thromboendarterectomy procedures where there lies the possibility of finding lesions produced by unilateral repercussions that require differential ventilation patterns, including the case of bilateral pulmonary injuries [1].

Currently there are three main methods for lung isolation: Double-Lumen endotracheal Tubes (consult the previous chapter), Bronchial Blockers (BBs) or single-lumen endotracheal tubes.

The double-lumen endotracheal tubes (DLTs) consist of a tube with two separate channels (endotracheal and endobronchial channels) that can be used to achieve the isolation of any of the lungs. There are two main types of DLTs, one including endobronchial lumen for the main right bronchus that has a ventilation orifice for the upper right hand lobe, as well as a left DLT, with endobronchial lumen for the left main bronchus. This left DLT is most commonly used for trainees with less clinical

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experience, because they think it seems easier than right DLT or BBs. Nevertheless, complications are still possible, making the BBs a more reliable option in other types of intervention.

BBs allow for the blocking of one main bronchus in order to achieve the collapse of lung tissue distal to the obstruction. There are two types of BBs, the first being an independent BB that is introduced through a standard endotracheal tube, and the second which is inserted through a specialised channel within a special tracheal tube, such as the Univent tube [2].

The final alternative consists in selective isolation using a conventional endotracheal tube that is directed towards the main bronchus of the lung in need of ventilation. This technique is currently not in use for adult patients due to the difficulties produced when inserting the tracheal tube into the main bronchus. Nevertheless, this technique has important disadvantages but this technique is still sometimes used for infant and lactating patients, guided using a paediatric bronchoscope. BBs, however, are currently decreasing in size and are replacing this technique for younger patients.

5.2 History of Bronchial Blockers

The first selective bronchial blockade was carried out by Gale and Waters in 1931. In 1936 Magill used for the first time a catheter with an inflatable balloon to block a lung. These devices, however, presented some limitations, needing a great deal of clinical experience for their correct handling and requiring the introduction of a rigid bronchoscope before intubation. The description of DLTs was carried out by Carlens in 1949 and by Björk in 1952. In the 1960s Robert Shaw designed a new DLT adapted for bronchial anatomy that greatly resembles those used today. The recommendations of Robertshaw gave way to the origin of different double-lumen tubes that were adaptable to the anatomy of both the right and the left main bronchi. The first tubes (Carlens) where manufactured using a red latex (Leyland, London, UK) and were reusable. Versions in Polyvinyl Chloride (PVC) were later produced by multiple manufacturers such as Rusch (double-lumen bronchial tubes, Willy Rüsch AG, Waiblinger, Germany), Sheridan (Sher-I-Bronch, Argyle, NY) and Mallinckroot (Broncho-Cath, Glen Falls, NY). These were disposable, eliminating the problem of cleaning and re-sterilising these pieces after each use [2].

The use of BBs was partially abandoned in the 1950s with the incorporation of the DLTs. Nevertheless, as seen in recent literature, reports exist of cases where BBs were unavoidable, considering cases where introducing DLTs produced additional complications [3].

Developments in optical fiber technology and the introduction of fiber bronchoscopes of a smaller calibre have been able to facilitate the creation of new tools that can achieve pulmonary separation.

In 1981 Ginsberg described the use of the Fogarty catheter (Baxter Healthcare Corporation, Santa Ana, CA) for the blocking of bronchi through a single-lumen tube. In 1982 Inoue described an endotracheal single-lumen tube that consisted of

a channel that included a Bronchial Blocker, known as the Univent® (Fuji Systems Corporation, Tokyo, Japan). Available since 1999, the endobronchial blocker Arndt (Cook Medical Inc., Bloomington, IN, USA) has been used to wire guided using a characteristic nylon loop protruding from the distal lumen. In more recent years, the Cohen blocker (Cook Medical Inc. Bloomington, IN, USA) has also appeared on the market, as well as the Uniblocker (Fuji-BB, Fuji Systems Corp., Tokyo, Japan). The most recent to appear has been the Rusch EZ blocker (Teleflex Medical Europe Ltd., Athlone, Ireland) presenting a forked point and inflatable balloon on each side [3].

In recent years clinical practice have begun to use new types of tubes, including single-lumen (VivaSight-SL, AMBU, USA) and double-lumen (VivaSight-DL, AMBU, USA) aided using miniature HD cameras on the distal tip. This facilitates orotracheal intubation using the camera (for SL) or endobronchial intubation (for DL), without the need for a fiberscope to guide the device, even in cases of tracheal stenosis. The VivaSight-SL can thus achieve lung isolation and unipulmonary ventilation with the use of any BB that could be inserted into a bronchus guided through the camera of the orotracheal tube during procedure [4].

5.3 Indications for Lung Isolation

The objective of separating or isolating a lung is for the selective interruption of ventilation of one lung (total pulmonary collapse) or a lung lobe (selective lobar collapse). Several absolute and relative indications for lung separation exists. There are some absolute indications of lung isolation using DLTs as the prevention of the contamination of the healthy lung in the case of abscess or haemorrhaging. In addition, other absolute indications are due to the need for differential ventilation of both lungs in the case of giant emphysematous bullae, bronchopleural fistulas or bronchial interruptions finally, some other absolute indications are lung transplants or about carrying out any type of unilateral, pulmonary lavage or cleaning activities. Relative indications using BBs or DLTs can consist in cases that need to improve the surgical exposure as in upper lobectomy and lesser lung resection, thoracic aorta aneurisms, lung volume reduction or minimally invasive cardiac surgery. On the other hand, unipulmonary ventilation is a highly useful practice, however is less useful in cases such as oesophageal surgery, middle or lower lobectomy, mediastinal mass resection (e.g. thymectomy), pleural procedures, orthopedic surgery on the chest (e.g. thoracic spine surgery) and bilateral sympathectomy [5].

5.4 General Indications for Bronchial Blockers (BBs)

To date, the majority of anaesthesiologists and most surgeons prefer to use DLTs rather than BBs in their everyday clinical practices [6]. This is due to the greater advantages produced when collapsing lung tissue in order to expose the lung. As clinical indications for pulmonary exposure have increased, multiple limitations of the use

of double-lumen tubes have grown. Because of this, alternative options have grown in importance for pulmonary isolation, such as BBs despite the lower availability of different BBs in many hospitals. Neither do many studies exist comparing the superiority of one technique in contrast with another in cases of pulmonary collapse [7, 8]. Morever, there are some comparative studies on the time needed to introduce these devices, with minimal differences between BBs and DLTs without clinical relevance [9, 10]. Finally, it has to be pointed out how BBs move more often than DLTs during the positioning of the patient and the surgical procedure, therefore the amount of attempts to reposition the device is higher than in DLTs [9].

In a number of specific disorders BBs can be found preferable over DLTs [11]. Patients with a known or predicted difficult intubation and patients who have undergone previous surgical oral or cervical operations may present a distorted upper airway and it can difficult the intubation, requiring pulmonary isolation for intrathoracic surgery. In these conditions, a single-lumen tube introduced into the trachea through the nasal or oral tract is preferred, performed while the patient is spontaneously breathing or using a previous tracheotomy that protects the respiratory tract. After that an independent bronchial blocker can be positioned to achieve lung isolation. Another group of patients who would benefit from BBs are oncological patients that have previously undergone contralateral pulmonary resection. In these cases, a selective lobar blockade is sometimes needed with a BB in the ipsilateral side of the surgery, thus improving the oxygenation and facilitating the surgical exposure [12, 13]. In this case, any BB is introduced into the lobar bronchus that needs to be collapsed guided by direct vision of the fiberscope or VivaSight SL or in a different way an Arndt BB can be introduced through the fiberscope to the selected lobar bronchus.

Other important advantages of BBs inserted through a tracheal tube is that this technique allows remove the BB at the end of surgery without changing for any other tube. This is very important during prolonged thoracic or oesophageal surgery. In many cases, these patients present a swollen respiratory tract towards the end of the surgical procedure.

It is also indicated the use of BBs in patients already intubated with orotracheal tubes for any other reason. Patients with a patent tracheostomy orifice are an indication of the use of BBs.

The impossibility of using DLTs for some pediatric patients implies the need to use pulmonary isolation with BBs.

5.5 Types of Bronchial Blockers

5.5.1 UNIVENT (Fuji Systems Corporation, Tokyo)

UNIVENT is not specifically a bronchial blocker, yet comprises of a conventional endotracheal tube of a single lumen, with a bronchial blocker incorporated. This design presents a channel in the wall where the blocker slides into place. A high volume distal balloon can be inflated between 2 and 6 cc, depending on the introduction into lobar or main bronchus. These consist in a channel of 2 mm lumen that

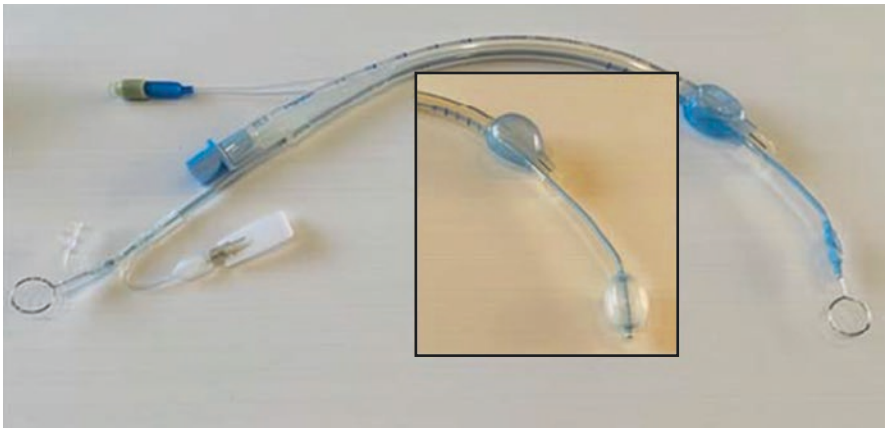

Fig. 5.1 The UNIVENT tube. It's an endotracheal tube with a channel in its walls where the blocker is passed through

allows for air aspiration once inflated, thus facilitating pulmonary collapse. Moreover, this channel facilitates the administration of oxygen or can be connected to a CPAP system (Fig. 5.1).

The external diameter of the Univent tube should always be noted, considering its considerably larger size that a conventional tube. The reason for this is the presence of the secondary channel for the blocker. This is especially important in paediatric patients, where the size of the Univent should be considered according to the age of the patient.

This device was initially used for patients with a difficult airway because double lumen tubes are more difficult to insert. In the last decade, the introduction of several independent BBs has produced a reduction in their use, so that they are no longer recommended in patients with difficult airway for its greater risk than the independent BBs [14].

Moreover this device has also been considerated necessary in cases when the bronchial bleeding from different etiologies must be controlled, using the bronchial blocker at the same time as isolating the healthy lung [15].

5.5.2 The Arndt Bronchial Blocker (William Cook Europe, Denmark)

The Arndt Bronchial Blocker was the first BB independently designed specifically for unipulmonary ventilation. It is characterised by a nylon loop that protrudes from the distal extremity, thus allowing for the guided insertion of the Arndt BB using a standard paediatric fiberscope that is passed throught the hole loop to introduce the Arndt BB that must be attached to the fibroscope (Fig. 5.2).

This BB is ideal to achieve selective lobar blockade, considering the ability to perfectly introduce the BB next to the fibroscope to the lobar bronchus of the

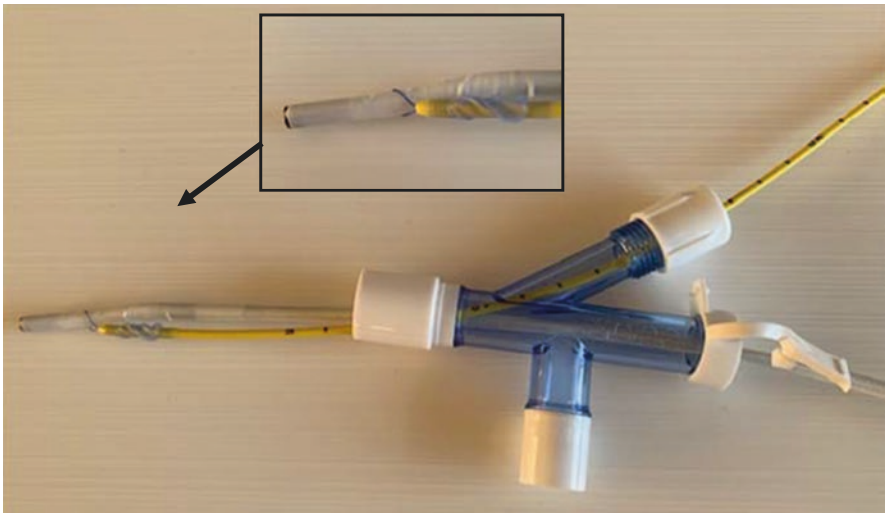

Fig. 5.2 The wire-guided Arndt Blocker with the nylon loop protruding from the distal end, allowing for a guided insertion via a standard pediatric fiberscope that is inserted into the interior of the loop

Table 5.1 Bronchial blockers' characteristics

	Arndt blocker	Cohen blocker	Fuji uniblocker	EZ-blocker
Size	5, 7 and 9 Fr	9 Fr	5 and 9 Fr	7 Fr
Length	5 Fr: 40 cm, 7 Fr: 65 cm, 9 Fr: 78 cm	65 cm	65 cm	75 cm
Balloon design	Spherical or Elliptical	Spherical or Elliptical	Spherical	Both are Spherical
Type of balloon	High volume, low pressure	High volume, low pressure	High volume, low pressure	High volume, high pressure
Average insuflation volume of the balloon	5 Fr: 0,5–2 ml 7 Fr: 2–6 ml 9 Fr spherical: 4–8 ml 9 Fr elliptical: 6–12 ml	6–9 ml	5 Fr: 3 ml 9 Fr: 8 ml	Left balloon: 11 ml Right balloon: 14 ml
Murphy eye	Present in 9 Fr	Present	Absent	Absent
Central canal diameter	1.4 mm	1.6 mm	2 mm	1.4 mm
Minimum recommended size of the endotracheal tube	5 Fr: TET 4.5 cm 7 Fr: TET 7 cm 9 Fr: TET 8 cm	TET 8 cm	9 Fr: TET 8 cm	TET 7 cm

pulmonary lobe that we wish to isolate [3]. The complete characteristics are specified in Table 5.1.

Before introducing the tube into the patient, the fiberscope and BB should be correctly positioned in the corresponding orifices of the multiport airway adapter. This step should assure that each instrument is connecting to the device in such a way that the output of both in the destination connection and the endotracheal tube connection should link, passing the distal extremity of the fiberscope through the loop of the Arndt BB, fixed 1 cm away from the distal extremity. Afterwards, both should be introduced inside the endotracheal tube and fixed to the multiport airway adapter with the endotracheal tube, orientating the point of the fiberscope until the bronchus that is intended to be blocked. Once inserted into this bronchus, the BB is pushed until it can be seen beyond the point of the fiberscope, leaving the BB positioned in place checked by the fiberscope view.

The largest problem presented by Arndt is seen in the difficulties found when adjusting its placement once the nylon loop has been retracted in order to achieve pulmonary collapse or apply CPAP. This issue is caused by how the loop cannot be redirected with the same accuracy, especially after having retracted the link that joined with the fiberscope. This Arndt BB is the device that presents the highest count of dislocations than all other BBs [9]. The difficulties in placement have consequently limited its general use, regardless of its success in general applications and use in selective lobar blocking.

5.5.3 The Cohen Bronchial Blocker (William Cook Europe Aps, Denmark)

The Cohen BB is one of the most used on a global scale and presents some highly favourable characteristics for its general use (Table 5.1). In principle, the method of insertion is similar to that of the Arndt. The device presents a multiport airway adapter, where the blocker and paediatric fiberscope is introduced separately. The Cohen BB also contains a small wheel in its proximal extremity that enables a 90° unidirectional movement of the distal extremity (Fig. 5.3). This device also presents a 9Fr caliber for adults. Above the balloon, an arrow is drawn so that, via the fiberscope, the specialist can see where the blocker is aimed. The proximal wheel can change the direction of the blocker, thus aiming at the lobe we try to block. This device also has two distal orifices that allow for the aspiration of secretions, facilitating the collapse of the lung and allows the application of a CPAP system.

In order to correctly position the device, the fiberscope is positioned more than 2 cm from the carina, thus allowing for the optimum visualisation of where the blocker will be placed. In the case where the BB is aimed directly at the bronchus of interest, all that is needed is the gentle insertion of the BB. In the opposite case, the arrow should be simply oriented towards the direction of the selected bronchus by applying a rotation to the BBs and the tip can be flexed by means of the proximal wheel, which facilitates the placement of the BBs. Once positioned, the balloon is

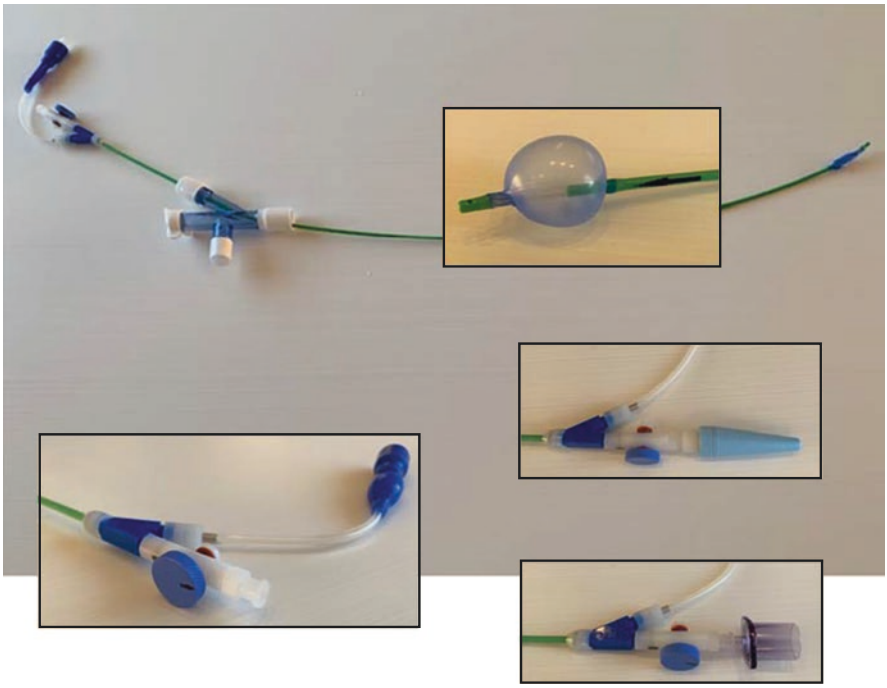

Fig. 5.3 The Cohen Blocker presenting a wheel in its proximal extremity that turns 90°, orientating the point of the blocker towards a designated area. Above the balloon there is a small arrow drawn, visible through the fiberscope indicating where the blocker is pointed to

inflated between 4 and 8 ml, controlled via the fiberscope or with the camera available in some endotracheal tubes such as the Viva Sight SL.

The Cohen BB is very easy to reposition in the case of accidental displacement, during the movement of the patient as well as during surgery, thus implicating a great advantage in relation to the Arndt BB [16].

5.5.4 Fuji Uniblocker Bronchial Blocker

The Uniblocker is another form of BB, and much like other blockers allows for selective isolation of the lung. This device shares multiple characteristics with UNIVENT (incorporated BBs), yet in this case is independent from the single-lumen tube (Fig. 5.4).

This piece of equipment includes multiple different sizes, including adult (9 Fr) and paediatric (5 Fr) models. The Uniblocker has, as most blockers do, a multiport airway proximal adapter that allows for the introduction of the blocker, paediatric fiberscope and respiration connections.

One of the main advantages of this equipment is found in its greater internal calibre that facilitates the collapsing of the lung and CPAP, as well as an easier insertion [17] through small movements of the proximal end of the BB. This is also made

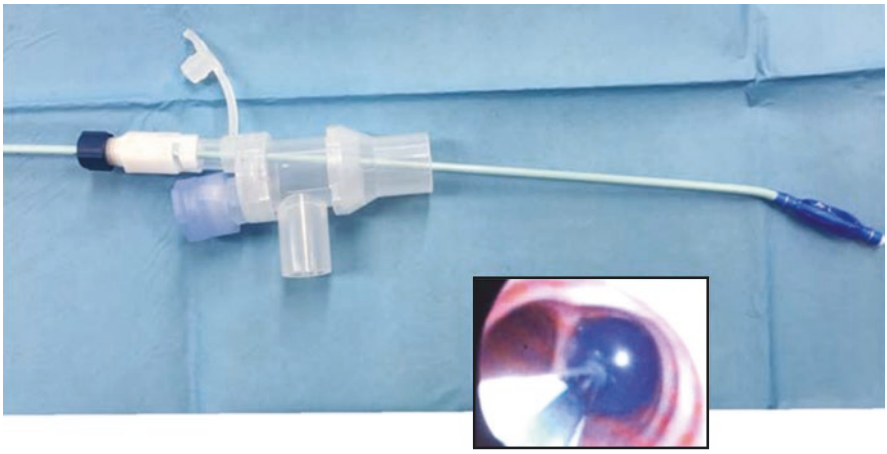

Fig. 5.4 The bronchial blocker Uniblocker, is easily introduced through the rotation of the proximal part of the BB to the left or right side and it must be inserted guided by direct vision using a fiberscope or a single-lumen tube with embedded camera

easier by the direct vision via fiberscope [13] or other optic device such as the VivaSight SL tube (Video nº1).

Blind lung isolation using the Uniblocker has presented a degree of success of over 85% in the case of right lung isolation and lower than 60% in the case of left lung isolation. Nevertheless, it is highly recommendable to use this BB guided by an optic device, unless such conditions are not available.

5.5.5 EZ-Blocker Bronchial Blocker (Teleflex Life Sciences Ltd., Athlone, Ireland) (EZB)

The EZ-Blocker BB, in comparison with the aforementioned blockers, presents a biforked distal extremity in a "Y" shape (Fig. 5.5). Each of the distal extensions includes a high pressure polyurethane balloon colour coded to coincide with each of the proximal balloons. This device has a distal point with a central lumen of 0.7 mm.

This design allows for the distal Y-shaped extremity to hook on to the tracheal carina during the insertion into the trachea, fixing the device in place and hindering its displacement. For this, its use in surgical practices associated with sequential episodes of isolation for either lung, such as the case of bilateral thoracoscopic sympathectomy, is highly recommended (video nº2). In such cases, once the procedure has been completed in a hemithorax, the only additional steps are the disinflation of the balloon in this side in order to reinflate the lung, followed by its contralateral balloon insufflation in order to collapse the other lung [8].

For the introduction of this device, it is recommended that the endotracheal tube is positioned approximately 4 cm from the tracheal carina, assuring that the vision through the FBS or endotracheal tube with incorporated camera (Viva Sight SL) has enough distance to allow for a separation between either terminals, facilitating the

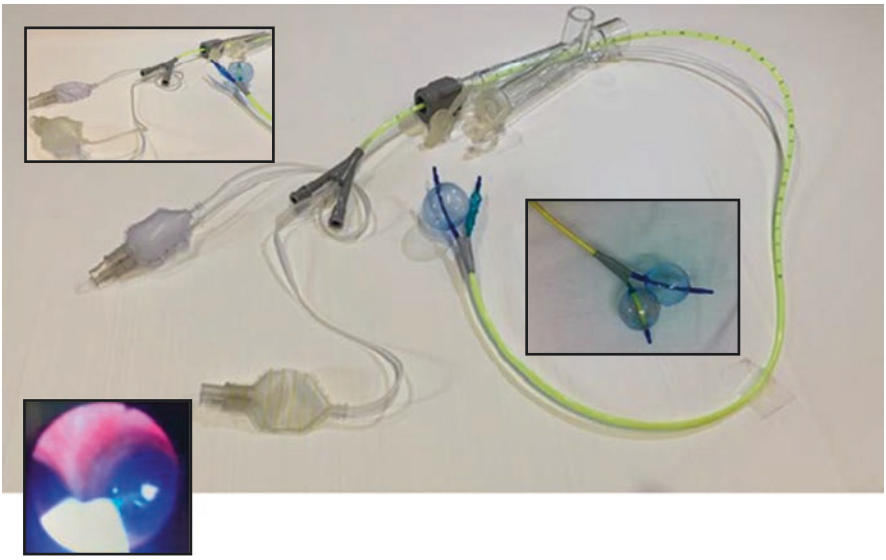

Fig. 5.5 The EZ-Blocker with its double extremity with two balloons that can be positioned in both main bronchi (left and right)

introduction of each extremity in the corresponding principal bronchi. Finally, two disadvantages are present in comparison with other BBs. The first is that the balloons are of high pressure, presenting difficulties and inconveniences in multiple situations [1]. The second is related to the internal diameter of both terminals (0.7 mm), presenting a distinct inconvenience that makes collapsing the lung a lengthy process. Because of this, the use of discontinuous aspiration through the internal channel or a period of disconnection or apnea to shorten it is recommended.

References

1. Campos JH. Progress in lung separation. Thorac Surg Clin. 2005;15:71–83.
2. Inoue H, Shohtsu A, Ogawa J, Kawada S, Koide S. New device for one-lung anesthesia: endotracheal tube with movable blocker. J Thorac Cardiovasc Surg. 1982;83(6):940–1.
3. Garcia-Guasch R, Campos JH, Granell M, Peña JJ. Applications for bronchial blockers in thoracic surgery. Rev Esp Anestesiol Reanim. 2001;54(9):547–55.
4. Granell M, Solís P, Cordova C, Cobo I, Guijarro R, de Andrés JA. Intubation in two patients with difficult airway management and tracheal stenosis after tracheostomy in thoracic surgery. Rev Esp Anestesiol Reanim. 2018;65(6):347–50.
5. Eisenkraft JFCE, Neustein SM. Anesthesia for thoracic surgery. In: Barash CB, Stoelting RK, Cahalan MK, Ortega R, Stock MC, editors. Clinical anesthesia. Philadelphia, PA: Lippincott Williams & Wilkins; 2013. p. 1030–75.
6. Brodsky JB. Con: a bronchial blocker is not a substitute for a double-lumen endobronchial tube. J Cardiothorac Vasc Anesth. 2015;29(1):237–9.
7. Campos JH, Kernstine KH. A comparison of a left-sided Broncho-Cath with the torque control blocker univent and the wire-guided blocker. Anesth Analg. 2003;96(1):283–9.

8. Mourisse J, Liesveld J, Verhagen A, van Rooij G, van der Heide S, Schuurbiers-Siebers O, et al. Efficiency, efficacy, and safety of EZ-blocker compared with left-sided double-lumen tube for one-lung ventilation. Anesthesiology. 2013;118(3):550–61.
9. Narayanaswamy M, McRae K, Slinger P, Dugas G, Kanellakos GW, Roscoe A, et al. Choosing a lung isolation device for thoracic surgery: a randomized trial of three bronchial blockers versus double-lumen tubes. Anesth Analg. 2009;108(4):1097–101.
10. Bauer C, Winter C, Hentz JG, Ducrocq X, Steib A, Dupeyron JP. Bronchial blocker compared to double-lumen tube for one-lung ventilation during thoracoscopy. Acta Anaesthesiol Scand. 2001;45(2):250–4.
11. Slinger PDCJ. Anestesia para la cirugía torácica. In: Miller RDEL, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller anestesia. Séptima edición ed. Barcelona: Elsevier; 2010. p. 1600.
12. Campos J. Update on selective lobar blockade during pulmonary resections. Curr Opin Anaesthesiol. 2009;22:18–22.
13. Morales J, Granell M, Biosca E, Guijarro R, Arnau A, de Andrés J. Right lobar isolation by different methods in two patients with previous left lung resection. J Cardiothorac Vasc Anesth. 2017;31:S53.
14. Granell M, Parra MJ, Jiménez MJ, et al. Review of difficult airway mangement in thoracic surgery. Rev Esp Anestesiol Reanim. 2018;65(1):31–40.
15. Nishiumi N, Nakagawa T, Masuda R, et al. Endobronchial bleeding associated with blunt chest trauma treated by bronchial occlusion with a Univent. Ann Thorac Surg. 2008;85(1):245–50.
16. Cohen E. Strategies for lung isolation: to block or not to block? Can J Anaesth. 2016;63(7):797–801.
17. Neustein SM. Pro: bronchial blockers should be used routinely for providing one-lung ventilation. J Cardiothorac Vasc Anesth. 2015;29(1):234–6.

Utility of Bronchoscope in Thoracic Surgery

6

Antonio Villalonga and Mohamed El Tahan

6.1 The Flexible Bronchoscope

The flexible bronchoscope (FB) is an optical instrument that allows visualization of the airway from the mouth or nose to beyond the tertiary bronchi. Its design has changed with the passage of time and its indications have been gradually increasing.

The technique of rigid bronchoscopy, preceded flexible bronchoscopy, was developed in 1897 by Gustav Killian, and perfected two decades later by Nathan Faux who managed to visualize the trachea and the main bronchi. This technique has persisted to this day, as a diagnostic and therapeutic procedure, although with more restricted indications.

In 1966 Shigeto Ikeda developed the first FB, he said: "There is more hope with the bronchoscope". It used filaments of coherent optical fiber, therefore it was called fiber-optic bronchoscope. In 1967 Murphy described the first tracheal intubation with a fibroscope [1, 2].

If a fiber is broken to the fiber-optic bronchoscopes a black dot appears in the image. The new FB have been improved and transmit the image by a system based on a charge coupled device (CCD) that is located at its end distal and have a definition 15 times greater. Although the term fibrobronchoscope is still used, in reality many are videobronchoscopes and it is more correct to call all of them flexible bronchoscopes. The FB is an instrument of high price, fragile and delicate, which

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requires a theoretical and practical training for its correct use and a careful cleaning and asepsis after its use to avoid the transmission of infections [3, 4].

6.1.1 Flexible Bronchoscope Dimensions

The most common type of FB currently used by anesthesiologists is the white light with a length of 600 mm that can cover the entire bronchial tree. There is a great variety of FB, the main trademarks are Olympus, Pentax, Storz, Machida, Fuji, Wolf, etc., in addition, other brands such as Ambu have developed the single-use FB that allows its availability at any time and avoid the cleaning process.

The FB can have different widths of the insertion cord that determine which can be used with a double lumen tube (DLT). Although DLTs can be positioned blindly, most anesthesiologists use the FB to see the correct position of both tracheal and bronchial lumen. For DLT from 35 to 41 Fr it is necessary to use a FB < 4 mm in diameter that can pass through both lumen. The FB of 4.8 mm can pass through the tracheal lumen of the DLT of 39 Fr and also of the bronchial lumen of the DLT of 41 Fr. For the DLT of 32 Fr it is necessary to use FB < 3.4 mm. There are pediatric FB of 2.7 mm for 35 Fr DLT and 1.8–2.2 mm for 26 Fr DLT.

In general bronchial blockers (BBs) need a thin FB to be placed in the desired place of the bronchial tree and see how the cuff is located once inflated.

6.1.2 Disposable Flexible Bronchoscope

Currently, disposable single-use videobronchoscopes (Ambu® aScope™ 4) are available, with an external monitor screen, and have the advantage of easy availability and transport to use it immediately and avoid the risks of cross-infection. The third generation has already been marketed, which has achieved a level of perfection similar to that of non-disposables, they are very ergonomic, the quality of vision is excellent and they have the possibility of recording in external video systems. Its drawback is the price, but by not incurring repair costs, nor those that entails cleaning, they become effective cost.

There are three different sizes, in relation to the external diameter of the insertion cord and the working channel of the instrument, the large 5.8 mm/2.8 mm, the regular 5.0 mm/2.2 mm and the slim 3.8 mm/1.2 mm, all have an insertion cord of 600 mm. The slim can be used for the DLT 35-37-39-41 Fr and tracheal tube (TT) 5 mm, the regular one serves for the DLT 41 Fr and TT 6 mm and the large one does not work for DLT but for TT ≥ 7 mm [5, 6].

6.1.3 Recommendations for Flexible Bronchoscopy

A flexible bronchoscope is considered to be the most reliable device for tracheal intubation in patients with difficult airways (see Chap. 10), and is fundamental for

the correct placement of DLTs (see Chap. 5) and BBs (see Chap. 6) and to solve problems related to thoracic surgery, but considerable skill with the FB is required. The practice of FB requires certain standards to be carried out safely and effectively. It begins with the correct training of the bronchoscopist and the staff, with this purpose there are resources to acquire this training, such as practical courses with dummies and simulators [7].

Proper patient preparation, monitoring of basic cardiorespiratory parameters, ensuring proper oxygenation and ventilation, and patient comfort and safety are essential through the application of adequate premedication, topical anesthesia, and sedation or anesthesia.

In addition, it is necessary to ensure the own safety and that of the staff avoiding the risk of contamination by infections of the patient by means of the use of masks, hat, gloves and gown and at the end to carry out a correct cleaning and disinfection of the equipment. It is necessary to know and avoid possible complications and treat them immediately when they appear. The British Thoracic Society published comprehensive guidelines in 2001, which have been updated in 2013, and include recommendations for the good practice of bronchoscopy [8].

6.1.4 Anesthesiologist's Role in Flexible Bronchoscopy

The anesthesiologist can be found in different scenarios regarding bronchoscopy: (1) The most common is as a user, usually to perform a tracheal intubation with FB. (2) Administering anesthesia or sedation in the bronchoscopy department of the pulmonology departments. (3) In the context of thoracic surgery and (4) In the critical patient either the postoperative thoracic or other. We will refer to these last three fields below.

6.1.4.1 Anesthesia in the Bronchoscopy Cabinet

The pulmonology bronchoscopy cabinets are increasing their procedures, is the so-called interventional pneumology that is a expanding specialty who often perform invasive procedures necessitating an anesthesiologist for deep sedation or general anesthesia. Consequently, anesthesiologists need to be familiar with these new procedures to formulate appropriate anesthetic plans and anticipate potential complications.

There are two main branches of interventional pneumology: diagnostic bronchoscopy and therapeutic bronchoscopy. The main diagnostic indications of FB are reported in Table 6.1.

Early detection is crucial to improve survival of lung cancer. Although tissue biopsy obtained by flexible bronchoscopy remains the gold standard for diagnosing malignant or premalignant airway disease, only 29% of carcinoma in situ (CIS) and 69% of microinvasive tumors are detectable using conventional white light bronchoscopy (WLB) alone [9, 10].

To increase the diagnostic accuracy new innovations in bronchoscopy incorporate developments in imaging technology [11, 12], such as endobronchial

Table 6.1 Diagnostic indications of flexible bronchoscopy

1. Taking microbiological samples: bronchial aspirate, bronchoalveolar lavage …
2. Sampling of masses and nodules: bronchial biopsy, transbronchial aspiration …
3. Staging of neoplasms. Diagnosis of dysphonia, stridor, cough and other pneumological signs and symptoms
4. Identification and treatment of hemoptisis
5. Lacerations or tracheal ruptures or bronchi. Thoracic trauma
6. Tracheoesophageal fistula
7. Bronchopulmonary fistula (after pneumonectomy)
8. Lung cryobiopsy in interstitial or diffuse lung diseases

Table 6.2 Developments in diagnostic bronchoscopy

1. Autofluorescence bronchoscopy (AFB) and narrow band imaging (NBI) [13]
2. High magnification bronchovideoscopy (HMB) [14]
3. Optical coherence tomography (OCT) [15]
4. Confocal laser endomicroscopy (CLE) [16]
5. Linear endobronchial ultrasound (EBUS) [17]
6. Radial endobronchial ultrasound (R-EBUS) [18]
7. Electromagnetic navigational bronchoscopy (EMB) [19]
8. Laser Raman spectroscopy (LRS) [20]

ultrasound-guided transbronchial needle aspiration, to improve the yield, sensitivity, and specificity of diagnostic pulmonary procedures which are summarized in Table 6.2 [13–20].

6.1.4.2 Diagnostic Bronchoscopy Before Thoracic Surgery

The diagnostic FB immediately before the surgery is a procedure that is fundamental to know the extension and type of the tumor and the possibility of resectability, and in the case of tracheal surgery it will indicate the height at which the tracheal narrowing is found, the tumor or the fistula, and also the remaining light to pass the orotracheal tube. After studying the airway we can know if it is possible to place a conventional endotracheal tube and the size of it, if possible ventilation with laryngeal mask or will have to perform jet ventilation through a cannula. The information provided by the FB is of great value in these cases.

6.2 Therapeutic Bronchoscopy

The field of interventional bronchoscopy using FB is rapidly advancing and include electrocautery-diathermy, argon plasma coagulation and thermal laser, cryotherapy, cryoextraction, photodynamic therapy, brachytherapy, tracheobronchial stenting, electromagnetic navigation bronchoscopy, endobronchial valves for emphysema and bronchial thermoplasty for asthma (Table 6.3).

Table 6.3 Therapeutic indications of bronchoscopy

1. Elimination of mucus and foreign bodies. Resolution of hypoxemia produced by atelectasis
2. Endotracheal intubation, placement of DLT or BB
3. Treatment of tumors or tissues that occlude the airway
4. Cryotherapy
5. Balloon dilatation/placement of tracheobronchial stents
6. Bronchial thermoplasty: weakening of the smooth bronchial musculature for the treatment of asthma refractory to medical treatment
7. Photodynamic therapy
8. Electrocoagulation
9. Placement of catheters for brachytherapy
10. Bronchoalveolar lavages in alveolar proteinosis
11. Lung volume reduction in emphysema
12. Assistance for percutaneous dilatational tracheostomy

Although bronchoscopic procedures are considered less invasive than their corresponding surgical ones, the risks should not be underestimated, since these patients usually have multiple comorbidities and are too sick, so they are excluded from surgery. On the other hand, these procedures are urgent or emergency and these patients are not optimized before their procedure, therefore, it is a great challenge for the anesthesiologist to perform the anesthesia or sedation of these patients given the high morbidity and mortality associated with these procedures [21].

6.2.1 FB, Pulmonary Emphysema and Lung Volume Reduction

In patients with pulmonary emphysema, duly selected, volume reduction surgery improves the clinical symptoms (dyspnea, ability to exercise, etc.) and also pulmonary function. However, this surgery is associated with high morbidity (30–50%) and mortality (4–7%). Therefore, less invasive techniques have been developed using FB to achieve the same results as surgery [22, 23]. These techniques include:

- Sclerosants and targeted lung denervation are additional modalities on the horizon for COPD treatment. Substances are administered by FB that produce inactivation of the surfactant and, later, an inflammatory and cicatricial reaction, with contraction of the affected parenchyma.
- Insertion of unidirectional valves, through bronchoscope, in the bronchial tree, prevent the entry of air into the isolated lung segment, but allow the drainage of secretions and exhaled gas, distal to the valve. This leads to the collapse of the isolated emphysematous segment, mimicking the result of surgical procedures for lung reduction [24].
- Endobronchial coils are a much newer technology for patients with emphysema and air trapping. Results of the latest randomized clinical trial showed improvement in exercise tolerance but with an increased likelihood of major complications [25].

Kemp et al. summarizes recent clinical trials for and emerging technologies in bronchoscopic treatment of COPD, including thermal ablation, valves, lung denervation, and cryospray [26].

6.2.2 Bronchial Thermoplasty for the Treatment of Refractory Asthma

Involves bronchoscopic delivery of radiofrequency energy to decrease smooth muscle thickness. The studies have shown BT to be safe and effective in reducing severe exacerbations, improving quality of life, and decreasing emergency department visits. Bronchial thermoplasty is performed in three separate visits [27, 28].

6.2.3 FB in Percutaneous Dilatational Tracheotomy

Percutaneous dilatational tracheostomy with flexible bronchoscopy assistance is effective and safe in critically ill patients under mechanical ventilation when performed by experienced specialists [29].

6.3 Sedation and Anesthesia in the Bronchoscopy Suite

The number and diversity of procedures performed by FB is increasing. At the same time, there is a flow of relocation of pulmonary interventional procedures including rigid bronchoscopy that were previously assigned to a traditional operating room and are now performed in the bronchoscopy suite because of improved provider flexibility, presents more cost-effective options while maintaining patient safety and satisfaction [30, 31].

With the widespread use of FB with more complex and longer procedures, the importance of proper sedation and anesthesia is crucial. It is debatable and controversial if it is acceptable for it to be administered by non-anesthesiologists. It is generally accepted that they could administer superficial sedation for short procedures in non-deteriorated patients. However, for the interventional bronchoscopy it is imperative an anesthesiologist [32].

The initial basis of a correct sedation or anesthesia is a correct topical anesthesia, usually performed with lidocaine and avoiding not exceeding toxic doses. There is a growing body of literature highlighting the advantages and benefits of propofol anesthesia for both flexible and rigid bronchoscopy. Propofol is the agent of choice, in boluses it is usually sufficient in brief procedures, and in the most complex ones administered by perfusion pumps and with other drugs such as opiates, alfentanil, remifentanil, etc. Most procedures can be performed in spontaneous ventilation, although they require a laryngeal mask or a tracheal tube and in an outpatient setting [33–36]. Dexmedetomidine has been used, which is a hypnotic with antisialagogue properties and minimal effects on the respiratory system. In addition, its vagolytic

effects are beneficial to attenuate the sympathetic response associated with intubation but for its prolonged recovery times, it is not favorable for outpatients [37–39].

6.4 Bronchoscopy in the Postoperative Period of Thoracic Surgery

Thoracic surgery includes procedures in which a high percentage of patients can develop serious complications. Therefore, the immediate postoperative period takes place in critical care units, where it is important to have a FB for the diagnosis and treatment of many of these complications. In intubated patients, preoxygenation is essential, increasing the FiO_2 up to 100%. It is advisable to continue with this concentration for the duration of the bronchoscopy and for a short period afterwards. The respirator must be adjusted in controlled mode to ensure ventilation. The limit pressure of the ventilator must be increased to ensure an adequate tidal volume during each cycle, but without exceeding the values at which a barotrauma can be caused. It is necessary to place a special connector with a perforated diaphragm between the endotracheal tube and the ventilator, so that the FB can be introduced through it and continue the ventilation and maintain the PEEP / CPAP. This is particularly important in patients with hypoxia or with adult respiratory distress syndrome (ARDS). In the patient without tracheal intubation, the preferred route for bronchoscopy in resuscitation is the nasal route. We highlight the following complications:

6.4.1 Atelectasis

Is the most frequent postoperative complication of thoracic surgery. It can occur in the operated lung or in the contralateral lung. The causes are multifactorial: due to mucociliary alteration, hypoventilation and alteration of diaphragmatic function, among other mechanisms. Other complications include hypoxemic respiratory failure. In this context, we are in need of a therapeutic bronchoscopy in a patient who may be in treatment with invasive mechanical ventilation. The FB allows in many cases to know its etiological, being the bronchial secretions the most frequent. In this case, the FB is useful for solving the problem, since it allows to aspirate the secretions through the working channel of the FB with the help of physiological serum or acetylcysteine.

6.4.2 Hemoptysis

A small bleeding is relatively frequent if it increases or persists, it is necessary through the FB to determine if its location and amount is possible. In cases of massive hemorrhage, the FB may be insufficient to locate the bleeding. In these cases, a rigid bronchoscopy may be necessary, through which the problem can be identified

and resolved more easily. Tracheal or bronchial injury or rupture. Its incidence is 1% with intubations with TDL. The clinic usually appears in the first hours of the postoperative period, in the form of dyspnea, subcutaneous emphysema in the neck and chest, hemoptysis and cyanosis. The FB together with the CT scan are the diagnostic methods of choice to determine the location and magnitude of the tracheobronchial break.

6.4.3 Torsion of Lobe or Lung Segment

In the postoperative period of pulmonary resections in the operated hemothorax, a rotation of part of the parenchyma on its bronchovascular pedicle may occur in the areas adjacent to the resection. The bronchoscopy is indicated in the presence of a pulmonary consolidation that does not improve with conservative measures, when carrying out a stenosis of the bronchus and its mucosa with engorged vessels. It may be feasible to pass the FB through the stenosis, but it collapses again upon removal. The treatment will be a new emergency thoracotomy that often requires lung resection.

6.4.4 Bronchopleural Fistula

It is one of the most feared complications in the postoperative period of thoracic surgery. The FB is useful as a diagnostic tool and in some cases therapeutic, as in small fistulas where it can be used, always under endoscopic vision, repeated cauterizations, placement of tissue adhesive materials, stents, etc.

6.4.5 Bronchoscopy in the Lung Transplantation

In lung transplantation (see Chap. 20), bronchoscopy may be required if problems such as those described above appear. In addition, at the end of the transplant, the endobronchial tube is changed to a tracheal tube and a bronchoscopy is performed to check the condition of the sutures and aspirate secretions and take samples for Gram and culture studies. It will also be repeated in the postoperative period before extubation of the patient. The FB remains the gold standard to establish the presence or absence of acute pulmonary allograft rejection or infection after lung transplantation. The use of FB modified clinical management in one third of airway evaluation and microbiological sampling procedures for critically ill lung transplantation recipients. No fatalities were attributed to bronchoscopy in this critically ill population [40, 41].

References

1. Ikeda S, Yanai N, Ishikawa S. Flexible bronchofiberscope. Keio J Med. 1968;17:1–16.
2. Murphy P. A fibre-optic endoscope used for nasal intubation. Anaesthesia. 1967;22:489–91.

3. Ovassapian A. Fiberoptic endoscopy and the difficult airway. 2nd ed. Philadelphia, PA: Lippincott; 1996.
4. Villalonga Morales A. Fibroscopia en anestesiología y reanimación. Madrid: Ergon; 2005.
5. Zaidi SR, Collins AM, Mitsi E, Reiné J, Davies K, Wright AD, et al. Single use and conventional bronchoscopes for Broncho alveolar lavage (BAL) in research: a comparative study (NCT 02515591). BMC Pulm Med. 2017;17:83. https://doi.org/10.1186/s12890-017-0421-7.
6. Marshall DC, Dagaonkar RS, Yeow C, Peters AT, Tan SK, Tai DY, et al. Experience with the use of single-use disposable bronchoscope in the ICU in a tertiary referral center of Singapore. J Bronchol Interv Pulmonol. 2017;24:136–43.
7. Baker PA, Weller JM, Baker MJ, Hounsell GL, Scott J, Gardiner PJ, Thompson JMD. Evaluating the ORSIM® simulator for assessment of anaesthetists' skills in flexible bronchoscopy: aspects of validity and reliability. Br J Anaesth. 2016;117(Suppl. 1):i87–91.
8. Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, et al. British Thoracic Society Guideline for diagnostic flexible bronchoscopy in adults. Thorax. 2013;68:i1–i44.
9. Andolfi M, Potenza R, Capozzi R, Liparulo V, Puma F, Yasufuku K. The role of bronchoscopy in the diagnosis of early lung cancer: a review. J Thorac Dis. 2016;8:3329–37.
10. Sardi AH, Islam S. Early lung cancer detection, mucosal, and alveolar imaging. Curr Opin Pulm Med. 2016;22:271–80.
11. Selzer AR, Murrell M, Shostak E. New trends in interventional pulmonology. Curr Opin Anesthesiol. 2017;30:17–22.
12. Dhillon SS, Harris K. Bronchoscopy for the diagnosis of peripheral lung lesions. J Thorac Dis. 2017;9(Suppl 10):S1047–58.
13. He Q, Wang Q, Wu Q, Feng J, Cao J, Chen BY. Value of autofluorescence imaging videobronchoscopy in detecting lung cancers and precancerous lesions: a review. Respir Care. 2013;58:2150–9.
14. Yamada G, Shijubo N, Kitada J, Takahashi M, Otsuka M, Fujii M, Takahashi H. Decreased subepithelial microvasculature observed by high magnification bronchovideoscope in the large airways of smokers. Intern Med. 2008;47:1579–83.
15. d'Hooghe JNS, Goorsenberg AWM, de Bruin DM, Roelofs JJTH, Annema JT, Bonta PI. Optical coherence tomography for identification and quantification of human airway wall layers. PLoS One. 2017;12(10):e0184145.
16. Wellikoff AS, Holladay RC, Downie GH, Chaudoir CS, Brandi L, Turbat-Herrera EA. Comparison of in vivo probe-based confocal laser endomicroscopy with histopathology in lung cancer: a move toward optical biopsy. Respirology. 2015;20:967–74.
17. d'Hooghe JNS, Goorsenberg AWM, de Bruin DM, Roelofs JJTH, Annema JT, Bonta PI, Gompelmann D, Herth FJF. Role of endobronchial and endoscopic ultrasound in pulmonary medicine. Respiration. 2014;87:3–8.
18. Ali MS, Trick W, Mba BI, Mohananey D, Sethi J, Musani AI. Radial endobronchial ultrasound for the diagnosis of peripheral pulmonary lesions: a systematic review and meta-analysis. Respirology. 2017;22:443–53.
19. Han KN, Kim HK. The feasibility of electromagnetic navigational bronchoscopic localization with fluorescence and radiocontrast dyes for video-assisted thoracoscopic surgery resection. J Thorac Dis. 2018;10(Suppl 6):S739–48.
20. Short MA, Lam S, McWilliams AM, Ionescu DN, Zeng H. Using laser Raman spectroscopy to reduce false positives of autofluorescence bronchoscopies: a pilot study. J Thorac Oncol. 2011;6:1206–14.
21. Ernst A, Simoff M, Ost D, Goldman Y, Herth FJF. Prospective risk-adjusted morbidity and mortality outcome analysis after therapeutic bronchoscopic procedures: results of a multiinstitutional outcomes database. Chest. 2008;134:514–9.
22. Slebos D-J, Shah PL, Herth FJF, Valipour A. Endobronchial valves for endoscopic lung volume reduction: best practice recommendations from expert panel on endoscopic lung volume reduction. Respir Int Rev Thorac Dis. 2017;93:138–50.
23. Flandes J, Soto FJ, Cordovilla R, Cases E, Alfayate J. Bronchoscopic lung volume reduction. Clin Chest Med. 2018;39:169–80.

24. Klooster K, ten Hacken NH, Hartman JE, et al. Endobronchial valves for emphysema without interlobar collateral ventilation. N Engl J Med. 2015;373:2325–35.
25. Sciurba FC, Criner GJ, Strange C, et al. Effect of endobronchial coils vs usual care on exercise tolerance in patients with severe emphysema: the RENEW randomized clinical trial. JAMA. 2016;315:2178–89.
26. Kemp SV, Shah DL. An update on bronchoscopic treatments for chronic obstructive pulmonary disease. Curr Opin Pulm Med. 2016;22:265–70.
27. Lee JA, Rowen DW, Rose DD. Bronchial thermoplasty: a novel treatment for severe asthma requiring monitored anesthesia care. AANA J. 2011;79:480–3.
28. Kheir F, Majid A. Bronchial thermoplasty: a nonpharmacologic therapy for severe asthma. Clin Chest Med. 2018;39:261–9.
29. Cheung NH, Napolitano LM. Tracheostomy: epidemiology, indications, timing, technique, and outcomes. Respir Care. 2014;59:895–919.
30. Jose RJ, Shaefi S, Navani N. Anesthesia for bronchoscopy. Curr Opin Anesthesiol. 2014;27:453–7.
31. Goudra BG, Singh PM, Borle A, Farid N, Harris K. Anesthesia for advanced bronchoscopic procedures: state-of-the-art review. Lung. 2015;193:453–65.
32. Kern M, Kerner T, Tank S. Sedation for advanced procedures in the bronchoscopy suite: proceduralist or anesthesiologist? Curr Opin Anesthesiol. 2017;30:490–5.
33. Carmi U, Kramer MR, Zemtzov D, et al. Propofol safety in bronchoscopy: prospective randomized trial using transcutaneous carbon dioxide tension monitoring. Respiration. 2011;82:515–21.
34. Grendelmeier P, Tamm M, Pflimlin E, Stolz D. Propofol sedation for flexible bronchoscopy: randomized, noninferiority trial. Eur Respir J. 2014;43:591–601.
35. Yoon HI, Kim J-H, Lee J-H, et al. Comparison of propofol and the combination of propofol and alfentanil during bronchoscopy: a randomized study. Acta Anaesthesiol Scand. 2011;55:104–9.
36. de Lima A, Kheir F, Majid A, Pawlowski J. Anesthesia for interventional pulmonology procedures: a review of advanced diagnostic and therapeutic bronchoscopy. Can J Anaesth. 2018;65:822–36.
37. Ryu JH, Lee SW, Lee JH, et al. Randomized double-blind study of remifentanil and dexmedetomidine for flexible bronchoscopy. Br J Anaesth. 2012;108:503–11.
38. Cai Y, Li W, Chen K. Efficacy and safety of spontaneous ventilation technique using dexmedetomidine for rigid bronchoscopic airway foreign body removal in children. Paediatr Anaesth. 2013;23:1048–53.
39. Wang HB, Yang CX, Zhang B, et al. Efficacy of target-controlled infusion of propofol and remifentanil with high frequency jet ventilation in fibre-optic bronchoscopy. Singap Med J. 2013;54:689–94.
40. Glanville AR. Bronchoscopic monitoring after lung transplantation. Semin Respir Crit Care Med. 2010;31:208–21.
41. Mohanka MR. Impact of bedside bronchoscopy in critically ill lung transplant recipients. J Bronchol Intervent Pulmonol. 2014;21:199–207.

Video Laryngoscopes in Thoracic Surgery

7

Mohamed El Tahan and Antonio Villalonga

7.1 Introduction

There are several supportive tools and adjuncts can facilitate endobronchial intubation and extubation like as flexible bronchoscope, videolaryngoscopes (VLs), fluoroscopy, and intubation/extubation adjuncts (e.g. Airway Exchange Catheter, Bougie, etc.).

VLs provide a better laryngeal view without the need for airway alignment for endobronchial intubation with double lumen tubes (DLTs). Shulman and Connelly [1] have been described the use of VL for placement of Double Lumen Tubes (DLT) using a Bullard VL in 1999. VL-assisted DLT intubation is associated with improved glottic visualisation [2], however, that does not always translate into easier tracheal intubation. A recent meta-analysis has shown that, compared with the direct laryngoscopy, the VLs provided a higher success rate at first attempt for DLT intubation, a lower incidence of oral, mucosal or dental injuries and postoperative sore throat, and comparable intubation time [3]. These observations are common when used by experienced operators [4]. Unfortunately, the use of VLs can be associated with a higher incidence of malpositioned DLT [3].

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7.2 Lung Separation in the Era of VLs

VLs have several potential roles in lung separation for thoracic surgery including: (1) placement of a DLT in patients with predicted or unanticipated difficult airway, (2) the airway can be secured with a single lumen tube (SLT), then exchange a DLT for the SLT, using a VL, (3) the trachea can be intubated, then a bronchial blocker can be advanced alongside the SLT under VL-guidance [5].

7.3 Classification of VLs

There are three main classes of VLs including the angulated-blade VL, those with a guidance channel that facilitate DLT or SLT guidance into the trachea, and video-stylets, however the performances are likely to be different between these devices [6].

A recent meta-analysis has shown that the performance of both channelled and non-channelled VLs was superior to the direct laryngoscopy in terms of improved glottic visualisation and success rate in obese patients, however, the intubation time was longer with the non-channelled VLs [7]. Compared with the angulated-blade VLs, the channelled VLs have equipped with thinner blades and pronounced curvature that make them useful in patients with limited mouth opening and restricted neck movement [8] (Fig. 7.1).

7.3.1 Angulated Blades VLs

7.3.1.1 GlideScope

There are several emerged types of the GlideScope (Verathon Medical Canada ULC, Burnaby, BC, Canada), a VL with a 60° angled blade, including: (1) lightweight and thin reusable GlideScope® Titanium angled (sizes: LoPro T3 and LoPro T4) and MAC-style blades (sizes: MAC T3 and MAC T4), (2) thin single-use GlideScope Titanium blades (angled sizes: LoPro S1, S2, S3 and S4, and MAC-style sizes: MAC S3 and S4), and (3) a portable GlideScope Go™ with single-use

Fig. 7.1 From left to right: the Clarus Trachway, King Vision™, Pentax AirwayScope, Yellow Airtraq, C-MAC (D-blade), McGrath series 5, and GlideScope Titanium angled LoPro T4

blades and 3.5″ colour display (Fig. 7.1). The GlideScope has been described for DLT intubation. The newly thinner blades can potentially facilitate intubation using the larger and more rigid DLTs particularly in patients with limited mouth opening. The GlideScope takes variable times to achieve DLT intubation according to the previous experience of the operators [9, 10].

Comparisons with Other VLs

Compared with the King Vision VL, the GlideScope was easier to use and required less frequent optimizing manoeuvers in the simulated easy airway scenario by novice operators [11]. Contradictory, the use of GlideScope for DLT intubation required a longer time for DLT intubation and was more difficult to use than the Airtraq in humans by operators with mixed experience, although failures did occur with the Airtraq [12, 13]. However, the GlideScope and Airtraq have comparable success rates of DLT intubation in patients with a predicted or known difficult airway [14].

Tips to Facilitate GlideScope-Guided Double-Lumen Tube Intubation

The use of GlideScope for DLT intubation can be facilitated with several tricks as follows: (1) Bending the stylet of the DLT so that the distal 20 cm of the DLT curve follows the curve of the GlideScope blade [15] (Fig. 7.2a). (2) The use of an Airway Exchange Catheter (AEC) alongside the GlideScope guidance for DLT intubation particularly in patients with the unanticipated difficult airway [16]. Compared with the Rusch (Bronchopart®, Teleflex, Research Triangle Park, NC) and Mallinckrodt (Broncho-Cath®, Covidien, Mansfield, MA) DLTs, the Fuji-Phycon DLT (Silbroncho®, Fuji Systems, Tokyo, Japan) can facilitate the passage of DLT over an

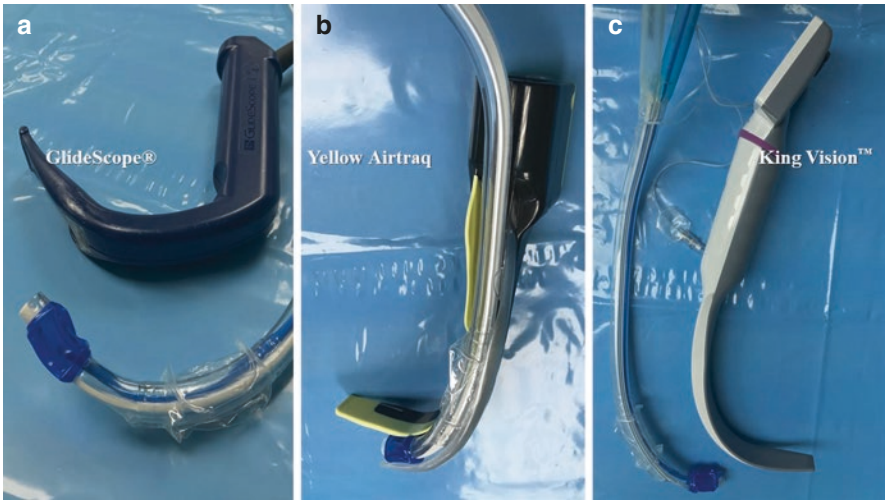

Fig. 7.2 (**a**) The GlideScope GVL blade size 4 with reshaped distal 20 cm of the stylet of DLT, (**b**) the Yellow Airtraq with a removed stylet of the DLT, and (**c**) the non-channeled King Vision blade with a reshaped distal 20 cm of the stylet of the DLT to follow the blade

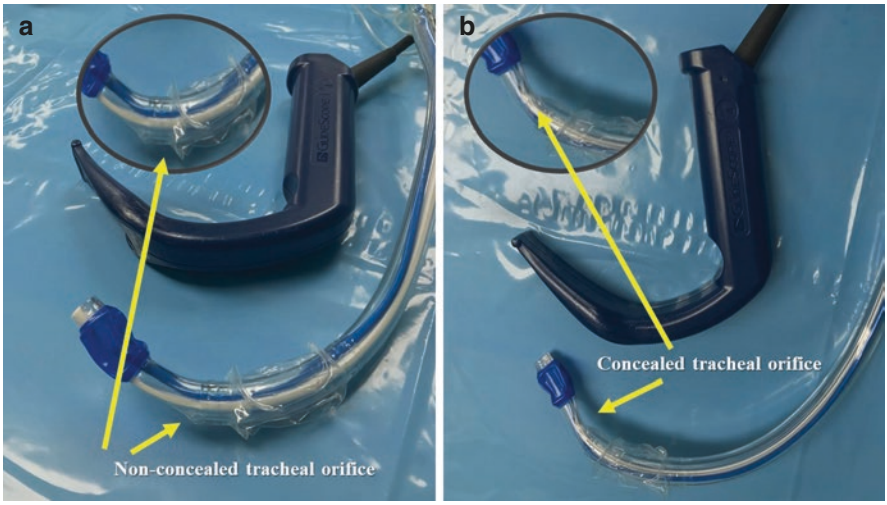

Fig. 7.3 (**a**) Non-concealed tracheal orifice and (**b**) angulating the distal tip of DLT to a hockey-stick shape with more acute angle concealing the tracheal orifice

AEC [17]. (3) Combined use of the GlideScope and fiber-optic bronchoscope for DLT intubation in a patient with difficult airway [18, 19]. (4) Sequential rotation of the DLT after introducing the tip of the bronchial lumen of the left-side DLT into the glottis using a bended malleable stylet with an initial 180° counter-clockwise rotation to align the axis of the bronchial lumen with the patient's tracheal axis, then, an additional 90° clockwise rotation is performed to align the DLT with the left main bronchus [20]. (5) Angulating the distal tip of DLT to a hockey-stick shape with more acute angle concealing the tracheal orifice [21] (Fig. 7.3). (6) Using a specifically designed semi-rigid intubating GlideRite DLT Stylet for the use with DLTs [22].

7.3.1.2 McGrath® Series 5

The McGrath® Series 5 VL, an angulated tip VL with reusable thin Mac blades, offers improved glottic visualisation for DLT intubation when used by experienced operators [23] (Fig. 7.1). However, this was associated with a longer time to achieve DLT intubation and more frequent DLT malposition [23]. Surprisingly, the use of McGrath® VL for placement of DLT by anaesthesia residents (>50 experiences with DLT intubation) took a shorter time to achieve DLT intubation and improved laryngeal visualisation than with the direct laryngoscopy [24]. However, that study was not powered to test that outcome variable [24]. Additionally, the use of McGrath® VL improved the glottic view and facilitated DLT intubation in patients with in-line stabilization [25].

Comparisons with Other VLs

Compared with the Airtraq, the use of the McGrath® VL for placement of a DLT resulted in a longer time for DLT intubation by 11 s and comparable intubation difficulty score and incidence of DLT misposition [26].

Tips to Facilitate McGrath®-Guided Double-Lumen Tube Intubation

These include: (1) the combined use of the McGrath® VL and the Parker Flex-IT™ Stylet (Parker Medical, CO, USA) can navigate the tip of the DLT towards the glottis by pushing the sum button at the top of the stylet [27]. (2) The use of a 12-cm pillow height to achieve an appropriate sniffing position [28]. (3) The combined use of McGrath® and fibre-optic bronchoscope in patients with difficult airway [29].

7.3.1.3 C-Mac D-Blade VL

The C-Mac with D-blade videolaryngoscope™ (Karl Storz GmbH and Co.KG, Tuttlingen, Germany) (Fig. 7.1) offers an 80° field of view which can facilitate DLT intubation using a reshaped distal curvature of the DLT to follow the curve of the D-blade [1]. Compared with direct laryngoscopy, the use C-Mac with D-blade has comparable time to achieve DLT intubation, improved laryngeal visualisation, however, it was more difficult to use, which can be explained with the less experience of operators in using the C-Mac with D-blade for placement of a DLT [30].

7.3.1.4 CEL-100 Videolaryngoscope™

The CEL-100 videolaryngoscope™ (Connell Energy Technology CO. Ltd., Shanghai, China) has a 40° angulated Macintosh blade.

Lin and colleagues [31] had demonstrated the successful use of the CEL-100 VL for DLT intubation in patients with difficult laryngoscopy and failed placement of a DLT using the Macintosh laryngoscope when used by experienced anaesthesiologists (>30 times) [31]. Similarly, the use of the CEL-100 VL for DLT was associated with improved laryngeal visualisation and success rate than with the direct laryngoscopy [32].

7.3.2 Channelled VLs

7.3.2.1 Airtraq

Airtraq (Prodol Limited, Vizcaya, Spain), a channelled VL, has a unique 90° shape which could potentially minimise cervical hyperextension and reduces force required (Figs. 7.1, 7.2b, and 7.4) Multiple viewing options are available for Airtraq including direct view, WiFi camera, Endo cams, and compatible phone adaptor with smart phones (Fig. 7.4). The yellow Airtraq can facilitate placement of the 35- and 37-Fr DLT without using the stylet (Fig. 7.4). Contradictory, a previous observational study showed that removal of the stylet could increase the possibilities of DLT misplacement, however it included few patients without predicted difficult airway [33]. Interestingly, Airtraq has been described to be used for awake intubation using a DLT in patients with predicted potential difficult airway [34].

Comparisons with Other VLs

Airtraq, when used by operators with limited prior experience in using VLs for DLT intubation, required more time over the MacIntosh laryngoscope for DLT intubation in simulated easy and difficult airways [11]. Obviously, growing the learning curve

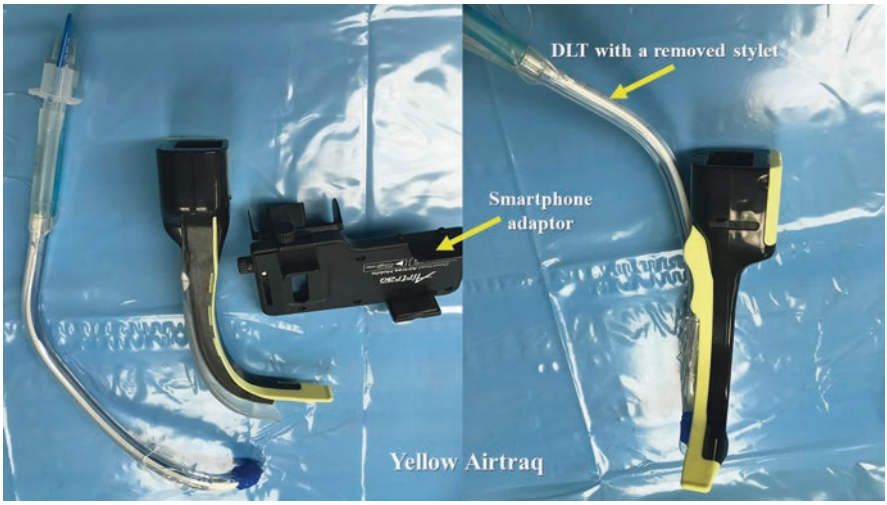

Fig. 7.4 Left: The DLT with a stylet inserted, a Yellow Airtraq, and smart phone adaptor, and Right: The 35-Fr DLT without using the stylet inserted through the channel of the Yellow Airtraq

can potentially reduce the time to DLT intubation. The use of channelled Airtraq by operators with mixed experience required less time for DLT intubation and was easier to use than the GlideScope, although failures were more frequent with Airtraq [12]. Of note, the success rates of DLT intubation were similar in patients with a predicted or known difficult airway when using either a GlideScope or Airtraq device [14].

7.3.2.2 Pentax Airway Scope

Pentax Airway Scope (AWS) (Hoya Corp., Tokyo, Japan), a 2.4-in., 300 kilo-pixel high-definition colour LCD monitor-integrated VL, has a cross-hair displays on-screen, which facilitates dependable intubation (Fig. 7.1). The disposable standard P-blade has 80° angle view (height: 131 mm; width: 52 mm; depth: 96 mm). The thinner P-Blade (height: 134 mm; width: 52 mm; depth: 95 mm) allows placement of tracheal tubes sizes 7.5–10.0 mm, which might potentially facilitate placement of the bulky DLT in patients with restricted mouth opening.

The guiding channel of the P-Blade cannot accommodate the DLT size 37 Fr or larger, however, it could be used in conjunction of an airway exchanger catheter to place a DLT [35, 36]. Sano et al. reported a successful endobronchial intubation with the AWS, equipped with the Intlock, using size 35 Fr DLT, in a patient with restricted mouth opening and head tilting [37]. Similarly, Ono et al. described the successful use of the AWS with an infant-size Intlock for placement of DLT size 32 Fr in a patient with predicted difficult airway [38]. AWS has been successfully used for placement of a DLT either over an airway exchanger catheter or through the guiding-channel during cricoid pressure for rapid sequence intubation [39, 40].

7.3.2.3 King Vision™

The King Vision™ VL (Ambu, Ballerup, Copenhagen, Denmark) has two blades styles: a standard non-channeled blade and a channeled blade. The former requires the use of a reformed stylet to direct the tracheal tube towards the glottis (Figs. 7.1 and 7.2c). The height and width of the standard non-channeled and channeled blades are 13 mm and 26 mm vs. 18 mm and 29 mm, respectively [41].

El Tahan et al. [41] have described the successful use of King Vision™ to place a left-side DLT in a morbidly obese patient with a predicted difficult airway using four steps: "first, bend the DLT stylet so that the distal curve of the DLT follows the curve of the standard non-channeled blade and the proximal curve of the DLT remains directed to the right side (Fig. 7.2c). Next, insert the DLT, exercising caution to avoid damage to the tracheal cuff by the upper teeth during its passage through the mouth opening. Then, after the bronchial cuff passes through the vocal cords, withdraw the stylet of the DLT. Finally, rotate the DLT 180° counterclockwise while advancing the DLT to the desired depth" [41].

Comparisons with Other VLs

The previous experience of the operators in using the King Vision™ might significantly shorten the time taken to achieve DLT intubation. A manikin study included 21 novice anaesthetists in using the VLs for DLT intubation showed that the use of King Vision™ for DLT intubation was more difficult than the GlideScope and Airtraq in both simulated easy and difficult airway scenarios and required more frequent optimizing manoeuvres than the GlideScope in the simulated easy airway [11]. A recent study included 133 patients undergoing thoracic surgery, the use of the GlideScope and King Vision™ laryngoscopes by operators with mixed experience resulted in longer DLT intubation times than those with Macintosh laryngoscopy [12].

7.3.3 Video-Stylet

7.3.3.1 Bonfils Intubation Fiberscope

The Bonfils intubation fiberscope (Karl Storz GmbH and Co.KG, Tuttlingen, Germany), a rigid endoscope with an optical stylet, has a 40° curved distal segment of the shaft. The length and diameter of shaft are 35 cm or 40 cm and 3.5 mm or 5.0 mm, respectively. These dimensions may make it a potential tool to place a DLT particularly in those with limited mouth opening or restricted neck movement [42]. The successful use of the Bonfils intubation fiberscope (length: 40 cm, an outer diameter of 5.0 mm) has been described for DLT intubation in patients with failed direct laryngoscopy [43, 44]. However, this required shortening the length of the connecting tubes of both tracheal and bronchial lumens of sizes 37 and 39 Fr DLT by 1.5 cm and 3.5 cm, respectively, to fit the length of the Bonfils intubation fiberscope [43, 44] (Fig. 7.5).

7.3.3.2 Clarus Video System (Trachway) Video Stylet and the OptiScope®

The Trachway intubating stylet (Biotronic Instrument Enterprise Ltd., Tai Chung, Taiwan, China), a 32-cm rigid intubating stylet with adjustable malleable angle and

rotatable monitor, allows using of tracheal tubes with an internal diameter of 6.0 mm or larger [45–47] (Fig. 7.1).

Hsu and colleagues [46] found that the Trachway video-stylet-guided DLT intubation was associated with a shorter time to intubation than the direct laryngoscopy by 20 s and reduced incidence of hoarseness of voice during the first postoperative day, however the studied patients had normal airway [46]. In similar to other video-stylets, the stylet of the Trachway is shorter than the length of the DLT that requires cutting off the DLT bronchial connector. Then, a 6.5-mm tracheal tube can be shortened and used as a modified connector following inserting the modified DLT [47] (Fig. 7.5).

The Clarus Video System (Trachway) intubating stylet has been used also for DLT intubation in a patient with limited neck movement [48].

The OptiScope® (Pacific Medical, Seoul, Republic of Korea), a specifically designed video-stylet for DLT intubation, has a rigid video-stylet with a malleable tip (length: 40.5 cm and an outer diameter of 5.0 mm) that is derived from the Clarus Video System (Clarus Medical, Minneapolis, MN, USA) and can accommodate a 35 Fr or larger Mallinckrodt DLT [49]. A previous study including 397 patients demonstrated faster DLT intubation (37 Fr for female and 39 Fr for male) using the OptiScope® [mean difference [95% confidence interval (CI)]: 5.5 (3.8–13.2) s, P = 0.010] and higher success rate of the first intubation [80.4% vs. 89.9%, P = 0.036] than with the direct laryngoscopy. However, that study was not blinded, and the operators had mixed experience [49].

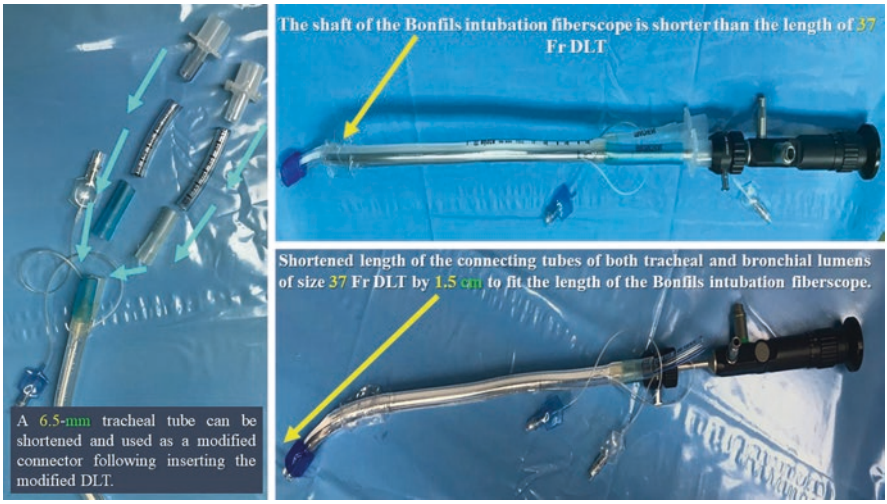

Fig. 7.5 Left: A 6.5-mm tracheal tube can be shortened and used as a modified connector following inserting the modified DLT. Upper right: The shaft of the Bonfils intubation fiberscope is shorter than the length of 37 Fr DLT. Lower right: Shortened length of the connecting tubes of both tracheal and bronchial lumens of size 37 Fr DLT by 1.5 cm to fit the length of the Bonfils intubation fiberscope

7.3.3.3 Shikani Optical Stylet

The Shikani optical stylet (Clarus Medical, Minneapolis, MN), a rigid video-stylet (length: 37.9 cm and an outer diameter of 5.01 mm), has a malleable stylet, high-resolution eyepiece, Turbo LED, and oxygen port for insufflation. Its dimensions do not make it fit to accommodate the DLT without removal tube-stop and shortening of the bronchial lumen.

Compared with the direct laryngoscopy, the use of Shikani optical stylet can potentially reduce the time to achieve successful DLT intubation and the incidence of mucosal and dental injury [50].The angulation of the tip of the Shikani optical stylet to a hockey-stick shape with alignment of the tracheal orifice of the DLT with the concave aspect of the distal curvature resulted in 11% shorter time to intubation and lower incidence of postoperative hoarseness and sore throat [51]. Unfortunately, that technique can potentially increase the incidence of malposition DLT [51].

7.3.3.4 Lighted Stylet

The lighted stylet (Light Way, Ace Medical, Seoul, Korea) relies on the principle of transillumination of the soft tissues of the neck to guide the tube into the larynx without direct visualization of the glottis. Chang and co-workers [52] have described the following steps for using the lighted stylet for placement of DLT: (1) cutting the proximal 1.5 cm of the tracheal and bronchial lumens of the DLT to accommodate the relatively shorter lighted stylet, (2) loading the DLT alongside the lighted stylet with an angulated distal end at 90°, (3) then the DLT with the lighted stylet is introduced through the oropharynx and directed anteriorly through the midline towards the cricothyroid membrane under transillumination guidance, (4) the lighted stylet is removed, and (5) the DLT is rotated 90° counter-clockwise after lifting the jaw anteriorly and advanced into the trachea.

Comparisons with Other VLs

Compared with GlideScope, the use of the lighted stylet reduced the time for achieving DLT intubation by 15 s [52].

7.4 Awake Endobronchial Intubation Using VLs

The VLs can offer a new merit for awake DLT intubation in patients with anticipated difficult airway where there is high priority to place a DLT rather than using a bronchial blocker.

7.4.1 GlideScope

GlideScope has been shown to provide topical anaesthesia and successful DLT intubation in an awake patient with predicted difficult airway and risk of pulmonary aspiration of gastric contents [53].

7.4.2 Airtraq

Similarly, Airtraq has been successfully used for awake DLT intubation in two cases with predicted difficult airway [34].

7.4.3 Clarus Video System

Seo and colleagues [54] have described the successful use of Clarus VL and for awake endobronchial intubation using a size 37 Fr DLT in a patient with a large epiglottic cyst under the combined use of superior laryngeal nerve block and topical anaesthesia [54].

References

1. Shulman GB, Connelly NR. Double lumen tube placement with the Bullard laryngoscope. Can J Anaesth. 1999;46(3):232–4.
2. Purugganan RV, Jackson TA, Heir JS, Wang H, Cata JP. Video laryngoscopy versus direct laryngoscopy for double-lumen endotracheal tube intubation: a retrospective analysis. J Cardiothorac Vasc Anesth. 2012;26(5):845–8.
3. Liu TT, Li L, Wan L, Zhan CH, Yao WL. Videolaryngoscopy vs. Macintosh laryngoscopy for double-lumen tube intubation in thoracic surgery: a systematic review and meta-analysis. Anaesthesia. 2018;73:997–1007.
4. Pieters BMA, Maas EHA, Knape JTA, van Zundert AAJ. Videolaryngoscopy vs. direct laryngoscopy use by experienced anaesthetists in patients with known difficult airways: a systematic review and meta-analysis. Anaesthesia. 2017;72(12):1532–41.
5. Brodsky JB. Lung separation and the difficult airway. Br J Anaesth. 2009;103(Suppl 1):i66–75.
6. El-Tahan MR. Videolaryngoscopes for placement of double lumen tubes: is it time to say goodbye to direct view? Saudi J Anaesth. 2016;10(2):218–27.
7. Hoshijima H, Denawa Y, Tominaga A, Nakamura C, Shiga T, Nagasaka H. Videolaryngoscope versus Macintosh laryngoscope for tracheal intubation in adults with obesity: a systematic review and meta-analysis. J Clin Anesth. 2018;44:69–75.
8. Suppan L, Tramèr MR, Niquille M, Grosgurin O, Marti C. Alternative intubation techniques vs Macintosh laryngoscopy in patients with cervical spine immobilization: systematic review and meta-analysis of randomized controlled trials. Br J Anaesth. 2016;116(1):27–36.
9. Russell T, Slinger P, Roscoe A, McRae K, Van Rensburg A. A randomised controlled trial comparing the GlideScope(®) and the Macintosh laryngoscope for double-lumen endobronchial intubation. Anesthesia. 2013;68:1253–8.
10. Hsu HT, Chou SH, Wu PJ, Tseng KY, Kuo YW, Chou CY, et al. Comparison of the GlideScope® videolaryngoscope and the Macintosh laryngoscope for double-lumen tube intubation. Anesthesia. 2012;67:411–5.
11. El-Tahan MR, Al'ghamdi AA, Khidr AM, Gaarour IS. Comparison of three videolaryngoscopes for double-lumen tubes intubation in simulated easy and difficult airways: a randomized trial. Minerva Anestesiol. 2016;82(10):1050–8.
12. El-Tahan MR, Khidr AM, Gaarour IS, Alshadwi SA, Alghamdi TM, Al'ghamdi A. A comparison of 3 videolaryngoscopes for double-lumen tube intubation in humans by users with mixed experience: a randomized controlled study. J Cardiothorac Vasc Anesth. 2018;32(1):277–86.
13. Yi J, Gong Y, Quan X, Huang Y. Comparison of the Airtraq laryngoscope and the GlideScope for double-lumen tube intubation in patients with predicted normal airways: a prospective randomized trial. BMC Anesthesiol. 2015;15:58.

14. Belze O, Lepage E, Bazin Y, Kerourin P, Fusciardi J, Remérand F, Espitalier F. Glidescope versus Airtraq DL for double-lumen tracheal tube insertion in patients with a predicted or known difficult airway: a randomised study. Eur J Anaesthesiol. 2017;34(7):456–63.
15. Hernandez AA, Wong DH. Using a glidescope for intubation with a double lumen endotracheal tube. Can J Anesth. 2005;52:658–9.
16. Chen A, Lai HY, Lin PC, Chen TY, Shyr MH. GlideScope-assisted double-lumen endobronchial tube placement in a patient with an unanticipated difficult airway. J Cardiothorac Vasc Anesth. 2008;22:170–2.
17. Gamez R, Slinger P. A simulator study of tube exchange with three different designs of double-lumen tubes. Anesth Analg. 2014;119:449–53.
18. Tateura N, Sato H, Arai T, Asai T, Okuda Y. Intubation using a double-lumen tube with a combination of fiberoptic bronchoscope and the glidescope in a patient with difficult airway. Masui. 2015;64(8):815–8.
19. Ara T, Mori G, Adachi E, Asai T, Okuda Y. Combined use of the GlideScope and fiberoptic bronchoscope for tracheal intubation in a patient with difficult airway. Masui. 2014;63(6):647–9.
20. Bustamante S, Parra-Sánchez I, Apostolakis J. Sequential rotation to insert a left double-lumen endotracheal tube using the GlideScope. Can J Anesth. 2010;57:282–3.
21. Hsu HT, Chou SH, Chou CY, Tseng KY, Kuo YW, Chen MC, et al. A modified technique to improve the outcome of intubation with a left-sided double-lumen endobronchial tube. BMC Anesthesiol. 2014;14:72.
22. Bussières JS, Martel F, Somma J, Morin S, Gagné N. A customized stylet for GlideScope® insertion of double lumen tubes. Can J Anaesth. 2012;59(4):424–5.
23. Yao WL, Wan L, Xu H, Qian W, Wang XR, Tian YK, Zhang CH. A comparison of the McGrath® Series 5 videolaryngoscope and Macintosh laryngoscope for double lumen tracheal tube placement in patients with a good glottic view at direct laryngoscopy. Anaesthesia. 2015;70(7):810–7.
24. Kido H, Komasawa N, Matsunami S, Kusaka Y, Minami T. Comparison of McGRATH MAC and Macintosh laryngoscopes for double-lumen endotracheal tube intubation by anesthesia residents: a prospective randomized clinical trial. J Clin Anesth. 2015;27(6):476–80.
25. Yoo JY, Park SY, Kim JY, Kim M, Haam SJ, Kim DH. Comparison of the McGrath videolaryngoscope and the Macintosh laryngoscope for double lumen endobronchial tube intubation in patients with manual in-line stabilization: a randomized controlled trial. Medicine (Baltimore). 2018;97(10):e0081. https://doi.org/10.1097/MD.0000000000010081.
26. Wan L, Liao M, Li L, Qian W, Hu R, Chen K, Zhang C, Yao W. McGrath Series 5 videolaryngoscope vs Airtraq DL videolaryngoscope for double-lumen tube intubation: a randomized trial. Medicine (Baltimore). 2016;95(51):e5739.
27. Ueshima H, Kitamura A. Combination of Parker Flex-IT™ Stylet and McGRATH MAC for effective double lumen tube intubation. Saudi J Anaesth. 2014;8(4):574.
28. Deguchi S, Komasawa N, Kido H, Ueno T, Minami T. Impact of pillow height on double-lumen endotracheal tube intubation with McGRATH MAC: a prospective randomized clinical trial. J Clin Anesth. 2016;34:339–43.
29. Imajo Y, Komasawa N, Minami T. Efficacy of broncho-fiberscope double-lumen tracheal tube intubation combined with McGRATH MAC for difficult airway. J Clin Anesth. 2015;27(4):362.
30. Shah SB, Bhargava AK, Hariharan U, Mittal AK, Goel N, Choudhary M. A randomized clinical trial comparing the standard Mcintosh laryngoscope and the C-Mac D-blade Video laryngoscope™ for double lumen tube insertion for one lung ventilation in onco-surgical patients. Indian J Anaesth. 2016;60(5):312–8.
31. Lin WQ, Quan SB, Liu WJ, Zhang TH, Li HT, Zhong ZJ, Cao LH. Evaluation of the CEL-100 videolaryngoscope(TM) for double-lumen tracheal tube insertion after failure using the Macintosh laryngoscope. Anaesthesia. 2012;67(11):1232–6.
32. Lin W, Li H, Liu W, Cao L, Tan H, Zhong Z. A randomised trial comparing the CEL-100 videolaryngoscope(TM) with the Macintosh laryngoscope blade for insertion of double-lumen tubes. Anesthesia. 2012;67:771–6.

33. Chastel B, Perrier V, Germain A, Seramondi R, Rozé H, Ouattara A. Usefulness of the Airtraq DL™ videolaryngoscope for placing a double-lumen tube. Anaesth Crit Care Pain Med. 2015;34:89–93.
34. Salazar Herbozo E, Planas B, Ramasco F, Gómez Rice A, Catalán P. Double lumen tube insertion in awake patients through the AirTraq laryngoscope in 2 cases of expected difficult airway. Rev Esp Anestesiol Reanim. 2011;58:315–7.
35. Iizuka T, Shimoyama N, Notoya A. Tube introducer catheter as an adjunct to the airway scope for tracheal intubation in a manikin model. Masui. 2010;59(12):1534–8.
36. Poon KH, Liu EH. The airway scope for difficult double-lumen tube intubation. J Clin Anesth. 2008;20(4):319.
37. Sano H, Komasawa N, Minami T. Efficacy of the Pentax-AWS Airwayscope with a newly developed Intlock for a double-lumen tracheal tube. J Clin Anesth. 2016;34:373–4.
38. Ono N, Komasawa N, Nakano S, Kuwamura A, Tatsum S, Minami T. Successful double-lumen tube insertion using Pentax-AWS Airwayscope with an infant-sized intlock in a rheumatoid arthritis patient with restricted mouth opening and head tilting. Masui. 2014;63(4):406–8.
39. Kurahashi N, Komasawa N, Hattori K, Minami T. Rapid-sequence intubation of a patient with difficult airway using a double-lumen endotracheal tube with the Pentax-AWS Airwayscope and a soft-tipped tube exchanger. J Clin Anesth. 2017;36:14–5.
40. Yamazaki T, Ohsumi H. The airway scope is a practical intubation device for a double-lumen tube during rapid-sequence induction. J Cardiothorac Vasc Anesth. 2009;23(6):926.
41. El-Tahan M, Doyle DJ, Khidr AM, Hassieb AG. Case report: double lumen tube insertion in a morbidly obese patient through the non-channelled blade of the King Vision (™) videolaryngoscope. Version 3. F1000Res. 2014;3:129. https://doi.org/10.12688/f1000research.4481.3. eCollection 2014.
42. Thong SY, Wong TG. Clinical uses of the Bonfils retromolar intubation fiberscope: a review. Anesth Analg. 2012;115(4):855–66.
43. Bein B, Caliebe D, Römer T, Scholz J, Dörges V. Using the Bonfils intubation fiberscope with a double-lumen tracheal tube. Anesthesiology. 2005;102(6):1290–1.
44. Subramani S, Poopalalingam R. Bonfils assisted double lumen endobronchial tube placement in an anticipated difficult airway. J Anaesthesiol Clin Pharmacol. 2014;30(4):568–70.
45. Ong J, Lee CL, Lai HY, Lee Y, Chen TY, Shyr MH. A new video intubating device: trachway intubating stylet. Anaesthesia. 2009;64(10):1145.
46. Hsu HT, Chou SH, Chen CL, Tseng KY, Kuo YW, Chen MK, Cheng KI. Left endobronchial intubation with a double-lumen tube using direct laryngoscopy or the Trachway® video stylet. Anaesthesia. 2013;68(8):851–5.
47. Hung KC. Trachway video stylet use in double lumen tube insertion. Anaesthesia. 2015;70(9):1093–4.
48. Kim YR, Jun BH, Kim JA. The use of the Clarus Video System for double-lumen endobronchial tube intubation in a patient with a difficult airway. Korean J Anesthesiol. 2013;65(1):85–6.
49. Yang M, Kim JA, Ahn HJ, Choi JW, Kim DK, Cho EA. Double-lumen tube tracheal intubation using a rigid videostylet: a randomized controlled comparison with the Macintosh laryngoscope. Br J Anaesth. 2013;111(6):990–5.
50. Xu T, Li M, Guo XY. Comparison of Shikani optical stylet and Macintosh laryngoscope for double-lumen endotracheal tube intubation. Beijing Da Xue Xue Bao. 2015;47(5):853–7.
51. Xu T, Li M, Xu M, Guo XY. Comparison of two shaping methods for double-lumen endotracheal tube intubation by Shikani optical stylet laryngoscope. Beijing Da Xue Xue Bao. 2016;48(6):1038–42.
52. Chang JE, Kim H, Min SW, Lee JM, Ryu JH, Yoon S, Hwang JY. A randomized controlled trial comparing the utility of Lighted Stylet and GlideScope for double-lumen endobronchial intubation. J Cardiothorac Vasc Anesth. 2018;32(1):290–6.
53. Onrubia X, Lluch-Oltra A, Armero R, Baldó J. Use of GlideScope for double lumen endotracheal tube insertion in an awake patient with difficult airway. Rev Esp Anestesiol Reanim. 2014;61(6):346–8.
54. Seo H, Lee G, Ha SI, Song JG. An awake double lumen endotracheal tube intubation using the Clarus Video System in a patient with an epiglottic cyst: a case report. Korean J Anesthesiol. 2014;66(2):157–9.

8 Intubation Guides, Tube Exchanger Catheter and Safe Extubation in Thoracic Surgery

Antonio Villalonga and Mohamed El Tahan

8.1 Intubation Guides

In 1973, Venn designed [1] the Eschmann endotracheal tube introducer also known as the gum-elastic bougie. It has a 35° curved tip, is longer in length (60 cm) and stiffness yet maintains flexibility, allowing it to enter the trachea with minimal trauma to the soft tissues and is reusable [2]. Now there are many single-use introducers available on the market: Frova (Cook UK Ltd., Letchworth, UK), Portex (Smiths Medical International), Pro-Breathe (Pro-Act Medical Ltd., Northampton, UK), Boussignac bougies (Vygon, Ecouen, France).

The tracheal tube introducers or intubation guides or bougie is a widely used device for facilitating tracheal intubation. It is one of the most widely, effective and commonly used device for management of the difficult airway and for this reason is in the intubation guide is an option of the 'Plan A' of the Difficult Airway Society (DAS) guidelines for management of the unanticipated difficult intubation [3]. It can also be helpful during videolaryngoscopy. Non-channelled videolaryngoscopes necessitate the use of a pre-shaped stylet or bougie to aid the passage of the tracheal tube through the cords [4, 5].

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The characteristics of bougies vary, and this may affect their performance. Janakiraman et al. [6] found higher significant successful placement of Frova and Eschmann that with Pro-Breathe and Portex tracheal introducers and that the peak force that could be exerted by the Pro-Breathe, Portex and Frova single-use introducers were 3–6 times greater than that which could be exerted by the Eschmann introducer that are more likely to cause tissue trauma during placement. For this reason, the 'hold-up' sign that may signal the passage of the bougie as far as small bronchi, it is associated with risk of airway perforation and trauma, should not be elicited if a single-use bougie is being used and great caution should be exercised if attempting to elicit the hold-up sign with Eschmann reusable bougie [7]. The main complications reported are airway bleeding, pneumothorax and mediastinitis [8].

When encountering a difficult airway with videolaryngoscopy with an endotracheal tube channel such as Airway Scope (AWS) a bougie can be inserted into the endotracheal tube in the channel. The angulated tip of the bougie can be guided toward the glottis by rotating it. Takenaka et al. tested the ease of rotating bougies (Eschmann reusable, Boussignac, Portex single-use, and Frova) in an endotracheal tube when placed in the AWS channel and conclude that Eschmann reusable and Boussignac bougies are a useful aid for intubation with an AWS and Portex single-use and Frova bougies seem to be less suitable for this technique [4].

8.1.1 Intubation Guides in Thoracic Surgery

In anesthesia for thoracic surgery the intubation guides are used mainly for tracheal intubation and is a help with both the Macintosh laryngoscope and the videolaryngoscopes and can be used as an adjunct to DLT intubation. A 10-Ch, 70-cm bougie can be inserted into the trachea, then the DLT is introduced over the bougie through its tracheal lumen [9]. Additionally, Gottlieb et al. recommended use the bougie in emergency department to facilitate single lung intubation when visualization is limited. After the bougie enter in the trachea, then to turn the bougie 90° clockwise (for right mainstem intubation) or 90° counter-clockwise (for left mainstem intubation). Subsequently, either an endobronchial tube or a DLT can be then advanced over the bougie [10].

The intubation guides have been used as tracheal tubes and double-lumen tube exchangers, but it is preferable to use instruments designed specifically for this purpose. In particular there are reports of a fragment of a Frova introducer becoming dislodged in the airway after use with a double-lumen tube [11].

8.2 Airway Exchange Catheter

The use of airway exchange catheter (AEC) had been proposed by Choby et al. in 1979, as a guide to facilitate nasal reintubation in patients with intermaxillary fixation without removing the dental fixation [12]. Nowadays the AEC has been a suggested as part of an extubation strategy when managing difficult airways that may

require re-intubation. No other specific tool or procedure to increase safety at extubation has gained wide acceptance or has been routinely adopted in clinical algorithms [13–18]. In fact, whit the use of AEC Mort [19] refers an overall success rate at reintubation of 92% (87% at first attempt) in intensive care unit (ICU) patients with "difficult airway."

8.2.1 Characteristics

The AEC should be a long semirigid tube inserted through a tracheal tube before extubation to minimize trauma. Hollow catheters are preferred, as they offer the ability to insufflate oxygen and/or ventilate through their lumen. Commonly used and recommended model and sizes: Cook AEC catheters 8 F length 45 cm and 11 F, 14 F and 19 F length 83 cm (Cook Critical Care, Bloomington, IN), compatible with tracheal tubes of internal diameters 3, 4, 5 and 7 mm, respectively. These sizes are large enough to provide adequate support in case of reintubation, and thin enough to be well tolerated by patients. In addition, it has connectors included for oxygen insufflation and capnography. After the tracheal tube is withdrawn over the AEC, it can serve as a conduit for re-intubation if required.

The Sheridan TTX tracheal tube exchanger (Sheridan Catheter Corp, Argyle, NY) and the Endotracheal Ventilation Catheter (CardioMed, Lindsay, Ontario, Canada) are other examples of hollow endotracheal tube exchangers. Nonhollow AEC have also been used, however the use of hollow catheters has been generally widely favored and recommended [16, 18].

An alternative 'next generation' is the Staged Extubation kit (Cook Critical Care, Bloomington, IN, USA). This recent modification has detachable connectors for emergency ventilation. This consists of a coated, high-quality wire and a re-intubation catheter. Similar to the exchange catheter, the guidewire is inserted down the tracheal tube before extubation and left in situ to provide access to the lower airway should the patient require re-intubation. In this case, the re-intubation catheter, that has a soft distal tip to attempt to decrease the risk of distal airway injury during tube exchange, is railroaded over the guidewire and this in turn facilitates railroading of a tracheal tube into the airway. Currently there is limited research concerning this two-step system for extubation [20, 21].

8.2.2 Indications

There are different clinical situations in which the AEC is useful:

- **Difficult tracheal tube exchange**. A tracheal tube may require urgent replacement if displaced, blocked, kinked, if the cuff has failed, or if a small tracheal tube has been inserted during difficult or fibre-optic airway management. The AECs provides the safest method of tracheal tube exchange ensures airway continuity is maintained throughout the procedure [22–25].

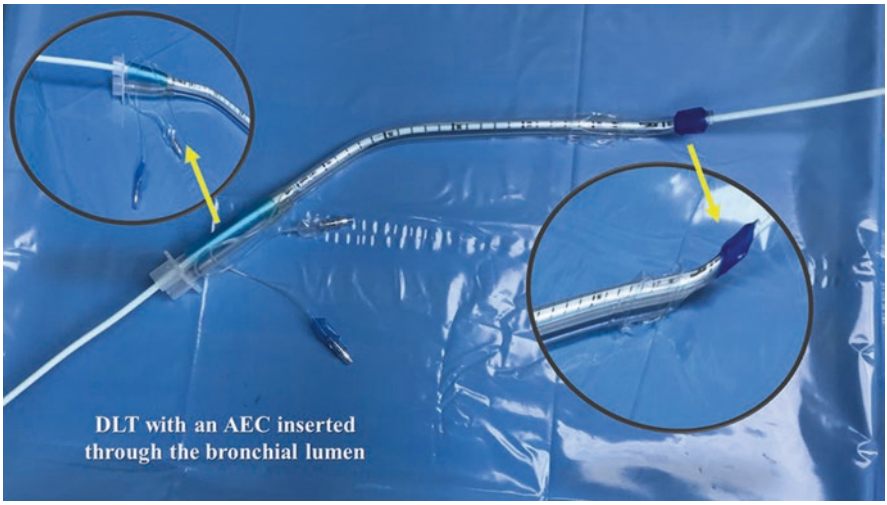

Fig. 8.1 Double lumen tube (DLT) with an Airway Exchange Catheter (AEC) inserted through the bronchial lumen

- **Extubation strategy**. AEC play an important role as part of an extubation strategy when managing difficult airways that may require re-intubation. It is included in all the guidelines on tracheal extubation. This may occur after certain surgeries, such as head and neck surgery, in patients that tracheal intubation has been difficult or in patients with prolonged tracheal intubation in critical care. AECs are placed prior to extubation and retained in situ after extubation and that act as a conduit for TT if reintubation is required [16–18].
- **Change a single tracheal tube for a double-lumen tube or vice versa**. The first case can occur in a difficult intubation in thoracic surgery and the opposite in the end of surgery in a patient that requires mechanical ventilation in the postoperative period as in the large esophageal surgery (Fig. 8.1).
- One study using two airway exchange catheters to exchange a DLT for a single-lumen endotracheal tube showed that there was a reduction in the incidence of glottis impingement of the tracheal tube and that there was a higher success rate of passage of the single-lumen endotracheal tube when compared with the use of a single airway exchange catheter [26].
- **Change a tracheal tube for a supraglotic dispositive at the end of surgery**. In cases of extubation in normal airway requiring suppression of haemodynamic responses at the end of surgery. The TT can be removed of over an AEC and railroading the laryngeal mask airway through its airway lumen into the pharynx for its placement [26].

8.2.3 Technics

The use of an AEC requires prior knowledge and training by the staff who will perform the technique. Tracheal tube exchange should always be approached as a high-risk intervention, with the same level of preparation and equipment provision as difficult intubation [27].

The patient. To perform the procedure the patient must be in an optimal position, slightly semi-incorporated and the 'sniffing' position, in a neutral head-neck position in case of cervical spine immobilization the results are worse [28]. The patient will be given oxygen at 100% to have a greater margin of safety in case of difficulties. Oropharyngeal secretions will be aspirated and lidocaine can be administered through TT to abolish reflexes.

The AEC. The choice of the size of the AEC is important to facilitate the exchange, the most suitable is the one that approaches the internal diameter of the TT to avoid the gap that would make the passage of the TT by the glottis difficult.

After applying lubricating jelly over the AEC, insert the AEC to its appropriate depth ensuring the tip remains above carina. It usually about 20–22 cm orally or 26–30 cm nasally. Never advance an AEC against resistance.

Remove the tracheal tube over the AEC, while maintaining the AEC position without advancing the AEC.

The TT. The gap between the catheter and the tracheal tube during re-intubation may cause the tube to impinge on upper airway structures such as the epiglottis and arytenoids, causing a 'hold-up' and insertion failure [29]. The tube with a blunt beveled tip for use with an intubating LMA (Intavent Direct Ltd., Maidenhed UK), or the Parker Flex-Tip™ tracheal tube (Parker Medical, Englewood, CO, USA) has a curved tip and posterior-facing bevel, which minimises this gap and allows smooth passage into the trachea [30]. These problems may be also reduced by passing an Aintree TM Intubation Catheter (William Cook Europe, Bjaeverskov, Denmark) over the AEC before re-intubation. This allows easier railroading of the tracheal tube, with less likelihood of hold-up [31–33].

Reintubation under laryngoscopy. Exchange tube should be performed with videolaryngoscopy better than direct laryngoscopy, leading to better glottic view to retract the tongue and improve visibility of the periglottic structures and facilitate advancement of the ETT into the trachea with higher success rate, and fewer complications [34]. Full neuromuscular blockade increase safety. After reintubation, confirm the position of the tracheal tube with capnography.

Use of an airway exchange catheter for 'at-risk' extubation.

Secure AEC to the cheek or forehead with tape and clearly label the AEC to prevent confusion with a nasogastric tube. The patient should be nursed in a critical care unit and remain nil by mouth until the AEC is removed. Most patients remain able to cough and vocalize. In case of cough check that the tip is above the carina and inject lidocaine via the AEC.

Supplemental oxygen can be given via a facemask, nasal cannula or CPAP mask better than via AEC. Oxygen insufflation and jet ventilation through AEC may be associated with significant risk of barotrauma and should be reserved to selected life-threatening situations. In the context of rapid decompensation of a patient with an AEC in situ, the priority should be given to attempt reintubation over attempting oxygenation and ventilation through the lumen of the catheter [34].

The optimal **timing for removal** of the AEC should be individualised in every situation. The Difficult Airway Society (UK) recommends retaining the AEC for

2 h, but the device may be kept for an extended period of up to 3 days. The guiding principle should be to leave the catheter in place as long as it is necessary to rule out complications that may lead to reintubation.

8.2.4 Complications

Most common complications associated with AEC use: pneumothorax (unilateral or bilateral, with or without subcutaneous emphysema), pneumoperitoneum and pneumomediastinum, hypoxia during airway management and unintended esophageal misplacement leading to gastric perforation.

Due to reports of barotrauma, it is now recommended that oxygen insufflation and manual ventilation through an AEC should only occur in emergency situations [34–39], if an AEC is left in place after extubation, it is safer to administer oxygen by other means [14]. Only experienced airway management personnel with a high level of training should use these devices or very closely supervise their use.

Postextubation complications may be prevented or mitigated by preemptive optimization of the patients' medical conditions, careful timing and logistics of the extubation process, preparation for urgent or emergent tracheal reintubation (including routine use of AECs in case of extubation of difficult airways), and adequate level of postextubation monitoring and care.

An AEC was impinged at the distal tracheal lumen and snapped during manipulation of a DLT replacement with a SLT. The authors suggest than AEC will be inserted into the bronchial lumen in optimal depth with the adjunct of video laryngoscope, as the safe method for double-lumen tube exchange [40].

8.3 Safe Extubation

In 1993, the ASA [41] developed the first difficult tracheal intubation guide, subsequently several societies introduced their own, and this has contributed to a marked decrease in morbidity and mortality related to tracheal intubation. It can be said that, rather than the introduction of new instruments, it has been the awareness of anesthesiologists to detect difficult airways and have concrete plans of action both in the planned and in the unforeseen and successive alternatives in case the initial approaches fail. The Practice Guidelines, updated in 2003, suggest that [42]:

"The preformulated extubation strategy should include

1. A consideration of the relative merits of awake extubation versus extubation before the return of consciousness.
2. An evaluation for general clinical factors that may produce an adverse impact on ventilation after the patient has been extubated.
3. The formulation of an airway management plan that can be implemented if the patient is not able to maintain adequate ventilation after extubation.
4. A consideration of the short-term use of a device that can serve as a guide for expedited reintubation."

However, those brief indications about tracheal extubation as those of the other guidelines have been insufficient, and in these years it has been proven that the complications in this phase of the intubated patient have increased as shown by the audits [43, 44]. For this reason, more recently review articles and specific guidelines for safe tracheal extubation have appeared [14–17], even specific for patients in intensive care [18], which will undoubtedly contribute to reducing the incidence of complications in this period.

At the time of extubation the patient may be more impaired than in the induction, the airway may be more altered and the effects of anesthesia and surgery may contribute and facilitate the appearance of complications when extubating the patient or later. In the thoracic surgery is added the fact of the greater manipulation of the airway that involves the placement of DLT and BB, and the concomitant limitations to pulmonary resections and pain by thoracotomy.

Complications can appear due to anatomical or physiological alterations of the respiratory tract. The problems related to airway reflexes may be due to an abnormal response of these causing stridor, laryngospasm or bronchospasm or an absence of response that facilitates bronchoaspiration. Laryngospasm, if not resolved early, can cause pulmonary edema due to obstruction or negative pressure. The result can be oxygen desaturation and if the initial treatment is not effective, it can be complicated by failed attempts of tracheal intubation that can damage the airway and cause arterial and intracerebral hypertension, myocardial ischemia and morbidity and mortality.

To avoid these disastrous consequences, the extubation guidelines recommend having a plan, specifically the DAS stages it in four steps (see Fig. 8.2) [14]:

The first step is the anticipation of the possibility of a difficult extubation by assessing the risks associated with the patient and surgery. It should be kept in mind

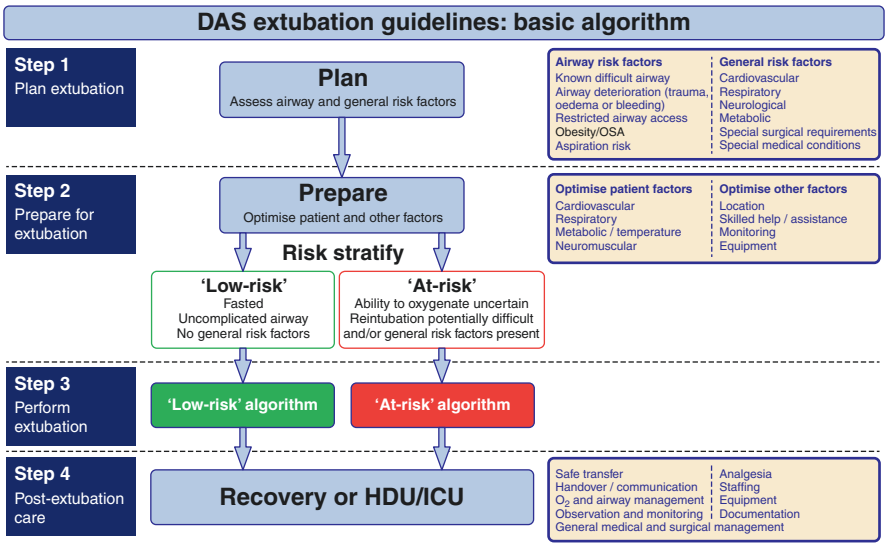

Fig. 8.2 Difficult Airway Society (DAS) extubation guidelines: basic algorithm [3]

Table 8.1 Sequence for 'low-risk' extubation in an awake patient

1. Deliver 100% oxygen through the breathing system
2. Remove oropharyngeal secretions using a suction device, ideally under direct vision
3. Insert a bite block to prevent occlusion of the tube
4. Position the patient appropriately
5. Antagonise residual neuromuscular blockade
6. Establish regular breathing and an adequate spontaneous minute ventilation
7. Allow emergence to an awake state of eye-opening and obeying commands
8. Minimise head and neck movements
9. Apply positive pressure, deflate the cuff and remove the tube while the lung is near vital capacity
10. Provide 100% oxygen with an anaesthetic breathing system and confirm airway patency and adequacy of breathing
11. Continue delivering oxygen by mask until recovery is complete

From: Popat et al. [3]

that difficult intubation is often followed by difficult extubation. Upper airway edema, vocal cord paralysis, upper airway bleeding, residual neuromuscular blockade, increased secretions and cough strength are the main risk factors for extubation failure. A TF ratio >0.9 [45], the visual assessment of the larynx by videolaryngoscopy or FB or ultrasound, and the cuff-leak test (loss of 10–25% tidal volume that was measured before cuff deflation, or more than 110 ml in the adult) [46], help identify at-risk situations.

The second step serves to optimize the factors related to extubation, once completed it can be determined whether the patient is extubated at low or high risk. The DAS has two other algorithms for each of these situations.

In the third step extubation is performed. The low-risk (routine) extubation is considered the one that is not expected to reintubate the patient. It can be carried out in two ways: with the patient awake that is the usual (see Table 8.1) or deep extubation only performed by clinicians familiar with this modality. The deep or asleep extubation, before return of consciousness, is indicated to avoids coughing and fighting against ventilator which may lead to increased risk of rebleeding (e.g., at the site of neck/upper airway surgery) due to increased venous pressure and straining on sutures. Regular and effective spontaneous breathing must be present and easy intubation and mask ventilation are important prerequisites. The risk of aspiration and airway obstruction is present and the risk of laryngospasm is increased if extubation is performed during transition between deeply anesthetized and awake state.

The respiratory criteria for tracheal extubation include a steady spontaneous breathing without difficulty (VT > 6 ml/kg), respiratory rate 12–25 breaths/min, negative inspiratory pressure <−20 cmH_2O and SpO_2 > 95% (air). Ensure that there is no residual neuromuscular blockade to prevent residual paralysis (TOF ratio should be greater than 0.9). It is important to remove the TT while the lung is in inspiration because reflex glottis closure and laryngospasm are facilitated by expiratory phase [47].

The at-risk extubation in relation to the degree of risk will involve awake extubation if it is low, and if greater extubation is done by advanced techniques (changing the TT by a LM or using an AEC) that require experience, or if the risk is high. Patient is not extubated waiting for conditions to improve or a tracheotomy is performed directly.

The fourth step is the post-extubation care that begins with a safe transfer to the recovery room or ICU.

The Indian guidelines to tracheal extubation are very interesting, presenting three different scenarios of increasing difficulty: 1. Extubation in normal airway. 2. (4 **D**s) Extubation in difficult airway including **d**ifficult mask ventilation, **d**ifficult intubation/reintubation, **d**elayed recovery or airway **d**ifficulty due to pre-existing disease: and 3. (3 **S**s) Extubation in difficult airway due to **s**urgical cause, **s**uspected airway oedema or **s**uspected airway collapse. Based on these assessments, patient may be planned an awake extubation, under deep anaesthesia or at times tracheostomy. A systematic approach complemented with good clinical judgement as outlined in this guideline could result in an uneventful extubation [16].

In conclusion, tracheal extubation is the final step of airway management, it is a routine manoeuvre but could be a high risk phase of anesthesia that required a predefined strategy, of risk stratification and management to anticipate and prevent complications.

References

1. Venn PH. The gum elastic bougie. Anaesthesia. 1993;48:274–5.
2. Rai MR. The humble bougie…forty years and still counting? Anaesthesia. 2014;69:195–207.
3. Frerk C, Mitchell VS, McNarry AF, Mendonca C, Bhagrath R, Patel A, Difficult Airway Society Intubation Guidelines Working Group. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. Br J Anaesth. 2015;115:827–48.
4. Takenaka I, Aoyama K, Iwagaki T, Takenaka Y. Bougies as an aid for endotracheal intubation with the Airway Scope: bench and manikin comparison studies. BMC Anesthesiol. 2017;17:133.
5. Batuwitage B, McDonald A, Nishikawa K, Lythgoe D, Mercer S, Charters P. Comparison between bougies and stylets for simulated tracheal intubation with the C-MAC D-blade videolaryngoscope. Eur J Anaesthesiol. 2015;32:400–5.
6. Janakiraman C, Hodzovic I, Reddy S, Desai N, Wilkes AR, Latto IP. Evaluation of tracheal tube introducers in simulated difficult intubation. Anaesthesia. 2009;64:309–14.
7. Marson BA, Anderson E, Wilkes AR, Hodzovic I. Bougie-related airway trauma: dangers of the hold-up sign. Anaesthesia. 2014;69:219–23.
8. Evans H, Hodzovic I, Latto IP. Tracheal tube introducers: choose and use with care. Anaesthesia. 2010;65:857–66.
9. Pandey R, Garg R, Chandralekha JB, Elakkumanan LB, Chaitra M, Darlong V. Laryngoscope-guided and bougie-aided correct placement of a double-lumen tube in a difficult airway. J Cardiothorac Vasc Anesth. 2009;23(4):583–4.
10. Gottlieb M, Sharma V, Field J, Rozum M, Bailitz J. Utilization of a gum elastic bougie to facilitate single lung intubation. Am J Emerg Med. 2016;34(12):2408–10.
11. Graham J, Von Heldreich C, Howard W, Fiddes C. Frova introducer and double-lumen tubes. Anaesthesia. 2013;68:775.

12. Choby WA, Ung KA, Abadir AR. Management of the post extubation airway in patients with intermaxillary fixation. Anesth Prog. 1979;26:124–5.
13. Higgs A, McGrath BA, Goddard C, Rangasami J, Suntharalingam G, Gale R, et al. Guidelines for the management of tracheal intubation in critically ill adults. Br J Anaesth. 2018;120:323–52.
14. Popat M, Mitchell V, Dravid R, Patel A, Swampillai C, Higgs A. Difficult Airway Society guidelines for the management of tracheal extubation. Anaesthesia. 2012;67:318–40.
15. Langeron O, Bourgain JL, Francon D, Amour J, Baillard C, Bouroche G. Intubation difficile et extubation en anesthésie chez l'adulte. Anesthesiol Reanim. 2017;3:552–71.
16. Kundra P, Garg R, Patwa A, Ahmed SM, Ramkumar V, Shah A, et al. All India Difficult Airway Association 2016 guidelines for the management of anticipated difficult extubation. Indian J Anaesth. 2016;60:915–21.
17. Cavallone LF, Andrea Vannucci A. Extubation of the difficult airway and extubation failure. Anesth Analg. 2013;116:368–83.
18. Sturgess DJ, Greenland KB, Senthuran S, Ajvadi FA, van Zundert A, Irwin MG. Tracheal extubation of the adult intensive care patient with a predicted difficult airway – a narrative review. Anaesthesia. 2017;72:248–61.
19. Mort TC. Continuous airway access for the difficult extubation: the efficacy of the airway exchange catheter. Anesth Analg. 2007;105:1357–62.
20. Ward EW, McManus SM. Novel use of a guidewire to facilitate intubation in an obstructing anterior mediastinal mass. Can J Anesth. 2014;61:660–3.
21. Corso RM, Cattano D, Maitan S. Experience using a new staged extubation kit in patients with a known difficult airway. Anaesth Intensive Care. 2015;43:137–8.
22. Hou RM, Crooke B, Greenland KB, Comadira G. A technique for safe endotracheal tube exchange in difficult airway patients. Anaesth Intensive Care. 2013;41:684–5.
23. Mort TC. Tracheal tube exchange: feasibility of continuous glottic viewing with advanced laryngoscopy assistance. Anesth Analg. 2009;108:1228–31.
24. Mort TC, Braffett BH. Conventional versus video laryngoscopy for tracheal tube exchange: glottic visualization, success rates, complications, and rescue alternatives in the high-risk difficult airway patient. Anesth Analg. 2015;121:440–8.
25. Cooper RM. The use of an endotracheal ventilation catheter in the management of difficult extubations. J Can Anesth. 1996;43:90–3.
26. Suzuki A, Uraoka M, Kimura K, Sato S. Effects of using two airway exchange catheters on laryngeal passage during change from a double-lumen tracheal tube to a single-lumen tracheal tube. Br J Anaesth. 2007;99:440–3.
27. McLean S, Lanam CR, Benedict W, Kirkpatrick N, Kheterpal S, Ramachandran SK. Airway exchange failure and complications with the use of the Cook Airway Exchange Catheter®: a single center cohort study of 1177 patients. Anesth Analg. 2013;117:1325–7.
28. Kim DK, Kim HK, Lee KM, Shin HY, Ryu JS. Poor performance of the pediatric airway exchange catheter in adults with cervical spine immobilization. Can J Anesth. 2008;55:748–53.
29. Higgs A, Swampillai C, Dravid R, et al. Re-intubation over airway exchange catheters – mind the gap. Anaesthesia. 2010;65:859–60.
30. Kitagawa H, Imashuku Y, Yamazaki T. The Parker Flex-Tip tube is useful in a bougie-assisted endotracheal tube exchange after lung lavage. J Cardiothorac Vasc Anesth. 2010;24:901.
31. Law J, Duggan L. Extubation guidelines: use of airway exchange catheters. Anaesthesia. 2012;67:918–9; author reply 21–2.
32. Farag E, Bhandary S, Deungria M, et al. Successful emergent reintubation using the Aintree intubation catheter and a laryngeal mask airway. Minerva Anestesiol. 2010;76:148–50.
33. Higgs A, Hammell C. Use of an Aintree catheter in a difficult tracheostomy tube change. Care Crit Ill. 2006;22:47–9.
34. Duggan LV, Law JA, Murphy MF. Brief review: supplementing oxygen through an airway exchange catheter: efficacy, complications, and recommendations. Can J Anaesth. 2011;58:560–8.
35. Cook TM, Bigwood B, Cranshaw J. A complication of transtracheal jet ventilation and use of the Aintree intubation catheter during airway resuscitation. Anaesthesia. 2006;61:692–7.

36. Benumof JL. Airway exchange catheters: simple concept, potentially great danger. Anesthesiology. 1999;91:342–4.
37. Baraka AS. Tension pneumothorax complicating jet ventilation via a cook airway exchange catheter. Anesthesiology. 1999;91:557–8.
38. Nunn C, Uffman J, Bhananker SM. Bilateral tension pneumothoraces following jet ventilation via an airway exchange catheter. J Anesth. 2007;21:76–9.
39. Axe R, Middleditch A, Kelly FE, Batchelor TJ, Cook TM. Macroscopic barotrauma caused by stiff and soft-tipped airway exchange catheters: an in vitro case series. Anesth Analg. 2015;120:355–61.
40. Wu HL, Tai YH, Wei LF, Cheng HW, Ho CM. Bronchial lumen is the safer route for an airway exchange catheter in double-lumen tube replacement: preventable complication in airway management for thoracic surgery. J Thorac Dis. 2017;9(10):E903–6.
41. ASA Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway. Anesthesiology. 1993;78:598–602.
42. American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Anesthesiology. 2003;98:1269–77.
43. Cook TM, Woodall N, Frerk C. Fourth National Audit Project. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 1: anaesthesia. Br J Anaesth. 2011;106:617–31.
44. Peterson GN, Domino KB, Caplan RA, Posner KL, Lee LA, Cheney FW. Management of the difficult airway: a closed claims analysis. Anesthesiology. 2005;103:33–9.
45. Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: methods to reduce the risk of residual weakness. Anesth Analg. 2010;111:129–40.
46. Prinianakis G, Alexopoulou C, Mamidakis E, Kondili E, Georgopoulos D. Determinants of the cuff-leak test: a physiological study. Crit Care. 2005;9:R24–31.
47. Ikari T, Saski CT. Glottic closure reflex control mechanisms. Ann Otol Rhinol Laryngol. 1980;89:220–4.

Difficult Airway Management in Thoracic Surgery

9

Javier H. Campos and Manuel Granell Gil

9.1 Introduction

One-lung ventilation (OLV) in the thoracic surgical patient who presents with a difficult airway can be achieved with the use of a double–lumen endotracheal tube (DLT) or a single-lumen endotracheal tube and or with a bronchial blocker [1]. It is estimated that between 5% and 8% of patients with primary lung carcinoma also have a carcinoma of the pharynx, usually in the epiglottic area many of these patients have undergone extensive surgery on the airway and the neck [2]. In addition, some of these patients have a potentially difficult airway because of previous radiation to the neck, or previous airway surgery, such as hemimandibulectomy or hemiglossectomy, making intubation and achievement of OLV difficult due to distorted upper airway anatomy. Also, a patient who requires OLV might have distorted anatomy at or beyond the tracheal carina, such as a descending thoracic aortic aneurysm compressing the entrance of the left mainstem bronchus or an intrabronchial or extrabronchial tumor near the tracheobronchial bifurcation that makes the insertion of a left-sided DLT relatively difficult or impossible.

This review will focus on the perioperative management of the difficult airway in the thoracic surgical patient requiring lung isolation and OLV.

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9.2 Preoperative Evaluation of the Difficult Airway

An airway is termed difficult when conventional laryngoscopy reveals a grade III view (just the epiglottis is seen) or grade IV view (just part of the soft palate is seen). Figure 9.1 displays the normal airway anatomy, the grade III just epiglottis seen and grade IV just part of the soft palate is seen.

Once the airway is recognized as being potentially difficult, a careful examination of the patient ensues [3]. Previous anesthesia records should be examined for a history of airway management in the patient. Patients should be asked to open their mouths as wide as possible and extend their tongues. The length of the submental space should also be noted. Patients should be evaluated from side to side to asses any degree of maxillary overbite and their ability to assume the sniffing positing. Also, the patency of the nostrils must be assed in patients who cannot open their mouths, as a nasotracheal approach might be considered. For patients who have a tracheostomy cannula in place, the inlet of the stoma and the circumferential diameter must be assed when considering replacing the tracheostomy cannula with a specific device to achieve OLV [4].

Another group of patients considered to have difficult airways during OLV are those who have distorted anatomy at the entrance of the mainstem bronchus [5]. Such anomalies can be found by reviewing the chest radiographs and the chest regarding the mainstem bronchus diameter and anatomy which can be distorted or compressed. In some instances a flexible fiber-optic bronchoscopy will be necessary to assess the degree of distorted anatomy of the airway prior to the selection of specific device or bronchial blocker to achieve OLV. Table 9.1 displays the patients at risk of having difficult intubation during OLV [6].

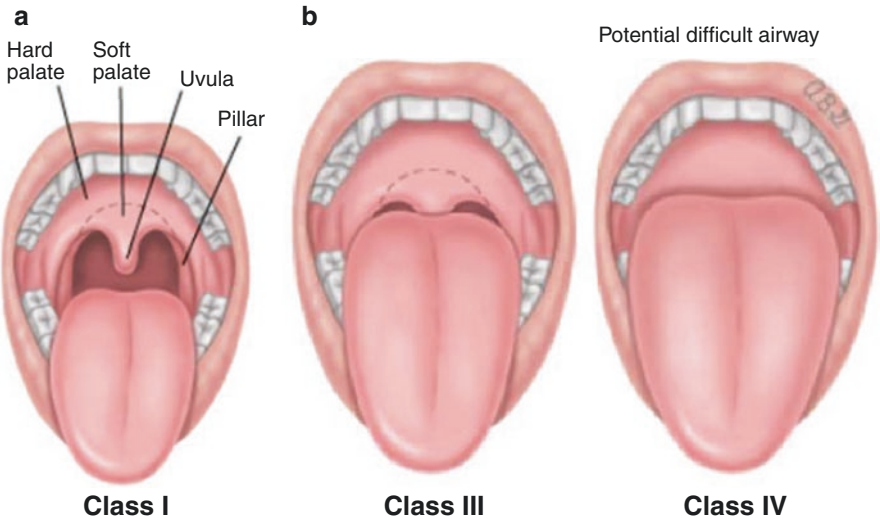


Fig. 9.1 Modified Mallampati classification for difficult laryngoscopy and intubation (**a**) normal (**b**) class III and IV

Table 9.1 Patients at risk of having a difficult intubation during one-lung ventilation

Upper airway
• Short neck and increased neck circumference
• Prominent upper incisors with a receding mandible
• Limited cervical mobility
• Limited jaw opening due to previous surgery
• Radiation therapy of the neck
• Hemiglossectomy/hemimandibulectomy
• Tumors (mouth, tongue, epiglottis)
Lower airway
• Existing tracheostomy in place
• Distorted anatomy (trachea/bronchus)
• Compression at the entrance of left mainstem bronchus

9.3 Difficult Airway and Lung Isolation

9.3.1 Securing the Airway a Must

In patients who require OLV and present with the dilemma of a difficult airway, the primary goal after appropriate anesthesia is achieved is to establish an airway with a single-lumen endotracheal tube placed orally with the aid of a flexible fiber-optic bronchoscope. In selected patients who seem easy to ventilate, this may be performed after induction of anesthesia with the use of a bronchoscope or with a video laryngoscope [7–10]. An alternative when securing the airway prior to placing a lung isolation device is the use of a laryngeal airway mask; with the aid of a flexible fiber-optic bronchoscope, a single-lumen endotracheal tube can be passed through the laryngeal mask airway [11].

9.4 Upper Airway Abnormalities and Lung Isolation

Patients requiring OLV can be identified during the preoperative evaluation to have a potentially difficult airway. This is in part because of the distorted airway anatomy caused by previous surgeries, radiation therapy or both. Distorted anatomy maybe found in the upper airway (tongue, pharynx, larynx). Various methods are available to provide lung isolation under these circumstances. The first step is to establish an airway with a single-lumen endotracheal tube placed orally when the patient is awake.

9.5 Use of a Flexible Fiber-Optic Bronchoscope During Awake Intubation in Difficult Airways

Patients undergoing an awake fiber-optic bronchoscopy must receive oxygen via nasal cannula and be monitored including the use of pulse oximetry. All local anesthetics used via spray or aerosolizes should be quantified to avoid overdose or complications post local anesthetics administration, such as seizures or methemoglobinemia. Also, patients undergoing an awake intubation should receive

an antisialagogue medication such as glycopyrrolate. A simple approach to anesthetize the posterior part of the tongue is to apply lidocaine 5% ointment to a tongue blade depressor and let the patient hold this in his/her mouth for about 5 min. After the tongue blade depressor is removed, the next step is to use a mucosal atomization device (MAD®) to spray the local anesthetic (lidocaine 4% 10 ml) directly to the pharynx, larynx and vocal cords. When the patient experience cough reflex it is very likely that the anesthetic has entered the vocal cords. The next step is to suction all residual secretions that were accumulated in the airway. In order to test that the gagging reflex is abolished, a Berman® intubating pharyngeal airway impregnated with lidocaine 5% ointment at the posterior tip end of the cannula is advanced in the middle of the tongue until it its completely inserted in the oral cavity. The advantage of using the Berman® cannula is that it facilitates a view of the epiglottis and allows the direct passage of the fiberscope followed by a single-lumen endotracheal tube. Also the cannula protects the fiberscope against damage from the patient's teeth.

The fiberscope must be positioned in the midline such that the single-lumen endotracheal tube faces posteriorly during the attempt for intubation. In some cases, retracting of the single-lumen endotracheal tube and 90° counter clock wise rotation will facilitate passage of the tube through the vocal cords. Sometimes it is necessary to complement the local anesthetic with an additional dose of lidocaine 4% (3 ml) through the suction channel of the fiberscope to abolish the cough reflex during manipulation of the airway. The best indicator of proper placement of the fiber-optic bronchoscope and the single-lumen endotracheal tube within the patient's trachea is the direct visualization of the tracheal rings and the tracheal carina with the fiberscope along with the view of the tip of the single-lumen endotracheal tube inside the trachea [12]. After the patient is intubated with a single-lumen endotracheal tube, then an independent bronchial blocker should be considered to achieve OLV.

Common independent bronchial blockers used through or extraluminal to the single-lumen endotracheal tube include the following: a wire-guided endobronchial Arndt® blocker sized 5.0, 7.0 and 9.0 Fr, the Cohen® FlexTip blocker size 9.0 Fr, the Fuji Uniblocker® sizes 4.5 and 9.0 Fr or the EZ-Blocker® size 7.0 Fr [13]. A different alternative to secure the airway if a patient cannot open the mouth due to previous surgery and cannot be intubated orally, then an awake nasotracheal intubation can be performed taking all precautions of a nasal intubation, including the application of a vasoconstrictor followed by a local anesthetic and the passage of a single-lumen endotracheal tube. Once the airway is established, then an independent bronchial blocker can be advanced [14, 15].

When an independent bronchial blocker is used, specifically size 9.0 Fr, the smallest acceptable single-lumen endotracheal tube size recommended is 8.0 I.D. mm, it is important to have enough space between the bronchial blocker and the flexible fiber-optic bronchoscope so that navigation can be achieved with the single-lumen endotracheal tube. Once the single-lumen endotracheal is secured in the patient's trachea, an independent bronchial blocker can be advanced with the aid of a flexible fiber-optic bronchoscope. An advantage of the Cohen, Fuji Uniblocker or the EZ-blocker over the Arnd® wire-guided endobronchial blocker is that while advancing it to a desired bronchus the distal tip of the blocker can be seen while entering a bronchus. With the Arndt blocker, the distal tip is looped into the

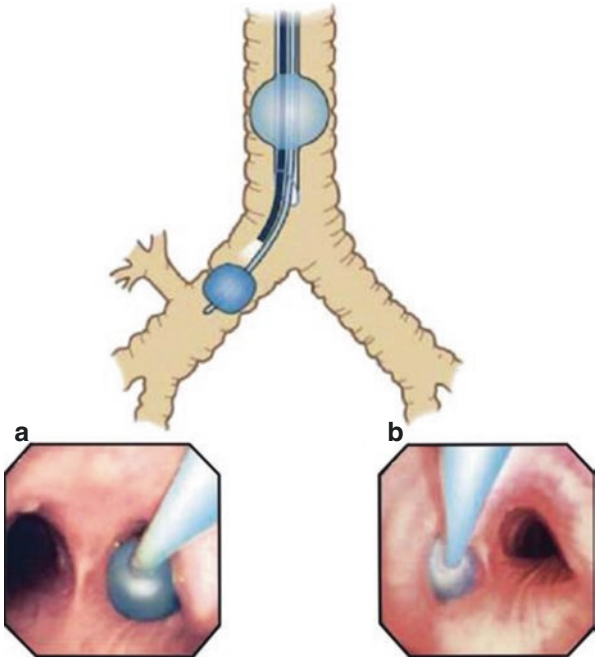


Fig. 9.2 (**a**) Displays the fully inflated balloon of the Fuji® Uniblocker in the right mainstem bronchus (**b**) displays the fully inflated balloon of the Fuji® Uniblocker in the left mainstem bronchus

fiberscope and cannot be seen until disengagement occurs. To achieve OLV the bronchial blocker must be advance to the bronchus where lung collapse is required. One of the advantages of one-time intubation with a single-lumen endotracheal tube in a patient with a difficult airway is that it allows for the conversion of OLV with insertion of an independent bronchial blocker and simple removal of the blocker at the end of the procedure of postoperative ventilatory support is needed [16]. Once the blocker is within the targeted bronchus and the patient is turned into lateral decubitus position the endobronchial balloon is inflated. The amount of air needed to achieve a complete seal within the bronchus in an adult varies between 5 and 8 ml of air. The EZ-blocker required higher amounts of air to achieve a seal [17].

The optimal position of a bronchial blocker in the left or right bronchus is when the blocker balloon's outer surface is seen at least 10 mm below the tracheal carina inside the blocked bronchus and proper seal achieved. Figure 9.2 shows the optimal position of the Fuji Uniblocker® through a single-lumen endotracheal tube.

9.6 Use of Laryngeal Mask Airway and a Bronchial Blocker During Difficult Airways

An alternative to achieve OLV in a patient with a difficult airway is with the use of a laryngeal mask airway in conjunction with the use of an independent bronchial blocker. The use of a ProSeal laryngeal mask airway has been used with a bronchial blocker in patients in whom the airway was deemed difficult and who required OLV during thoracoscopic surgery [18, 19].

9.7 Use of a Double-Lumen Endotracheal Tube in Patients with Difficult Airways

Intubation with a DLT can be more difficult than intubation with a single-lumen endotracheal tube. The larger size, the rigidity, and the shape of the DLT without a bevel at the tip of the tube can obscure the view of the glottis. In practice there are different ways to place a DLT in a patient with a difficult airway. The first involves the use of airway topical anesthesia an awake fiber-optic bronchoscopy with passage of the flexible fiber-optic bronchoscope through the endobronchial lumen of the DLT, where the tube is advanced under bronchoscopy guidance [20]. The second technique involves the use of ancillary lighted devices or video laryngoscopes that increase the visualization field of the epiglottis, vocal cords and passage of the tube. The use of a malleable lighted Stylette had been reported, it was used within the endobronchial lumen of the DLT where the tip of the bulb was positioned distally at the tip of the DLT in patients with difficult airways [21].

Others have reported the use of a fiber-optic laryngoscope, the WuScope during placement of a DLT in patients with abnormal airway anatomy [22]. One of the advantages of the fiber-optic laryngoscope is that it protects against rupture of the endotracheal cuff during laryngoscopy because the DLT is enclosed with the laryngoscope blade. One of the limitations of this device is the need for smaller size DLT's such as 35–37 Fr. The GlideScope is a videolaryngoscope that has been used in patients with a difficult airway during placement of a DLT [23].

9.8 Tube Exchanger Technique for a Double-Lumen Endotracheal Tube

Another alternative is to intubate the patient's trachea with a single-lumen endotracheal tube during an awake fiber-optic bronchoscopy or after induction of anesthesia, and then tube exchange technique can be used to replace the existing tube for a DLT after general anesthesia is induced [11].

For an airway exchange catheter to work, it must have a hollow center channel and universal adapter to insufflate oxygen. The exchange catheter must have a flextip distally to avoid airway lacerations, be long in length, and have outer markings to control the depth of insertion while in use. For a DLT, the exchange catheter should be at least 83 cm long. The airway Aintree tube exchanger has a large internal diameter that allows fiber-optic bronchoscopy guidance. Also, a 14 Fr airway exchange catheter can be used to facilitate insertion of 39 and 41 Fr DLT's. For a 35 or 37 Fr DLT an 11 Fr airway exchange catheter can be used.

The airway exchange catheter, single-lumen endotracheal tube and the DLT combination should be tested in vitro before the exchange [24]. A sniffing position will facilitate tube exchange. After the airway exchange catheter is lubricated it is advanced through a single-lumen endotracheal tube. The airway catheter should not be inserted deeper than 24 cm from the lips to avoid accidental rupture or laceration of the trachea, bronchi or lung [25, 26]. After cuff deflation the single-lumen endotracheal tube is withdrawn then the endobronchial lumen of the DLT is advanced over the exchange catheter. It is optimal to use a video laryngoscope during the tube exchange to guide the DLT through the glottis under direct vision [27].

If a video laryngoscope is not available, then having an assistant to perform a standard laryngoscopy during tube exchange partially straightens out the alignment of the oropharynx and glottis and facilitates the exchange. Proper final position of the DLT is then achieved with auscultation, presence of end tidal carbon dioxide ($ETCO_2$) wave form and a fiber-optic bronchoscopy examination.

9.9 Exchange of a Double-Lumen Endotracheal Tube for a Single-Lumen Endotracheal Tube

Replacement of a DLT for a single-lumen endotracheal tube can be done at the conclusion of surgery with the use of a double airway exchange catheter. Figure 9.3 displays the double airway exchange catheter technique. (a) Displays the video laryngoscope, (b) displays a view of the airway exchange catheter through the vocal cords and (c) displays a DLT advanced with two airway exchange catheters 11 Fr, one through the tracheal lumen and one through the endobronchial lumen. One study using two airway exchange catheters to exchange a DLT for a single-lumen endotracheal tube showed

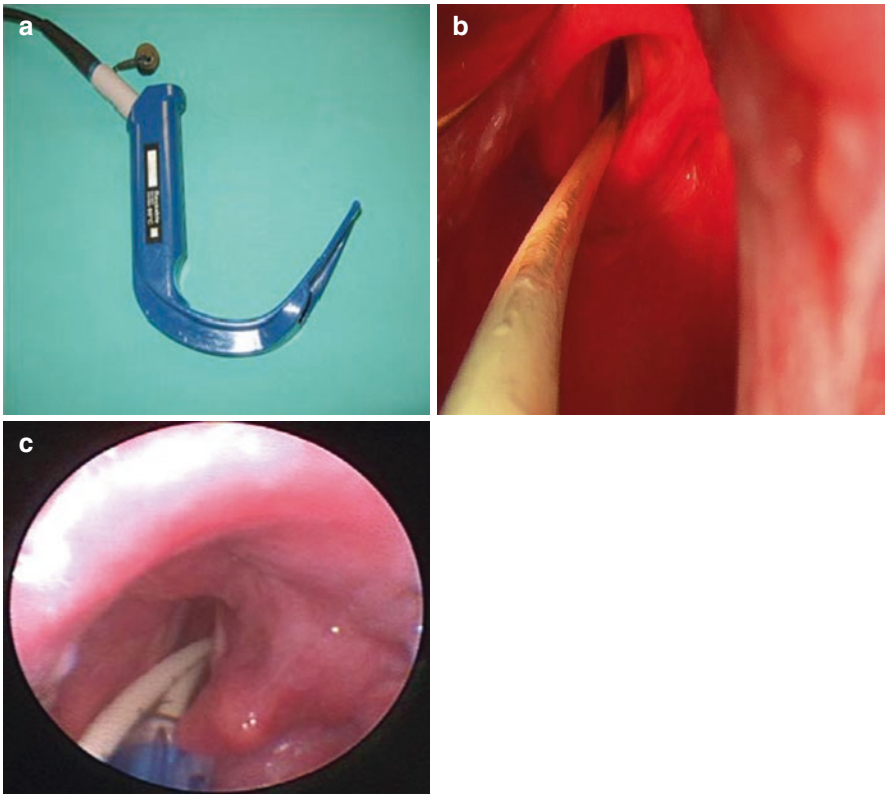


Fig. 9.3 Double airway exchange catheter technique. (**a**) Displays the video laryngoscope, (**b**) displays a view of the airway exchange catheter through the vocal cords and (**c**) displays a DLT advanced with two airway exchange catheters 11 Fr, one through the tracheal lumen and one through the endobronchial lumen

that there was a reduction in the incidence of glottis impingement of the tracheal tube and that there was a higher success rate of passage of the single-lumen endotracheal tube when compared with the use of a single airway exchange catheter [28].

The use of a double airway exchange catheter involves the following techniques: two 11 Fr 83 cm long airway exchange catheters from Cook® Critical Care are used. One catheter is passed through the endobronchial lumen of the DLT, making sure that the tip of the airway exchanger does not protrude distally in the tip of the DLT. A second exchange catheter is passed through the tracheal lumen; both wires provide easy placement of the new single-lumen endotracheal tube because of the increase rigidity with the two tube exchangers. For this technique to work, an 8.0 I.D. mm single-lumen endotracheal tube must be used. Another variation of the tube exchanger technique is using a double-diameter coaxial airway exchange catheter. This consists of a 4.0 mm outer diameter exchanger inside a 7.0 mm outer diameter exchanger. This device allows for a more rigid guide-wire for replacing DLT with a single-lumen endotracheal tube. During tube exchanger techniques, it is recommended to use a video laryngoscope to visualize the proper exchange and move the tongue away from the tube. Figure 9.4 displays the Aintree airway catheter from Cook® Critical Care.

Fig. 9.4 Displays the Cook® airway catheter Aintree (Cook® Critical Care) for exchange between double-lumen endotracheal tubes and a single-lumen endotracheal tube. This recent modification has a soft distal (purple) tip to attempt to decrease the risk of distal airway injury during tube exchange (right). The proximal stiffer green end (left) has detachable connectors for emergency ventilation. Shown is the standard 15-mm outside diameter breathing circuit connector

9.10 Lung Isolation Techniques in Patients with Tracheostomies

The patient with a tracheostomy in situ needs special airway management because the airway has been shortened or because a total laryngectomy will limit oral-tracheal intubation. Although a left-sided DLT is the most common device used for lung isolation, opportunities for using a DLT in a patient with a tracheostomy in situ are limited because the DLT is too long or has a large outside diameter and rigidity, or the tracheostomy stoma may be too small to accommodate the DLT, which can damage the airway easily. Factors to consider when managing lung isolation devices in a tracheostomized patient include early-stage stoma within 7 days of insertion [29] when the airway can be lost immediately while attempting to remove the Shiley tube, versus a long-term tracheostomy where the is a well-formed stoma [30]. All of these factors play an important role in selecting the appropriate lung isolation device to be place thought a tracheostomy stoma [4].

In a patient with a tracheostomy in situ who had an early-stage tracheostomy, the Shiley tube and a bronchial blocker can be used [4]. In contrast for patients with a long-term tracheostomy stoma a single-lumen endotracheal tube can be used and guided it to a selective bronchus where lung isolation take place. A different alternative is the use of a single-lumen endotracheal tube followed by intraluminal or extraluminal placement of an independent bronchial blocker guided with the use of flexible fiber-optic bronchoscopy to achieve optimal position of the bronchial blocker. One-lung ventilation in tracheostomized patients has been reported with the use of Arndt® wire-guided endobronchial blocker, Cohen® flexitip blocker, Fuji® Uniblocker and EZ®-blocker with good results [4, 31]. Although a DLT has been used [32], the author (J. Campos), recommends as a first choice the use of a bronchial blocker unless there is an absolute indication for the use of a DLT. For all these cases a small-size fiber-optic bronchoscope (i.e. 3.5 mm outer diameter) is recommended. Figure 9.5 displays a patient with an existing tracheostomy where an Arndt® blocker has been used to achieve OLV. Table 9.2 displays the

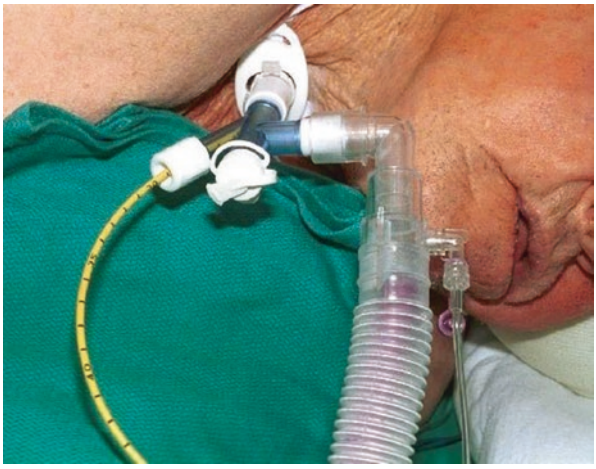
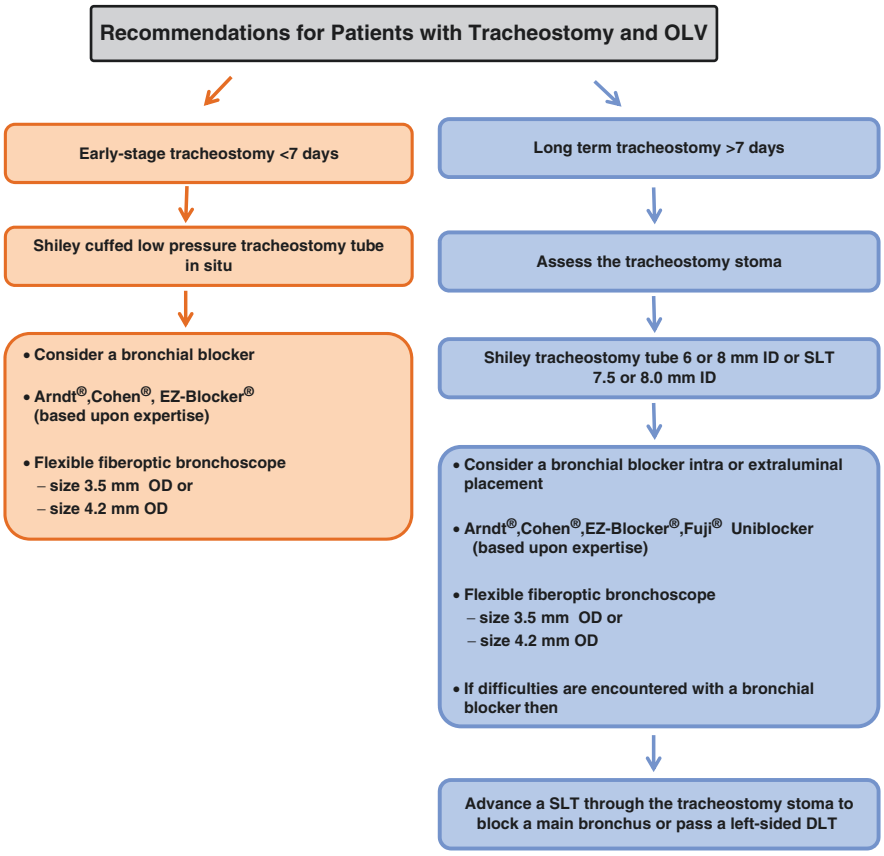


Fig. 9.5 Patient with an existing tracheostomy. an Arndt® blocker [4] is advanced through a multiport connector attached to the Shiley tracheostomy cannula. (With permission: Campos JH, et al: J Cardiothorac Vasc Anesth 2019 [4])

Table 9.2 Displays recommendations to manage lung isolation in a patient with an existing tracheostomy



With permission: Campos JH, et al: J Cardiothorac Vasc Anesth 2019 [4]

recommendations for patients with tracheostomy in situ based upon 70 cases with permission Campos JH, et al, J Cardiothorac Vasc Anesth, 2019 [4].

9.11 Lung Isolation in Patients with Lower Airway Abnormalities

Another important group to consider when dealing with the difficult airway and OLV is patients who present with lower airway abnormalities, specifically distal trachea or bronchial lesions. The common problems that will preclude or contraindicate the use of left-sided DLT include an intraluminal tumor of the left mainstem bronchus or a descending thoracic aortic aneurysm that compressed the entrance of the left main bronchus. One option in these cases is to use a right-sided DLT guided with flexible fiber-optic bronchoscopy [33].

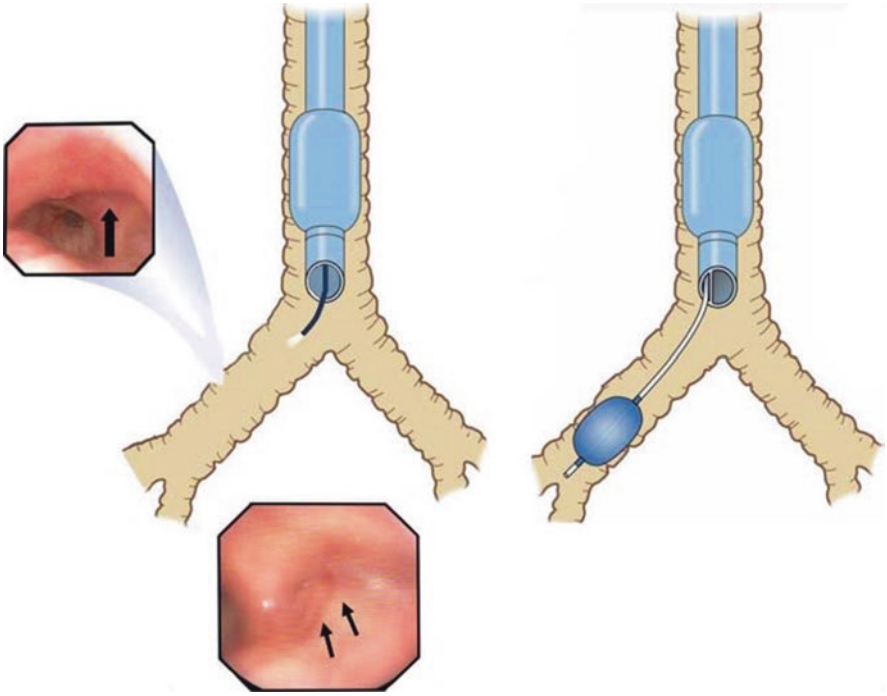


Fig. 9.6 Patient with previous lobectomy the missing (stapled) segmental bronchus for a right upper lobectomy (please see arrows)

Another group of patients that has lower airway abnormalities and require OLV are patients with previous lobectomy. Sometimes in these cases the distorted anatomy may contribute to difficulties in recognizing the right and left bronchus because the loss of anatomical landmarks [34]. In these patients a complete fiberoptic bronchoscopy exam of the trachea and bronchi prior to placement of lung isolation device is required in order to properly identify the anatomy of the tracheobronchial tree. Figure 9.6 displays a patient with a previous lobectomy indicating the missing (stapled) segmental bronchus for a right upper lobectomy.

9.12 Extubation or Mechanical Ventilation After Surgery

Extubation at the completion of surgery in a patient who has a difficult airway represents a challenge. Factors to consider prior to extubation include any mucosal edema, bleeding or lacerations to the pharynx during intubation, the length of surgery, and the amount of fluid administered during the intraoperative period. Continuous access to the airway should be maintained in case re-intubation is needed. The single-lumen endotracheal tube or the DLT can be removed with an airway catheter exchanger in place prior to extubation [35]. In some circumstances, in a patient with a difficult airway and a DLT may require mechanical ventilation in

the postoperative period. One option for extubation of these patients is to deflate both cuffs of the DLT, withdraw the tube above the carina, then reinflate the tracheal cuff and convert the DLT to two-lung ventilation, particularly if the conversion to exchange a DLT for a single-lumen endotracheal tube is considered too risky. Another alternative technique is to exchange a DLT for a single-lumen endotracheal tube using an airway catheter exchanger under direct vision with a laryngoscope or video laryngoscope [36–38].

9.13 Summary

Patients who require OLV, a key element during the preoperative assessment is the recognition and identification of the potentially difficult airway [39]. The safest way to establish an airway is by securing the airway with a single-lumen endotracheal tube placed orally or nasotracheally with the aid of flexible fiberoptic bronchoscopy. Lung isolation in these patients is achieved best with the use of an independent bronchial blocker. An alternative can be the use of a DLT with an airway exchange technique. For the patient who has a tracheostomy in place, the use of an independent bronchial blocker through a single-lumen endotracheal tub or through a Shiley tracheostomy cannula in place is recommended. For all these devices, a flexible fiberoptic bronchoscopy examination is recommended prior, during placement and at the conclusion of the use of lung isolation device [40].

References

1. Campos J. Lung isolation in patients with difficult airways. In: Slinger P, editor. Principles and practice of anesthesia for thoracic surgery. New York, NY: Springer; 2011. p. 247–58.
2. Campos JH. Lung isolation techniques for patients with difficult airway. Curr Opin Anaesthesiol. 2010;23:12–7.
3. American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Anesthesiology. 2003;98:1269–77.
4. Campos JH, Musselman ED, Hanada S, Ueda K. Lung isolation techniques in patients with early stage or long term tracheostomy: a case series report of 70 cases and recommendations. J Cardiothorac Vasc Anesth. 2019;33(2):433–9.
5. Collins SR, Titus BJ, Campos JH, Blank RS. Lung isolation in the patient with a difficult airway. Anesth Analg. 2018;126:1968–78.
6. Campos JH. Difficult airway and one-lung ventilation. Curr Rev Clin Anesth. 2002;16:197–208.
7. Poon KH, Liu EH. The airway scope for difficult double-lumen tube intubation. J Clin Anesth. 2008;20:319.
8. El-Tahan MR, Khidr AM, Gaarour IS, et al. A comparison of 3 videolaryngoscopes for double-lumen tube intubation in humans by users with mixed experience: a randomized controlled study. J Cardiothorac Vasc Anesth. 2018;32:277–86.
9. Liu TT, Li L, Wan L, et al. Videolaryngoscopy vs. Macintosh laryngoscopy for double-lumen tube intubation in thoracic surgery: a systematic review and meta-analysis. Anaesthesia. 2018;73:997–1007.

10. Granell M, Parra MJ, Jiménez MJ, et al. Review of difficult airway management in thoracic surgery. Rev Esp Anestesiol Reanim. 2018;65:31–40.
11. Perlin DI, Hannallah MS. Double-lumen tube placement in a patient with a difficult airway. J Cardiothorac Vasc Anesth. 1996;10:787–8.
12. Campos JH. Fiberoptic bronchoscopy in anesthesia. Curr Rev Clin Anesth. 2008;29:61–72.
13. Campos J. Lung isolation. In: Slinger P, editor. Principles and practice of anesthesia for thoracic surgery, 2011. New York, NY: Springer; 2017. p. 227–46.
14. Campos JH, Kernstine KH. Use of the wire-guided endobronchial blocker for one-lung anesthesia in patients with airway abnormalities. J Cardiothorac Vasc Anesth. 2003;17:352–4.
15. Angie Ho CY, Chen CY, Yang MW, et al. Use of the Arndt wire-guided endobronchial blocker via nasal for one-lung ventilation in patient with anticipated restricted mouth opening for esophagectomy. Eur J Cardiothorac Surg. 2005;28:174–5.
16. Cohen E. Pro: the new bronchial blockers are preferable to double-lumen tubes for lung isolation. J Cardiothorac Vasc Anesth. 2008;22:920–4.
17. Mourisse J, Liesveld J, Verhagen A, et al. Efficiency, efficacy, and safety of EZ-blocker compared with left-sided double-lumen tube for one-lung ventilation. Anesthesiology. 2013;118:550–61.
18. Ozaki M, Murashima K, Fukutome T. One-lung ventilation using the ProSeal laryngeal mask airway. Anaesthesia. 2004;59:726.
19. Tsuchihashi T, Ide S, Nakagawa H, et al. Differential lung ventilation using laryngeal mask airway and a bronchial blocker tube for a patient with unanticipated difficult intubation. Masui. 2007;56:1075–7.
20. Patane PS, Sell BA, Mahla ME. Awake fiberoptic endobronchial intubation. J Cardiothorac Anesth. 1990;4:229–31.
21. O'Connor CJ, O'Connor TA. Use of lighted stylets to facilitate insertion of double-lumen endobronchial tubes in patients with difficult airway anatomy. J Clin Anesth. 2006;18:616–9.
22. Smith CE, Kareti M. Fiberoptic laryngoscopy (WuScope) for double-lumen endobronchial tube placement in two difficult-intubation patients. Anesthesiology. 2000;93:906–7.
23. Hernandez AA, Wong DH. Using a glidescope for intubation with a double lumen endotracheal tube. Can J Anaesth. 2005;52:658–9.
24. Benumof JL. Difficult tubes and difficult airways. J Cardiothorac Vasc Anesth. 1998;12:131–2.
25. Thomas V, Neustein SM. Tracheal laceration after the use of an airway exchange catheter for double-lumen tube placement. J Cardiothorac Vasc Anesth. 2007;21:718–9.
26. deLima LG, Bishop MJ. Lung laceration after tracheal extubation over a plastic tube changer. Anesth Analg. 1991;73:350–1.
27. Chen A, Lai HY, Lin PC, et al. GlideScope-assisted double-lumen endobronchial tube placement in a patient with an unanticipated difficult airway. J Cardiothorac Vasc Anesth. 2008;22:170–2.
28. Suzuki A, Uraoka M, Kimura K, et al. Effects of using two airway exchange catheters on laryngeal passage during change from a double-lumen tracheal tube to a single-lumen tracheal tube. Br J Anaesth. 2007;99:440–3.
29. Mitchell RB, Hussey HM, Setzen G, et al. Clinical consensus statement: tracheostomy care. Otolaryngol Head Neck Surg. 2013;148:6–20.
30. De Leyn P, Bedert L, Delcroix M, et al. Tracheotomy: clinical review and guidelines. Eur J Cardiothorac Surg. 2007;32:412–21.
31. Rispoli M, Nespoli MR, Salvi R, et al. One-lung ventilation in tracheostomized patients: our experience with EZ-blocker. J Clin Anesth. 2016;31:288–90.
32. Yaney LL. Double-lumen endotracheal tube for one-lung ventilation through a fresh tracheostomy stoma: a case report. AANA J. 2007;75:411–5.
33. Campos JH, Ajax TJ, Knutson R, Moyers J, Rossi N, Kuretu RM, Shenag S. Case conference a 76 year old needs an emergency surgery for a descending thoracic aortic aneurysm repair, has multiple intraoperative and postoperative complications. J Cardiothorac Anesth. 1990;5:631–45.

34. Campos JH. Update on selective lobar blockade during pulmonary resections. Curr Opin Anaesthesiol. 2009;22:18–22.
35. Mort TC. Continuous airway access for the difficult extubation: the efficacy of the airway exchange catheter. Anesth Analg. 2007;105:1357–62.
36. Benumof JL. Airway exchange catheters: simple concept, potentially great danger. Anesthesiology. 1999;91:342–4.
37. Merli G, Guarino A, Della Rocca G, et al. Recommendations for airway control and difficult airway management in thoracic anesthesia and lung separation procedures. Minerva Anestesiol. 2009;75:59–78.
38. Thong SY, Lim Y. Video and optic laryngoscopy assisted tracheal intubation—the new era. Anaesth Intensive Care. 2009;37:219–33.
39. Campos JH. Guidelines, algorithms, and recommendations during the management of the difficult airways in the thoracic surgical patient: are they supported by evidence based. Rev Esp Anestesiol Reanim. 2018;65:1–4.
40. Campos JH. Progress in lung separation. Thorac Surg Clin. 2005;15:71–83.

10 Respiratory Mechanics and Gas Exchange in Thoracic Surgery: Changes in Classical Knowledge in Respiratory Physiology

Jakob Wittenstein, Paolo Pelosi, F. Javier Belda, Göran Hedenstierna, and Marcelo Gama de Abreu

10.1 Respiratory Mechanics

Usually, global respiratory mechanics is used to determine the settings of mechanical ventilation; nevertheless, this approach does not take into account alveolar mechanics, which might be different [4]. Furthermore, monitoring of respiratory mechanics and graphics during mechanical ventilation describe the lungs as a single compartment [1]. Additionally, variations in body position lead to changes in the direction of gravitational force and therefore influence pulmonary blood flow distribution, ventilation and respiratory mechanics. Most research of respiratory mechanics during OLV has been undertaken in lateral decubitus position. All of this must be kept in mind when interpreting bedside respiratory system mechanics. Thereby, the information can be used to evaluate lung function and optimize mechanical ventilator support accordingly.

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10.1.1 Plateau, Peak Inspiratory Pressure and Transpulmonary Pressure

The driving force of spontaneous ventilation is the pressure difference between atmosphere and the alveoli, which becomes negative during inspiration. During positive pressure mechanical ventilation, this gradient is determined by the pressure in the airway and at end-expiration, which can be mathematically described by the so-called equation of motion:

$$\text{Paw} = V_T / C_{RS} + \text{Raw} \times \text{Flow} + \text{PEEP}$$

Where Paw is proximal airway pressure applied by the ventilator, V_T is the tidal volume, C_{RS} is the respiratory system compliance, Raw is the airway resistance and PEEP is the positive end-expiratory pressure.

At constant inspiratory flow, the peak inspiratory pressure depends importantly on Raw. In the intubated and ventilated patient, Raw is mainly determined by the diameter of the endotracheal tube. Therefore, peak inspiratory pressure during constant inspiratory flow likely plays a minor role in VILI.

In the context of lung protection, the inspiratory plateau airway pressure, which is a surrogate of the alveolar pressure, plays a key role. Whereas in volume-controlled ventilation, (VCV) plateau pressure can be measured by means of an appropriate inspiratory pause, in pressure-controlled ventilation (PCV) inspiratory pressure equals the plateau pressure when flow decreases to zero at the end of inspiration. Thus, in both modes, zero-flow is necessary to determine the plateau pressure.

The alveolar distending pressure is the transpulmonary pressure, which equals the alveolar pressure (plateau pressure) minus the pleural pressure. During no flow conditions, while an inspiratory or expiratory pause maneuver is performed, transpulmonary pressure equals the alveolar distending pressure. During the clinical routine, the pleural pressure is usually not measured directly. A surrogate of pleural pressure, namely the oesophageal pressure, as measured with a balloon catheter placed in the lower third of the oesophagus, may be used instead [5]. Different factors influence the pleural pressure, including body position, lung elastance and chest wall elastance, which are influenced by the weight of thoracic organs and abdominal pressure. In order to protect the lungs from high distending pressures and to avoid so called barotrauma or volutrauma, the plateau pressure should ideally be kept at values <30 cmH_2O or even below 25 cmH_2O, since higher values may overdistend lungs [1].

10.1.2 Positive End-Expiratory Pressure and Recruitment Maneuvers

OLV has major effects on ventilation/perfusion (V/Q) matching, and is associated with a reduction of the functional residual capacity of the ventilated lung [6]. In this

context, PEEP can improve the function of the ventilated lung by limiting formation of atelectasis, which leads to ventilation within a more compliant portion of the pressure-volume curve [7]. Also, PEEP may reduce atelectrauma, that is, cyclic opening and closing of terminal airways and alveoli [1]. However, PEEP can also result in over-distension of already open alveoli [1]. In the latter case PEEP will increase shunt by diverting blood to the non-ventilated lung, thus increasing functional dead space [8]. There is intense debate on which PEEP should be set, and whether it should be individualized. Studies on this issue have brought conflicting results, with some investigations showing improvement [6, 9, 10], while others showed no effects [11] and even worsening of oxygenation due to PEEP [12].

Despite this controversy, the application of PEEP during OLV became part of standard of care during OLV in an attempt to improve gas exchange and respiratory mechanics [10, 13]. The physiological and clinical effects of a particular level of PEEP are different when PEEP is used isolated or in combination with an alveolar recruitment maneuver (RM) [8]. In fact, only when the critical opening pressure of closed alveoli is reached, appropriate PEEP levels will be able to maintain them opened throughout the respiratory cycle.

A RM is a maneuver aimed at increasing the transpulmonary pressure in an attempt to revert alveolar collapse [13]. Different RMs have been described to achieve this aim in the ventilated, and also the non-ventilated lung. These RM share a temporary increase of the airway pressure, usually with values $\geq$30 cmH_2O.

During OLV in lateral decubitus position, a RM of the dependent lung can result in an increased compliance and improved arterial oxygenation [6, 14]. In order to keep the recruited alveoli open after the RM, PEEP can be set to optimize respiratory mechanics while minimizing alveolar over distension [8]. In contrast to a preset PEEP, it can be titrated to reach the best compliance (C_{RS}), e.g. by a decremental PEEP trial. Thereby driving pressure (ΔP = plateau pressure − PEEP) can be reduced and C_{RS} improved [8, 15–17].

10.1.3 Auto-PEEP

Auto-PEEP, also known as intrinsic PEEP or occult PEEP, occurs when the expiratory phase is terminated prematurely and gas remains trapped in the lungs at end-expiration. It can be measured by an end-expiratory pause during muscle relaxation and under controlled ventilation. The pressure measured at the end of this maneuver in excess of the PEEP set on the ventilator corresponds to the auto-PEEP [1]. However, if airways collapse during exhalation and air is trapped in the alveoli, auto-PEEP is underestimated.

On the one hand, air trapping in the ventilated and non-ventilated lung can have positive effects, reducing atelectasis, preserving oxygenation and delaying the onset of desaturation and hypoxemia [18]. On the other hand, it can have also deleterious effects, causing over-distension of the lung with increased deadspace, shift of blood flow towards the non-ventilated lung and hemodynamic impairment. In certain

cases, the auto-PEEP may be reduced by an RM or adjustments of the PEEP set at the ventilator [6], but allowing more time for the expiratory phase [19] is key.

10.1.4 Driving Pressure

In patients with ARDS, a driving pressure below 15 cmH_2O has been suggested to be lung-protective [20]. Recently, a post-hoc analysis of a large observational trial [21] showed that when RM combined with PEEP led to a decrease of driving pressure, the rate of postoperative pulmonary complications was reduced [22].

In a trial during OLV, [23], a driving pressure–guided ventilation resulted in improved lung protection as compared to a fixed level of PEEP at 5 cmH_2O. However, that study was relatively small.

One has to keep in mind that the driving pressure is not the real lung-distending pressure. In fact, it is the transpulmonary driving pressure that effectively results in lung strain, which can be estimated using the oesophageal pressure. Transpulmonary driving pressure may be useful to understand how much of the driving pressure is due to elastance of the lungs and how much to chest wall elastance [24]. Accordingly, a high driving pressure that results from a high chest-wall elastance is likely less harmful to the lungs.

10.1.5 Tidal Volume

OLV with high tidal volumes has been shown to induce tidal lung over-distension (volutrauma), promoting VILI [25, 26]. During OLV, the tidal volume should be set between 5 and 6 mL/kg of predicted body weight (PBW) [27, 28]. The use of PBW is based on the assumption that volutrauma might be minimized by delivering a volume appropriate to the patient's lung capacity [29]. Lung capacity and respiratory system compliance relate more closely to height than to weight [3, 30, 31]. Predicted weight for male and female patients can be calculated by the following formulas:

$$\text{Male}: \text{PBW} = 50 + 0.91\left(\text{centimetres of height} - 152.4\right)$$

$$\text{Female}: \text{PBW} = 45.5 + 0.91\left(\text{centimetres of height} - 152.4\right)$$

10.1.6 Compliance and Functional Residual Capacity

When addressing the respiratory system mechanics, both static and dynamic conditions must be taken into account. Static assessment is performed under no-flow conditions, while dynamic assessment is done during ventilation. Respiratory system mechanics measured under dynamic conditions is usually preferable, since it reflects the full respiratory system [4]. Quasi-static C_{RS} can be calculated by the following formula when ventilated in volume-controlled mode:

$$C_{RS} = V_T / (\text{plateau pressure} - \text{PEEP})$$

The resistance of the respiratory system (R_{RS}) can be calculated by the following formula when ventilated in volume-controlled mode:

$$(R_{RS}) = (\text{peak airway pressure} - \text{plateau pressure}) / \text{flow}$$

In lateral decubitus position the dependent hemi-thorax is compressed by the mediastinal structures and cephalad displacement of the lower diaphragm [32]. Therefore the static pressure-volume curve of the lung (P/V curve) has a rightward horizontal shift as compared to the upright position, with consequent reduced C_{RS} [33]. Furthermore, in lateral decubitus position, the compliance of the dependent hemi-thorax is about two-thirds of the contra-lateral one, when both lungs are ventilated (two-lung ventilation, TLV). When switching to OLV, the static P/V curve of the dependent lung, is shifted to the left and steeper, as compared to the P/V curve obtained in the same lung during TLV [34]. During OLV the elastic recoil of the non-dependent, collapsed lung and the compression of the dependent lung are lower than the elastic, expanding force in the chest wall [24]. The consequence is that the compliance of the ventilated hemi-thorax increases during OLV compared to TLV of the same lung in the lateral decubitus position. Importantly, C_{RS} is altered by the formation of atelectasis, increased pulmonary fluid content, surfactant dysfunction and increased pleural and abdominal pressure.

The functional lung size is the volume of aerated lung available for tidal ventilation [35], which is the end-expiratory lung volume (EELV). During mechanical ventilation, EELV can be determined by computer tomography, washout methods or indicator gas dilution. OLV abruptly reduces EELV. Usually, the left lung accounts for 45%, and the right lung for 55% of EELV [25]. Alveolar derecruitment during OLV further reduces EELV [36]. RM combined with appropriate PEEP can restore EELV [6]. A low preoperative EELV combined with the further reduction during anaesthesia might result in a EELV below closing volume. Closing volume is the lung volume at which airway closure occurs. When the closing volume is bigger than EELV, meaning that end-expiratory lung collapse is present, pulmonary shunt is increased. In this case PEEP can be used to increase EELV above closing volume to reduce shunt and improve gas exchange [17].

Once more it has to be kept in mind that respiratory mechanics mostly displays the lungs as a single compartment. The lungs are a constitute of different compartments with a different time constant, so-called τ, which is the product of resistance and compliance. Lung units with a higher resistance and/or compliance will have a longer time constant and require more time to fill and to empty. In contrast, lung units with a lower resistance and/or compliance will have a lower time constant and thus require less time to fill and to empty [37].

10.1.7 Inspiratory to Expiratory Time Ratio

A prolonged inspiratory time with an ratio of inspiratory to expiratory time (I:E) of 1:1 during OLV can result in a modest improvement in oxygenation and decreased

shunt fraction [38]. However, in patients with obstructive lung disease, expiratory time must be long enough though, to allow complete expiration and avoid air trapping.

10.1.8 Stress and Strain

In lungs, stress is the pressure applied to the lung parenchyma. Shear stress is generated when the force is applied at an angle. Strain is the physical deformation or change in shape of a structure, such as an alveolus, usually caused by stress [1]. The clinical equivalent of stress is the distending, transpulmonary pressure, while the equivalent of strain is the ratio of V_T to the functional residual capacity (FRC) [1]. Lung stress and strain are global values and therefore do not reflect regional conditions. Heterogeneity between lung units, in particular the interface between atelectasis and normally expanded alveoli, has been described as a stress modifier [39] which results in shear stress [40].

Due to the loss of EELV during OLV high lung strain is present, especially when, large V_T are used [2]. The consequence is an elevated risk for VILI. The use of PEEP can reduce the dynamic strain by increasing EELV, however it introduces an potentially injurious static strain component [3].

The so-called stress index, which is the coefficient of a power equation, can be used to guide ventilation. The stress index can be assessed qualitatively from the shape of the pressure-time curse during volume control ventilation. Thereby a linear increase of pressure equals a stress index of one, meaning that compliance is constant and alveolar recruitment is adequate without over-distension taking place. If compliance worsens during increase of pressure, which is resampled by an upward concavity of the pressure time curve, stress index is >1, meaning over-distension is present. In this case, V_T should be decreased in order to prevent VILI. When compliance increases during inspiration, this leads to a downward concavity of the pressure time cure and a stress index <1. This can be due to tidal recruitment, which might be stabilized when PEEP is increased [1].

10.2 Gas Exchange

Pulmonary gas exchange depends upon three processes: ventilation, diffusion and perfusion. Especially ventilation and perfusion can be altered during OLV. Hypoventilation occurs because of atelectasis formation and perfusion might be altered because of positive pressure ventilation with increased intra-thoracic pressure. During OLV, the absence of ventilation in the non-dependent lung and the atelectasis induced by anaesthesia in the dependent lung result in V/Q mismatch and hypoxemia [17]. Changes in the direction of gravitational force due to positional changes as well as mediastinal structure shifting, impact pulmonary blood flow distribution, ventilation, and therefore oxygenation [41]. Surgical positions influence the deterioration speed and the nadir value of PaO_2 after the start of OLV [13]. The

diversion of blood flow from the non-ventilated lung to the ventilated lung is gravity related and best in the lateral decubitus position [42]. Given that the right lung is larger than the left one, derangement of gas exchange is more pronounced in right thoracotomies [43].

During the first successful performed pneumonectomies in 1931 and 1933, hypoxemia was a major issue during OLV [44, 45]. Currently, hypoxemia during OLV is less common, but may still pose difficulties, particularly in the supine position. By increasing F_IO_2 hypoxemia can be prevented, nevertheless high F_IO_2 increases the risk of resorption atelectasis, which itself increases shunt and thereby causes hypoxemia. Furthermore, RM of both lungs before OLV and RM of the ventilated and/or non-ventilated during OLV can improve arterial oxygenation and ventilator efficiency during thoracic surgery not only in the supine position [13].

During OLV a mild hypercapnia can usually accepted, if there are no contraindications. In fact, a mild hypercapnia was shown to reduce pulmonary inflammation during OLV [46]. An increase in respiratory rate to counteract hypercapnia is limited by the expiratory time on one hand, with possible auto-PEEP, and inspiratory time on the other hand, which may result in high inspiratory pressures [46].

10.3 Ventilation-Perfusion-Matching

The V/Q ratio describes the efficiency of gas exchange, ranging from zero (shunt) to infinite (alveolar dead space). Blood oxygenation (partial arterial oxygen pressure) is mainly impaired by shunt, whereas dead space impact more pronouncedly on CO_2 removal [10]. The physiological pattern of regional pulmonary blood flow is mainly determined by the relationship among pulmonary arterial, venous, and alveolar pressures [43]. The lungs can be divided in three functional different zones, the so called West zones [47]. The classic West zones of the lungs represent the relationship between the dynamic differential regional distribution of alveolar, arterial, and venous pressures in the lung. The different lung regions experience a transition between the zones depending on the phase of the respiratory and cardiac cycle, as external forces and regional blood flow change [46]. Zone 1 is the zone that experiences the least gravity. There alveolar pressure (PA) exceeds both arterial (Pa) and venous (Pv) pressure (PA > Pa > Pv). Therefore, ventilation takes place without perfusion, which is alveolar dead space. The most gravity depended zone is zone 3 wherein both Pv and PA are lower than Pa, resulting in perfusion of non-ventilated lung units, which is shunt. The zone in-between, zone 2, is where gas exchange takes place. Here Pa is higher than PA and Pv.

10.4 Ventilation

Ventilation describes the movement of gas during inspiration and expiration between atmosphere/ventilator and alveoli. The driving force is the pressure difference between these. While inspiration is an active process, contraction of the respiratory

muscles or applied pressure by the ventilator, expiration is usually passive. During OLV, the lung volume available for ventilation, the EELV, is significantly reduced because of the exclusion of one lung and development of intraoperative atelectasis, with an increasing risk for VILI [48]. Risk factors for lung injury include preoperative characteristics such as age, history of chronic alcohol use, and multi-morbidity, whereas intraoperative risk factors include pneumonectomy, extended resection and duration of OLV [46].

10.5 Perfusion

During OLV perfusion is redistributed away from the collapsed lung to the ventilated lung. Gravity is a major determinant of shunt fraction and perfusion, and therefore influences oxygenation. PaO_2 is higher during OLV in patients operated in the lateral position compared with the supine position. During OLV in a lateral decubitus position, gravity supports the redistribution of perfusion to the ventilated, gravity dependent lung, improving and maintaining V/Q matching [49].

During one-lung ventilation (OLV) in the lateral position, pulmonary shunt usually ranges from 15% to 40% because of the total collapse of the non-dependent lung [50]. Both atelectasis and hypoventilated zones in the dependent lung contribute to a V/Q mismatch and have an additive effect to the shunting in the non-dependent lung [51].

Shunt, perfusion of non-ventilated lung units, activates hypoxic pulmonary vasoconstriction (HPV), which leads to contraction of vascular smooth muscles in the pulmonary circulation in response to a low regional partial pressure of alveolar oxygen. HPV decreases shunt and redirects pulmonary blood flow to the well-oxygenated and dependent lung [49, 52]. If HPV is intact, shunt fraction during OLV is 20–30% of cardiac output, as opposed to the 50% in the absence of HPV [32]. The maximal HPV response during OLV decreases blood flow to the non-dependent lung by 50% [53]. However, if the hypoxic compartments are substantial in their size, e.g. bigger than 70% of the total lung, the effectiveness of HPV is reduced, since the size of normoxic lung units is not sufficient to receive diverted blood flow [54].

HPV is a biphasic reaction with an early response that usually starts within seconds and reaches a peak between 20 and 30 min during OLV, followed by a delayed response during the next 2 h when the maximal vasoconstrictor response is reached [49]. This explains, why PaO_2 gradually increases during OLV.

HPV might be altered during OLV by hypotension, hypocapnia, hypothermia, the presence of chronic obstructive pulmonary diseases and by the use of vasodilators, vasoconstrictors and anaesthetic agents [49]. On the other hand, pulmonary hypoperfusion functionally enhances the effects of HPV. Pulmonary hypoperfusion can be due to decreased cardiac output and pulmonary arterial pressure which result in a decreased shunt fraction [32].

10.6 Considerations for Non-tubed Procedures

The interest in the so-called non-tubed, or non-intubated, anesthetic management is increasing rapidly. Non-tubed thoracic anesthesia refers to thoracic procedures that are performed in spontaneously breathing subjects without endotracheal airway devices [55]. Thereby, adverse effects, including airway injury, prolonged mechanical ventilation and VILI can be reduced, or even completely avoided.

During non-tubed procedures, efficient contraction of dependent hemi-diaphragm is preserved and results in a high ventilation and perfusion matching especially in lateral decubitus position. Even though the evidence is low, patients seem to tolerate non-tubed surgical procedure relatively well, with minor intraoperative impairment in gas exchange [55].

Nevertheless, paradoxical breathing patterns causing rebreathing of carbon dioxide from the non-dependent surgical lung can occur. Furthermore, the need for an open hemithorax causes a mediastinal shift with a consecutive reduction of the compliance of the dependent lung and a reduction of tidal volume [56]. Hypercapnia might be more frequent in non-tubed procedures compared with invasive OLV, but is usually well-tolerated and rapidly resolves after the operation [57]. This has to be kept in mind especially in patients with elevated pulmonary pressures, raised intracranial pressures and arrhythmias where a hypercapnia should be avoided [58].

Low oxygenation and hypercapnia during non-tubed video-assisted thoracoscopy can be resolved when a chest tube is inserted at the beginning of the operation. Thereby the trocars can be closed intermittently allowing re-expansion of the non-dependent lung during surgery [59]. A facial oxygen mask usually provides sufficient oxygen supply, but if conversion to intubated general anesthesia and mechanical ventilation becomes necessary, a skilled anesthetist with expertise in this type of procedure is necessary [57].

References

1. Hess DR. Respiratory mechanics in mechanically ventilated patients. Respir Care. 2014;59(11):1773–94.
2. Lohser J, Slinger P. Lung injury after one-lung ventilation: a review of the pathophysiologic mechanisms affecting the ventilated and the collapsed lung. Anesth Analg. 2015;121(2):302–18.
3. Ball L, Robba C, Gama de Abreu M, Pelosi P. Lung protection during one-lung ventilation: another piece in the puzzle. Eur J Anaesthesiol. 2018;35(10):724–6.
4. Schwenninger D, Runck H, Schumann S, Haberstroh J, Priebe HJ, Guttmann J. Endoscopic imaging to assess alveolar mechanics during quasi-static and dynamic ventilatory conditions in rats with noninjured and injured lungs. Crit Care Med. 2013;41(5):1286–95.
5. Mauri T, Yoshida T, Bellani G, Goligher EC, Carteaux G, Rittayamai N, et al. Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. Intensive Care Med. 2016;42(9):1360–73.
6. Cinnella G, Grasso S, Natale C, Sollitto F, Cacciapaglia M, Angiolillo M, et al. Physiological effects of a lung-recruiting strategy applied during one-lung ventilation. Acta Anaesthesiol Scand. 2008;52(6):766–75.

7. Valenza F, Ronzoni G, Perrone L, Valsecchi M, Sibilla S, Nosotti M, et al. Positive end-expiratory pressure applied to the dependent lung during one-lung ventilation improves oxygenation and respiratory mechanics in patients with high FEV1. Eur J Anaesthesiol. 2004;21(12):938–43.
8. Ferrando C, Mugarra A, Gutierrez A, Carbonell JA, García M, Soro M, et al. Setting individualized positive end-expiratory pressure level with a positive end-expiratory pressure decrement trial after a recruitment maneuver improves oxygenation and lung mechanics during one-lung ventilation. Anesth Analg. 2014;118(3):657–65.
9. Tusman G, Böhm SH, Melkun F, Staltari D, Quinzio C, Nador C, et al. Alveolar recruitment strategy increases arterial oxygenation during one-lung ventilation. Ann Thorac Surg. 2002;73(4):1204–9.
10. Tusman G, Böhm SH, Sipmann FS, Maisch S. Lung recruitment improves the efficiency of ventilation and gas exchange during one-lung ventilation anesthesia. Anesth Analg. 2004;98(6):1604–9.
11. Mascotto G, Bizzarri M, Messina M, Cerchierini E, Torri G, Carozzo A, et al. Prospective, randomized, controlled evaluation of the preventive effects of positive end-expiratory pressure on patient oxygenation during one-lung ventilation. Eur J Anaesthesiol. 2003;20(9):704–10.
12. Slinger PD, Kruger M, McRae K, Winton T. Relation of the static compliance curve and positive end-expiratory pressure to oxygenation during one-lung ventilation. Anesthesiology. 2001;95(5):1096–102.
13. Choi YS, Bae MK, Kim SH, Park J-E, Kim SY, Oh YJ. Effects of alveolar recruitment and positive end-expiratory pressure on oxygenation during one-lung ventilation in the supine position. Yonsei Med J. 2015;56(5):1421–7.
14. Madke GR, Forgiarini LA Jr, Grun G, Fontena E, Pereira RB, de Moraes MM, et al. Effect of positive end-expiratory pressure after porcine unilateral left lung transplant. Exp Clin Transplant. 2013;11(1):50–5.
15. Ferrando C, Suarez-Sipmann F, Tusman G, León I, Romero E, Gracia E, et al. Open lung approach versus standard protective strategies: effects on driving pressure and ventilatory efficiency during anesthesia - a pilot, randomized controlled trial. PLoS One. 2017;12(5):e0177399.
16. Ferrando C, Soro M, Unzueta C, Suarez-Sipmann F, Canet J, Librero J, et al. Individualised perioperative open-lung approach versus standard protective ventilation in abdominal surgery (iPROVE): a randomised controlled trial. Lancet Respir Med. 2018;6(3):193–203.
17. Spadaro S, Grasso S, Karbing DS, Fogagnolo A, Contoli M, Bollini G, et al. Physiologic evaluation of ventilation perfusion mismatch and respiratory mechanics at different positive end-expiratory pressure in patients undergoing protective one-lung ventilation. Anesthesiology. 2018;128(3):531–8.
18. Purohit A, Bhargava S, Mangal V, Parashar VK. Lung isolation, one-lung ventilation and hypoxaemia during lung isolation. Indian J Anaesth. 2015;59(9):606–17.
19. Szegedi LL, Barvais L, Sokolow Y, Yernault JC, d'Hollander AA. Intrinsic positive end-expiratory pressure during one-lung ventilation of patients with pulmonary hyperinflation. Influence of low respiratory rate with unchanged minute volume. Br J Anaesth. 2002;88(1):56–60.
20. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med. 2015;372(8):747–55.
21. Hemmes SNT, de Abreu MG, Pelosi P, Schultz MJ. ESA Clinical Trials Network 2012: LAS VEGAS--Local assessment of ventilatory management during general anaesthesia for surgery and its effects on postoperative pulmonary complications: a prospective, observational, international, multicentre cohort study. Eur J Anaesthesiol. 2013;30(5):205–7.
22. Neto AS, Hemmes SN, Barbas CS, Beiderlinden M, Fernandez-Bustamante A, Futier E, et al. Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. Lancet Respir Med. 2016;4(4):272–80.

23. Park M, Ahn HJ, Kim JA, Yang M, Heo BY, Choi JW, et al. Driving pressure during thoracic surgery: a randomized clinical trial. Anesthesiology. 2019;130(3):385–93.
24. Rauseo M, Mirabella L, Grasso S, Cotoia A, Spadaro S, D'Antini D, et al. Peep titration based on the open lung approach during one lung ventilation in thoracic surgery: a physiological study. BMC Anesthesiol. 2018;18(1):156. https://doi.org/10.1186/s12871-018-0624-3.
25. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med. 2013;369(22):2126–36.
26. Marret E, Cinotti R, Berard L, Piriou V, Jobard J, Barrucand B, et al. Protective ventilation during anaesthesia reduces major postoperative complications after lung cancer surgery: a double-blind randomised controlled trial. Eur J Anaesthesiol. 2018;35(10):727–35.
27. Sundar S, Novack V, Jervis K, Bender SP, Lerner A, Panzica P, et al. Influence of low tidal volume ventilation on time to extubation in cardiac surgical patients. Anesthesiology. 2011;114(5):1102–10.
28. Slinger PD. Optimizing one-lung ventilation: moving beyond tidal volume. J Cardiothorac Vasc Anesth. 2018;32(6):2673–5.
29. ARDS-Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med. 2000;342(18):1301–8.
30. Cressoni M, Gallazzi E, Chiurazzi C, Marino A, Brioni M, Menga F, et al. Limits of normality of quantitative thoracic CT analysis. Crit Care. 2013;17(3):R93. https://doi.org/10.1186/cc12738.
31. Martin DC, Richards GN. Predicted body weight relationships for protective ventilation - unisex proposals from pre-term through to adult. BMC Pulm Med. 2017;17(1):85. https://doi.org/10.1186/s12890-017-0427-1.
32. Vidal Melo MF, Musch G, Kaczka DW. Pulmonary pathophysiology and lung mechanics in anesthesiology: a case-based overview. Anesthesiol Clin. 2012;30(4):759–84.
33. Washko GR, O'Donnell CR, Loring SH. Volume-related and volume-independent effects of posture on esophageal and transpulmonary pressures in healthy subjects. J Appl Physiol (1985). 2006;100(3):753–8.
34. Klingstedt C, Baehrendtz S, Bindslev L, Hedenstierna G. Lung and chest wall mechanics during differential ventilation with selective PEEP. Acta Anaesthesiol Scand. 1985;29(7):716–21.
35. Gattinoni L, Pesenti A. The concept of "baby lung". Intensive Care Med. 2005;31(6):776–84.
36. Larsson A, Malmkvist G, Werner O. Variations in lung volume and compliance during pulmonary surgery. Br J Anaesth. 1987;59(5):585–91.
37. Carvalho AR, Ichinose F, Schettino IA, Hess D, Rojas J, Giannella-Neto A, et al. Tidal lung recruitment and exhaled nitric oxide during coronary artery bypass grafting in patients with and without chronic obstructive pulmonary disease. Lung. 2011;189(6):499–509.
38. Lee SM, Kim WH, Ahn HJ, Kim JA, Yang MK, Lee CH, et al. The effects of prolonged inspiratory time during one-lung ventilation: a randomised controlled trial. Anaesthesia. 2013;68(9):908–16.
39. Gattinoni L, Carlesso E, Langer T. Towards ultraprotective mechanical ventilation. Curr Opin Anaesthesiol. 2012;25(2):141–7.
40. Plataki M, Hubmayr RD. The physical basis of ventilator-induced lung injury. Expert Rev Respir Med. 2010;4(3):373–85.
41. Lan CC, Chang CY, Peng CK, Wu CP, Huang KL, Lee SC, et al. Effect of body positions on hemodynamics and gas exchange in anesthetized pigs shortly after pneumonectomy. Shock. 2010;34(5):482–7.
42. Reinius H, Borges JB, Engström J, Ahlgren O, Lennmyr F, Larsson A, et al. Optimal PEEP during one-lung ventilation with capnothorax: an experimental study. Acta Anaesthesiol Scand. 2019;63(2):222–31.
43. Ribas J, Jimenez MJ, Barbera JA, Roca J, Gomar C, Canalis E, et al. Gas exchange and pulmonary hemodynamics during lung resection in patients at increased risk: relationship with preoperative exercise testing. Chest. 2001;120(3):852–9.
44. Brewer LA. The first pneumonectomy. Historical notes. J Thorac Cardiovasc Surg. 1984;88(5 Pt 2):810–26.

45. Graham EA, Singer JJ. Landmark article Oct 28, 1933. Successful removal of an entire lung for carcinoma of the bronchus. By Evarts A. Graham and J. J. Singer. JAMA. 1984;251(2):257–60.
46. Bender SP, Anderson EP, Hieronimus RI, Bensimhon A. One-lung ventilation and acute lung injury. Int Anesthesiol Clin. 2018;56(1):88–106.
47. West JB, Dollery CT, Naimark A. Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures. J Appl Physiol. 1964;19:713–24.
48. Downs JB, Robinson LA, Steighner ML, Thrush D, Reich RR, Rasanen JO. Open lung ventilation optimizes pulmonary function during lung surgery. J Surg Res. 2014;192(2):242–9.
49. Campos JH, Feider A. Hypoxia during one-lung ventilation—a review and update. J Cardiothorac Vasc Anesth. 2018;32(5):2330–8.
50. Torda TA, McCulloch CH, O'Brien HD, Wright JS, Horton DA. Pulmonary venous admixture during one-lung anaesthesia. The effect of inhaled oxygen tension and respiration rate. Anaesthesia. 1974;29(3):272–9.
51. Hedenstierna G, Tokics L, Strandberg A, Lundquist H, Brismar B. Correlation of gas exchange impairment to development of atelectasis during anaesthesia and muscle paralysis. Acta Anaesthesiol Scand. 1986;30(2):183–91.
52. Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. Anesthesiology. 2015;122(4):932–46.
53. Glasser SA, Domino KB, Lindgren L, Parcella P, Marshall C, Marshall BE. Pulmonary blood pressure and flow during atelectasis in the dog. Anesthesiology. 1983;58(3):225–31.
54. Benumof JL. One-lung ventilation and hypoxic pulmonary vasoconstriction: implications for anesthetic management. Anesth Analg. 1985;64(8):821–33.
55. Tacconi F, Pompeo E. Non-intubated video-assisted thoracic surgery: where does evidence stand? J Thorac Dis. 2016;8(Suppl 4):S364–75.
56. Hung M-H, Hsu H-H, Cheng Y-J, Chen J-S. Nonintubated thoracoscopic surgery: state of the art and future directions. J Thorac Dis. 2014;6(1):2–9.
57. Guo Z, Yin W, Pan H, Zhang X, Xu X, Shao W, et al. Video-assisted thoracoscopic surgery segmentectomy by non-intubated or intubated anesthesia: a comparative analysis of short-term outcome. J Thorac Dis. 2016;8(3):359–68.
58. Irons JF, Martinez G. Anaesthetic considerations for non-intubated thoracic surgery. J Vis Surg. 2016;2:61. https://doi.org/10.21037/jovs.2016.02.22. eCollection 2016.
59. Pompeo E, Rogliani P, Tacconi F, Dauri M, Saltini C, Novelli G, et al. Randomized comparison of awake nonresectional versus nonawake resectional lung volume reduction surgery. J Thorac Cardiovasc Surg. 2012;143(1):47–54.

Non-intubated Video-Assisted Surgery: A Critical Review

11

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11.1 Introduction

The development of thoracic surgery and thoracic anesthesia was revolutionized by the ability to collapse the operated lung using double lumen tubes (DLT) or, more recently, bronchial blockers (BB). A collapsed, motionless lung provides an optimal operating condition and thus expedites surgery. A DLT not only provided a collapsed lung, it also helped avoid cross-contamination of the lungs with blood or pus from the contralateral lung. In cases such as broncho-pleural injuries, DLT provided the possibility of ventilation and oxygenation as such.

An important development in thoracic surgery has been the introduction of video-assisted thoracoscopic surgery (VATS). This approach minimizes tissue injury, reduces postoperative pain and improves postoperative recovery. General anesthesia protocols using either DLT or BB are commonly used and are the mainstay of VATS and open lung surgery worldwide. Usually, two or three ports are used to introduce instruments into the thoracic cavity during VATS. More recently, surgeons have explored using two or even a single port to perform complex operations. The use of a single port introduced through one single small incision dramatically

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decreases the invasiveness of surgery and improves patient well-being postoperatively. In 2004, Gaetano Rocco [1] introduced a uniportal VATS approach for lung wedge resection, which opened new horizons for minimal invasive video-assisted thoracic surgery.

Since intraoperative pain is reduced during VATS, it has been recently questioned whether all patients undergoing this procedure need general anesthesia and intubation with a DLT and lung collapse. Anesthetists has therefore recently explored less invasive approaches during VATS such as avoiding intubation and maintaining spontaneous breathing during the procedure. During such non-intubated VATS (NI-VATS), anesthetics and regional anesthesia have been used to provide sedation and pain relief during the procedures. Various anesthetics have been used to keep the patient arousable but sedated, pain relieved, and comfortable while maintaining sufficient spontaneous breathing during NI-VATS procedure. Regional anesthesia for more intensive pain relief used during the procedures has ranged from epidural anesthesia to local anesthesia applied selectively to intercostal nerves. In some series, local anesthetics have been applied to the vagal nerve to suppress cough during the procedure. NI-VATS is now one of the most widely discussed topics in thoracic surgery in last few years.

Today at least some of VATS procedures can be performed without general anesthesia, without invasive airway management, and without mechanical ventilation but equally safely, without discomfort to the patient nor undue difficulty for the surgeon. A survey among the members of the European Society of Thoracic Surgery (ESTS) shows that non-intubated VATS technique has already been adopted especially for minor procedures in many European centers [2]. However, non-intubated, awake VATS (NI-VATS) procedures call for skilled and an experienced thoracic team. Careful patient selection is important, possible contraindications should be considered, short and long term risks and benefits for the patient should be taken into account.

11.2 History of Non-intubated Thoracoscopy

Awake thoracoscopic intervention has a long history. Limited, mostly diagnostic thoracoscopic procedures were performed by pulmonologist long before thoracic surgeons started using it. Medical thoracoscopy started at the beginning of twentieth century when Jacobaeus applied the emerging technology of cystoscopy (visual examination of a cavity) to the thoracic cavity [3]. Jacobaeus named the procedure thoracoscopy and used the method both for diagnostic and limited therapeutic purposes. Medical thoracoscopy is still used today applying local anesthesia and mild sedation [4, 5].

Surgeons and anesthesiologists came to use NI-VATS occasionally in geriatric patients, in patients with limited respiratory reserve, in sick and frail patients in whom general anesthesia was considered too risky. In 1998 Mukaida and coworkers [6] reported successful VATS procedure for intractable pneumothorax using only epidural analgesia without general anesthesia in four high risk patients. The non-intubated VATS procedure was soon extended to less sick patients and more

complex surgical procedures. Today, NI VATS is reported not only for minor surgical procedure such as pleural and lung biopsies, metastasectomies, empyema evacuation and pneumothorax treatment but also for major resections, such as lung reduction surgery, thymectomy and lung anatomical resections [7–10]. The development has been especially rapid in China and Taiwan, there major lung resection for cancer such as lobectomy, sleeve resections and even tracheal resections have been performed in non-intubated patients [9, 11, 12]. However, as major resections are usually more time-consuming and may more often lead to bleeding and other complication, having the patient without a secured airway and without anesthesia may lead to risky management problems. Therefore, the decision to use the awake procedure should be well indicted, supported by surgeons and anesthetist, and the well-informed patient. The level of evidence for these risky and sometimes adventurous procedures is very low and patient safety not well regarded.

While using awake procedures, all professionals in the operating room should be familiar with the procedure and its potential for major complications. An emergency protocol especially for an immediate induction of anesthesia and management of the airway known to all professionals in the operating room should be available.

11.3 Pathophysiology of Breathing with an Open Pneumothorax

11.3.1 Decrease in Lung Volumes and Lung Function

During NI-VATS procedure, the patient (awake or sedated) breaths spontaneously with an open non-dependent thoracic cavity and is positioned in the lateral decubitus position. Without muscle relaxation diaphragm activity is intact and allows spontaneous ventilation of the dependent lung. However, the dependent lung is under pressure from the weight of abdominal content caudally and from the pressure of the operation table from below. Since the surgical-induced pneumothorax usually results in the spontaneous collapse of the non-dependent lung, its weight also increases the mediastinal pressure on the dependent lung. These pressures, in combination, lead inevitably to a reduction in lung volumes such as vital capacity (VT), functional residual capacity (FRC), residual volume (RV) and total lung capacity (TLC) [13–15]. Pompeo investigated lung volumes in sick and healthy patients in the lateral decubitus position and open pneumothorax. He found reductions in forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) which were more prominent in patients with healthy lungs (45% and 52% respectively) as compared to patients with chronic obstructive pulmonary disease (COPD) (34% and 30% respectively) [14].

Clinically, the extent of lung collapse of the non-dependent lung as a result of surgical incision in the spontaneously breathing patient will depend on pulmonary, airway, and pleural pathology. Emphysema, increase in airway resistance (COPD), airway obstruction from secretions, and pleural adhesions would probably result in less effective lung collapse and less convenient surgical conditions.

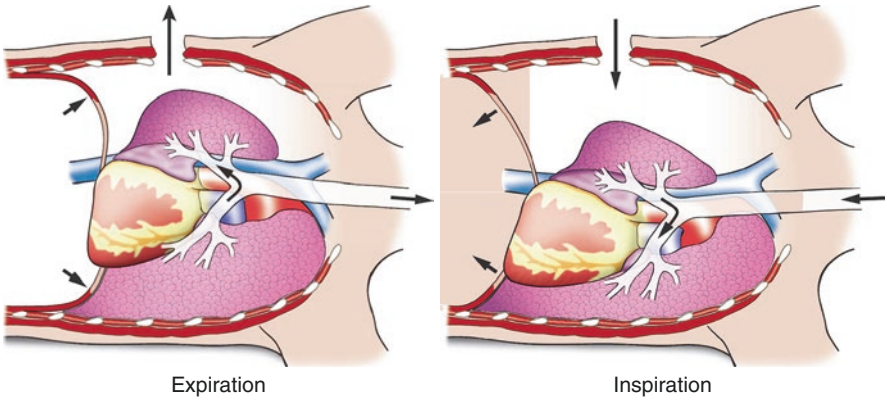

Fig. 11.1 Gas exchange during surgical pneumothorax in the spontaneously breathing patient. During expiration, air is expired partly to the atmosphere and partly to the upper, operated lung. During inspiration, influx of fresh air from the atmosphere is mixed with waste air from the non-dependent, collapsed lung. This complex abnormalities decrease the efficacy of gas exchange

Lung collapse and the reduction in available lung volume for breathing leads to changes in lung function. One such change is *paradoxic respiration* which can lead to decreases in oxygenation and increases in carbon dioxide tension (Fig. 11.1). Paradoxical respiration results from active inspiration of the spontaneously breathing patient with a pneumothorax, where an influx of fresh air from the atmosphere is mixed with waste air from the non-dependent, collapsed lung. During expiration, air is expired partly to the atmosphere and partly to the upper, operated lung. These complex changes in the spontaneous ventilation of the two lungs can decrease the efficacy of gas exchange and lead to hypercapnia and hypoxemia, which is may increase with sedation [15]. Hypercapnia due to paradoxic respiration may lead to an increase in respiratory rate.

Another physiological mechanism, contributing to impaired gas exchange during awake VATS, is intrapulmonary shunt fraction. Although the upper lung is collapsed, it is still perfused. Perfusion to the upper, collapsed, and only partially ventilated lung is a reason for increased shunt fraction and hypoxemia. The more collapsed the upper lung, the larger is the intrapulmonary shunt. Hypoxic pulmonary vasoconstriction and gravity reduce the perfusion of the non-ventilated lung and help reduce the risk of hypoxemia. Theoretically, since the patient during NI-VATS is breathing spontaneously, airway pressure in the dependent lung will be low (i.e. much lower than during ventilated VATS), the expected diversion of blood flow to the nonventilated, collapsed lung may well be less than that during ventilated VATS. This mechanism will decrease shunt and improve oxygenation.

Despite these complex changes, especially hypoxemia and but also hypercapnia rarely pose a severe problem during NI-VATS. This will be especially the case when the procedure is not very long and sedation is not unduly deep. Supplemental oxygen administration helps compensate for decreases in oxygenation. In one large study, hypoxemia as a problem was reported in only 2 out of 446 patients [11].

11.3.2 Hemodynamic Changes of an Open Pneumothorax with Breathing

Surgical pneumothorax during spontaneous ventilation leads to non-dependent lung collapse and spontaneous breathing in the dependent lung leads to periodic downward mediastinal shift. Downward mediastinal shift is due to the negative pressure generated by active diaphragmatic contraction during inspiration in dependent lung. The mediastinum then returns to its previous position during expiration. The periodic mediastinal shift during spontaneous respiration in the lateral decubitus position with an open hemithorax may theoretically lead to hemodynamic instability and could represent a difficulty for surgery [13, 15]. However, this has seldom been explicitly reported as a clinical problem in the many NI-VATS series studied in the last 10–15 years.

Changes in $PaCO_2$ may occur during NI-VATS and have affect hemodynamics. Severe hypercapnia ($PaCO_2$ over 90 mmHg) may theoretically lead to arrhythmias and hemodynamic instability. However, severe hypercapnia is rare when sedation is controlled and not unduly deep. Mild hypercapnia due to hypoventilation and rebreathing from the collapsed lung increases cardiac output by sympathetic stimulation and by peripheral vasodilation [16, 17]. Pulmonary vascular resistance is usually increased in hypercapnia because of hypoxic pulmonary vasoconstriction in the non-dependent lung but also because of increases in $PaCO_2$ and acidosis [16] Hypercapnia may also increase cerebral perfusion and increase intracranial pressure. These facts suggest that NI-VATS will be less suitable and probably unsafe for patients with right ventricular dysfunction, pulmonary hypertension, and increased intracranial pressure.

In summary, hemodynamic changes during NI-VATS are modest, blood pressure and heart rate are usually stable throughout the operation and major hemodynamic disturbances do not occur in the setting of a spontaneously breathing patient with an open hemithorax in the lateral decubitus position. Surgical stimulation which increases sympathetic activity may also be a factor in preserving cardiovascular function.

11.4 Patient Selection for Non-intubated Video-Assisted Thoracic Surgery

11.4.1 Indications

The indication for NI-VATS should be well supported by scientific evidence, good clinical judgement and assessment of risk for the individual patients. Informing the patients of the potential risks and benefits is mandatory.

Patients with good indications for NI-VATS are those in whom the risk of surgery is low but the risk of general anesthesia is considered to be high. Procedures such as simple lung and pleura biopsy, bullae and small nodule excision, pleurodesis, simple decortication, and simple metastasectomy are those reported most often under this indication [5, 18, 19].

Recent studies show NI-VATS can also be used for simple and short procedures for normal patients i.e. those with no apparent risk for general anesthesia. This might be an acceptable alternative for such patients as the need for conversion during the procedure may be small and well balanced against avoiding general anesthesia and DLT intubation. Furthermore, operating room turnover time may be reduced [18].

Reviewing recent literature, especially from China, but also in limited scale from Europe, it would seem that as long as VATS as such is theoretically possible there is no clear cut surgical contraindication to NI-VATS anymore. Indeed, complex operations such as lobectomy, thymectomy and even sleeve-resections have been performed without airway security with double lumen tube [7, 11, 20, 21]. However, as major resections are usually more time-consuming and may more often lead to bleeding and other complication, having the patient without a secured airway and without anesthesia may lead to risky management problems without apparent benefits. At this time point, there is no scientific evidence, i.e. large, multicenter, randomized and controlled studies, showing the superiority of NI-VATS to intubated VATS in major lung surgery in terms of short and especially long-term reduction of morbidity and mortality. As the method does not show superiority and 3–5% rates conversion to risky intubations, sound clinical judgment should preclude its use in complex and "open-end" procedures. It might be considered particularly premature, risky and irresponsible to use this method for cancer surgery. Recent studies show that minimally invasive surgery as such may presumably lead to less radical resection and to a long-term increase in cancer recurrence and decrease survival as compared to open surgery [22]. Adding more risky scenarios such as non-intubated status with a more mobile operative field may lead to even greater chance of incomplete resection and decrease in long term survival. Were NI-VATS it a new cancer drug, it would have not been allowed to use it in this reckless manner. Therefore, for more complex surgery and especially for cancer surgery, the safety and long term survival of the patients should be our first priority and the indication NI-VATS should be used for limited non cancer surgery until hard evidence in properly conducted studies for cancer surgery is available. Only in this setting is NI-VATS a good method and leads to more benefits than risks.

11.4.2 Contraindications to Non-intubated VATS (Table 11.1)

As a rule, NI-VATS is not suitable in patients who refuse or are very reluctant to undergo NI-VATS. Patient cooperation is important to a successful NI-VATS procedure. An unprepared team should also be also considered a problem for a NI-VATS procedure.

Usually patients with known dense and extensive pleural adhesions, previous thorax surgery or radiation, or with large tumors (>6 cm) are not considered good surgical choices. Morbid obesity may also pose a technical problem because of cranial displacement of the diaphragm and less space in thorax cavity. Patients with risk of excessive bleeding because of coagulation disorders or for other operative

Table 11.1 Possible contraindication for non-intubated video-assisted thoracic surgery

Surgical factors	• Dense pleural adhesions • Long duration of surgery • Large lesions >6 cm • Curative cancer resection surgery
Anesthesiological factors	• Anticipated difficult airway • Risk of aspiration • Risk of hemodynamic instability
Patient factors	• Patient who refuse or are reluctant to consent • Uncooperative patients • Patients with increased intracranial pressure • Patients with pulmonary hypertension • Obesity (>30 kg/m^2) • Patients with coagulopathy • Respiratory compromised patients (hypoxemia and/or hypercapnia) • Persistent cough • Profuse, uncontrollable bronchial secretions

reasons would be safer under general anesthesia. The same goes for patients in whom surgery is anticipated to be difficult. Liu [23] did not include some of the following patients in their randomized study for NI-VATS: lesion size >6 cm, structural abnormalities, or tumor involvement of the trachea or bronchi; extensive pleural adhesion, and body mass index ≥30 kg/m^2. Long duration of surgery (>2–3 h) may also be considered a relative contraindication.

Patient with known or anticipated difficult airways should not be selected for NI-VATS. When emergent conversion to general anesthesia is needed, difficult airway management would endanger the patient. Patients with mental or neurological impairment are also problematic because of poor communication and unintentional movements. Patients with sleep apnea or with high risk of aspiration should not be considered for NI-VATS for obvious reasons. On the one hand, severely compromised patients and especially those with hemodynamic instability are considered poor choices for NI-VATS. On the other hand, limited surgery may nevertheless be performed on a case-to-case basis on patients using NI-VATS who are considered poor choices for general anesthesia. This may then indeed involve patients with limited cardiopulmonary reserve.

11.5 Anesthesia for Non-intubated Video-Assisted Thoracic Surgery

Ni-VATs at best usually means keeping the patient moderately sedated with minimum effects on spontaneous respiration, using regional anesthesia for pain relief and improving oxygenation with an oxygen mask. However, NI-VATS, as practiced, represents a wide range of techniques ranging from awake procedures in epidural anesthesia [18] to those under more profound sedation needing supraglottic devices for airway patency [24].

11.5.1 Regional Anesthesia

Regional anesthesia techniques include local infiltration, intercostal blocks, serratus anterior plane blocks, paravertebral block and epidural block as successful regional analgesia for NI-VATS [25]. Local infiltration is usually performed by the surgeon and can be best used for short, single-port procedures. However, depending on depth of the sedative regiment, local infiltration can also be used for more extensive surgery. There is no very clear-cut difference between intercostal blocks and infiltration blocks, because local infiltration can only make sense if local anesthetics are applied in the intercostal space where the port is to be inserted. Another option used by the surgeons is "internal", camera-guided, multiple intercostal blocks after local infiltration of one intercostal space through the skin (external infiltration) and introducing camera [26].

Thoracic epidural anesthesia (TEA) provides excellent pain relief and would therefore seem to be a very good choice for providing analgesia for NI-VATS, specially for awake NI-VATS. However, epidurals need more time to be performed and are associated with hemodynamic side effects and the potential risk of neurological injury. Effective blockade of the intercostal muscles by epidural anesthesia can reduce FVC and FEV1 [27]. In a retrospective study in 238 patients intercostals block as compared to epidural analgesia was associated with like shorter anaesthesia time and less haemodynamic side effects [11]. Serratus anterior plane blocks [28], erector spinae plane block [29], and paravertebral blocks have also been used for NI-VATS [30].

11.5.2 Sedation for NI-VATS

Sedative drugs used for Ni-VATS should, on the one hand, attenuate the tachypnea due to pain, anxiety and mild hypercapnia. On the other hand, sedation should not lead to hypoventilation i.e. low respiratory rates or shallow breathing thus potentially leading to hypoxemia or excessive hypercapnia.

Sedation can be provided by many drugs and drug combination. Both long-acting (fentanyl, ketamine, midazolam) and short-acting drugs (propofol, dexmedetomidine and remifentanil) have been used to induce sedation and provide additional analgesia. BIS guided, target-controlled infusion of propofol and remifentanil is often used [21, 25]. Infusion of remifentanil and propofol have ideal pharmacokinetic properties for use during sedation. Their short context-sensitive half-lives and the ease of increasing or decreasing levels of sedation and analgesia make them ideal agents for sedation. Furthermore, remifentanil can be readily antagonized with naloxone. Propofol in doses of 1–2 mg/kg/h with remifentanil in doses of 0.025–0.05 μg/kg/min is used routinely by one of the authors (W.K.) for non-intubated thoracoscopic interventions and has a very good record of safety, patient satisfaction and ease of use. Ketamine has some appeal as a preferred agent in COPD patient because it preserves inspiratory muscle tone and functional residual capacity [31], however, recovery period could be prolonged. Ketamine has

central nervous side effects which might be problematic during the procedure or during emergence. Dexmedetomidine, an alpha-2-adrenoreceptor agonist, is used for sedation in intensive care units but has recently also been adopted for intraoperative needs. Excellent respiratory profile and good analgesic effects are its' main advantage, although moderate cardiovascular depression (bradycardia and hypotension) should be taken into consideration [32]. Iwata et al. have described the combination of dexmedetomidine and epidural analgesia in patients with severe respiratory dysfunction undergoing VATS [33].

11.5.3 Airway and Oxygenation During NI-VATS

"Non-intubated", "awake" or "tubeless" VATS usually means intubation is avoided and the patient is provided with oxygen face mask or nasal prongs to a mostly sedated but arousable patient. However, in some series nasopharyngeal airway or laryngeal mask airway have been used for airway patency in cases of deep sedation [23, 24]. Thus the choice of airway depends on the level of sedation one wants to achieve. Intermittent positive pressure ventilation using a face mask, laryngeal mask or non-invasive ventilation have been suggested as methods to improve ventilation and oxygenation during NI-VATS. However, if deep sedation is needed, it might be more prudent and safer to us a laryngeal mask airway or to opt for an intubated VATS in the first place.

Emergency intubation in lateral decubitus position during ongoing NI-VATS is not a rare event and may be needed in about 5% of the cases. Intubation in the lateral decubitus position should be considered difficult and a challenge for the anesthesia team. Intubation in the lateral decubitus position needs not only skill but also good preparation and coordination. Teams performing NI-VATS should have a standard procedure on how to proceed when emergent conversion to tracheal intubation is inevitable. The anesthesia team should be well prepared for conversion and have all necessary devices needed for a difficult airway ready at short notice. This should include a videolaryngoscope and a fiber-optic bronchoscope. Although the DLT is considered an airway device of choice, a single-lumen tube and lung isolation with an endobronchial blocker would be easier to employ in the lateral decubitus position. In case of intrabronchial bleeding or other difficult issues the preferable but albeit more difficult choice would be to use a DLT.

11.5.4 Monitoring During NI-VATS

Standard monitoring during NI-VATS includes ECG, peripheral oxygen saturation (SpO_2), and non-invasive blood pressure and end-tidal CO_2 ($EtCO_2$, capnography). A decrease in respiratory rate and shallow breathing are early signs of respiratory depression which precede hypoxemia and decreases in SpO_2. Capnography can reliably detect decreases in respiratory rate and, to a degree, also shallow breathing. Without capnography, the first sign of respiratory depression will be

hypoxemia ($SpO_2 < 90\%$) which would need immediate measures to alleviate it. With capnography, a decrease in respiratory rate would merely need readjusting sedatives with no immediate danger to the patient. Capnography is also crucial when adjusting opiate doses to patient's needs. Arterial line should be considered in procedures lasting more than an hour, in all patients who have significant cardiovascular or respiratory disease and also in cases in which lung resection is planned. To monitor sedation levels, Ramsay sedation score or Bi-spectral index (BIS) have been used. It may be helpful to keep the patient sleeping but easily arousable. In terms of Ramsay sedation score this should be a target score of level 3, which translates as "moderately sedated, follows simple commands". With deeper sedation (BIS < 60) airway patency and hypoventilation may call for—at least—a supraglottic airway device. High-flow nasopharyngeal cannula is also an option to improve oxygenation during NI-VATS, it doesn't, of course, protect against the effects of respiratory depression [34].

11.6 Benefits of NI-VATS

Limited, mostly diagnostic, thoracoscopic procedures were performed awake by pulmonologist much before thoracic surgeons started using it. Such procedures which at the most involve evacuating pleural effusions, taking some biopsies and pleurodesis have a long history of safety and are accepted methods in the disciplines involved [5]. Stepping beyond those simple procedures and toward major VATS resection may mean leaving the safe zone. Nevertheless, proponents of NI-VATS argue that leaving the established practice is worth the trouble because it may be beneficial for the patients [35].

The proponents attack the established intubated VATS practice on several fronts. Risks of tracheal intubation with double-lumen tubes and its potential for minor and major airway injury is one such attack. Sore throat and hoarseness is indeed a most common side-effect of using a DLT [36]. The major and very serious complication is tracheobronchial trauma, which, especially when undetected, may be associated with morbidity but also mortality. However, the incidence of a tracheal tear is very low [37]. Although we do have some case reports of tracheal tears using DLTs [38], in a large series of patients, Brodsky and Lemmens did not have a single tracheal tear in more than 1100 patients [39]. In the department of one of the authors (W.K.) we have had one tracheal tear since 2001 and we have a yearly volume of over 700–800 DLT uses. This single tear was treated successfully with repeated endobronchial application of fibrin glue, no surgery was needed. With the introduction of video-laryngoscopes and other airway devices for improved view of the glottis, double lumen intubation became less traumatic even in patients with potential difficult airway [40]. Difficult airway in thoracic anesthesia is frequently a topic of reviews in major publications [41–43]. Mandatory bronchoscopy for tube positioning also reduces the incidence of malposition of the tube and possible hazard due to tube's blind movement [44]. However, using hazards of DLT intubation to promote NI-VATS may be self-defeating as emergency intubation of the patient in fixed

lateral decubitus position places the NI-VATS patient at an increased risk for complications for airway complications.

Another line of argumentation involves the side effects of ventilation and acute lung injury. Although lung injury occurs may occur in after lung resections and carries a mortality rate, however, the etiology of lung injury is multifactorial and ventilation does not seem to be the sole or the major causal problem [45]. Of course, high ventilating pressures can induce barotrauma, unusually large tidal volumes can lead to over-distension of the lung (volutrauma), and a ventilation strategy favoring repetitive closing and reopening of the alveoli (atelectrauma) may lead to lung injury. However, such ventilation strategies are rarely used today. Modern ventilation strategies use smaller tidal volumes, lower airway pressures and positive end-expiratory pressure which are not associated with lung injury [46]. Implementation of lung protective ventilation into thoracic surgery, the standard of day-to-day practice, has dramatically reduced any adverse effects older ventilation strategies may have had [47].

Side effects of general anesthesia, like nausea and vomiting, may also occur in NI-VATS since similar anesthetics are used for sedation. Avoiding muscle relaxation and its potential postoperative effects in NI-VATS may partly be a good argument as the incidence of postoperative residual curarization (PORC) is still high [48]. However, with good clinical practice and using readily available monitoring devices the incidence and side effects of postoperative residual curarization can be minimized. Therefore, neuromuscular monitoring techniques has become a standard of general anesthesia. Furthermore, the modern reversing agent sugammadex, a specific antidote for vecuronium and rocuronium, has brought an increased level of safety into postoperative care of patients under general anesthesia. A recent study by Brueckmann et al. report a 0% PORC rate in patients reversed with sugammadex versus 46% in neostigmine group [49].

Still another line of argumentation involves inflammatory mediators found in ventilated lungs. It has been frequently shown that OLV induces a pro-inflammatory reaction in the intra-alveolar compartment characterized by elevated levels of pro-inflammatory mediators. In these studies however, increases in those cytokines in have not been shown to reliably and causally translate in overt lung injury. NI-VATS, as compared to intubated VATS, is associated with lower levels of inflammatory cytokines, including TNF alfa in broncho-alveolar lavage fluid and lower plasma levels of C-reactive protein, as well as preserved function of natural killer cells [50, 51]. In a small retrospective study Ambrogi [52] showed a significant decrease of natural killer lymphocytes and increase of serum IL-6 level in intubated VATS as compared to NI-VATS. A follow-up retrospective study of the same group [53] did not add any further evidence. However, these small mostly nonrandomized studies in very small patient population show these abnormalities but fail to show any clinical correlates of increase mediators. As of now, there is no convincing evidence that NI-VATS decreases clinical lung injury.

Still another line of argumentation involves operative time, hospital stay, costs and duration of postoperative fast. Non-intubated VATS technique could accelerate the possibility of the enhanced recovery after surgery (ERAS) in hospitals, shortens

the hospital stay and general costs [54]. Operation time as such might not be very different between NI-VAT and intubated VATS. Overall time might vary; anesthesiologist would save the time needed for tracheal intubation etc. but need more time for regional block or local infiltration. A good case might be made for NI-VATS pleurodesis because of limited surgical trauma, low risk of bleeding, short operation time, no lung resection and especially its very long history of safety.

In conclusion, the line of argument, that NI-VATS is less dangerous than intubated VATS, is not convincing. However, NI-VATS in minor thoracic procedures and biopsies could lead to a decrease in operating room time and other perioperative resources and promote short term wellbeing of the patients.

11.7 Safety of NI-VATS

Is non-intubated VATS surgery safe enough to be widely performed and recommended? Yes and no. Yes, the evidence of many studies shows that NI-VATS is a reasonable choice for minor VATS procedures. No, because there is no evidence however, that it can be widely performed safely beyond these indications. Furthermore, no, it may be unsafe to use the procedure in major lung resections and especially in curative cancer surgery without concluding evidence in properly performed randomized controlled trials.

One major problem with the "evidence" for NI-VATS depends mostly on a long list of publication with small sample size, usually retrospective case series, only one credible and properly performed small randomized study, a variety of different methods of sedation, regional anesthesia, airway management and operative procedures. Also a small group of active proponents seem to produce a large proportion of these studies. It is therefore very difficult to extract "evidence" for sound clinical practice from these studies. Robust safety studies confirm that NI-VATS is a safe procedure with postoperative benefits in minor thoracic procedure, especially in pleurodesis or minor resections (biopsy). Bertolaccini a prominent thoracic surgeon, therefore correctly asses that "the currently available studies about non-intubated VATS under loco-regional anaesthesia were all carried out in a small sample size, which lacks robust evidence to elucidate its actual feasibility and safety for thoracic surgery". Therefore, large randomized studies are needed to show long term safety of any surgical method which involves tumor and lymph node resection. Since long term survival is at stake, it is difficult to endorse a method not yet properly studied for this indication. As long as no such study exists, long term patient safety may be at risk. This might also pose a legal issue to use an as yet experimental method where cancer survival (life time) is a concern and informed consent limited. A recent study published in the New England Journal of Medicine [22] points to hazards of easy answers to complex questions and of using retrospective studies and conclusions thereof as sole evidence to change established practice.

Coughing, simple physiological reflex, could become a safety problem during NI-VATS, interfering with surgery. Coughing may be induced by traction of hilar structures, stripping interlobar vessels, handling incomplete fissures, pulling at a

bronchus or the carina during major VATS procedures. Coughing may be difficult to control. Different methods are recommended. Unilateral infiltration with local anesthetic of the vagal nerve blocks afferent and afferent fibers to the cough center in the brain stem and can block the cough reflex effectively for 2–3 h [11]. He recommends 2–3 ml of 0.25% bupivacaine injected close to the vagus nerve at the level of lower trachea in the right thorax or in the aorto-pulmonary window in the left thorax. The proximity of the vagal nerve to major vessels calls for good needle control when applying the local anesthetic. Preoperative administration of an aerosolized 5 ml solution of 2% lidocaine immediately before procedure and pleural surface dispersion of another lidocaine dose (5 ml of 2% lidocaine) are more simple methods, effective in minor procedures [52]. However, avoiding hilar traction and careful manipulation of hilar structures may obviate the need for local anesthetic infiltration of the vagal nerve [55].

Technical issues as extensive adhesions, major bleeding, and unexpected anatomy are possible reasons for conversion to general anesthesia. Surgical problems during NI-VATS major resections are mediastinal movement, cough control and precise balance of sedation to overcome severe hypercapnia. Time of non-intubated surgery should be limited as well. Two to three hours are reasonable and expected safe [56].

Conversion rate to general anesthesia and intubation was reported to be 2.3–10% or more, depending on the type of procedure and the experience of the surgical teams [7]. Intubation in the lateral-decubitus position is difficult and may cause hypoxemia and airway injuries. Furthermore, in case of complications such as major intratracheal bleeding, the patient the patient would be put in a double jeopardy: clot formation in both lungs leading to hypoxemia and need for lung separation (preferably with DLT) which would take time. In infectious cases, in which emptying of lung abscess of pleural empyema into the airway is a possibility, general anesthesia and DLT should be considered first choice. The published studies on NI-VATS do not have enough patients to adequately rule out such complication which are not trivial and put patients unduly at risk. It is of note, that even in experienced hands, conversion rates are especially high (>5%) in risky indications such as segment resection and lobectomy [11].

11.8 Conclusions

Intubated VATS procedures have been shown to minimizes tissue injury, reduce intraoperative and postoperative pain and improve postoperative recovery. Recently, anaesthetic management of VATS patients has also undergone changes and less invasive anaesthetic approaches have been explored. One such approach is avoiding intubation while providing monitored sedation, pain relief using regional anesthesia and maintaining spontaneous breathing during VATS procedure. Although no large prospective randomized trial has studied the short- and long-term efficacy and safety of NI-VATS, a large number of retrospective studies and some prospective studies show that NI-VATS is a surgically and anesthesiologically feasible and, when employed

appropriately, a safe method of intraoperative care. This especially the case for minor VATS, where increased turnover times in operating room, improved immediate recovery after surgery and reduction in material costs have been shown for NI-VATS. The concerns which remain are problems of emergency intubation during the procedure and selecting appropriate patients for NI-VATS since properly randomized studies showing reduction of major morbidity and mortality in complex and long operations are lacking. This is especially the case for cancer surgery.

We are aware that innovative minimally invasive methods in anesthesiology deserve to be integrated into our daily practice. However, in the excitement of innovation we should not to forget that the first principle of our profession is not to do harm.

References

1. Rocco G, Martin-Ucar A, Passera E. Uniportal VATS wedge pulmonary resections. Ann Thorac Surg. 2004;77(2):726–8.
2. Pompeo E, et al. Non-intubated thoracic surgery-a survey from the European Society of Thoracic Surgeons. Ann Transl Med. 2015;3(3):37.
3. Braimbridge MV. The history of thoracoscopic surgery. Ann Thorac Surg. 1993;56:610–4.
4. Katlic MR, Facktor MA. Video-assisted thoracic surgery utilizing local anesthesia and sedation: 384 consecutive cases. Ann Thorac Surg. 2010;90:240–5.
5. Katlic MR. Five hundred seventy-six cases of video-assisted thoracic surgery using local anesthesia and sedation: lessons learned. J Am Coll Surg. 2018;226(1):58–63.
6. Mukaida T, et al. Thoracoscopic operation for secondary pneumothorax under local and epidural anesthesia in high-risk patients. Ann Thorac Surg. 1998;65:924–6.
7. Pompeo E. State of the art and perspectives in non-intubated thoracic surgery. Ann Transl Med. 2014;2:106.
8. Gonzalez-Rivas D. Uniportal thoracoscopic surgery: from medical thoracoscopy to non-intubated uniportal video-assisted major pulmonary resections. Ann Cardiothorac Surg. 2016;5:85–91.
9. Hung MH, et al. Nonintubated thoracoscopic surgery: state of the art and future directions. J Thorac Dis. 2014;6:2–9.
10. Bedetti B, et al. Uniportal non-intubated thoracic surgery. J Vis Surg. 2018;4:18.
11. Chen KC, et al. Nonintubated thoracoscopic surgery using regional anesthesia and vagal block and targeted sedation. J Thorac Dis. 2014;6:31–6.
12. Liu J, et al. Non-intubated resection and reconstruction of trachea for the treatment of a mass in the upper trachea. J Thorac Dis. 2016;8(3):594–9.
13. David P, et al. Surgical pneumothorax under spontaneous ventilation-effect on oxygenation and ventilation. Ann Transl Med. 2015;8:106.
14. Pompeo E. Pathophysiology of surgical pneumothorax in the awake patient. In: Pompeo E, editor. Awake thoracic surgery. Sharja, U.A.E: Bentham Science Publishers; 2012. p. 9–18.
15. Triantafillou AN, Benumof J, Lecamwasam HS. Physiology of the lateral decubitus position, the open chest, and one-lung ventilation. In: Kaplan JE, Slinger P, editors. Thoracic anesthesia. Philadelphia: Elsevier Science; 2003. p. 71–94.
16. Sticher J, et al. Controlled hypercapnia during one-lung ventilation in patients undergoing pulmonary resection. Acta Anaesthesiol Scand. 2001;45(7):842–7.
17. Cullen DJ, Eger EI II, Gregory GA. The cardiovascular effects of carbon dioxide in man, conscious and during cyclopropane anesthesia. Anesthesiology. 1969;31(5):407–13.
18. Pompeo E, Mineo TC. Awake pulmonary metastasectomy. J Thorac Cardiovasc Surg. 2007;133:960–6.

19. Tacconi F, et al. Awake video-assisted pleural decortication for empyema thoracis. Eur J Cardiothorac Surg. 2010;37:594–601.
20. Gonzalez-Rivas D, et al. Non-intubated video-assisted thoracoscopic lung resections: the future of thoracic surgery? Eur J Cardiothorac Surg. 2016;49:721–31.
21. Shao W, et al. Non-intubated complete thoracoscopic bronchial sleeve resection for central lung cancer. J Thorac Dis. 2014;6:1485–8.
22. Ramirez PT, et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. N Engl J Med. 2018;379(20):1895–904.
23. Liu J, et al. Nonintubated video-assisted thoracoscopic surgery under epidural anesthesia compared with conventional anesthetic option: a randomized control study. Surg Innov. 2015;22:123–30.
24. Irons JF, et al. Intubated versus nonintubated general anesthesia for video-assisted thoracoscopic surgery-a case-control study. J Cardiothorac Vasc Anesth. 2017;31(2):411–7.
25. Sunaga H, Blasberg JD, Heerdt PM. Anesthesia for nonintubated video-assisted thoracic surgery. Curr Opin Anaesthesiol. 2017;30(1):1–6.
26. Hung MH, et al. Non-intubated thoracoscopic surgery using internal intercostal nerve block, vagal block and targeted sedation. Eur J Cardiothorac Surg. 2014;46:620–5.
27. Groeben H. Epidural anesthesia and pulmonary function. J Anesth. 2006;20:290–9.
28. Corso RM, et al. The serratus anterior plane block for pediatric non-intubated video-assisted thoracoscopic surgery. Minerva Anestesiol. 2017;83(7):775–6.
29. Hu B, Zhou H, Zou X. The erector spinae plane block (ESPB) for non-intubated video-assisted thoracoscopic surgery. J Clin Anesth. 2018;54:50–1.
30. Kiss G, Castillo M. Non-intubated anesthesia in thoracic surgery-technical issues. Ann Transl Med. 2015;3(8):109.
31. Tokics L, et al. Computerized tomography of the chest and gas exchange measurements during ketamine anaesthesia. Acta Anaesthesiol Scand. 1987;31:684–92.
32. Candiotti KA, et al. Monitored anesthesia care with dexmedetomidine: a prospective, randomized, double-blind, multicenter trial. Anesth Analg. 2010;110:47–56.
33. Iwata Y, Hamai Y, Koyama T. Anesthetic management of nonintubated video-assisted thoracoscopic surgery using epidural anesthesia and dexmedetomidine in three patients with severe respiratory dysfunction. J Anesth. 2016;30(2):324–7.
34. Wang ML, Hung MH, Chen JS, Hsu JS, Cheng YJ. Nasal high-flow oxygen therapy improves arterial oxygenation during one-lung ventilation in non-intubated thoracoscopic surgery. Eur J Cardiothorac Surg 2018;53(5):1001–6.
35. Pompeo E. Awake thoracic surgery—is it worth the trouble? Semin Thorac Cardiovasc Surg. 2012;24:106–14.
36. Knoll H, et al. Airway injuries after one-lung ventilation: a comparison between double-lumen tube and endobronchial blocker: a randomized, prospective, controlled trial. Anesthesiology. 2006;105:471–7.
37. Liu H, et al. Tracheobronchial rupture after double-lumen endotracheal intubation. J Cardiothorac Vasc Anesth. 2004;18(2):228–33.
38. Fitzmaurice BG, Brodsky JB. Airway rupture from double-lumen tubes. J Cardiothorac Vasc Anesth. 1999;13:322–9.
39. Brodsky JB, Lemmens HJ. Left double-lumen tubes: clinical experience with 1,170 patients. J Cardiothorac Vasc Anesth. 2003;17:289–98.
40. El-Tahan MR. Videolaryngoscopes for placement of double lumen tubes: is it time to say goodbye to direct view? Saudi J Anaesth. 2016;10(2):218–27.
41. Campos JH. Lung isolation techniques for patients with difficult airway. Curr Opin Anaesthesiol. 2009;23:12–7.
42. Collins SR, et al. Lung isolation in the patient with a difficult airway. Anesth Analg. 2018;126(6):1968–78.
43. Brodsky JB. Lung separation and the difficult airway. Br J Anaesth. 2009;103(Suppl 1):i66–75.
44. Klein U, et al. Role of fiberoptic bronchoscopy in conjunction with the use of double-lumen tubes for thoracic anesthesia: a prospective study. Anesthesiology. 1998;88:346–50.

45. Hedenstierna G, Edmark L. Protective ventilation during anesthesia. Is it meaningful? Anesthesiology. 2016;125:1079–82.
46. Kim SH, et al. Application of intraoperative lung-protective ventilation varies in accordance with the knowledge of anaesthesiologists: a single-centre questionnaire study and a retrospective observational study. BMC Anesthesiol. 2018;18(1):33.
47. Licker M, et al. Impact of intraoperative lung-protective interventions in patients undergoing lung cancer surgery. Crit Care. 2009;13:R41.
48. Fuchs-Buder T, Nemes R, Schmartz D. Residual neuromuscular blockade: management and impact on postoperative pulmonary outcome. Curr Opin Anaesthesiol. 2016;29(6):662–7.
49. Brueckmann B, et al. Effects of sugammadex on incidence of postoperative residual neuromuscular blockade: a randomized, controlled study. Br J Anaesth. 2015;115(5):743–51.
50. Tacconi F, et al. Surgical stress hormones response is reduced after awake videothoracoscopy. Interact Cardiovasc Thorac Surg. 2010;10:666–71.
51. Vanni G, et al. Impact of awake videothoracoscopic surgery on postoperative lymphocyte responses. Ann Thorac Surg. 2010;90:973–8.
52. Ambrogi V, et al. Uniportal video-assisted thoracic surgery colorectal lung metastasectomy in non-intubated anesthesia. J Thorac Dis. 2017;9(2):254–61.
53. Mineo TC, et al. Immunological and inflammatory impact of non-intubated lung metastasectomy. Int J Mol Sci. 2017;18(7):E1466.
54. Tacconi F, Pompeo E. Non-intubated video-assisted thoracic surgery: where does evidence stand? J Thorac Dis. 2016;8(Suppl 4):S364–75.
55. Navarro-Martinez J, et al. Intraoperative crisis resource management during a non-intubated video-assisted thoracoscopic surgery. Ann Transl Med. 2015;3(8):111.
56. Galvez C, et al. Nonintubated uniportal VATS pulmonary anatomical resections. J Vis Surg. 2017;3:120.

Changes in Ventilation Strategies During Thoracic Surgery: Do We Have to Focus "Only" in Oxygenation?

12

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12.1 Introduction

One-lung ventilation (OLV) is a "unique" ventilation method: one lung is excluded from ventilation, but the perfusion to the non-ventilated lung continues, leading to a significant increase in intrapulmonary shunt (Qs/Qt) and consequently a higher risk of hypoxemia. Until approximately 15 years ago, hypoxemia was considered as the most important—if not the only—problem during OLV. In 1970s, the incidence of hypoxemia during (OLV) was assumed to be between 20 and 25%. Therefore; the historical ("classical") guidelines for OLV were primarily aimed at preventing and treating the hypoxemia (Table 12.1) [1].

Several mechanisms (above all, the "Hypoxic Pulmonary Vasoconstriction (HPV)") cause a decrease of blood flow to the non-ventilated lung, resulting in a

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Table 12.1 Historical recommendation for OLV (to avoid hypoxemia)

• FiO2: 1.0
• High TV (e.g. 10 mL/kg)
• Normocapnia (if necessary, increase respiratory rate)
• CPAP, if necessary
• PEEP, only if necessary, should be <CPAP
• TIVA instead of inhalational anaesthetics

decreased Qs/Qt. For anaesthesia and intensive care, the knowledge of the basic (patho)physiology of HPV is essential [2]. The historical guidelines suggest also the use of IV anaesthetics, as inhalational agents are known to inhibit HPV, leading to a further increase in pulmonary shunt.

Although the incidence has declined to 5–10% today, hypoxemia should still be considered as an important challenge of OLV because of several reasons.

However, the paradigm has changed. A growing number of studies have shown that lung injury (ALI) associated with/induced by the OLV is also an important problem [3]. Thoracic surgery is unique on that the target organ of both the surgeon and the mechanical ventilation is the same: the lung. One can assume that the post-operative lung injury would be more likely due to the surgical trauma; however, it has been shown that the degree of radiological density increase was significantly greater in the non-operative lung compared to operative lung after lobectomy [4].

The mechanism of ALI and/or increased inflammation induced by the OLV has been explained recently [3, 5]. As a matter of fact, there are similarities of OLV and ARDS: OLV can be assumed as a "variation" of ventilation in ARDS, not at least because they both deal with smaller volumes of lung ("baby lung" in ARDS, and the "one-lung" in OLV) [6].

Consequently, it can be assumed that the "new paradigm" of the ventilation strategy during OLV should deal not only with the maintenance the adequate gas exchange, but also with the protection of the lung: "protect both the lung and its functions".

Mechanisms of hypoxemia during OLV:

- It should be noted that one of the most common reasons of hypoxemia (e.g. 38%) during OLV is dislocation of OLV devices [7], but this is out of the topic of this chapter.
- During OLV, the ventilation of one lung is interrupted, while the perfusion persists: Qs/QT increases.
- Hypoventilation in the dependent lung as a result of derecruitment of the alveoli (increased risk of atelectasis).
- Inhibition of HPV: The "older" inhalational agents are claimed to have a relevant inhibitory effect on HPV. But there are also several other factors that can lead to an inhibition of HPV.
- Any application causing a diversion of blood flow to the non-ventilated lung (e.g. high airway pressures in ventilated lung) can lead, even without any impact of HPV, to hypoxemia [8].

Mechanisms of lung injury during OLV:

- Application of the whole tidal volume into the—only—ventilated lung (as suggested in classical guidelines) can lead to baro- and/or volutrauma, as experienced in ARDS ventilation.
- No or very low PEEP to ventilated lung can lead to atelectasis as this lung is already under external pressure; opening of this collapse during inhalation can result in "cyclic recruitment" and consequently in atelectotrauma
- Atelectasis and the possible atelectotrauma can be worsened by application of high FiO2 (i.e. 1.0) [9].
- OLV is also associated with an increased pulmonary immune response [10] ("biotrauma") and furthermore, the alveolar damage during OLV can be even more exaggerated than the one during two-lung ventilation [11].
- Recent findings have shown that the atelectasis and the re-expansion at the end of OLV lead to 'oxidative stress' with formation of reactive oxygen and reactive nitrogen species [5].
- The magnitude of oxidative stress correlates with the duration of SLV [5].

12.2 "Protective Ventilation"

The "protective ventilation" was defined and determined in ARDS patients [12]. For intraoperative management, it has three components:

1. Low tidal volumes (TV)
2. Recruitment manoeuvres (RM)
3. Positive end-expiratory pressure (PEEP).

It has been shown that this approach is also appropriate in "healthy" lungs (but not thoracic surgery!) [13]. The effects of the combination of RM, low TV, and PEEP were examined. During 5 postoperative days, intraoperative protective ventilation was associated with an improvement in oxygenation (higher SpO2), fewer alterations on chest X-ray, and a lower "modified Clinical Pulmonary Infection Score". However, during OLV, the classical guidelines controvert to all of the components of protective ventilation in some degree. Therefore, precise changes in the "classical" guidelines have been necessary (Table 12.2).

We only "assume" that the application of the combination of all *three components* of protective ventilation can be beneficial for *both* oxygenation *and* lung protection during OLV [14]. It is being discussed that in "healthy" lungs, applying PEEP and recruitment manoeuvre does not improve the postoperative outcome and is even associated with intraoperative hemodynamic instability, as shown in PROVHILO-study [12]. The debate about this so-called "permissive atelectasis" approach continues [15]. New studies entitled "PROTHOR" and "iPROVE-OLV" are running to test the effects of PEEP and recruitment manoeuvre during OLV.

Table 12.2 Current recommendation for OLV (to avoid hypoxemia and lung injury)

• FiO2 < 1.0
• Low tidal volume (max. 6 mL/kg)
• Low driving pressure of ventilation
• Permissive hypercapnia
• Inhalational anaesthetics
• Routine use of CPAP (if not contraindicated [VATS])
• One-lung RM
• Routine use of PEEP

12.2.1 Tidal Volume (VT)

The detrimental effects of high VT during OLV are well documented. High TV during OLV produces end-inspiratory lung overdistension, a recognized risk factor of lung injury [3, 16, 17]. Several clinical studies have proved it, showing that low VT is associated with a lower incidence of postoperative acute lung injury [17, 18]. Besides, low VT compared with high VT decreases the proinflammatory systemic response [10, 19, 20]. On the contrary, high VT during OLV induces diffuse alveolar damage [11]. Another factor involved in lung injury is the repeated alveolar opening and closing of unstable alveoli with each breath cycle.

Low TV ventilation based on predicted body weight (PBW) should be routine to avoid the use of excess TV. Predicted body weight is calculated by a formula based on gender and height. VT should be restricted to 4–5 mL/kg PBW. The use of a tidal volume of 4 mL/kg during OLV was associated with less lung water content than with larger tidal volumes of 6–8 mL/kg [21].

A recent meta-analysis has shown that the use of low VT can worsen gas exchange but reduces airway pressure. Preservation of postoperative oxygenation and reduction in infiltrates suggest a lung-protective modality with low TV [22]. Another meta-analysis has reported that low VT was associated with the reduced incidence of postoperative pulmonary complications [23].

Another study confirming the advantages of low VT has underlined that low VT without adequate PEEP, does not prevent postoperative respiratory complications. Thus, use of physiologic VT may represent a necessary, but not independently sufficient, component of lung protective ventilation (LPV) [24]. This finding leads again to the recent question of how the different components of LPV should be combined to achieve the best results.

12.2.2 Lung Recruitment Manoeuvres

Recruitment manoeuvres (RM) are ventilatory strategies aimed to improve lung aeration by applying a brief and controlled increment in airways pressures. Originally this kind of ventilatory treatment was designed for ARDS patients in the ICU. Nowadays, RM are applied in the operating rooms because it was demonstrated that lung function deteriorates and VILI potentially occurs even in patients with healthy lungs undergoing general anesthesia.

There are two types of RM described in the literature: one is the sustained inflation (SI) manoeuvre, which consist in the application of 40 cmH_2O of continuous

airways pressure during 10–30 s [25]. The other type, the cycling RM, is characterized by a step-wise increment in PEEP keeping a constant driving pressure in PCV mode. Each step of PEEP is increased every 5 cmH_2O and maintained for 5 breaths until reach a final PEEP of 20 cmH_2O and a plateau pressure of 40 cmH_2O [26]. Although the first method is easier to perform, it is related to unacceptable hemodynamic repercussion and high stress on the lung tissue [27, 28]; so that the second one is the preferred and the most accepted kind of RM.

The classical clinical response of lung recruitment in mechanically ventilated patients is an improvement in gas exchange, FRC and lung mechanics. Following some case-series studies showed those beneficial effects when RM was done during OLV [29, 30], controlled and randomized studies confirmed an increment in PaO2, a decrement in dead space and an improvement in respiratory mechanics when compared patients with RM than those without having RM [31, 32].

The positive effect of RM on gas exchange during OLV suggested that part of the total shunt effect was caused by atelectasis in the dependent ventilated lung [29]. An experimental animal model using CT-scan images showed atelectasis in the most dependent zones of the ventilated lung and hypoventilated areas in the rest of the lung parenchyma [33]. Atelectasis was successfully treated and most of the ventilated lungs became well aerated after lung recruitment.

RM has also been shown to decrease the "dead space" (Vd/Vt) enabling a higher elimination of CO_2 per breath during OLV [32, 34].

Lung mechanics improved after RM because normalizing FRC decreases airways resistance and increases compliance [35]. The final result is a decrement in driving pressure when compared to protective ventilation without recruitment. Following RM, a decreased driving pressure can be obtained to achieve the same tidal volume [31, 32]. Driving pressure (DP) is the difference between the airway pressure at the end of inspiration (plateau pressure, Ppl) and PEEP; in that terms the denominator of the static compliance, whereas Cstat = VT/(Ppl − PEEP) = Vt/DP. In the Unzueta et al. study [32], the differences in DP between protective ventilation vs RM groups during OLV was around 2–3 cmH_2O. Both groups used the same level of PEEP (8 cmH_2O). However, in the study of Ferrando et al. PEEP was individualized in the RM group (10 ± 2 cmH_2O) while kept fixed (5 cmH_2O) in the called protective ventilation group [31]. The differences found in DP between groups during OLV were higher than the one observed in the previous study. The conclusion of these results is that lung recruitment decreases DP and reaches it maximum effect when the selected PEEP is individualized by performing a PEEP titration trial. A current study of the same group has shown that incremental PEEP titration was also associated with a decrease in postoperative pulmonary complications [36].

Obviously, RM is a non-physiological manoeuvre, can lead to some complications, such as the hemodynamic compromise and lung tissue stress [28, 35]. To avoid these complications:

- The pathophysiology behind the lung collapse-recruitment phenomenon should be well-known and should be well trained doing RM.
- There are contraindications of RM. Some of these contraindications can be very important during thoracic surgery, e.g. patients with a broncho-pleural fistula

- The patient must be clinically and hemodynamically stable because the hemodynamic repercussion is minimized in normovolemic patients.
- The type of RM plays a major role in those negative effects.

12.2.3 Positive End-Expiratory Pressure (PEEP)

RM opens the collapsed alveoli, but the effects of the RM are usually transitory or insufficient when they are not accompanied by a post-titration PEEP to "keep them open".

Besides, the PEEP level has been always controversial because the negative effects in oxygenation described in several clinical studies [37–39]. This may be because PEEP per se does not restore functional residual capacity and just an arbitrarily set "higher" level of PEEP can contribute to overdistension which in turn can increase shunt by diverting pulmonary blood flow to nonaerated areas, and can cause unwanted hemodynamic side effects, especially in heterogeneous lungs. Moreover, the protective role of PEEP and its potential beneficial effects have not been clearly established, neither in patients during anesthesia (two or one-lung ventilation) [12] nor in ARDS patients [40, 41].

More recently, after the inclusion of the RM as part of the standard ventilatory strategy during one-lung ventilation, all this changed because the physiological and clinical effects of a particular level of PEEP are different when PEEP is used isolated or in combination with a RM.

As it is known, the lungs heterogeneity of those patients undergoing one-lung ventilation is high including obstructive, restrictive pulmonary diseases or even patients with healthy lungs. Which in turn means that a same PEEP value probably would have different effects on lung mechanics, efficiency, oxygenation, and potentially in the prevention of postoperative pulmonary complications. From a more physiological point of view, we advocate for the use of an individualized PEEP. Nowadays, several bedside parameters such as Cdyn, VTCO2 or VDBohr can be used to individualized PEEP, showing that this strategy better maintains oxygenation, lung efficiency and lung mechanics after the RM [31, 42, 43]. The benefits of an individualized PEEP titration compared with a standard PEEP level after a RM have been shown both in peroperative oxygenation and lung mechanics [31], and also in postoperative pulmonary complications [36].

A recent study has also shown that during low VT one-lung ventilation, high positive end-expiratory pressure levels improve pulmonary function without increasing high V/Q and reduce driving pressure [44].

12.3 Ventilatory Modes

Pressure-controlled ventilation (PCV) and volume-controlled ventilation (VCV) have different working principles. In VCV the VT is preset and constant. It is delivered by means of a constant flow with a square waveform. In PCV the inspiratory

pressure is set and the pattern in flow is decelerating. The high initial flow rates are delivered to quickly achieve and maintain the set inspiratory pressure followed by rapidly decelerating flow. These high initial rates of flow lead to a more rapid alveolar inflation. From a physiologic point, the decelerating flow pattern could allow a more homogenous gas distribution than a square flow. Initial studies had suggested a possible advantage in terms of gas exchange [45]. However, several other studies have not observed the alleged benefits of PCV [45–49]. Thus, the beneficial effect on gas exchange of PCV compared with VCV remains inconclusive.

The main advantage of PCV versus VCV appears to be lower peak airway pressure that might decrease the risk for barotrauma during mechanical ventilation [50]. Nevertheless, peak airway pressure does not reflect peak alveolar pressure: peak airway pressure is much greater, and depends on endotracheal tube resistance, inspiratory flow, and the respiratory mechanics of the lung. Further, there appears to be only a weak correlation between peak airway pressure and the incidence of barotrauma. In contrast, there is a strong correlation between plateau airway pressure and mechanical ventilation-induced barotrauma when plateau airway pressure levels exceed 35 cmH_2O [51]. Therefore, during VCV the risk of lung injury can be minimized by limiting the plateau airway pressure to 30 cmH_2O. Senay found that there is no difference regarding inflammatory marker levels between VCP and PCV in prone position [51]. On the other hand, another study has shown that the use of PCV offers more improved right ventricular function than the use of VCV during OLV [52].

So far, there is no clear evidence to support the advantage of any one of these ventilation modes over the others. It is rather more important to keep the "driving pressure" (Plateau pressure − PEEP) as low as possible [53].

12.4 CPAP to the Nondependent Lung

Several studies have clearly shown that CPAP applied to the nondependent lung increased PaO2 [54, 55]. With the exceptions of VATS operation (where the total collapse is often absolutely necessary) and airway surgery, CPAP of 4–5 cmH_2O is tolerated easily by many surgeons. This approach would also allow a wider margin of protection of the ventilated lung and lower FIO2 levels [55, 56]. It should be noted that CPAP has to be applied after delivering a VT to the nondependent lung; otherwise the application to collapsed alveoli would not obtain an adequate expansion.

CPAP also prevents the nondependent lung from complete collapse. In a recent RCT, it has been shown that CPAP to the nondependent lung was associated with a lower local immune response during OLV in oesophagectomies [57]. This new finding suggests that CPAP is beneficial for both oxygenation and lung protection. A recent animal study has confirmed the previous findings and has shown that CPAP applied to the nonventilated lung during OLV suppresses blood flow shift and decreases inflammatory cytokines and water content in both lungs. Application of CPAP may attenuate lung injury during and after OLV [50].

12.5 Inhalational vs IV Anaesthetics

Historical guidelines discourage using inhalational anaesthetics as they inhibit HPV, and recommends TIVA during OLV which was found to be associated with an increased PaO2 and a decreased Qs/Qt [58, 59]. Today, we know that in "equi-anaesthetic" doses, inhalational agents do not aggravate hypoxemia when compared with intravenous propofol; at least the difference in PaO2 is not clinically relevant, probably because of the interaction of other hemodynamic effects of anaesthetics (both inhalational and IV) [60]. Very probably, the inhibitory effects of the newer generation of inhalational anaesthetics (sevoflurane and desflurane) are less relevant than the older ones (halothane, enflurane, isoflurane). A RCT has shown that sevoflurane and propofol at equivalent doses, as measured by bispectral index, were not associated with a significant difference in oxygenation between the two types of anaesthetic was found [61].

Regarding the effects on ALI, there are several studies showing that IV anaesthesia is associated with an increased inflammatory response during OLV; this has been shown in the increase of the release of different mediators in broncho-alveolar lavage fluid of dependent [62], and non-dependent lung [63]; the further one was also associated with lower postoperative complications.

Regarding a very recent meta-analysis, "Inhalation anesthesia can preserve intraoperative cardiac function and reduce postoperative pulmonary complications in patients undergoing thoracic surgery with OLV; although it decreases intraoperative pulmonary function, inhalation anesthesia may be superior to intravenous anesthesia in thoracic surgery" [64].

12.6 Conclusion

To obtain both a sufficient gas exchange and lung protection during OLV, using low FiO2, appropriate PEEP, low TV and RM are necessary. However, the "fine tunings" of the components of this approach (e.g. PEEP titration, the degree of "low" tidal volume, pro's and con's of recruitment manoeuvres) have to be examined. If possible, CPAP to the non-dependent lung is beneficial for both challenges. It is probably not very important which ventilatory mode have to be used, it is rather more important to keep the "driving pressure" as low as possible.

References

1. Benumof JL. Conventional and differential lung management of one-lung ventilation. In: Benumof JL, editor. Anesthesia for thoracic surgery. Philadelphia: WB Saunders; 1995. p. 406–31.
2. Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. Anesthesiology. 2015;122:932–46.
3. Lohser J, Slinger P. Lung injury after one-lung ventilation: a review of the pathophysiologic mechanisms affecting the ventilated and the collapsed lung. Anesth Analg. 2015;121:302–18.

4. Padley SP, Jordan SJ, Goldstraw P, et al. Asymmetric ARDS following pulmonary resection: CT findings initial observations. Radiology. 2002;223:468–73.
5. Heerdt PM, Stowe DF. Single-lung ventilation and oxidative stress: a different perspective on a common practice. Curr Opin Anaesthesiol. 2017;30(1):42–9.
6. Sentürk M. New concepts of the management of one-lung ventilation. Curr Opin Anaesthesiol. 2006;19:1–4.
7. Campos JH, Hallam EA, Van Natta T, Kernstine KH. Devices for lung isolation used by anesthesiologists with limited thoracic experience: comparison of double-lumen endotracheal tube, Univent torque control blocker, and Arndt wire-guided endobronchial blocker. Anesthesiology. 2006;104:261–6.
8. Conacher ID. 2000—Time to apply Occam's razor to failure of hypoxic pulmonary vasoconstriction during one lung ventilation. Br J Anaesth. 2000;84:434–6.
9. Okahara S, Shimizu K, Suzuki S, Ishii K, Morimatsu H. Associations between intraoperative ventilator settings during one-lung ventilation and postoperative pulmonary complications: a prospective observational study. BMC Anesthesiol. 2018;18(1):13.
10. Schilling T, Kozian A, Huth C, et al. The pulmonary immune effects of mechanical ventilation in patients undergoing thoracic surgery. Anesth Analg. 2005;101:957–65.
11. Kozian A, Schilling T, Röcken C, et al. Increased alveolar damage after mechanical ventilation in a porcine model of thoracic surgery. J Cardiothorac Vasc Anesth. 2010;24:617–23.
12. Hemmes SN, Gama de Abreu M, Pelosi P, Schultz MJ. High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): a multicentre randomised controlled trial. Lancet. 2014;384:495–503.
13. Severgnini P, Selmo G, Lanza C, et al. Protective mechanical ventilation during general anesthesia for open abdominal surgery improves postoperative pulmonary function. Anesthesiology. 2013;118:1307–21.
14. Şentürk M, Slinger P, Cohen E. Intraoperative mechanical ventilation strategies for one-lung ventilation. Best Pract Res Clin Anaesthesiol. 2015;29:357–69.
15. Güldner A, Kiss T, Serpa Neto A, Hemmes SN. Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. Anesthesiology. 2015;123:692–713.
16. Jeon K, Yoon JW, Suh GY, Kim J, Kim K, Yang M, Kim H, Kwon OJ, Shim YM. Risk factors for post-pneumonectomy acute lung injury/acute respiratory distress syndrome in primary lung cancer patients. Anaesth Intensive Care. 2009;37:14–9.
17. Fernández-Pérez ER, Keegan MT, Brown DR, Hubmayr RD, Gajic O. Intraoperative tidal volume as a risk factor for respiratory failure after pneumonectomy. Anesthesiology. 2006;105:14–8.
18. Licker M, Diaper J, Villiger Y, et al. Impact of intraoperative lung-protective interventions in patients undergoing lung cancer surgery. Crit Care. 2009;13:R41.
19. Shen Y, Zhong M, Wu W, Wang H, Feng M, Tan L, Wang Q. The impact of tidal volume on pulmonary complications following minimally invasive esophagectomy: a randomized and controlled study. J Thorac Cardiovasc Surg. 2013;146:1267–73.
20. Michelet P, D'Journo XB, Roch A, Doddoli C, Marin V, Papazian L, Decamps I, Bregeon F, Thomas P, Auffray JP. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. Anesthesiology. 2006;105:911–9.
21. Qutub H, El-Tahan MR, Mowafi HA, El Ghoneimy YF, Regal MA, Al Saflan AA. Effect of tidal volume on extravascular lung water content during one-lung ventilation for video-assisted thoracoscopic surgery: a randomised, controlled trial. Eur J Anaesthesiol. 2014;31(9):466–73.
22. El Tahan MR, Pasin L, Marczin N, Landoni G. Impact of low tidal volumes during one-lung ventilation. A meta-analysis of randomized controlled trials. J Cardiothorac Vasc Anesth. 2017;31(5):1767–73.
23. Liu Z, Liu X, Huang Y, Zhao J. Intraoperative mechanical ventilation strategies in patients undergoing one-lung ventilation: a meta-analysis. Springerplus. 2016;5(1):1251.

24. Blank R, Colquhoun D, Durieux M, Kozower B, McMurry T. Management of one-lung ventilation. Impact of tidal volume on complications after thoracic surgery. Anesthesiology. 2016;216(124):1286–95.
25. Rothen HU, Sporre B, Wegenius G, et al. Reexpansion of atelectasis during general anaesthesia: a computed tomography study. Br J Anaesth. 1993;71:788–95.
26. Tusman G, Böhm SH, Vazquez de Anda GF, do Campo JL, Lachmann B. Alveolar recruitment strategy improves arterial oxygenation during general anaesthesia. Br J Anaesth. 1999;82:8–13.
27. Marini JJ. Recruitment by sustained inflation: time for a change. Intensive Care Med. 2011;37:1572–4.
28. Tusman G, Bohm SH, Suarez-Sipmann F. Alveolar recruitment during mechanical ventilation – where are we in 2013? Trends Anesth Crit Care. 2013;3:238–45.
29. Tusman G, Böhm SH, Suarez-Sipmann F, et al. Lung recruitment improves the efficiency of ventilation and gas exchange during one-lung ventilation anesthesia. Anesth Analg. 2004;98:1604–9.
30. Cinella G, Grasso S, Natale C, Sollitto F, Cacciapaglia M, Angiolillo M, Pavone G, Mirabella L, Dambrosio M. Physiological effects of a lung-recruiting strategy applied during one-lung ventilation. Acta Anaesthesiol Scand. 2008;52:766–75.
31. Ferrando C, Mugarra A, Gutierrez A, Carbonell JA, García M, Soro M, Tusman G, Belda FJ. Setting individualized positive end-expiratory pressure level with a positive end-expiratory pressure decrement trial after a recruitment maneuver improves oxygenation and lung mechanics during one-lung ventilation. Anesth Analg. 2014;118:657–65.
32. Unzueta C, Tusman G, Suarez-Sipmann F, Bohm SH, Moral V. Alveolar recruitment improves ventilation during thoracic surgery: a randomized controlled trial. Br J Anaesth. 2012;108:517–24.
33. Kozian A, Schilling T, Schütze H, Heres F, Hachenberg T, Hedenstierna G. Lung computed tomography density distribution in a porcine model of one-lung ventilation. Br J Anaesth. 2009;102:551–60.
34. Tusman G, Böhm SH, Suarez-Sipmann F. Dead space during one-lung ventilation. Br J Anaesth. 2015;28:10–7.
35. Tusman G, Bohm SH. Prevention and reversal of lung collapse during the intra-operative period. Best Pract Res Clin Anaesth. 2010;24:183–97.
36. iPROVE Network Investigators, Belda J, Ferrando C, Garutti I. The effects of an open-lung approach during one-lung ventilation on postoperative pulmonary complications and driving pressure: a descriptive, multicenter national study. J Cardiothorac Vasc Anesth. 2018;32(6):2665–72.
37. Michelet P, Roch A, Brousse D, D'Journo XB, Bregeon F, Lambert D, Perrin G, Papazian L, Thomas P, Carpentier JP, Auffray JP. Effects of PEEP on oxygenation and respiratory mechanics during one-lung ventilation. Br J Anesth. 2005;95:267–73.
38. Hoftman N, Canales C, Leduc M, Mahajan A. Positive end expiratory pressure during one-lung ventilation: selecting ideal patients and ventilator settings with the aim of improving arterial oxygenation. Ann Card Anesth. 2011;14:183–7.
39. Sentürk NM, Dilek A, Camci E, Sentürk E, Orhan M, Tuğrul M, Pembeci K. Effects of positive end-expiratory pressure on ventilatory and oxygenation parameters during pressure-controlled one-lung ventilation. J Cardiothorac Vasc Anesth. 2005;19:71–5.
40. Meade MO, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ, Davies AR, Hand LE, Zhou Q, Thabane L, Austin P, Lapinsky S, Baxter A, Russel J, Skrobik Y, Ronco JJ, Stewart TE for the lung open ventilation study investigators. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome. A randomized controlled trial. JAMA. 2008;299:637–45.
41. Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL, Lefrant JY, Prat G, Richecoerur J, Nieszkowska A, Gervais C, Baudot J, Bouadma L, Brochard L, Expiratory Pressure (Express) Study Group. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2008;299:646–55.

42. Tusman G, Groisman I, Fiolo F, Scandurra A, Martinez J, Krumrick G, Bohm S, Suarez-Sipmann F. Noninvasive monitoring of lung recruitment maneuvers in morbidly obese patients: the role of pulse oximetry and volumetric capnography. Anesth Analg. 2014;118:137–44.
43. Maisch S, Reissmann H, Fuellekrug B, Weismann D, Rutkowski T, Tusman G, Bohm S. Compliance and dead space fraction indicate an optimal level of positive end-expiratory pressure after recruitment in anesthetized patients. Anesth Analg. 2008;106:175–81.
44. Spadaro S, Grasso S, Karbing DS, Fogagnolo A, Contoli M, Bollini G, Ragazzi R, Cinnella G, Verri M, Cavallesco NG, Rees SE, Volta CA. Physiologic evaluation of ventilation perfusion mismatch and respiratory mechanics at different positive end-expiratory pressure in patients undergoing protective one-lung ventilation. Anesthesiology. 2018;128:531–8.
45. Tugrul M, Camci E, Karadeniz H, et al. Comparison of volumen controlled with pressure controlled ventilation during one-lung anaesthesia. Br J Anaesth. 1997;79:306–10.
46. Unzueta MC, Casas JI, Moral MV. Pressure-controlled versus volume-controlled ventilation during one-lung ventilation for thoracic surgery. Anesth Analg. 2007;104:1029–33.
47. Pardos PC, Garutti I, Piñeiro P, Olmedilla L, de la Gala F. Effects of ventilator mode during one-lung ventilation on intraoperative and postoperative arterial oxygenation in thoracic surgery. J Cardiothorac Vasc Anesth. 2009;23:770–4.
48. Choi Y, Shim J, Na S, Hong S, Hong Y, Oh Y. Pressure-controlled versus volume-controlled ventilation during one-lung ventilation in the prone position for robot-assisted esophagectomy. Surg Endosc. 2009;23:2286–91.
49. Montes F, Pardo D, Charrís H, Tellez L, Garzón J, Osorio C. Comparison of two protective lung ventilator regimes on oxygenation during one-lung ventilation: a randomized controlled trial. J Cardiothorac Surg. 2010;5:99–103.
50. Tojo K, Goto T, Kurahashi K. Protective effects of continuous positive airway pressure on a nonventilated lung during one-lung ventilation: a prospective laboratory study in rats. Eur J Anaesthesiol. 2016;33:776–83.
51. Şenay H, Sıvac R, Kokulu S, Koca B, Bak E, Ela Y. The effect of pressure-controlled ventilation and volume-controlled ventilation in prone position on pulmonary mechanics and inflammatory markers. Inflammation. 2016;39(4):1469–74.
52. Al Shehri AM, El-Tahan MR, Al Metwally R, Qutub H, El Ghoneimy YF, Regal MA, Zien H. Right ventricular function during one-lung ventilation: effects of pressure-controlled and volume-controlled ventilation. J Cardiothorac Vasc Anesth. 2014;28:880–4.
53. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, Stewart TE, Briel M, Talmor D, Mercat A, Richard JC, Carvalho CR, Brower RG. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med. 2015;372:747–55.
54. Capan LM, Turndorf H, Patel C, et al. Optimization of arterial oxygenation during one-lung anesthesia. Anesth Analg. 1980;59:847–51.
55. Şentürk M, Layer M, Pembeci K, et al. A comparison of the effects of 50% oxygen combined with CPAP to the non-ventilated lung vs. 100% oxygen on oxygenation during one-lung ventilation. Anasthesiol Intensivmed Notfallmed Schmerzther. 2004;39:360–4.
56. Grichnik KP, Shaw A. Update on one-lung ventilation: the use of continuous positive airway pressure ventilation and positive end-expiratory pressure ventilation – clinical application. Curr Opin Anaesthesiol. 2009;22:23–30.
57. Verhage RJ, Boone J, Rijkers GT, et al. Reduced local immune response with continuous positive airway pressure during one-lung ventilation for oesophagectomy. Br J Anaesth. 2014;112:920–8.
58. Abe K, Shimizu T, Takashina M, et al. The effects of propofol, isoflurane, and sevoflurane on oxygenation and shunt fraction during one-lung ventilation. Anesth Analg. 1998;87:1164–9.
59. Karzai W, Haberstroh J, Priebe HJ. Effects of desflurane and propofol on arterial oxygenation during one-lung ventilation in the pig. Acta Anaesthesiol Scand. 1998;42:648–52.
60. Ng A, Swanevelder J. Hypoxaemia associated with one-lung anaesthesia: new discoveries in ventilation and perfusion. Br J Anaesth. 2011;106:761–3.

61. Pruszkowski O, Dalibon N, Moutafis M, et al. Effects of propofol vs sevoflurane on arterial oxygenation during one-lung ventilation. Br J Anaesth. 2007;98:539–44.
62. Schilling T, Kozian A, Senturk M, et al. Effects of volatile and intravenous anesthesia on the alveolar and systemic inflammatory response in thoracic surgical patients. Anesthesiology. 2011;115:65–74.
63. De Conno E, Steurer MP, Wittlinger M, et al. Anesthetic-induced improvement of the inflammatory response to one-lung ventilation. Anesthesiology. 2009;110:1316–26.
64. Pang QY, An R, Liu HL. Effects of inhalation and intravenous anesthesia on intraoperative cardiopulmonary function and postoperative complications in patients undergoing thoracic surgery. Minerva Anestesiol. 2018;84:1287–97.

Part III

Perioperative Medicine: Analgesia, Applied Pharmacology, Hemodynamic Control and Infections

Change in "Gold Standard" of Thoracic Epidural in Thoracic Surgery

13

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13.1 Introduction

Postoperative analgesia is an essential component of functional recovery after surgery. Blocking nociceptive stimuli contributes to decreasing the response to surgical stress, accelerating rehabilitation and reducing the incidence of chronic postoperative pain. Both the surgical technique and the operative team's organization are among the most important factors influencing the process of nociceptive development. Thoracic surgery and, more specifically, thoracotomy are some of the most intense surgical pain experiences that we know. The surgical insult, along with the associated postoperative pain, triggers a pathophysiological cascade which can be extremely noxious for patients, many times already afflicted by multiple pre-existing conditions which can easily decompensate.

Several strategies have been described to reduce postoperative pain following thoracic surgery, including parenteral opioids, non-steroidal anti-inflammatory drugs (NSAIDs), regional anesthetic blocks and cryotherapy.

Among regional blocks with local anesthetics, epidural analgesia has achieved great popularity, especially in surgeries with high prevalence of pain, such as thoracic surgery [1, 2] and high abdominal surgery [3, 4]. Epidural analgesia is still

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considered superior to intravenous analgesia in several surgical settings and during labor and remains a widely practiced analgesic technique worldwide [3, 6].

There is no evidence suggesting that epidural analgesia is no longer a first-line option in thoracic surgery [7, 8], but the development of less invasive regional techniques and the newer and increasingly common thoracoscopic approaches have led to questioning its pre-eminent role, which had been generally accepted until only a few years ago [1].

This chapter presents an overview of the evolution of regional analgesic techniques for pain management in thoracic surgery, describing them in parallel to the development of surgical procedures over time.

13.2 Thoracic Surgery: From Thoracotomy to Video-Assisted Thoracoscopic and Robotic Surgery—Toward Minimally Invasive Procedures—Fast-Track Surgery and Eras

Thoracic surgery emerged as a surgical specialty throughout the twentieth century [9] and has evolved continuously until present times, ever since the first successful pulmonary resection performed by Evarts Graham in 1933. Over the last two decades of the twentieth century, the number of technologies used in surgical applications grew considerably. Together with the greater availability of analgesic techniques for the management of perioperative pain, this has facilitated less invasive surgical approaches and ever shorter recovery and hospitalization periods [2, 10]. Video-assisted surgery originated in classical thoracoscopy. Jacobeus performed the first successful thoracoscopic procedure in 1910, to resect adhesions in therapeutic intrapleural pneumolysis for the treatment of pulmonary tuberculosis [11]. With the emergence of antibiotic therapy, thoracoscopy practically faded into oblivion, until it was rediscovered in the 1980s [12, 13], especially for diagnostic purposes. The earliest reports on lobectomies performed with video-assisted thoracoscopic surgery (VATS) were published in 1992 and 1993 [14, 15].

The advantages of this type of surgery are obvious. More complex diagnostic and therapeutic maneuvers could now be performed using sophisticated endoscopic materials and video cameras; in addition, all members of the surgical team could now take part in the procedure and the entire intrathoracic area could be inspected [16].

With the turn of the twenty-first century, robotic surgery was slowly introduced in our operating rooms. The first documented use of an assisting robot in surgery dates back to 1985, when the PUMA 560 robotic arm was used in a neurosurgical procedure. In thoracic surgery, the first robot-assisted thoracoscopic procedure was reported in 1998, after Okada et al. performed a successful segmental resection [17]. Robot-assisted surgery is now implemented in multiple centers and involves the use of four arms. One arm is connected to a three-dimensional camera inserted into the sixth or seventh intercostal space at the mid-clavicular line; two arms work as the right and left arms; and the fourth arm can be used to assist the left arm or be kept in reserve.

Although thoracoscopic approaches (and robotic surgery) are used with increasing frequency, they have not resulted in the expected favorable impact in terms of reducing the pain caused by the procedure. Certainly, with smaller incisions and less rib retraction, the incidence of acute pain is lower. However, outcomes are not better in terms of chronic pain. This is mainly due to the use of wide-diameter trocars inserted at several levels, which increases the probability of damaging intercostal nerves [18].

Another development that has greatly impacted the choice of the analgesic techniques and the multimodal management of pain has been the concept of "fast-track surgery", also known as enhanced recovery after surgery (ERAS), introduced by Kehlet and Wilmore [2, 19, 20]. Fast-track surgery is based on the rapid recovery of the patient and early discharge as a result of reduced response to surgical stress, less organ dysfunction and a lower rate of postoperative complications [21, 22]. The fast-track concept was introduced to thoracic surgery by Cerfolio et al. [23]. Several factors should be taken into account when fast-tracking thoracic surgery, including [24]:

- Comprehensive anesthetic assessment in the preoperative phase. Patients should be given information about every aspect of the hospital experience which they are about to undergo. This is also the time to implement smoking and drinking cessation interventions, which are associated with better survival.
- Surgical technique: The VATS approach has several advantages compared to thoracotomy, as described above, including lower mortality rates and shorter hospital stays. Major studies have reported similar 5-year survival rates with VATS and thoracotomy.
- Anesthetic technique: An anesthetic fast-track strategy involves general anesthesia with endotracheal intubation, avoidance of fluid overload, maintenance of normothermia, use of short-acting anesthetics and effective multimodal analgesia.

Regarding the latter point, the use of regional anesthesia (either thoracic paravertebral or thoracic epidural blocks) in thoracic surgery is well established for both thoracotomy and VATS, with no definitive evidence pointing to one technique being superior to the other. Therefore, both can be considered as the gold standard [25].

The current trend in fast-track surgery is paravertebral block, although it is still underused. Paravertebral blocks provide excellent analgesia with lower opioid consumption, facilitate early mobilization and are associated with lower rates of adverse effects.

It is the responsibility of the multidisciplinary team to remove systemic barriers and improve clinical practice in order to implement an ERAS protocol in thoracic surgery.

13.3 Thoracic Surgery and Analgesia: Together into the Future

As seen in the section above, thoracic surgery evolved exponentially in the twentieth century, especially during its second half, with the introduction of thoracoscopy and minimally invasive procedures. This has been fundamental for modifying classical analgesic protocols in complex surgery.

The pre-eminence of epidural analgesia has been questioned as a result of evolving regional anesthesia techniques and emerging concepts such as preventive and multimodal analgesia, along with the selective assessment of the benefit/risk ratio for each modality of postoperative analgesia. However, the evidence in clinical practice still supports the role of epidural analgesia for both video-assisted thoracoscopy and open thoracotomy [26]. There is no evidence to support the impact of postoperative analgesia on major surgical outcomes such as mortality, morbidity or mean length of stay, which are dependent on multiple and heterogenous factors. The assessment of analgesic efficacy in the surgical process must be based on patient-oriented outcomes, such as analgesic quality, adverse effects or postoperative well-being, in addition to global perioperative management and postoperative pain.

In order to delineate its current role in modern thoracic surgery, we provide an overview of the development of epidural analgesia since its inception to present times, describing techniques that are still in use in our operating rooms and others which have fallen into disuse for various reasons.

13.3.1 Thoracic Epidural Analgesia

Griffiths et al. evaluated the feasibility of epidural (then extradural) analgesia in thoracic surgery in 1975 [27], following earlier investigations of similar techniques in abdominal surgery. They conducted a study in 17 patients aged 46–70 who underwent thoracotomy for lung cancer. Before the operation and under general anesthesia, the patients were placed in the lateral position. An extradural cannula was inserted, via a Tuohy needle, through the midline, between the second and sixth thoracic spines. All patients had a test dose of 2 ml, followed by a subarachnoid injection of 4–6 ml of 0.5% bupivacaine with 1:200,000 adrenaline. Following surgery, the patients were transferred to the intensive care unit (ICU), where the block was continued for 48 h. According to the authors, “patients receiving extradural analgesia need constant supervision”, which, at their hospital, “is available only in the intensive care unit”. In the postoperative phase, the extradural block was maintained with intermittent injections of 0.5% bupivacaine with 1:200,000 adrenaline up to target analgesic levels by pinprick test or with 0.25% bupivacaine, 0.125% bupivacaine or continuous infusion of 0.25 mg/kg/h of 0.25% bupivacaine. Analgesic effectiveness and adverse effects such as tremor, urinary retention and hemodynamic stability were assessed. The authors concluded that thoracic “extradural” analgesia produced very efficient relief of pain, but that a disadvantage of the technique was that it required more skilled and demanding nursing care than conventional systemic analgesics [27]. A year later, Shuman et al. [28] reported the use of epidural anesthesia in a series of eight subjects with lung cancer and chronic obstructive pulmonary disease. Epidural analgesia provided successful pain relief, improved the postoperative course and avoided the use of narcotics or a respirator in seven of the eight patients.

Over the following years, driven by the success of Griffiths et al., there was an increase in the number of reports on post-thoracotomy epidural analgesia. In 1981,

James et al. [29] reported on a series of 53 patients who underwent thoracotomy for different diagnoses and had epidural analgesia with bupivacaine. In these patients, epidural analgesia was effective for pain relief, but the incidence of hypotension and other comorbidities raised questions on its relevance in this type of surgery.

With the focus now shifting to reducing the complications of epidural anesthesia in thoracotomy, Logas et al. [30] conducted a prospective randomized study in 1987. The study included five experimental groups with epidural morphine chloride and 0.1% bupivacaine alone or combined, versus epidural saline or intramuscular morphine. The authors concluded that the continuous infusion of morphine and bupivacaine provided excellent pain relief with an acceptable level of adverse effects.

In 1993, Grosmanová et al. [31] compared two groups of patients undergoing thoracotomy. The first group (23 patients) was given analgesics by the classical bolus administration, whereas epidural morphine was applied to the second group (15 patients). The second group had significantly greater pain relief on the first post-surgical day. There were some adverse effects described by the authors as "insignificant" in 60% of cases (vomiting, urine retention).

13.3.2 Intercostal Nerve Block

Following the introduction of epidural analgesia in thoracic surgery, and probably out of fear of its side effects, which were then poorly controlled, intercostal blocks began to be used in thoracotomies in the 1980s. Sabanathan et al. [32] reported in 1988 a series of 81 patients who had an intercostal catheter inserted in the paravertebral space, through a small pleural incision, under direct surgeon observation, with an infusion of 0.5% bupivacaine for 5 days. Effective analgesic control was attained and 66 (81.5%) patients required no additional analgesic in the subsequent 4 days.

The same group of investigators, driven by the benefits of preventive analgesia in major surgery procedures, described percutaneous paravertebral nerve block (the origins of which will be explained below) followed by an intercostal extrapleural block using a postoperative catheter (inserted by the surgeons), with good control of perioperative pain [33].

After the efficacy of intercostal nerve blocks in thoracic surgery was demonstrated in the studies conducted by these authors, Richardson, Sabanathan et al. [34] compared a continuous intercostal block to epidural morphine for the management of post-thoracotomy analgesia. They conducted a controlled study in 20 patients randomized into two groups of 10 patients each. Toward the end of the surgery, one of the groups received epidural morphine (2–6 mg depending on age) through a catheter inserted before the surgery. The other group received 20 ml 0.5% bupivacaine through an intercostal catheter placed in the paravertebral space by a surgeon. The study assessed pain relief, respiratory performance, oxygen saturation by pulse oximetry and incidence of complications. The authors concluded that continuous intercostal nerve block was effective for post-thoracotomy pain, with adequate

analgesic control, normal pulmonary mechanics, and absence of the side effects normally associated with epidural block, such as pruritus, postoperative nausea and vomiting and urinary retention.

13.3.3 Interpleural Nerve Block

Already in the 1990s, Bachman et al. [35] evaluated the benefits of intrapleural analgesia in order to investigate the effect of different pain-relief methods (regional and systemic) following thoracotomies on the cardiovascular system, pulmonary gas exchange, various endocrine parameters and subjective pain perception. They compared this new regional analgesia technique to other established methods such as intercostal or thoracic epidural nerve blocks. Bachmann et al. concluded that there were no statistically significant differences in catecholamine concentrations among the different study groups. The plasma concentrations of the "stress metabolites", such as glucose and lactate, as well as the hemodynamic (mean arterial pressure and heart rate) and pulmonary parameters (blood gas analyses), showed no significant differences among study groups. Pain management results, however, were not promising. Indeed, in contrast to the other pain-relieving methods, seven out of ten patients with interpleural analgesia needed supplementary systemic opioid therapy [35].

Parallel to the development of alternatives to thoracic epidural analgesia such as interpleural or intercostal nerve blocks, paravertebral blocks regained relevance between the 1970s and 1990s (with the collection and report of cases) for the management of pain in both thoracic surgery and in cholecystectomies and nephrectomies.

13.3.4 Paravertebral Nerve Block

Paravertebral nerve blocks were introduced in clinical practice in 1906 [36] but later fell into disfavor until 1979. It was even said that "paravertebral somatic block is now of more interest to historians than to practical anesthetists". It was then when Eason and Wyatt [37] described the thoracic paravertebral block technique with a loss of resistance test and placement of a catheter for thoracic surgery (thoracotomy), performed on 75 cases—50 with catheter placement and 25 with single-shot blocks. Paravertebral block was satisfactory for pain relief and much easier to perform, with few side effects. The authors even considered it superior to other techniques described previously for similar surgeries, such as intercostal or epidural blocks.

In light of the increasing number of studies showing its clinical efficacy, Richardson and Sabanathan [38] considered it necessary in 1995 to review and establish the importance and feasibility of paravertebral block. In this review, the authors discussed the history of the technique and explained the anatomy of the paravertebral space, the indications for blockade and the mechanism of analgesia

and analgesic efficacy. They described the paravertebral catheter placement technique using loss of resistance as reported by Eason and Wyatt [37], as well as the direct vision method with stripping up of the parietal pleura reported by Sabanathan [33]. They compared paravertebral block to other types of afferent blocks such as epidural analgesia, intercostal blocks and intrapleural analgesia. Finally, they described potential toxicity, the performance of bilateral blocks, contraindications, the need for nursing surveillance and the incidence of side effects and complications such as intrapleural catheter placement or migration, hypotension and neurological complications. The authors conclude that the overall efficacy of this block is impressive. It is relatively easy to learn, it has less than 5% complications and it requires no additional nursing surveillance postoperatively. For bilateral surgery, they consider that further study is warranted in relation to doses of local anesthetic required for maximal benefit versus risks of accumulation and toxicity. For all these reasons, the authors were the first to recommend paravertebral nerve block as the "gold standard" for unilateral surgery of the chest or trunk [38].

In their references of this review, Richardson and Sabanathan included a prospective randomized study of their own in which they had compared interpleural and paravertebral blocks for thoracic surgery. In this study [38], they included 53 patients undergoing posterolateral thoracotomy and divided them into two groups. In group 1, patients received continuous percutaneous paravertebral blocks with 20 ml of 0.5% bupivacaine and subsequent placement of a catheter in the paravertebral space under direct vision, following the method of Sabanathan et al. In group 2, patients had interpleural block with gradual advancement of a Tuohy needle in the mid-scapular line until a "click" and loss of resistance to saline were noted. Once the interpleural space was identified, patients were administered 20 ml of 0.5% bupivacaine. Towards the end of the surgery, patients in this group also had a catheter placed into the interpleural space under direct vision, with its tip at the intercostal level of the incision. In both groups, pain scores and patient-controlled morphine needs were similar, with patients comfortable at rest. However, spirometric values and postoperative respiratory morbidity were better in the paravertebral block group, probably because of the "local" spread of the drug as opposed to the gravity-dependent caudal spread in the intercostal block group. In addition, hospital stay was shorter in the paravertebral block group (by 1 day). Finally, five patients showed confusion in the interpleural block group, probably because of bupivacaine toxicity. The authors concluded that bupivacaine deposited paravertebrally produced greater preservation of lung function and fewer side effects than bupivacaine administered interpleurally, and questioned the use of interpleural analgesia in thoracic surgery [39].

Other authors, including Kruger [40], also concluded that there was insufficient evidence to favor the use of interpleural block over epidural analgesia in patients undergoing thoracotomy [25]. For these reasons, interpleural block was slowly abandoned in favor of other established techniques such as thoracic epidural block or the increasingly popular paravertebral block.

Paravertebral block slowly became the norm in our operating rooms in Europe. Català et al. [41] compared a single paravertebral puncture with administration of

intermittent bolus doses versus continuous paravertebral infusion of bupivacaine in 30 patients. Their results suggested that continuous paravertebral block provides better analgesic control than the bolus regime.

In the United States, however, thoracic epidural analgesia remained the gold standard in post-thoracotomy pain management. Authors like Bimston [42] began to question this, noting that epidural analgesia provided adequate pain control but was more or less associated with complications that include improper placement, pulmonary complications, pruritus, nausea and vomiting, respiratory depression, mental status changes, postural hypotension, paresthesias, and urinary retention. For these reason, Bimston et al. conducted a prospective controlled study in 50 patients undergoing thoracotomy who were randomized into two groups. The patients in one group received thoracic epidural analgesia preoperatively and were controlled by anesthesiologists postoperatively. Patients in the second group had a paravertebral catheter placed under direct vision following the method described by Sabanathan. In both groups, a solution containing a mixture of opioids (fentanyl 10 μg/ml) and a local anesthetic (0.1% bupivacaine) was infused through the catheter, and the infusion rates were titrated to provide adequate postoperative pain control. Pain levels were tested by visual analog scale (VAS), patients had blood drawn for fentanyl and bupivacaine levels and bedside pulmonary function tests performed, including forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC). Analgesia-related complications such as catheter insertion difficulties, pruritus, nausea and vomiting, postural hypotension, paresthesias, respiratory depression, mental status changes, urinary retention, pulmonary complications, deep vein thrombosis and wound infection were recorded. The authors concluded that both techniques provided excellent pain control. Paravertebral block was associated with less frequent urinary retention, easier insertion and postoperative control by surgeons, less anesthetic expenditure and minimal occurrence of pulmonary or cardiovascular complications. Discharge times from both the ICU and the hospital were similar in the epidural and paravertebral block groups. Given these results, the authors recommended continuous paravertebral infusion as the new gold standard for postoperative pain control in thoracic surgery [42]. Some colleagues, nevertheless, questioned the use of paravertebral blocks with catheters placed by surgeons, as they considered that it excluded the benefits of preemptive analgesia associated with epidural block [42].

13.3.5 Fascial Blocks on the Thoracic Wall

There is no evidence that ultrasounds have a significant effect on the incidence of peripheral nerve damage. However, the development of ultrasound technologies and their use in regional anesthesia offers several potential advantages over the use of nerve stimulators or anatomical landmarks on the skin.

Blanco et al. [43] recently reported the application of a serratus plane block. In this block, the local anesthetic is deposited either above or below the serratus anterior muscle in the mid-axillary line. Blockade of the lateral cutaneous branches of

the intercostal nerves results in anesthesia of thoracic dermatomes T2 to T9. This technique is intended to prevent autonomic block and the potential injury to neuroaxial structures associated with thoracic epidural analgesia, as well as the potential pleural damage associated with paravertebral block. The ultrasound anatomy of serratus block is easily identified and the virtually superficial trajectory of the needle facilitates its location, unlike in paravertebral block. For these reasons, this approach appears to be easy to perform.

Khalil et al. [44] conducted a prospective randomized study in which they attempted to assess the effectiveness of ultrasound-guided serratus anterior block versus thoracic epidural analgesia in 40 patients scheduled for thoracic surgeries (metastatectomy, lobectomy, pneumonectomy or pleuro-pneumonectomy) with posterolateral incisions. The primary endpoint was mean arterial blood pressure after thoracotomy, measured after initiation of infusion with local anesthetic 0.125% levobupivacaine at 5 ml/h (following an initial 30 ml bolus of 0.25% levobupivacaine for the serratus block and 15 ml of 0.25% levobupivacaine for the epidural analgesia). Secondary endpoints were pain scores, morphine consumption, and incidence of postoperative nausea and vomiting in the first 24 h after surgery.

Compared to preoperative values, mean arterial blood pressure in the serratus block group did not change significantly, whereas it decreased significantly in the thoracic epidural group. VAS scores and the total dose of morphine consumed were comparable in the two groups. For these reasons, the authors concluded that serratus anterior plane block appeared to be a safe and effective alternative for postoperative analgesia after thoracotomy. Furthermore, they added that serratus anterior block is the subject of several clinical trials that have not been published yet, including the evaluation of this approach in VATS compared to thoracic epidural analgesia and local anesthetic infiltration at the site of the thoracoscopy. The expected results of these studies should boost the increasingly relevant role of serratus anterior block in thoracic wall surgery, just like transversus abdominis plane block has become popular in abdominal surgery.

In the same line, a novel erector spinae plane block has been reported recently [45]. This block was applied successfully to patients with chronic thoracic neuropathic pain and in acute postoperative pain. It provided similar analgesia as epidural block, although unilaterally. An ultrasound-guided needle is advanced in a cephalad-to-caudad direction through the trapezius, rhomboid major and erector spinae to gently contact the transverse process. The injection is administered into the interfascial plane deep to the erector spinae. The analgesic effect was postulated to be due to the spread of the local anesthetic in the paravertebral space, blocking the dorsal ramus of the spinal thoracic nerve, and allowing the local anesthetic to reach the ventral rami. This block provided analgesia to the posterior and anterior thorax safely and with medium to low difficulty.

So far, no large case series or studies have been conducted to compare the erector spinae block to epidural, paravertebral or intercostal blocks in thoracic surgery. The experience with the use of this block falls within multimodal strategies for perioperative analgesic control or rescue of failed neuroaxial techniques.

A series of four cases was reported recently in VATS for pulmonary resection in which patients had ultrasound-guided erector spinae plane blocks [46]. These four patients had the ultrasound-guided block and the catheter inserted before surgery and anesthetic induction. At the completion of the surgery and before emergence, an infusion of 0.15% ropivacaine was initiated at infusion rates between 7 and 12 ml/h. The authors concluded that erector spinae block is an alternative to thoracic epidural or paravertebral blocks in thoracic surgery. It is an interesting approach in VATS or as an alternative to thoracic epidural or paravertebral blocks when these techniques fail or are not feasible [46].

13.4 Gold Standard in Thoracic Surgery

Because pain was and is (and probably will be) one of the major challenges of thoracic surgery, there have been several gold standards defined in the history. Recent findings will probably lead to changes in the perception and the determination for the analgesia methods. For an appropriate definition, we have first to answer some questions:

1. What is the aim of the post-thoractomy analgesia: A low VAS (visual analog scale) during rest (in other words, a peaceful sleeping patient) is naturally desired; but can not be considered as the primary target of the analgesic approach.
   (a) Overall postoperative outcome: This includes not only a shorter stay in the PACU, ICU and in the hospital, but also incidence of postoperative pulmonary complications (e.g. there is a direct relationship between the analgesia and complications like pneumonia, atelectasis etc.) [47].
   (b) Less chronic post-thoractomy pain (CPTP): Persisting pain after a certain time (2–6 months) after thoracotomy is a very important problem with a frequency of up to 60% [48, 49]. Even after less invasive thoracoscopic operations, the incidence is still high (approx. 20–30%) [50].

       Unfortunately, the majority of the studies about analgesia is still dealing with VAS, mainly VAS in rest. Beneficial effects of thoracic epidural (TEA) to decrease atelectasis and infections have been shown, but only in comparison to systemic analgesia. More recent techniques such as paravertebral and peripheral blocks appear to have similar successful effects. But whether any analgesic method can have a direct effect on postoperative outcome is still have to be examined.

       Regarding CPTP, TEA has been shown in several studies to decrease the frequency [51, 52]. The effect of paravertebral and peripheral blocks have been studied less; but considering the fact that appropriate treatment of acute pain is associated with less CPTP [53] can lead us to hypothesize that the newer methods can be as effective, too.
2. How effective are different approaches? In the previous decades, different approaches such as “multimodal analgesia”, “preemptive analgesia”, “patient controlled analgesia” have been introduced to daily practice. Following the ini-

tial optimism, all these methods are still under examination. Today we know that:

(a) The combination of different drugs (and strategies) acting on different sites of central and peripheral nervous system is beneficial as side effects of high-dose opioids can be avoided with better analgesia. A commonly used strategy is to combine local anesthetics (regional analgesia or infiltration), opioids, and non-opioid analgesics with regional anesthesia as mainstay of pain relief [54].

(b) "Preventive" (but not the "preemptive") analgesia prevents the establishment of central sensitization caused not only by incisional but also by inflammatory injuries, covering the whole preoperative and early postoperative periods [55]. This should lead to an equal effective analgesia with lower doses of analgesics. In a prospective randomized trial comparing the effects of preoperative- or postoperative-initiated thoracic epidural anesthesia (TEA) versus intravenous opioids, it has been found that the preoperative initiation of TEA was associated with a significant improvement in both acute and chronic postthoracotomy pain [51].

3. Comprehensive pain management in thoracic surgery cannot be fully conceived nowadays in the absence of a multimodal (and preventive) model. Although preventive analgesia has been a frequent topic of discussion, several studies strongly suggest that, in the case of thoracic surgery, such strategies result in clear reductions in pain and/or consumption of analgesics. A multimodal approach takes into account the multiple pathways by which nociceptive input is conveyed to the central nervous system (CNS), the number of pharmacologically distinct mechanisms of modulating this input, the need for effective analgesia throughout the perioperative period and after discharge, and the importance of minimizing side effects, particularly respiratory depression [54]. Finally, but most importantly, with regard to the questions above, is TEA still the gold standard, or are the newer techniques (paravertebral and the more recent peripheral blocks) superior to TEA?

Regarding the long-standing discussion of whether thoracic epidural or paravertebral blocks are the gold standard for perioperative pain management, the *Journal of Cardiothoracic and Vascular Anesthesia* recently published testimonials that are both for [56] and against [57] the superiority of thoracic epidural analgesia.

Paravertebral block, which has become more popular in recent years, has a similar analgesic profile as thoracic epidural block, with lower rates of minor adverse events such as hypotension, nausea and vomiting, urinary retention or pruritus. Paravertebral block is not free of complications, such as inadvertent pleural puncture, pneumothorax or ipsilateral Horner syndrome. The incidence of neurological damage is lower, as a result of the greater distance to the epidural space and the spinal cord compared to thoracic epidural block. Absolute contraindications to paravertebral block are cutaneous or intrathoracic infection and tumors near the target site of the block. Relative contraindications include severe coagulopathy, severe respiratory diseases (with ventilation depending on intercostal musculature),

ipsilateral diaphragm paresis, severe spinal deformities such as hyperkyphosis or scoliosis and dilation of intercostal vessels (which may occur in case of coarctation or aneurysm). Paravertebral block may be performed with the classical technique under direct vision of the surgeon or under ultrasound guidance. In the former setting, the costovertebral ligament is pierced, which may or may not feel like a "pop". If a low-resistance syringe is used, loss of resistance can be felt. However, both are highly subjective sensations. In addition, the use of a nerve stimulator has been reported to verify the correct location of the needle, especially in the event of technical difficulties (obesity or altered thoracic anatomy). The motor response to this, based on the puncture level, is a contraction of the relevant intercostal muscle or the muscles of the abdominal wall (transversus abdominis or obliquus externus abdominis). If there is a single puncture, the technique will not suffice to achieve analgesia over all dermatomes involved in the pain input of surgery. Insertion of a catheter appears to be a solution to this problem. However, progression of the catheter is not easy and the failure rate is not negligible. Insertion by a surgeon does not appear to be a preventive analgesic management alternative, even though the effectiveness of this approach is still under discussion. Finally, ultrasonography for this type of block appears to be an effective alternative for a safer approach.

The success rate of thoracic paravertebral block depends on operator experience and there are still no studies to confirm its actual effectiveness. The use of ultrasound may be reasonable to assure successful placement of the catheter in the paravertebral space, although, at this time, studies evaluating paravertebral catheter placement under ultrasound guidance are mostly limited to human cadaveric subjects [58].

Thoracic epidural block remains the technique of choice for most anesthesiologists. Epidural block reduces post-thoracotomy pain both at movement and at rest and improves mucociliary clearance and postoperative respiratory mechanics. In addition, it reduces cardiovascular complications via a number of mechanisms including diminished response to stress and sympathetic input, both systemically and through blockage of cardioaccelerator fibers, thereby promoting dilation of constrained coronary arteries. Also, thoracic epidural block results in lower rates of supraventricular arrhythmia, present in up to 30% of patients undergoing thoracotomy.

Nonetheless, epidural analgesia is not exempt from complications and risks. On the one hand, placing a thoracic epidural catheter can be a real challenge, given the anatomical particulars of this space, especially to unskilled hands. The most serious risks are dural puncture and neurological damage. These complications are usually transient and less frequent, in any case, than in a lower thoracic approach.

The theoretical difficulty of performing the technique and placing the catheter is comparable, and in no case superior to, identifying the paravertebral space and channeling the catheter paravertebrally. The loss of resistance test for identifying the epidural space is more obvious than in paravertebral block, as the paravertebral catheter is frequently placed percutaneously. In addition, the sympathetic blockade resulting from the dose test can be useful to demonstrate accurate positioning of the catheter. In any case, the success of both techniques is operator-dependent. The

technique should always be performed in conscious, cooperating patients, and there are several contraindications, including lack of consent, coagulopathy, infection at the puncture site, severe systemic infection, tattoos at the puncture site, acute CNS disorders or space-occupying brain tumors.

Minor complications of epidural block, such as pruritus, hypotension, urinary retention or nausea and vomiting, may be due to inappropriate use of the drugs. The synergistic activity of local anesthetics with an opioid has been shown to provide a better analgesic profile than epidural use of local anesthetics alone or thoracic paravertebral block. In addition, the combination of these drugs administered epidurally results in lower rates of hypotension than with epidural use of the local anesthetic alone, which requires higher dosages to attain similar analgesic effects [59]. Some authors suggest that the limitations of epidural analgesia could be solved easily by maintaining the right preload and using the synergistic effects of local anesthetics and opioids. An additional advantage of thoracic epidural analgesia is its effectiveness in reducing chronic post-thoracotomy pain, while no studies confirm such properties in the case of paravertebral block.

It should be noted that neither approach is useful for post-thoracotomy shoulder pain. Studies show that over 85% of post-thoracotomy patients under epidural analgesia complain of shoulder pain [60]. Several hypotheses have been put forward to explain this pain, including excessive strain of the posterior thoracic ligaments that may occur when positioning the patient, elongation of the brachial plexus and musculoskeletal pain or referred pain from irritation of the pleural surface. The pain transmitted by the ipsilateral phrenic nerve appears to contribute significantly to post-thoracotomy shoulder pain. Phrenic nerve infiltration has been shown to reduce post-thoracotomy pain in several studies, without significant effects on respiratory function [61].

In conclusion, we believe that the choice of the technique should be based on the experience of the anesthesiologist, the familiarity with the procedure, the clinical and anatomical particulars of the patient and a multimodal analgesic management plan. We cannot recommend one technique over the other, since both have good analgesic profiles. The difficulty of performing thoracic epidural block is intermediate, although it can be easy for experienced hands. It is easy to detect loss of resistance and its effect can be sustained over time with placement of a catheter. Management of its complications involves adequate vascular filling and accurate use of drugs with synergistic actions, such as local anesthetics and opioids. On the other hand, the paravertebral approach is similar to epidural block for analgesic control and post-thoracotomy pain, with a better adverse effect profile. The theoretical difficulty of locating the paravertebral space can be overcome with ultrasonography.

Nevertheless, some clinical conditions such as post-thoracotomy shoulder pain and chronic pain are not resolved with the use of either technique alone. For this reason, clinicians should be familiar with the therapeutic arsenal against post-thoracotomy pain (including intravenous opioids, NSAIDs, ketamine, gabapentinoids, cryoanalgesia, intercostal or thoracic wall blocks such as serratus and erector spinae blocks) and the implementation of a multimodal analgesic strategy. This will result in lower patient morbidity, earlier discharge and ultimately lesser health expenditure.

References

1. Rawal N. Epidural technique for postoperative pain: gold standard no more? Reg Anesth Pain Med. 2012;37(3):310–7.
2. Kehlet H, Dahl J. Epidural analgesia and postoperative outcomes. A need for a different approach. Acta Anaesthesiol Scand. 2008;52:1311–2.
3. Oh TK, Lim MC, Lee Y, et al. Improved postoperative pain control for cytoreductive surgery in women with ovarian cancer using patient-controlled epidural analgesia. Int J Gynecol Cancer. 2016;26:588–93.
4. Tang GL. Increased survival secondary to decreased perioperative complications in open aortic aneurysm repair using epidural anesthesia. JAMA Surg. 2016;151:1123–4.
5. Mohamad MF, Mohammad MA, Hetta DF, et al. Thoracic epidural analgesia reduces myocardial injury in ischemic patients undergoing major abdominal cancer surgery. J Pain Res. 2017;10:887–95.
6. Capdevila X, Moulard S, Plasse C, et al. Effectiveness of epidural analgesia, continuous surgical site analgesia, and patient-controlled analgesic morphine for postoperative pain management and hyperalgesia, rehabilitation, and health-related quality of life after open nephrectomy: a prospective, randomized, controlled study. Anesth Analg. 2017;124:336–45.
7. Bos EME, Hollmann MW, Lirk P. Safety and efficacy of epidural analgesia. Curr Opin Anaesthesiol. 2017;30(6):736–42.
8. Blackshaw WJ, Bhawnani A, Pennefather SH, Al-Rawi O, Agarwal S, Shaw M. Propensity score-matched outcomes after thoracic epidural or paravertebral analgesia for thoracotomy. Anaesthesia. 2018;73(4):444–9.
9. Paris-Romeu F, González-Aragoneses F. Figuras pioneras de la cirugía torácica española. Arch Bronconeumol. 2002;38:37–48.
10. Fry WA. Chirurgie thoracique: historique et comparaison des développements en Europe et en Amérique du Nord. Rev Mal Respir. 2004;21:369–71.
11. Jacobeus HC. The practical importance of thoracoscopy in surgery of the chest. Surg Gynecol Obstet. 1922;34:289–96.
12. Cantó A, Blasco E, Casillas M. Thoracoscopy in the diagnosis of pleural effusion. Thorax. 1977;32:550–4.
13. Boutin C, Viallat JR, Cargnino P, Farisse P, Choux R. La thoracoscopie en 1980. Revue générale. Poumon et Coeur. 1981;37:11–9.
14. Roviaro G, Rebuffat C, Varoli F, et al. Thoracoscopy assisted pulmonary lobectomy. Surg Laparosc Endosc. 1992;2:244–7.
15. Hazelrigg SR, Nunchuck SK, Locicero J III. Video assisted thoracic surgery study group data. Ann Thorac Surg. 1993;56:1039–44.
16. Izquierdo JM, Pac J, Casanova J, Mariñán M, Rojo R, Rumbero JC, Vara F. Videotoracoscopia en el tratamiento quirúrgico del neumotórax: a propósito de 46 casos. Arch Bronconeumol. 1996;32:76–8.
17. Okada S, Tanaba Y, Yamauchi H, Kimura K, Sato S. A voice-controlled robot assisted thoracoscopic surgery for pulmonary tumor. Kyobu Geka. 1998;51:735–8.
18. Morales JE, De Andrés J, Guijarro R, Granell M. Dolor crónico tras la cirugía torácica. Prevención y tratamiento. In: Granell M, editor. Manual de anestesia en cirugía torácica. 6th ed. Spain: Editorial Panamericana; 2018. p. 163–74.
19. Kehlet H, Wilmore DW. Fast-track surgery. Br J Surg. 2005;92:3–4.
20. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg. 2008;248(2):189–98.
21. Kehlet H. ERAS implementation-time to move forward. Ann Surg. 2018;267(6):998–9.
22. Kehlet H. Enhanced recovery after surgery (ERAS): good for now, but what about the future? Can J Anaesth. 2015;62(2):99–104.
23. Cerfolio RJ, Pickens A, Bass C, Katholi C. Fast-tracking pulmonary resections. J Thorac Cardiovasc Surg. 2011;122:318–24.

24. Loop T. Fast track in thoracic surgery and anesthesia: update of concepts. Curr Opin Anesthesiol. 2016;29:20–5.
25. Crumley S, Schraag S. The role of local anaesthesic techniques in ERAS protocols for thoracic surgery. J Thorac Dis. 2018;10:1998–2004.
26. Obuchi T, Yoshida Y, Moroga T, Miyahara N, Iwasaki A. Postoperative pain in thoracic surgery: re-evaluating the benefits of VATS when coupled with epidural analgesia. J Thorac Dis. 2017;9(11):4347–52.
27. Griffiths DP, Diamond AW, Cameron JD. Postoperative extradural analgesia following thoracic surgery: a feasibility study. Br J Anaesth. 1975;47:48–55.
28. Shuman RL, Peters RM. Epidural anesthesia following thoracotomy in patients with chronic obstructive airway disease. J Thorac Cardiovasc Surg. 1976;71:82–8.
29. James EC, Kolberg HL, Iwen GW, Gellatly TA. Epidural analgesia for post-thoracotomy patients. J Thorac Cardiovasc Surg. 1981;82:898–903.
30. Logas WG, El-Baz N, El-Ganzouri A. Continuous thoracic epidural analgesia for postoperative pain relief following thoracotomy: a randomized prospective study. Anesthesiology. 1986;87:787–91.
31. Grosmanová T, Koutná J, Scheinarová A. Analgesia after intercostal thoracotomy. Acta Univ Palacki Olomuc Fac Med. 1993;136:53–5.
32. Sabanathan S, Smith PJ, Pradhan GN, Hashimi H, Eng JB, Mearns AJ. Continuous intercostal nerve block for pain relief after thoracotomy. Ann Thorac Surg. 1988;46:425–6.
33. Sabanathan S, Richardson J, Mearns AJ. Management of pain in thoracic surgery. Br J Hosp Med. 1993;50:114–20.
34. Richardson J, Sabanathan S, Eng J, Mearns AJ, Rogers C, Evans C, Bembridge J, Majid M. Continuous intercostal nerve block versus epidural morphine for posthoracotomy analgesia. Ann Thorac Surg. 1993;55:377–80.
35. Bachmann-Mennenga B, Biscoping J, Kuhn DF, Schurg R, Ryan B, Erkens U, Hempelmann G. Intercostal nerve block, interpleural analgesia, thoracic epidural block or systemic opioid application for pain relief after thoracotomy? Eur J Cardiothorac Surg. 1993;7:12–8.
36. Sellheim H. Verh Dtch Ges Gynak. 1906;176
37. Eason MJ, Wyatt R. Paravertebral thoracic block—a reappraisal. Anaesthesia. 1979;34:638–42.
38. Richardson J, Sabanathan S. Thoracic paravertebral analgesia. Acta Anaesthesiol Scand. 1995;39:1005–15.
39. Richardson J, Sabanathan S, Mearns AJ, Shah RD, Goulden C. A prospective, randomized comparison of interpleural and paravertebral analgesia in thoracic surgery. Br J Anaesth. 1995;75:405–8.
40. Kruger M. Is interpleural analgesia better than thoracic epidural analgesia after thoracotomy? J Cardiothorac Vasc Anesth. 1999;13:653–5.
41. Català E, Casas JI, Unzueta MC, Diaz X, Aliaga L, Villar-Landeira JM. Continuous infusion is superior to bolus doses with thoracic paravertebral blocks after thoracotomies. J Cardiothorac Vasc Anesth. 1996;10:586–8.
42. Bimston DN, McGee JP, Liptay MJ, Fry WA. Continuous paravertebral extrapleural infusion for post-thoracotomy pain management. Surgery. 1999;126:656–7.
43. Blanco R, Parras T, Mc Donell JG, Prats-Galino A. Serratus plane block: a novel ultrasound-guided thoracic wall nerve block. Anaesthesia. 2013;68:1107–013.
44. Khalil A, Abdallah N, Bshandy G, Kaddah TA. Ultrasound guided serratus anterior plane block versus thoracic epidural analgesia for thoracotomy pain. J Cardiothorac Vasc Anesth. 2017;31:152–8.
45. Forero M, Adhikary S, López H, Tsui C, Chin KJ. The erector spinae plane block: a novel analgesic technique in thoracic neuropathic pain. Reg Anesth Pain Med. 2016;41:621–7.
46. Luis-Navarro JC, Seda-Guzmán M, Luis-Moreno C, López-Romero JL. Bloqueo del plano del músculo erector de la columna en 4 casos de cirugía torácica videoasistida. Rev Esp Anestesiol Reanim. 2018;65:204–8.
47. Senturk M. Acute and chronic pain after thoracotomies. Curr Opin Anaesthesiol. 2005;18:1–4.

48. Bayman EO, Brennan TJ. Incidence and severity of chronic pain at 3 and 6 months after thoracotomy: meta-analysis. J Pain. 2014;15(9):887–97.
49. Rodríguez-Aldrete D, Candiotti K, Janakiraman R, Rodríguez-Blanco Y. Trends and new evidence in the management of acute and chronic post-thoracotomy pain – an overview of the literature from 2005 to 2015. J Cardiothoracic Vasc Anesth. 2016;30:762–72.
50. Wildgaard K, Ringsted TK, Hansen HJ, et al. Persistent postsurgical pain after video-assisted thoracic surgery—an observational study. Acta Anaesthesiol Scand. 2016;60(5):650–8.
51. Sentürk M, Ozcan PE, Talu GK, Kiyan E, Camci E, Ozyalçin S, Dilege S, Pembeci K. The effects of three different analgesia techniques on long-term postthoracotomy pain. Anesth Analg. 2002;94:11–5.
52. Khoronenko V, Baskakov D, Leone M, Malanova A, Ryabov A, Pikin O, Golovashchenko M. Influence of regional anesthesia on the rate of chronic postthoracotomy pain syndrome in lung cancer patients. Ann Thorac Cardiovasc Surg. 2018;24(4):180–6.
53. Hetmann F, Kongsgaard UE, Sandvik L, et al. Prevalence and predictors of persistent postsurgical pain 12 months after thoracotomy. Acta Anaesthesiol Scand. 2015;59(6):740–8.
54. Gottschalk A, Cohen S, Yang S, Ochrong EA. Preventing and treating pain after thoracic surgery. Anesthesiology. 2006;104:594–600.
55. Katz J, Clarke H, Seltzer Z. Preventive analgesia: quo vadimus? Anesth Analg. 2011;113:1242–53.
56. Teeter E, Kumar P. Pro: thoracic epidural block is superior to paravertebral blocks for open thoracic surgery. J Cardiothoracic Vasc Anesth. 2015;29:1717–9.
57. Krakowski J, Arora H. Con: thoracic epidural block is not superior to paravertebral blocks for open thoracic surgery. J Cardiothoracic Vasc Anesth. 2015;29:1720–2.
58. D'Ercole F, Arora H, Kumar P. Paravertebral block for thoracic surgery. J Cardiothoracic Vasc Anesth. 2018;32:915–27.
59. Grider JS, Mullet TW, Saha SP, et al. A randomized, double-blind trial comparing continuous thoracic epidural bupivacaine with and without opioid in contrast to a continuous paravertebral infusion of bupivacaine for post thoracotomy pain. J Cardiothoracic Vasc Anesth. 2012;2:83–9.
60. Mac TB, Girard F, Chouinard P, et al. Acetaminophen decreases early post-thoracotomy ipsilateral shoulder pain in patients with thoracic epidural analgesia: a double-blind placebo-controlled study. J Cardiothoracic Vasc Anesth. 2005;19:475–8.
61. Danelli G, Berti M, Casati A, et al. Ipsilateral shoulder pain after thoracotomy surgery: a prospective, randomized, double-blind, placebo-controlled evaluation of the efficacy of infiltrating the phrenic nerve with 0.2% wt/vol ropivacaine. Eur J Anaesthesiol. 2007;24:596–601.

14 Are There New Evidences on the Use of Neuromuscular Blocking Agents and Reversal Drugs in Thoracic Surgery?

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14.1 Introduction

Anesthetic management affects patient's perioperative morbidity and mortality [1]. It is under scrutiny whether neuromuscular blocking agents (NMBA), especially postoperative residual neuromuscular block (RNMB) affects immediate or delayed outcomes. If the answer was yes, one possibility is to avoid these drugs during surgical procedures. However, NMBA use and its clinical indications are both evidence based [2].

Thoracic surgery procedures present some distinct characteristics. Adequate anesthetic management including neuromuscular blockade (NMB) is essential for airway management procedures and to allow controlled ventilation. From a surgical point of view optimal visceral exposition in order to minimize surgical times and complications is important. Although in permanent debate, neuromuscular blockade monitoring (NMM) throughout the whole surgical procedure permits to administer the precise dose of NMBA, and, at the end of the procedure, the adjusted dose of the reversal drug to allow safe extubation with adequate spontaneous ventilation reassumption, avoiding RNMB. Muscle relaxation is a standard during thoracic surgery. Most of the invasive surgical procedures benefits from NMBA use, as those performed by means of thoracotomy, sternotomy, video-assisted thoracoscopy

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(VATS), and other as rigid bronchoscopy or echobronchoscopy. Notwithstanding, a few studies or case series described thoracic procedures performed without muscle relaxation with good results [3].

NMBA use allow airway management, manipulations and tracheal intubation decreasing pharyngolaryngeal and tracheobronchial related lesions. On the other hand, mechanical ventilation is allowed, as is the surgical field access and closing. Muscle contractions due to electric scalpel are attenuated, as were patient's involuntary movements. During surgery, diaphragm and reflex coughing movements can induce dangerous situations, mainly when surgeons work near vital anatomical structures as bronchus, great vessels, heart or nerves, and this is the one of the causes why abdominal muscles and diaphragm should be completely relaxed. In addition, during thoracic surgery selected ventilatory strategies will be necessary to improve gas exchange, for instance recruitment maneuvers, in several patient positions—supine, prone, lateral decubitus—after postural changes, after endotracheal tube repositioning or change, and once one-lung-ventilation started and finished. Before these maneuvers are carried out, profound neuromuscular relaxation is recommended as complete thoracic muscles and diaphragm paralysis would permit to open collapsed alveoli without the opposition of this component (the "respiratory muscles") of the thoracic cage. One more reason that justify profound NMB is the pre- or intra-operative use of bronchofiberscopes or other intraluminal devices. These are frequently used to check for the correct placement of the double lumen endotracheal tubes or bronchial blockers, and can induce unexpected movements, cough or bronchial secretions or hemorrhage.

It should be mentioned VATS, procedures that can need profound NMB. There is evidence that profound NMB improve surgical conditions during abdominal laparoscopic surgery [4]. This might be extended to thoracic surgery, but studies are necessary to confirm this. Classical textbooks do not address this topic in depth, and recent articles evaluating intraoperative conditions and outcomes in oncologic thoracic surgery and postoperative cognitive dysfunction does not take into account NMB management [5]. One additional point of view is that it seems that anesthesiologists themselves do not consider important the use of the NMBA (and the way it should be used), or the NMB reversal in thoracic surgery.

In this chapter we will try to review these topics, and suggest to change these beliefs.

14.2 Aspects of Interest for the Clinician About the Neurobiology of the Neuromuscular Junction

The interested reader can found extensive information in Naguib et al. [6].

The main components of the neuromuscular junction are the motor nerve ending and the muscle fiber (muscle cell). In between are the cell membranes of both separated by the synaptic cleft, that has a width of 20–50 nm. A Schwann cell covers the synaptic cleft, because at this level there is no myelinated covering. In the adult full developed neuromuscular junction, every muscle cell use to receive only one nerve

ending. In the motor nerve ending there are vesicles near the cell membrane (active zone) containing the neurotransmitter acetylcholine (ACh), whereas in the muscle membrane there are ACh receptors (AChR). The synthesis and storage of neurotransmitter occurs in the vesicles (every vesicle containing 5000–10,000 molecules); in addition, there are a reserve of ACh vesicles in the cytoplasm and out-of-the-active zone storage.

In the motoneuron an action potential is generated that arrives at the nerve ending. Through voltage-gated calcium channels opening in the nerve membrane and calcium inflow, in the active zone around 200–400 vesicles fused with the cell membrane and released ACh to the synaptic cleft. The neurotransmitter binds to the AChR producing an ionic flux through the channel, this causing electric minipotentials that finally originates a threshold electrical potential being transmitted through the muscle membrane. In the T-tubules (an invagination of the muscle cell membrane), calcium inflow occurs producing the contraction after activation of several intracellular mechanisms finishing in the actin-myosin interaction.

Complex mechanisms control ACh release. Both ACh and the vesicles itself are rapidly recycled. After releasing from the AChR, the ACh molecules are hydrolyzed by ACh-esterase, an enzyme anchored to the postsynaptic membrane, mainly in the synapse (grouped as three tetramers). The ACh-esterase activity is regulated, in part, by muscle activity.

The proteinic AChR (channel) that is inserted in the muscle membrane lipidic bilayer, is composed by five subunits (pentameric). In the mature adult form of the channel the subunits are one ε type, whereas in the immature embryonic-fetal and neonatal form is of γ type, the other (common) being two α, one β and one δ type. This is important because it determines physiological and pharmacological properties of the junction. For instance, this determines function in myasthenia gravis and myasthenic syndromes, both congenital and autoimmune.

There are presynaptic (pre-junctional) AChR as well. These differ structurally from the postsynaptic ones. Although not completely elucidated, it have a role in the presynaptic ACh reserve pool migration facilitation (i.e. when ACh concentration falls or after repeated electrical stimulation, as in tetanic stimulation). As the postsynaptic ones, these receptors are inhibited by non-depolarizing NMBA (this explaining, in part, fade appearing during recovery from NMB). On the other hand, extra-junctional AChR have been described in striated muscle fiber's surface.

14.3 Some Considerations on NMBA Pharmacology

From a clinical point of view there are two main families of NMBA, depolarizing and non-depolarizing NMBA [7]. Succinylcholine is the only depolarizing NMBA clinically in use at the present time. After iv injection fasciculations use to precede the clinical relaxation, that in a proportion of patients might cause postoperative myalgia. Its onset time is rapid as is clinical recovery, whereas economic cost is low, these factors favoring wide utilization. However, experts and some studies recommend to restrict the use to selected cases for rapid sequence induction of anesthesia.

From a neurophysiologic point of view, the depolarizing block does not show fading, thus neuromuscular monitoring (NMM) is not useful in the recovery phase. Moreover, its action cannot be reverted with anticholinesterase drugs. In cases where pre- and extra-junctional immature AChR exists, hyperpotassemia can appear after succinylcholine that is life-threatening. The readers are referred to textbooks and review articles that address other adverse effects and contraindications.

Non-depolarizing NMBA are classified according to chemical structure in aminosteroidal and benzylisoquinolines. Its mechanism of action is as competitive antagonists of ACh in the AChR but, opposite to depolarizing agents, impeding the channel to open. These agents inhibit presynaptic AChR as well. From an electrophysiological point of view fading and post-tetanic potentiation are characteristic of the non-depolarizing block.

The neuromuscular system has a great safety margin. In fact, 70–90% of receptors can be blocked without affecting function. So, in order to start the pharmacologic action the NMBA should be administered in high doses; afterwards, as there are occupied AChR low doses use to be enough for NMB maintenance both as bolus re-injections of iv continuous infusions. Again, at the end of the surgical procedure more than 70% of receptors can be occupied without apparent clinical signs of block. A small ACh or NMBA plasma changes (both absolute or relative) could induce relevant signs of curarization.

Aminosteroidal NMBA are represented by vecuronium and rocuronium (pancuronium, pipecuronium and rapacuronium being other drugs in this group). The chemical structure contains a steroidal nucleus. These drugs do not induce significant histamine release. Plasma drug elimination is preceded by hepatic metabolism, that produces desacetyl metabolites, carrying diverse degrees of activity. Kidney elimination follows. Renal and hepatic insufficiency can have a role in drug accumulation due to slow plasma clearance. Benzylisoquinolines included atracurium besylate and cis-atracurium (one of the isomers of atracurium). These molecules induced a dose-dependent histamine release that can cause vasodilation and tachycardia. Metabolism occurs mainly via Hoffmann degradation, a non-enzymatic chemical process, that consists in spontaneous degradation at physiological pH and temperature, and by ester hydrolysis, both being independent of renal and hepatic function. Thus dose adjusting is not necessary in patients with renal or hepatic alterations. There are no active metabolites, but laudanosine, an inactive metabolite that is cleared by kidney, is potentially neurotoxic at high doses (Table 14.1 and Fig. 14.1).

Regarding reversal of the NMBA actions, spontaneous reversal is possible allowing the drug metabolism and elimination, but pharmacologic reversal is frequently used. ACh-esterase antagonists or aminosteroidal selective binding agents can be used. The firsts ones act blocking the ACh lysis, thus increasing available molecules in the synaptic cleft (i.e. an indirect mechanism). This is the main reason why ACh-esterase inhibitors require some degree of spontaneous recovery. The drugs used are neostigmine (most used), pyridostigmine and edrophonium. Moreover, these drugs

Table 14.1 Pharmacological characteristics of the most used NMBA

	ED 95 (mg/kg)	Induction dose (mg/kg)	Maintenance dose (μg/kg/min)	Start time (s)	Duration of action (min)
Atracurium	0.2–0.25	0.5	4–12	150–200	20–30
Cis-atracurium	0.05	0.1	2.3–3	150–180	20–30
Rocuronium	0.3	0.6–1.2	9–12	60–75	20–30
Vecuronium	0.04	0.6	0.8–1.4	120	30–40

ED effective dose

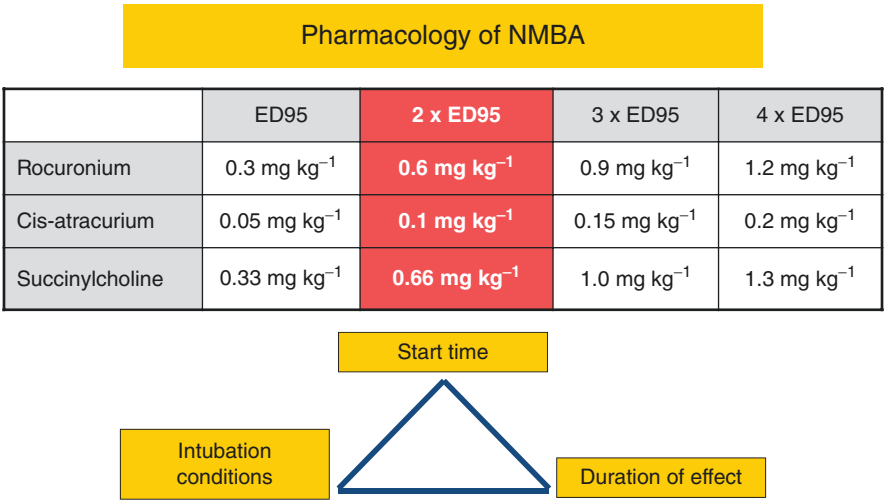

Fig. 14.1 Schematic comparison of the potency of NMBA in clinical use. *ED* effective dose. (Modified from Sparr HJ. Drugs 2001; 61: 919–942)

act outside the synapsis in muscarinic receptors (producing bradycardia, bronchoconstriction, miosis, gland hypersecretion and sialorrhea), and this is because parasympatholytic drugs (atropine or glycopyrrolate) are required to be administered together. Sugammadex is a gamma-cyclodextrin that has been designed to encapsulate the aminosteroidal drugs in plasma, thus creating a gradient with the synaptic cleft and facilitating NMBA release from the AChR, leaving it free for ACh interaction. No spontaneous recovery is required provided the drug dose administered is adapted to the existing block deepness. As it has no anticholinesterase activity, no parasympatholytics are required. The drug has few hemodynamic adverse events. In Fig. 14.2 the mechanism of action is summarized.

NMM is based in electrical stimuli application to a peripheral nerve recording the muscle response (Table 14.2). This has an important role to control the clinical evolution of the NMB and recovery. In Fig. 14.3 the standardized terms are showed.

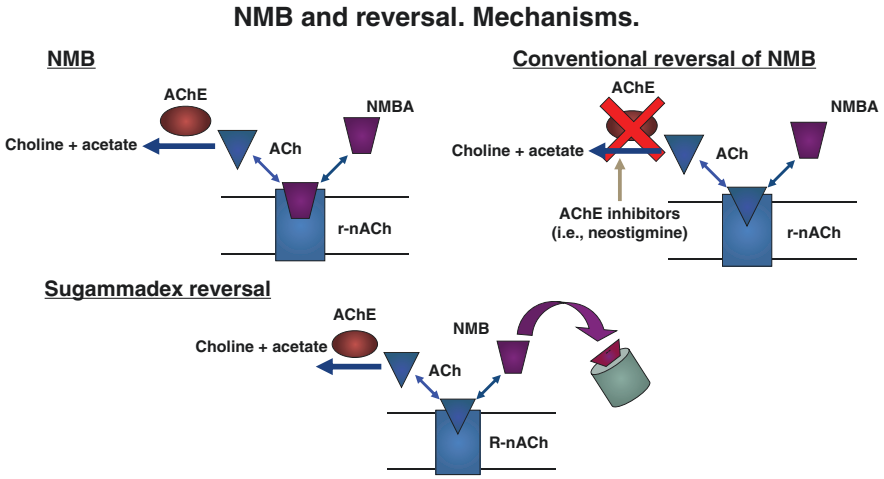

Fig. 14.2 Mechanism of action of NMBA reversal drugs. The process of the block by a non-depolarizing NMBA of a nicotinic AChR is showed. Indirect reversal by an anticholinesterase (right) and direct reversal by means of sugammadex (lower part of the figure) is showed as well. *ACh* acetylcholine, *AChE* acetylcholinesterase, *R-nACh* nicotinic Ach receptor. (Modified from Adam JM et al. J Med Chem 2002;45:1806–1816)

Table 14.2 Neurostimulation patterns and muscle responses of the different stimuli used in clinical practice

Single twitch: variable frequency stimulation (1–0.1 Hz). This stimulus is useful if a reference is obtained.
TOF: four stimuli 2 Hz (0.5 s), separated of the following one at least 10 s are applied and responses registered. Once NMB is stablished the T4/T1 responses relationship can be used (TOF ratio, TOFr). It is useful to evaluate the start and recovery times of NMB, as well as the NMB course; being (relatively) unuseful if profound or intense NMB occurs. It is used for subjective (with limitations) or objective evaluation/diagnosis of RNMB.
DBS: double burst stimulation, two 50 Hz stimuli separated 750 ms are applied, every one of them composed of three impulses separated 20 ms. It is used for visual or tactile subjective monitoring.
Tetanic stimulus: high frequency stimulus (50–200 Hz) of 5 s is applied. It is combined with several single twitch stimulus (10–20) to evaluate postetanic facilitation (postetanic count, PTC). It is used when no TOF responses are seen (profound NMB).

Mechanomyography, electromyography, acceleromyography, kinemyography and phonomyography have been used to register the responses. Acceleromyography is the most used in clinical practice.

14.4 Characteristics of Patients Under Oncologic Thoracic Surgery Related to Muscle Function

The diseases behind thoracic surgical procedures are diverse as are the patients suffering the diseases. They can vary from a young adult otherwise healthy patient with repeated pneumothoraces, apical bullae or hyperhidrosis, to the middle aged or

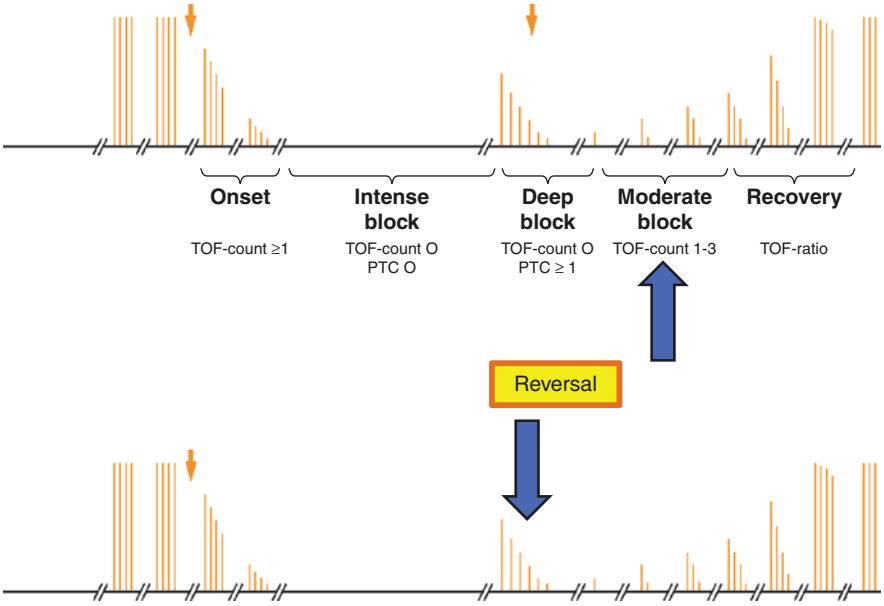

Fig. 14.3 Response to electrical stimulation during a typical surgical procedure with non depolarizing NMBA. The usual standardized terminology is showed

older patients with an oncologic bronchopulmonary process requiring aggressive therapy. Frequently cancer is the main cause of the surgical indication, and the subjects can be debilitated and with associated malnutrition. They are, as a general rule, heavy smokers or with smoking antecedents, with altered respiratory spirometry due to pulmonary obstructive or restrictive diseases or both.

It has been reported that thoracic surgery is the type of surgery most related with postoperative pulmonary complications (PPC). On the other hand, due to life long expectancy in economically developed countries, there is an increasing number of patient candidates to high complexity surgery, no matter the age they have.

From an surgical perspective, an adequate NMB should be achieved, followed by complete respiratory muscle function recovery in order to early and safely extubate the patient's trachea, thus avoiding complications [8]. As patient's age increase cardiac output is reduced, and hepatic and kidney functions are affected; moreover, muscle mass decrease and body temperature is regulated worse, especially over 70 years (frailty syndromes) [9–11].

A proportion of thoracic surgery patients have previous (or basal) muscle weakness and respiratory dysfunction that would be intensified by the surgery-associated inflammation together with pharmacokinetic and pharmacodynamic alterations of perioperative drugs, typically extending drug's clinical effects. Age is an independent predictive factor of perioperative mortality, mainly in urgent surgery and if the patient has organ systems affected. Preoperative respiratory insufficiency is especially important in this sense. The specificities of the respiratory system of elderly patients make it prone to postoperative complications: loss of pulmonary elasticity, thoracic rigidity, alveolar surface decrease, residual volume increase, expiratory

flow decrease, and increased heterogeneity in the ventilation-perfusion relationship (inspiratory muscle force diminution with increased work of breathing) [12].

In addition, a positive perioperative fluid balance, the surgical positioning, or increases of the metabolic demands can produce respiratory failure. Sarcopenia, a characteristic of the frail elderly patient, can strongly affect neuromuscular function. Partial blockade increases pharyngolaryngeal dysfunction from 37% to 71% in the elderly [13], but in other patients as well, thus, upper airway obstruction susceptibility or pulmonary aspiration risk are frequent.

14.5 Muscle Relaxation Requirements During Thoracic and Esophageal Surgical Procedures

One of the features of the clinical course of NMB is that it is unpredictable [2], because it depends on several factors, both patient related (age, sex, physical status, associated comorbidities, alterations in the ACh physiology, altered number or responsiveness of the AChR in the motor end plate, etc.), and drug related (as the selected NMBA itself). In addition, other conditions, pharmacologic characteristics, mode of NMBA use, particular patient populations, or direct drug use-related problems, are needed to be known in depth by the specialist.

The so called profound NMB is useful during pulmonary resection surgery [14], allowing the procedure, avoiding risks in complex surgical approaches or in the dissection near to vital anatomical structures, avoiding the physiological responses to airway manipulations, including repeated bronchofiberscopic explorations, and allowing adequate recruitment maneuvers and diaphragm muscle relaxation, a muscle resistant to paralysis. Moreover, experts recommend that degree of block in this surgical indication [15].

Some considerations about the pharmacophysiology of the muscles related to respiration and ventilation follows. Laryngeal adductor muscles, the diaphragm and abdominis rectus muscles are among the most resistant to NMBA effects, whereas muscles involved in swallowing and airway protection are very sensitive to NMBA. Clinical NMB starts in the diaphragm and laryngeal muscles before than in the adductor pollicis (the most used for monitoring), due to better vascular supply (and density of AChR, among other factors) compared to other neuromuscular peripheral systems, thus receiving a higher NMBA mass (number of molecules). With this in mind it is easy to understand why, in thoracic surgery (and other types of surgery as well) the NMB should involve the diaphragm, that is, a profound muscle relaxation is needed. The NMBA dose required to completely block these muscles use to be 1.5–2 times those to block the adductor pollicis [16]. In the recovery phase, the diaphragm recovers its function before, but at the same time (same plasma levels of NMBA) monitoring of adductor pollicis show absence of response. This means that for optimal relaxation a very profound one should be obtained [17], and that the response to NMM can confound and/or should be correctly interpreted.

From the NMB management perspective most of the esophageal surgical procedures requires an approach similar to that of thoracic ones.

Especially the esophageal cancer therapy needs a multidisciplinary management as it involves radiotherapy and chemotherapy in addition to a wide surgical resection. However, neoadjuvant treatment, radical resections and the extension of operative lymphadenectomy can increase perioperative morbimortality. Esophagectomy is a complex procedure with high morbimortality. Combined thoraco-abdominal approach is one of the factors contributing to PPC that are frequent after this type of surgery. Moreover, one lung ventilation is another cause of acute lung injury during thoracic surgery [18].

Several surgical techniques have been described, as the transhiatal and transthoracic ones. The first one allows the whole mobilization and resection of the intrathoracic esophagus and regional lymphatic nodes (but limited to the superior abdomen and inferior mediastinum) through two incisions, abdominal and cervical, thus avoiding thoracotomy. Transthoracic approaches consist in right thoracotomy (the patient sited in left lateral decubitus) plus laparotomy, or a thoracoscopic plus laparoscopic approaches. These permit excellent views of the tumor, allowing a more extensive lymphadenectomy compared to transhiatal technique and better local control of the disease. Following esophagus resection the anastomosis is performed at intrathoracic level (Ivor-Lewis) or cervical level (McKeown). From the anesthesiologist point of view, one lung ventilation is required with double lumen endotracheal tubes or bronchial blockers in order to collapse the lung in the operating side.

Recently, a minimally invasive approach in the prone position has been described. Of course, the anatomical exposure of the mediastinum became modified. Posterior structures became superior, and the anterior ones, inferior. Although prone thoracoscopy was first described in 1992 by Cushieri, the spread to practice is recent. Esophageal dissection is made easier because the posterior mediastinum is found in the superior part of the surgical field, and blood and secretions go down by gravity, optimizing esophagus view. This way, surgical times decrease and there are few respiratory complications.

A series including 130 patients [19] showed results supporting this. Surgical outcomes were non inferior compared to other minimally invasive approaches and open conventional surgery. Postoperative mortality decreased to 1.54%, there were few hospital readmissions and a low incidence of postoperative pneumonia. It was suggested that this technique would replace the classical one. In addition to the technical advantages, the prone position improved oxygenation through more homogeneous ventilation/perfusion relationship. However, selective intubation is needed as is one lung ventilation (with its inherent problems). Access to the airway or endotracheal tube manipulations can be difficult. But gravity itself facilitates the retraction of the right lung from the surgical field and when combined with low pressure induced pneumothorax (6–8 mmHg) allow to perform the surgery using single lumen tubes and two lung ventilation (Fig. 14.4).

The anesthesiologist should combine strategies to diminish morbimortality, as preoperative optimization, protective pulmonary ventilation, fluid restriction, epidural analgesia and postoperative care. In fact, in some settings, patients are included in a complete fast track enhanced recovery surgery pathway.

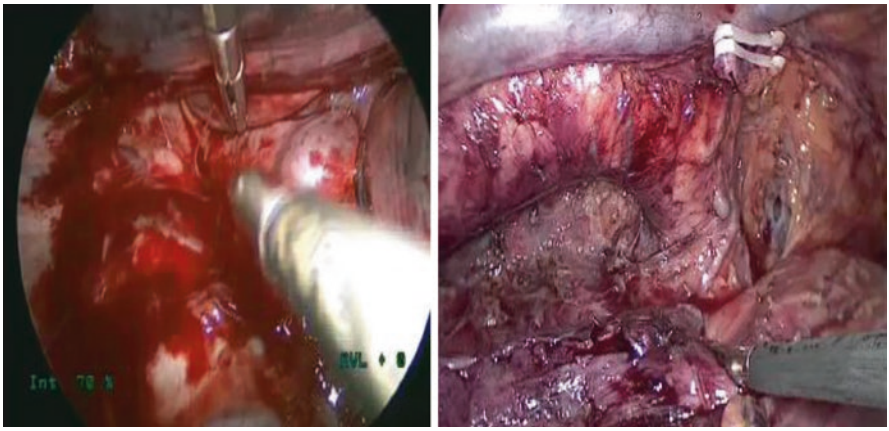

Fig. 14.4 Comparison of the surgical field during thoracoscopy for esophagectomy performed in left lateral decubitus (left) versus prone position (right)

Intraoperatively, in addition to standard monitoring, continuous cardiac output monitoring, active warming and neuromuscular monitoring are mandatory. Initial protective pulmonary ventilation consists in low VT (8 ml/kg), allowing for normocapnia, with FiO2 0.5, and PEEP 5 cmH_2O. Careful positioning is recommended with additional protection. Profound NMB throughout the procedure permits ventilation and positioning. After trocar's insertion capnothorax is induced until 8 mmHg are reached. A 30 s apneic maneuver allows partial right lung collapse. During this phase, volume controlled ventilation with 5 ml/kg VT, FiO2 0.8, 12–14 bpm and PEEP of 5 cmH_2O is recommended. If SaO2 decrease <90%, the tube position should be checked, FiO2 increased (0.8–1), and other possibilities should be taken into account, as hemodynamic alterations (hemorrhage, hypotension or low cardiac output due to other causes), otherwise, PEEP can be increased until intracavitary pressure level, i.e. 6–8 mmHg, is reached. If hypoxia persists, complete bipulmonary ventilation can be needed for a few cycles (the trocars should be withdrawn and the capnothorax stopped), and recruitment maneuvers carried out. Vasoactive drugs are usually required during the operative period. Apart from epidural anesthesia and analgesia, if possible, opioid free anesthesia is recommended. After surgery, early extubation is recommended, usually in the intensive care unit. Epidural analgesia, restrictive fluids, and enteral nutrition should be promptly initiated.

14.6 Recovery from Neuromuscular Blockade After Thoracic Surgery

As it has been stated before, recovery of the respiratory function is essential after thoracic surgery, because, in addition to secondary neuromuscular involvement (muscle transection, drugs, previous physical status, frailty) the surgery is performed on the respiratory organs.

Table 14.3 Clinical signs of RNMB observed in awake patients [modified from [72, 73]]

– TOFr 0.7: reduced ventilatory response to hypoxia, diplopia and ptosis, difficult swallowing, difficult in bite maintaining. Feel of discomfort. Speaking requires great effort.
– TOFr <0.9: alteration of respiratory, and pharyngeal function and airway protection.
– TOFr 0.9: discoordinated swallowing with aspiration episodes, decreased function of the superior esophageal sphincter, discoordination of laryngeal constriction muscles and esophageal sphincter; diplopia, disartria and difficult to swallow. Pharyngeal dysfunction and discoordinated deglution in some volunteers persisting more than 15 min.
– TOFr 0.91–0.95: recovery of respiratory function in most of subjects.
– TOFr 1: some volunteers experiment swallowing difficulties. Few subjects showed altered respiratory function.

It is important to know the definition of RNMB. There is enough scientific evidence that RNMB, defined by a "train-of-four" stimuli response ratio (TOFr) <0.9, increases the risk of PPC, length of ICU and in-hospital stay, and healthcare costs. It was demonstrated that a TOFr 0.7 does not guarantee sufficient muscle recovery, and there was consensus in considering that a TOFr of at least 0.9 should be reached. By subjective monitoring it is difficult to appreciate at a TOFr 0.3–0.4 tactile or visual fade to TOF stimulation (Table 15.3). Another type of stimulus, the double burst stimulation (DBS) allow to detect TOFr 0.6, but this is again insufficient to exclude RNMB [20].

Despite this, provided repeated boluses of NMBA (or infusion) have been administered during surgery, recovery of TOFr >0.9 does not exclude some alteration of the neuromuscular function, and muscle weakness could persist [21]. This suggest that a new RNMB standard will be foreseen [22] (Table 14.3).

From a pathophysiological point of view there is direct pulmonary function alteration due to RNMB [23]: forced vital capacity and peak expiratory flow decreases, chemosensitive carotid receptors sensitivity to hypoxia decrease [24], there is pharyngeal and upper esophageal sphincter dysfunction [25], and this can translate into postoperative aspiration pneumonitis [26, 27].

Monitoring use spread permits to decrease RNMB and the frequency of severe respiratory adverse events during transport to the PACU and PACU stay. Moreover, this facilitates early tracheal extubation in the operating room, thus allowing to start spontaneous ventilation. Patient's safety is improved and associated morbidity decreased [28–30].

The published incidence of RNMB vary between 4% and 57% [31]. Furthermore, despite evidence supporting its use, continuous or intermittent NMM is not performed by an important proportion of anesthesiologists during daily practice. NMB was involved in at least 6% of re-intubations in the PACU in a study involving more than 100,000 patients [32]. Incomplete recovery during the immediate postoperative period, gastric contents aspiration, respiratory failure or re-intubation, and prolonged PACU stay were found to be associated to NMBA use [8, 31, 33]. In a prospective observational study, high risk surgery was related to RNMB and reintubation was necessary in a case of thoracic surgery [34].

Factors related to prolonged NMB, RNMB and pulmonary complications are summarized in Tables 14.4, 14.5 and 14.6.

Table 14.4 Factors related with prolonged NMB

Drug interactions (Table 14.5).
Patient's factors: age and sex (until 30% higher sensibility to NMBA in women).
Clinical situation or comorbidities: renal or hepatic insufficiency, intrathoracic septic processes (high atracurium resistance), cholestasis, hypothyroidism, cardiac output alterations, immaturity of biologic systems, alterations in number or sensitivity of AChR, weight or BMI, obesity, genetic factors, moment of day, unexplained variability (interindividual or in the same person), enzymatic induction/inhibition, diseases (Table 14.7), Vd and pharmacokinetic variations, respiratory and metabolic acidosis.
Other perioperative factors: no drug reversal, normovolemic acute hemodilution, hypothermia.

Table 14.5 Drugs related with NMB course modifications

NMBA potentiation: anxiolytics (benzodiazepines, chlorpromazine), local anesthetics, opiates (fentanyl, morphine), hypnotics (thiopental, propofol, ketamine), halogenated drugs, antibiotics (aminoglucosides, clindamicine, tetraciclines, vancomicyn, metronidazole, cholistine, polymixine B), magnesium, lytium, calcium channel blockers, beta-blocking drugs, vasodilators (nitroglicerin), adrenergic agonists (salbutamol, ephedrine), immunosupresors (cyclophosphamide, cyclosporine), dantrolene, diuretics (furosemide, tiazide), antihystamines, corticoids, "natural medicine products".
Halogenated agents (NMB potentiation in order of magnitude; -depending of duration of anesthesia and concentration as well-): desflurane, sevoflurane, isoflurane, halotane.
NMBA: combinations, perfusion, reinjections.
NMBA action antagonism: phenytoin, carbamazepine, valproate, teophyline, aminophyline, ranitidine, corticoids, potassium, calcium.

Table 14.6 Factors related to RNMB

Patient and procedure related factors (more prevalent)
– Advanced age[a]
– Women[a]
– Duration of surgery (prolonged)
– Procedures with short duration
– Anesthesiologist experience[a]
– Temperature (low)
– Short interval last NMBA reinjection to reversal
– Short interval reversal to extubation
– Major surgery[a]
– Long duration NMBA
– Benzylisoquinoline NMBA[a]
– Halogenated anesthetic agents
– No intraoperative neuromuscular blockade monitoring[a]
– No drug reversal
– Reversal with neostigmine
Predictive factors of RNMB
– Atracurium (versus rocuronium)
– Halogenates
– Absence of reversal (versus neostigmine or sugammadex)
– Reversal with neostigmine (versus sugammadex)

[a]Studies showing contradictory or variable results. Modified from [15, 31]

Regarding the above mentioned problems, it can be understood the role of an adequate and complete reversal of the effects of the NMBA. Until few years ago, recommendation was to administer anticholinesterases after some degree of spontaneous recovery of the neuromuscular blockade is achieved. In patients with profound NMB, due to the ceiling effect (doses higher than 0.07 mg/kg does not produce increased effect) and to the different action times and duration, recurarization is possible. At least 10–15 min are necessary to TOFr 0.9 be reached provided the reversal drug is administered when 2 TOF responses appeared in the monitor. On the other hand, although somewhat controversial, it has been demonstrated that if high to moderate anticholinesterase drug doses are administered with shallow block, the NMB could be strengthened and airway collapse follow because of inadequate laryngeal muscles recovery. This is another reason why neostigmine administration should be guided by objective NMM, and injected when at least the four TOF response is observed [35–38]. In the thoracic surgery patient during the recovery phase, these aspects are of special interest.

Sugammadex induces a more rapid reversal, even from a profound NMB (when aminosteroidal NMBA are used), anticholinergic drug association is not necessary and RNMB is significantly decreased. Again, the dose depends on the NMB deepness, that is estimated by means of objective quantitative monitoring. As a general rule, and as per package insert, 2 mg/kg are recommended with T2 reappearance, 4 mg/kg when there are 2 PTC responses (profound block)—Table 14.3—and 16 mg/kg immediately after an induction dose of rocuronium or vecuronium (possible intense block, in the clinical context of an emergent 'cannot intubate cannot ventilate', or 'cannot oxygenate' situation). Moreover, in a pilot study, Amorim et al. [39] observed that after sugammadex the physiological and nociceptive recovery improved, with better patient's satisfaction. Sugammadex allows to maintain a profound block until near the end of the surgical procedure inducing a quick reversal not delaying recovery. Recovery of a typical NMB course is showed in Figs. 14.5 and 14.6.

Notwithstanding, the feasibility of partial reversal (as in intraoperative neurophysiological monitoring) [40] and low dose sugammadex in the case of high degrees of spontaneous recovery [41, 42] are under investigation. Additional studies analyzing cost-benefit balance are warranted.

14.7 Day Case Thoracic Surgical Procedures

Ambulatory surgery indications are now increasing, decreased costs and in-hospital beds limitation, added to improved perioperative safety are among the causes. An implication of the previous statement is that surgical techniques and drugs used in the anesthetic procedure might add to the efficacy—rapid recovery—together with low adverse or residual effects (with optimization of perioperative nausea and vomiting and pain prophylaxis and treatment). Thoracic surgical procedures include long procedures under general anesthesia and ambulatory explorations or invasive techniques. NMBA can interfere with organizational aspects, as well as with the

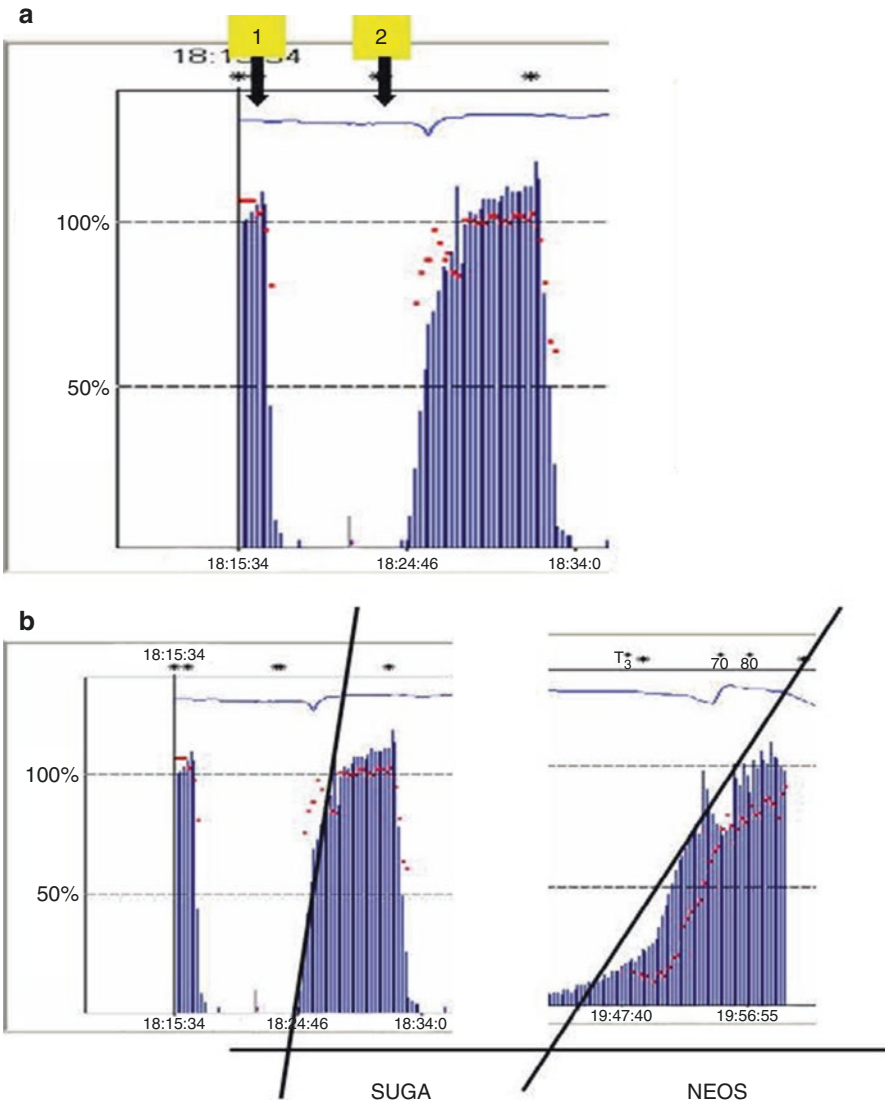

Fig. 14.5 Real time graphic representation (TOF Watch SX) of a typical course of NMB. Blue lines show TOF high every 15 s. (**a**) Rocuronium 1.2 mg/kg (1) and rapid reversal after sugammadex 16 mg/kg administered after intense block (2). (**b**) The TOF slope after reversal with sugammadex (SUGA) and neostigmine (NEOS) is showed for comparison in two different surgical procedures

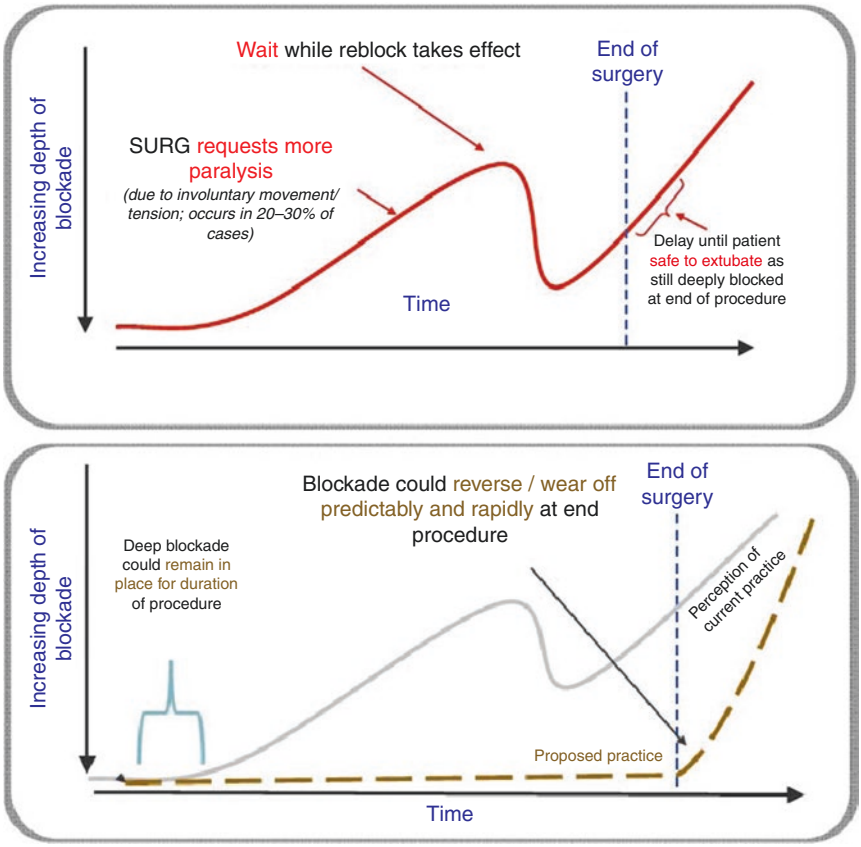

Fig. 14.6 Schematic representation of standard NMB management with gradual recovery and re-block near end of surgery, with subsequent delayed recovery or inappropriate surgical conditions (upper part) compared with maintenance of profound NMB throughout all the surgical procedure followed by rapid reversal with sugammadex

postoperative wellbeing of the patients. Avoiding these problems and facilitating a rapid and safe recovery is mandatory. Use of NMBA in some circumstances is neither counter-productive nor counter-indicated, because it is important do not forget the adverse effects of not using NMBA.

14.8 Thoracic Procedures in Patients with Neuromuscular Diseases and Rare Diseases

Patients suffering from myasthenia gravis presented with increased sensitivity to non-depolarizing NMBA and a variable response to depolarizing NMBA. Typical surgical procedures comprised thymectomy with or without thoracotomy, and surgery with propofol based total intravenous anesthesia with no NMBA has been suggested and

performed for the whole procedure including tracheal intubation. However, a common fact in almost all hereditary and acquired neuromuscular diseases, is the variable response to NMBA [43, 44]. NMBA can be used with specific quantitative NMM. Exceptions are diseases affecting mainly the nervous system, that sometimes precludes this type of monitoring. Also, sugammadex use is considered safe and has been used in a variety of these diseases. In Tables 14.7, 14.8, 14.9, and 14.10 the recommendations for the management of these group of diseases are summarized. Readers can find additional information in www.orphananesthesia.eu and www.orpha.net.

Table 14.7 Recommendations for anesthesia of patients affected with neuromuscular diseases

Preoperative period (previous neuromuscular status, as well as respiratory, cardiac and nutritional)[a,b]
Assess bronchoaspiration risk. Prophylaxis.
Avoid sedatives in premedication.
Assess dificult intubation.
Consider rocuronium-sugammadex.
Respiratory physiotherapy should be initiated.
Intraoperative period
If possible use regional anesthesia. However, muscle weakness should be considered if high neuraxial blocks or blocks affecting diaphragm are used (no important muscle weakness related with epidural anesthesia has been reported, specially during thoracic surgery for myasthenia gravis).
General anesthesia.
Consider difficult tracheal intubation.
Consider techniques without NMBA.
Avoid succinylcholine.
NMB course should be monitored. NMBA should be dosed by this guidance.
Avoid anticholinesterases.
Consider rocuronium-sugammadex.
Avoid hypothermia (central temperature).
Postoperative period
Adequate analgesia (epidural, paravertebral).
Ensure extubation criteria.
Early enteral or parenteral nutrition.
Respiratory physiotherapy.

[a]Patients with myasthenia, optimization of the preoperative treatment by a neurologist
[b]Cardiac evaluation in patients with suspected or diagnosed cardiopathy: clinical-functional, echocardiography, etc.

Table 14.8 Recommendations for tracheal extubation of patients under thoracotomy that suffer a neuromuscular disease

Extubation in the operating room should be attempted. This should be individualized.
If possible, avoid reversal with neostigmine.
Consider rocuronium-sugammadex.
A TOFr of 1 guarantee complete recovery of the diaphragm.
Assess swallowing and cough before extubation.
Maximal inspiratory force −20 cmH_2O attained, VT 1000 ml, PaO2 250 mmHg with FiO2 1 (but preoperative status of the patient should be taken into account).

Table 14.9 Thymectomy in myasthenia gravis

– Preoperative optimization.
– Individual evaluation of the neuromuscular status (including possible alteration of the medullary driven muscle respiratory function).
– Preferably endoscopic surgery vs. cervicotomy vs. broaden sternotomies or thoracotomies.
– Avoid NMBA[a] and neostigmine[b].
– Monitoring of NMBA[a].
– Combined epidural-general anesthesia, postoperative analgesia should be ensured.
– Avoid NMBA-halogenated agent (use of sevoflurane and desflurane if possible).
– Early tracheal extubation.

[a]Use vecuronium, rocuronium, atracurium, cis-atracurium. Sensibility to non depolarizing NMBA does not predict postoperative respiratory insufficiency
[b]Controversial, dose-dependent

Table 14.10 Summary of the main alterations in the response to NMBA with clinically important features of the most frequent neuromuscular diseases

Disease	NMB[a]	Succinylcholine[a]	Risk of aspiration	Central respiratory depression	Cardiac alterations	Disautonomy
Superior motoneurone	DS	IS, >K	High	Yes	No	Yes
Amyotrophic lateral sclerosis	IS, AR	IS, >K	High	Yes	No	Yes
Multiple sclerosis	AR	IS	High	No	No	No
Denervation	AR	IS	Normal	No	No	No
Polineuropathies	IS, AR	IS, >K	High[b]	No	Yes	Yes
Myastenia gravis	IS	DS, AR	Moderate	No	Yes	No
Myastenic syndromes	IS	IS	Normal	No	No	No
Miotonic syndromes (Steinert)	AR, N	IS, >K	High	Yes	Yes	No
Muscular dystrophies (Duchenne)	IS, AR	IS, >K	High	No	Yes	No

[a]*DS* decreased sensibility (low intensity and/or duration of NMB), *IS* increased sensibility (higher intensity and/or duration of NMB), *AR* altered response in a variable sense, *N* normal response
[b]Variable depending on the patient. K: potassium

14.9 Neuromuscular Blockade and Invasive Bronchology (Bronchoscopy and Echobronchoscopy-EBUS)

Indications and requirements for this invasive explorations are not the aim of this chapter. Flexible and rigid bronchoscopic explorations are essential to visualize and access the airways, both for diagnostic and therapeutic procedures. General anesthesia with NMB is frequently employed for rigid bronchoscopy, in the operating

room or in the endoscopic explorations area. Total intravenous anesthesia is the most used technique. To insert the devices used, succinylcholine with or without priming with non depolarizing NMBA can be used, but spontaneous ventilation is sometimes preferred (for instance in some foreign body obstructions extraction or vocal cords evaluation). A non depolarizing NMBA adds safety for the procedure, and if used, pharmacological reversal is indicated. In some environments a laryngeal mask is inserted as a step to extubation in the recovery phase. More recently echobronchoscopy with or without needle tissue aspiration (endobronchial ultrasound-transbronchial needle aspiration, EBUS), became an essential tool for bronchopulmonary cancer, as well as mediastinal masses as tumors or adenopathies diagnosis or staging. Pneumologists and thoracic surgeons use to be the professionals involved and the ultrasound probe can be lineal or radial. Moreover, in some obstructive entities, laser resection could be needed. These approaches can substitute or complement mediastinoscopy, mediastinotomy, extended cervical mediastinoscopy or videothoracoscopy. In some series more than 60% of the procedures were carried out with profound sedation or general anesthesia, and sustain specific complications (general rate is <2%; and hemorrhage requiring intervention, pneumothorax, airway lesions and persistent hypoxia occurs 0.1–0.5%, and respiratory failure in the first 24 h in 0.2%). The duration of the procedures was >60 min in the 50% of the cases (in experienced services) and use to be followed by bronchoalveolar lavage. Muscle relaxation (together with general intravenous anesthesia) can be indicated in long lasting procedures or if anatomical at risk areas should be accessed.

14.10 Postoperative Pulmonary Complications: The Role of (Neglected) Residual Neuromuscular Blockade

As stated in the introduction, PPC after general anesthesia are frequent. These determined the immediate postoperative outcomes in an important proportion of patients, and perhaps some medium- or long-term outcomes. Respiratory complications are multifactorial, but it is possible that RNMB take part in the genesis of these complications in at least two ways: as the main cause, or by adding to other factors. In previous sections of this chapter other factors involved have been detailed, linked to thoracic procedures.

A TOFr <0.9 determines and is the diagnostic of RNMB. However, a TOFr <0.7 was first used. Controversy persist in this aspect of NMB management: the TOFr used as threshold has been suggested to be changed to TOFr 1.0. On the other hand, although the TOFr was the same irrespective of the monitoring used, the usefulness and the accuracy of the different type of devices and stimuli (mainly mechanomyography, electromyography and acceleromyography) is not equivalent; a TOFr <0.7, <0.9 or >0.9 can be related with no clinical effects in some patients but with residual effects clinically relevant in others; and, to be underlined, the actual TOFr measured in the clinical setting can be erroneous due to a lot of factors, as has been reported [45].

Several aspects should be taken into account when clinical issues are translated to thoracic surgery and/or thoracic anesthesia, and to high risk surgical procedures in

general. Perhaps the single item that has enough scientific evidence is that the clinical tests are unuseful compared to monitoring in the evaluation of RNMB. None of the multiple tests used in the clinical setting warrant adequate recovery of the neuromuscular function (especially if used isolated). Contrary to the general perception of clinicians, RNMB is the fourth cause of postoperative respiratory complications [32], opioids being ranked the fifth. As stated before, an important aspect of clinical practice is the real knowledge of the practitioners about the incidence of complications and adverse events (and of the complications existence itself), and that incidence in their own daily practice. It was surprising that, in a survey, anesthesiologists reported that RNMB occurrence was <1%. In addition, there is a suboptimal knowledge of both NMM and RNMB by professionals, despite recommendations issued.

Despite monitoring and reversal of the NMB, RNMB has not completely disappeared. The correct use of NMM and reversal drugs (neostigmine and Sugammadex to date) allowed to decrease RNMB and PPC. Notwithstanding, studies lacks to completely demonstrate a near zero decrease of this complication. Spread of the correct use of reversal drugs and monitoring by means of teaching could be one of the pending approaches [46].

Another aspect that has been sufficiently demonstrated at a theoretical, experimental and clinical level is the relationship between RNMB and PPC. In a subset of surgical patients, the high risk surgical patients including thoracic surgery subjects, that link has not been directly explored [34], and there is an unclear relationship with conflicting results among studies.

On the other hand, after an extensive revision of the scientific bibliography, it seems that there are at least two important aspects that have been not addressed. The first one is the lack of studies on the effects of NMBA, NMM, RNMB in thoracic surgery, and the second one is the lack of reference to neuromuscular management in capital studies of epidemiology [47], prevention/treatment [48–56] or scores development [57–61] of PPC, or were not considered to be included [62, 63]. Only in some review articles [33, 64–69] and studies [51, 58] are cited, but not analyzed in-depth. It has been suggested that inclusion of information on NMB management would be mandatory in studies on PPC [70]. In a secondary analysis of one of these studies [51] PPC incidence was higher in patients whose NMB was not pharmacologically reversed, that is, spontaneous reversal of NMB was an independent risk factor for PPC (Garutti I, Ferrando C, Mazzinari G, Díaz-Cambronero O, Errando CL, et al.; Spontaneous recovery of neuromuscular blockade is an independent risk factor for postoperative pulmonary complications after abdominal surgery. A secondary analysis of the individualized PeRioperative Open-lung approachVersus standard protectivE ventilation in abdominal surgery (iPROVE) randomized controlled trial. Eur J Anaesthesiol, in press).

14.11 Conclusions

Adequate neuromuscular blockade management is a key point in thoracic anesthesia. Intra and postoperative outcomes and patient safety are probably related with this apparently minor anesthesia-related aspect. Residual neuromuscular blockade

is a neglected aspect of the drugs used, and teaching, together with full pharmacologic reversal (as in the ongoing postoperative residual curarization-zero, PORC-zero, study; Díaz-Cambronero O, Mazzinari G, Errando CL, et al., unpublished data) could be an important step to decrease its incidence. Future studies will focus on general effects of neuromuscular blocking agents [71–73] .

References

1. Arbous MS, Meursing AE, van Kleef JW, de Lange JJ, Spoormans HH, Touw P, et al. Impact of anesthesia management characteristics on severe morbidity and mortality. Anesthesiology. 2005;102(2):257–68.
2. Alvarez Gomez JA, Arino Irujo JJ, Errando Oyonarte CL, Martinez Torrente F, Roige i Sole J, Gilsanz Rodriguez F. [Use of neuromuscular blocking agents and reversal of blockade: guidelines from Sociedad Espanola de Anestesiologia, Reanimacion y Terapeutica del Dolor]. Rev Esp Anestesiol Reanim. 2009;56(10):616–27.
3. El-Tahan MR, Regal M. Target-controlled infusion of remifentanil without muscle relaxants allows acceptable surgical conditions during thoracotomy performed under sevoflurane anesthesia. J Cardiothoracic Vasc Anesth. 2015;29(6):1557–66.
4. Ledowski T. Laparoscopic surgery and muscle relaxants: is deep block really not helpful? Anesth Analg. 2016;122(1):290–3.
5. Egawa J, Inoue S, Nishiwada T, Tojo T, Kimura M, Kawaguchi T, et al. Effects of anesthetics on early postoperative cognitive outcome and intraoperative cerebral oxygen balance in patients undergoing lung surgery: a randomized clinical trial. Can J Anesth. 2016;63(10):1161–9.
6. Naguib M, Flood P, McArdle JJ, Brenner HR. Advances in neurobiology of the neuromuscular junction: implications for the anesthesiologist. Anesthesiology. 2002;96(1):202–31.
7. Fuchs-Buder T. Neuromuscular monitoring in clinical practice and research. Heilderberg: Springer; 2010.
8. Stewart PA, Liang SS, Li QS, Huang ML, Bilgin AB, Kim D, et al. The impact of residual neuromuscular blockade, oversedation, and hypothermia on adverse respiratory events in a postanesthetic care unit: a prospective study of prevalence, predictors, and outcomes. Anesth Analg. 2016;123(4):859–68.
9. Pietraszewski P, Gaszynski T. Residual neuromuscular block in elderly patients after surgical procedures under general anaesthesia with rocuronium. Anaesthesiol Intensive Ther. 2013;45(2):77–81.
10. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Vender JS, et al. Residual neuromuscular block in the elderly: incidence and clinical implications. Anesthesiology. 2015;123(6):1322–36.
11. Partridge JS, Harari D, Dhesi JK. Frailty in the older surgical patient: a review. Age Ageing. 2012;41(2):142–7.
12. Sprung J, Gajic O, Warner DO. Review article: age related alterations in respiratory function - anesthetic considerations. Can J Anesth. 2006;53(12):1244–57.
13. Cedborg AI, Sundman E, Boden K, Hedstrom HW, Kuylenstierna R, Ekberg O, et al. Pharyngeal function and breathing pattern during partial neuromuscular block in the elderly: effects on airway protection. Anesthesiology. 2014;120(2):312–25.
14. Garutti Martinez I, Gonzalez Aragoneses F, Ramirez JM. Multimodal rehabilitation program in thoracic surgery. Arch Bronconeumol. 2015;51(4):159–60.
15. Errando-Oyonarte CL, Moreno-Sanz C, Vila-Caral P, Ruiz de Adana-Belbel JC, Vazquez-Alonso E, Ramirez-Rodriguez JM, et al. Recommendations on the use of deep neuromuscular blockade by anaesthesiologists and surgeons. AQUILES (Anestesia QUIrurgica para Lograr Eficiencia y Seguridad) consensus. Rev Esp Anestesiol Reanim. 2017;64(2):95–104.

16. Kopman AF, Naguib M. Neostigmine: you can't have it both ways. Anesthesiology. 2015;123(1):231–3.
17. Kopman AF, Naguib M. Laparoscopic surgery and muscle relaxants: is deep block helpful? Anesth Analg. 2015;120(1):51–8.
18. Lohser J, Slinger P. Lung injury after one-lung ventilation: a review of the pathophysiologic mechanisms affecting the ventilated and collapsed lung. Surv Anesthesiol. 2016;60:98–9.
19. Palanivelu C, Prakash A, Senthilkumar R, Senthilnathan P, Parthasarathi R, Rajan PS, et al. Minimally invasive esophagectomy: thoracoscopic mobilization of the esophagus and mediastinal lymphadenectomy in prone position—experience of 130 patients. J Am Coll Surg. 2006;203(1):7–16.
20. Fruergaard K, Viby-Mogensen J, Berg H, el-Mahdy AM. Tactile evaluation of the response to double burst stimulation decreases, but does not eliminate, the problem of postoperative residual paralysis. Acta Anaesthesiol Scand. 1998;42(10):1168–74.
21. Eikermann M, Gerwig M, Hasselmann C, Fiedler G, Peters J. Impaired neuromuscular transmission after recovery of the train-of-four ratio. Acta Anaesthesiol Scand. 2007;51(2):226–34.
22. Piccioni F, Mariani L, Bogno L, Rivetti I, Tramontano GT, Carbonara M, et al. An acceleromyographic train-of-four ratio of 1.0 reliably excludes respiratory muscle weakness after major abdominal surgery: a randomized double-blind study. Can J Anesth. 2014;61(7):641–9.
23. Kumar GV, Nair AP, Murthy HS, Jalaja KR, Ramachandra K, Parameshwara G. Residual neuromuscular blockade affects postoperative pulmonary function. Anesthesiology. 2012;117(6):1234–44.
24. Jonsson M, Lindahl SG, Eriksson LI. Neuromuscular blocking agents and carotid body oxygen sensing. Adv Exp Med Biol. 2003;536:135–40.
25. Sundman E, Witt H, Olsson R, Ekberg O, Kuylenstierna R, Eriksson LI. The incidence and mechanisms of pharyngeal and upper esophageal dysfunction in partially paralyzed humans: pharyngeal videoradiography and simultaneous manometry after atracurium. Anesthesiology. 2000;92(4):977–84.
26. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. Anesth Analg. 2008;107(1):130–7.
27. Norton M, Xara D, Parente D, Barbosa M, Abelha FJ. Residual neuromuscular block as a risk factor for critical respiratory events in the post anesthesia care unit. Rev Esp Anestesiol Reanim. 2013;60(4):190–6.
28. Thilen SR, Hansen BE, Ramaiah R, Kent CD, Treggiari MM, Bhananker SM. Intraoperative neuromuscular monitoring site and residual paralysis. Anesthesiology. 2012;117(5):964–72.
29. Naguib M, Kopman AF, Lien CA, Hunter JM, Lopez A, Brull SJ. A survey of current management of neuromuscular block in the United States and Europe. Anesth Analg. 2010;111(1):110–9.
30. Baillard C. [Incidence and complications of post operative residual paralysis]. Ann Fr Anesth Reanim. 2009;28 Suppl 2:S41–5.
31. Errando CL, Garutti I, Mazzinari G, Diaz-Cambronero O, Bebawy JF, Grupo Espanol De Estudio Del Bloqueo Neuromuscular. Residual neuromuscular blockade in the postanesthesia care unit: observational cross-sectional study of a multicenter cohort. Minerva Anestesiol. 2016;82(12):1267–77.
32. Lee PJ, MacLennan A, Naughton NN, O'Reilly M. An analysis of reintubations from a quality assurance database of 152,000 cases. J Clin Anesth. 2003;15(8):575–81.
33. Sabate S, Mazo V, Canet J. Predicting postoperative pulmonary complications: implications for outcomes and costs. Curr Opin Anaesthesiol. 2014;27(2):201–9.
34. Errando CL, Mazzinari G, Diaz-Cambronero O, Garutti I, Grupo Espanol de Estudio Del Bloqueo Neuromuscular. Residual neuromuscular blockade in the postanesthesia care unit. A secondary analysis of the ReCuSS. Observational cross-sectional study of a multicenter cohort. Rev Esp Anestesiol Reanim. 2017;64(7):419–22.

35. Eikermann M, Zaremba S, Malhotra A, Jordan AS, Rosow C, Chamberlin NL. Neostigmine but not sugammadex impairs upper airway dilator muscle activity and breathing. Br J Anaesth. 2008;101(3):344–9.
36. Fuchs-Buder T, Meistelman C, Alla F, Grandjean A, Wuthrich Y, Donati F. Antagonism of low degrees of atracurium-induced neuromuscular blockade: dose-effect relationship for neostigmine. Anesthesiology. 2010;112(1):34–40.
37. Meyer MJ, Bateman BT, Kurth T, Eikermann M. Neostigmine reversal doesn't improve postoperative respiratory safety. BMJ. 2013;346:f1460.
38. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Deshur MA, et al. Neostigmine administration after spontaneous recovery to a train-of-four ratio of 0.9 to 1.0: a randomized controlled trial of the effect on neuromuscular and clinical recovery. Anesthesiology. 2018;128(1):27–37.
39. Amorim P, Lagarto F, Gomes B, Esteves S, Bismarck J, Rodrigues N, et al. Neostigmine vs. sugammadex: observational cohort study comparing the quality of recovery using the Postoperative Quality Recovery Scale. Acta Anaesthesiol Scand. 2014;58(9):1101–10.
40. Errando CL, Blanco T, Diaz-Cambronero O. Repeated sugammadex reversal of muscle relaxation during lumbar spine surgery with intraoperative neurophysiological multimodal monitoring. Rev Esp Anestesiol Reanim. 2016;63(9):533–8.
41. Kopman A, Brull S. Low-dose sugammadex reversal: there is no such thing as a free lunch. Anesthesiology. 2013;119(1):10–2.
42. Schaller SJ, Fink H, Ulm K, Blobner M. Sugammadex and neostigmine dose-finding study for reversal of shallow residual neuromuscular block. Anesthesiology. 2010;113(5):1054–60.
43. Errando CL, Perez-Caballero P. Anaesthetic management in patients with Duchenne muscular dystrophy. Eur J Anaesthesiol. 2013;30(5):257.
44. Galvez Canellas JL, Errando CL, Ordonez Arana A, Falco E, Mazzinari G, Robles D, et al. [Sugammadex, efficacious in reversing a neuromuscular block in a woman with Becker muscular dystrophy]. Rev Esp Anestesiol Reanim. 2011;58(10):614–7.
45. Mazzinari G, Errando CL, Diaz-Cambronero O, Martin-Flores M. Influence of tetanic stimulation on the staircase phenomenon and the acceleromyographic time-course of neuromuscular block: a randomized controlled trial. J Clin Monit Comput. 2018; https://doi.org/10.1007/s10877-018-0157-9.
46. Todd MM, Hindman BJ. The implementation of quantitative electromyographic neuromuscular monitoring in an academic anesthesia department: follow-up observations. Anesth Analg. 2015;121(3):836–8.
47. Fernandez-Bustamante A, Frendl G, Sprung J, Kor DJ, Subramaniam B, Martinez Ruiz R, et al. Postoperative pulmonary complications, early mortality, and hospital stay following noncardiothoracic surgery: a multicenter study by the Perioperative Research Network Investigators. JAMA Surg. 2017;152(2):157–66.
48. Neto AS, Bos LD, Campos PPZA, Hemmes SNT, Bluth T, Calfee CS, et al. Association between pre-operative biological phenotypes and postoperative pulmonary complications. An unbiased cluster analysis. Eur J Anaesthesiol. 2018;35:702–9.
49. Prove Network Investigators for the Clinical Trial Network of the European Society of Anaesthesiology, Hemmes SN, Gama de Abreu M, Pelosi P, Schultz MJ. High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): a multicentre randomised controlled trial. Lancet. 2014;384(9942):495–503.
50. D'Antini D, Huhle R, Herrmann J, Sulemanji DS, Oto J, Raimondo P, et al. Respiratory system mechanics during low versus high positive end-expiratory pressure in open abdominal surgery: a substudy of PROVHILO randomized controlled trial. Anesth Analg. 2018;126(1):143–9.
51. Ferrando C, Soro M, Unzueta C, Suarez-Sipmann F, Canet J, Librero J, et al. Individualised perioperative open-lung approach versus standard protective ventilation in abdominal surgery (iPROVE): a randomised controlled trial. Lancet Respir Med. 2018;6(3):193–203.
52. Marret E, Cinotti R, Berard L, Piriou V, Jobard J, Barrucand B, et al. Protective ventilation during anaesthesia reduces major postoperative complications after lung cancer surgery: a double-blind randomised controlled trial. Eur J Anaesthesiol. 2018;35(10):727–35.

53. Futier E, Constantin JM, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med. 2013;369(5):428–37.
54. Futier E, Paugam-Burtz C, Constantin JM, Pereira B, Jaber S. The OPERA trial - comparison of early nasal high flow oxygen therapy with standard care for prevention of postoperative hypoxemia after abdominal surgery: study protocol for a multicenter randomized controlled trial. Trials. 2013;14:341.
55. Futier E, Paugam-Burtz C, Godet T, Khoy-Ear L, Rozencwajg S, Delay JM, et al. Effect of early postextubation high-flow nasal cannula vs conventional oxygen therapy on hypoxaemia in patients after major abdominal surgery: a French multicentre randomised controlled trial (OPERA). Intensive Care Med. 2016;42(12):1888–98.
56. i Prove Network Investigators, Belda J, Ferrando C, Garutti I. The effects of an open-lung approach during one-lung ventilation on postoperative pulmonary complications and driving pressure: a descriptive, multicenter national study. J Cardiothorac Vasc Anesth. 2018; https://doi.org/10.1053/j.jvca.2018.03.028.
57. Arozullah AM, Daley J, Henderson WG, Khuri SF. Multifactorial risk index for predicting postoperative respiratory failure in men after major noncardiac surgery. The National Veterans Administration Surgical Quality Improvement Program. Ann Surg. 2000;232(2):242–53.
58. Brueckmann B, Villa-Uribe JL, Bateman BT, Grosse-Sundrup M, Hess DR, Schlett CL, et al. Development and validation of a score for prediction of postoperative respiratory complications. Anesthesiology. 2013;118(6):1276–85.
59. Canet J, Gallart L, Gomar C, Paluzie G, Valles J, Castillo J, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. Anesthesiology. 2010;113(6):1338–50.
60. Canet J, Sabate S, Mazo V, Gallart L, de Abreu MG, Belda J, et al. Development and validation of a score to predict postoperative respiratory failure in a multicentre European cohort: a prospective, observational study. Eur J Anaesthesiol. 2015;32(7):458–70.
61. Mazo V, Sabate S, Canet J, Gallart L, de Abreu MG, Belda J, et al. Prospective external validation of a predictive score for postoperative pulmonary complications. Anesthesiology. 2014;121(2):219–31.
62. Griffiths SV, Conway DH, POPC-CB Investigators, Sander M, Jammer I, Grocott MPW, et al. What are the optimum components in a care bundle aimed at reducing post-operative pulmonary complications in high-risk patients? Perioper Med (Lond). 2018;7:7.
63. Neto AS, da Costa LGV, Hemmes SNT, Canet J, Hedenstierna G, Jaber S, et al. The LAS VEGAS risk score for prediction of postoperative pulmonary complications: an observational study. Eur J Anaesthesiol. 2018; https://doi.org/10.1097/EJA.0000000000000845.
64. Ball L, Battaglini D, Pelosi P. Postoperative respiratory disorders. Curr Opin Crit Care. 2016;22(4):379–85.
65. Ferrando C, Belda FJ. Personalized intraoperative positive end-expiratory pressure: a further step in protective ventilation. Minerva Anestesiol. 2018;84(2):147–9.
66. Futier E, Marret E, Jaber S. Perioperative positive pressure ventilation: an integrated approach to improve pulmonary care. Anesthesiology. 2014;121(2):400–8.
67. Guldner A, Kiss T, Serpa Neto A, Hemmes SN, Canet J, Spieth PM, et al. Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. Anesthesiology. 2015;123(3):692–713.
68. Pelosi P, Hedenstierna G, Ball L, Edmark L, Bignami E. The real role of the PEEP in operating room: pros & cons. Minerva Anestesiol. 2018;84(2):229–35.
69. Fuchs-Buder T. Residual neuromuscular blockade and postoperative pulmonary outcome: the missing piece of the puzzle. Eur J Anaesthesiol. 2014;31(8):401–3.
70. Errando CL. Some considerations regarding the Pro and Con articles between Drs. Hedenstierna and Pelosi on intraoperative ventilation and pulmonary outcomes. Turk J Anaesthesiol Reanim. 2017;45(1):59–60.

71. Errando CL, Díaz-Cambronero O. Sugammadex, an antagonist of neuromuscular blocking agents, reverses immediate postoperative neurologic depression by a central pro-cholinergic mechanism. Med Sci Hypotheses. 2016;3:1–11.
72. Claudius C, Garvey LH, Viby-Mogensen J. The undesirable effects of neuromuscular blocking drugs. Anaesthesia. 2009;64(Suppl 1):10–21.
73. Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: methods to reduce the risk of residual weakness. Anesth Analg. 2010;111(1):129–40.

Are Anticoagulants and Antiplatelet Agents Important in Thoracic Surgery?

15

Juan V. Llau and Raquel Ferrandis

15.1 Are Anticoagulants and Antiplatelet Agents Important in Thoracic Surgery?

Thoracic surgery needs a careful anaesthetic preoperative evaluation. It includes the assessment of the perioperative risk mainly focused on the "patient medical morbidities" and their impact on the outcome after surgery. Although thoracic surgical patients commonly have respiratory impairment and the assessment of respiratory mechanics, gas exchange and cardiorespiratory interaction are of cornerstone importance, we need to address our preoperative evaluation also to the management of some common drugs taken by these patients: antiplatelet (APA) and anticoagulant (AC) agents.

Their management is a common challenging problem because patients could require temporary interruption of their administration, or could need to receive a new anticoagulant for thromboprophylaxis in the perioperative period. So, it is necessary to balance the risk of a thromboembolic event (venous or arterial) during the possible interruption of the therapy with the risk for bleeding if the antithrombotic drug is administered close to surgery.

AC and APA are very important in thoracic surgery. Recent years have seen new developments, mostly therapeutic, in their perioperative management. In this chapter, current recent guidelines are revised.

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15.2 Is It Important the Bleeding and Thrombotic Risk Assessment?

The perioperative management of patients on AC or APA treatment is based on a correct assessment of the thrombotic and haemorrhagic risk. To date, a method of specific stratification for the perioperative period has not been validated, so it has been necessary to adapt the general scales proposed and used in other contexts. In general and in order to do some easy recommendations, bleeding and thrombotic risk can be stratified in low, moderate or high risk.

15.2.1 Bleeding Risk in Thoracic Surgery

Most of the thoracic surgical procedures are assessed as having moderate or high bleeding risk (Table 15.1) [1, 2].

Besides a simple list of procedures, there are two interesting proposals that approach the idea of stratification of haemorrhagic risk in patients undergoing antithrombotic treatment. First, the stratification of the perioperative haemorrhagic risk is based on four predictors, which are the patient's bleeding history, to be a mechanical mitral valve carrier, to have an active cancer and a low platelet count, generically called "Bleed MAP" [3]. The other proposal is called the "HASBLED" score, and includes hypertension, impaired renal and/or hepatic function, history of stroke or previous bleeding, a labile normalized international ratio (INR), age older than 65 years and the history of drug use or alcoholism as predictors of bleeding; a result equal to or greater than 3 in patients chronically anticoagulated, was classified as an independent predictor of bleeding in the original prospective-observational-multicentre study [4].

Table 15.1 Proposal for the stratification of haemorrhagic risk in thoracic surgery procedures[a]

Low haemorrhagic risk	Moderate haemorrhagic risk	High haemorrhagic risk
Soft tissue biopsy	Pleural drain	Oesophageal surgery
Wall biopsy	Mediastinal drain	Pleural decortication
Dorsal sympathectomy	Metastasectomy	Lobectomy
Diagnostic thoracoscopy	Pleural resection	Bilobectomy
	Tracheal resection	Pneumonectomy
	Segmentectomy	Reinterventions
	Timectomy	Diaphragm rupture
	Thoracoplasty	Lung transplant
	Therapeutic thoracoscopy	
	Exploratory thoracotomy	

[a]Note from the authors: This list is intended to be merely indicative, and must be modified and applied by each particular Service

Table 15.2 Thrombotic risk stratification in patients receiving anticoagulation

	Mechanical heart valves	Atrial fibrillation	Venous thromboembolism
High thrombotic risk	– Mitral position – Tricuspid position (included biological) – Aortic position (mono-disc prosthesis) – Stroke <6 months	– CHA_2DS_2-VASc 7–9 – Stroke <3 months – Rheumatic mitral valvulopathy	– VTE <3 months – Severe thrombophilia
Moderate thrombotic risk	– Aortic position + 1 RF: AF or Stroke	– CHA_2DS_2-VASc 5–6 – Stroke >3 months	– VTE 3–12 months – Moderate thrombophilia
Low thrombotic risk	– Aortic position without RF	– CHA_2DS_2-VASc 1–4 – Stroke <3 months	– VTE >12 months

RF risk factor, *AF* atrial fibrillation, *VTE* venous thromboembolism
CHA_2DS_2-VASc: 1 point: cardiac insufficiency, hypertension, mellitus diabetes, female, age 65–74 years and vascular disease; 2 points for age ≥75 years and history of stroke or peripheral embolism

Table 15.3 Easy thrombotic risk stratification in patients receiving antiplatelet drugs (for more details, please see references from the text)

Risk	Low	Moderate	High
Indication	>12 months after: • ACS • CAGB • PCI: DES • PCI: CS • Stroke	6–12 months after: • ACS • CAGB • PCI: DES • PCI: CS • Stroke >12 months if complications or RF (DM, low EF, CKD) or complex PCI	<6 months after: • ACS • CAGB • PCI: DES • PCI: CS • Stroke 6–12 months if complications or RF (DM, low EF, CKD) or complex PCI

ACS acute coronary syndrome, *CAGB* coronary artery graft bypass surgery, *CKD* chronic kidney disease, *CS* conventional stent, *DM* diabetes mellitus, *EF* ejection fraction, *PCI* percutaneous coronary intervention, *RF* risk factors

15.2.2 Thrombotic Risk

Thrombotic risk is not specific for thoracic surgeries. In anticoagulated patients it stratifies the risk as low, moderate and high risk (Table 15.2) [2]. The stratification is different for patients receiving APA and an easy and practical approach is summarized in Table 15.3 [2, 5]. Both scales are only indicatives because they do not consider full personal circumstances that could modify the thrombotic risk and that should be assessed individually.

15.3 How to Manage Anticoagulation in Patients Scheduled for Thoracic Surgery?

Atrial fibrillation, mechanical heart valve and several other indications including cerebrovascular pathology (repeated strokes) or prevention of recurrences of previous thromboembolic events, are main indications for anticoagulation. Vitamin K antagonist (VKAs) as acenocoumarol or warfarin and direct oral anticoagulants (DOAC), as dabigatran, apixaban, edoxaban or rivaroxaban, are the drugs used in patients needing chronic anticoagulation.

The decision to withdraw anticoagulants depends on the patient's thrombotic risk versus haemorrhagic risk. Assessment of both will show the physician the best management of anticoagulant therapy in thoracic surgery.

15.3.1 Is It Necessary to Withdraw the Anticoagulant?

In patients scheduled for the vast majority of thoracic surgery procedures the interruption of the AC is required to achieve normal or near-normal haemostasis at the time of surgery because they are related with moderate to high bleeding risk.

15.3.1.1 Vitamin K Antagonists

In general, after stopping VKAs 3–5 days (acenocoumarol or warfarin respectively) most anticoagulant effect is eliminated and the haemostatic power is enough for performing a surgery (with acenocoumarol 3 days seem to be enough and with warfarin the delay should be up 5 days). So, main recommendation in patients scheduled for thoracic surgery that require temporary interruption of a VKA before the operation, is to stop VKAs approximately 5 days before surgery in the case of warfarin and 3 days if the VKA is acenocoumarol [6]. Last Spanish multidisciplinary consensus document modify this easy recommendation looking at the basal INR and modify it prolonging or shortening it (Table 15.4) [2].

During many time, the temporary discontinuation of VKAs has been managed with the administration of a short anticoagulant when the VKA is withdrawn. This strategy is called "bridging therapy", but recently some controversies have been published for this topic [7–11], mainly for a possible tendency to increase bleeding without any decrease of thrombotic events. Current main recommendation is to avoid the systematic administration of bridging therapy, being only a possibility (no a need) in patients at high thrombotic risk [2, 12–14].

15.3.1.2 Direct Oral Anticoagulants

DOACs are given orally and they do not need antithrombin for their action, but they are different drugs acting in different targets of the coagulation cascade: apixaban, edoxaban and rivaroxaban directly inhibit factor Xa; dabigatran is a direct inhibitor of factor IIa. They can be used for the prevention of a stroke in patients on atrial fibrillation and for the treatment and secondary prevention in patients with venous thromboembolism [15].

Table 15.4 Suggested elapsed time for anticoagulants before thoracic surgery in procedures considered with moderate-high bleeding risk (see the text)

Days before surgery	−7	−6	−5	−4	−3	−2	−1	0
Dabigatran			X (CrCl ≤50)	X (CrCl >50)				Surgery
Apixaban Edoxaban Rivaroxaban				X (CrCl 15–30)	X (CrCl >30)			Surgery
Vitamin K antagonists[a]								
7 days before INR < 2			X Warfarin		X Acenocoum.		Control INR	Surgery
7 days before INR 2–3		X Warfarin		X Acenocoum.			Control INR	Surgery
7 days before INR > 3	X Warfarin		X Acenocoum.				Control INR	Surgery

X = Last intake of anticoagulant
Acenocoum = Acenocoumarol
INR international normalized ratio
[a]No bridging therapy with low-molecular-weight heparin as general recommendation; consider only in high thrombotic risk patients

No bridging strategy is accepted nowadays for their management in the perioperative period. Best recommendation is to stop the drug before surgery. Based on DOAC rapid onset of action and short half-life, it has been proposed their withdrawal some days before surgery. As DOAC have different half-lives and different renal clearance rates, this proposal should be adapted to each drug, to the patient, to the creatinine clearance and to the procedure's bleeding risk. After recent articles revision and large discussions, it has been proposed an easy and practical protocol, summarized in Table 15.4 [2, 15–21].

15.3.2 What About Anticoagulation After Surgery?

After surgery it is necessary to restart the administration of the anticoagulant, and the most important decision is to determine "when". As a general rule, the answer is "when the haemostasis is achieved", taking into account the risk of bleeding, the type of medication, and the venous and arterial thromboembolic risk [2, 17, 21, 22]:

- *Patients on VKA*:
  - Begin with a low-molecular-weight heparin (LMWH) at prophylactic dose from 6 h after surgery (acting as venous thromboprophylaxis).
  - Increase the dose of LMWH up to therapeutic dose, begin the VKA from at day 3 or 4 after surgery, maintaining the LMWH until the INR ≥ 2.
- *Patients on DOAC*:
  - Begin with a low-molecular-weight heparin (LMWH) at prophylactic dose from 6 h after surgery (acting as venous thromboprophylaxis).
  - Do not increase the dose of LMWH and prescribe a "therapeutic" dose of the anticoagulant between 24 and 72 h postoperatively, stopping then the LMWH (no overlap both drugs).
- *In both cases*: In the presence of an epidural catheter, therapeutic administration with VKA or DOAC should be started when the catheter has been withdrawn.

15.4 How to Manage Antiplatelet Drugs in Patients Scheduled for Thoracic Surgery?

It is very common that patients who are scheduled for thoracic surgery are treated with APA due to their wide indications and the characteristics of these patients. They are drugs of diverse origin, whose prophylactic and therapeutic effects are especially important in the prevention and treatment of the arterial thrombosis. The most common APA used as chronic treatment are cyclooxygenase inhibitors such aspirin, adenosine diphosphate receptor P2Y12 antagonist such clopidogrel or prasugrel; new antiplatelet agents include ticagrelor and cilostazol. Their main characteristics are shown in Table 15.5 [5, 6, 23].

Table 15.5 Main characteristics of some current antiplatelet agents

Drug	Mode of action	Half life	Onset of action	Duration of action
Aspirin	Irreversible inhibition of the enzyme COX-1	15–20 min	Few minutes	Platelet life span[a]
Clopidogrel	Irreversible binding to the ADP P2Y12 receptor of the platelets	About 8 h (active metabolites after liver action)	2 h if given loading dose	Platelet life span[a]
Prasugrel	Irreversible binding to the ADP P2Y12 receptor of the platelets	Fast conversion in active metabolites	About 30 min	Platelet life span[a]
Cilostazol	Selective inhibition of phosphodiesterase IIIA (reversible inhibition of platelet aggregation)	Around 21 h	2–3 h	12–48 h

[a]For the recovery of haemostatic competence it could not be necessary the recovery of the function of all platelets. So 5 days after the last administration of the majority of these antiplatelet agents could be enough

Although the management of the APA in the perioperative period is not easy, main challenge for the anaesthesiologist and the thoracic surgeon is those patients receiving an APA with a coronary stent (mainly, drug-eluting coronary stents).

15.4.1 Which Are Main Recommendations for Patients Scheduled for Thoracic Surgery?

Although continuing APA during the perioperative period does not guarantee complete protection against ischaemic events, discontinuation is a further risk factor to be taken into account in the preoperative workup, and is added to the risk of delaying the resumption of the drug after surgery. Therefore, the decision to continue chronic APA treatment, or when to interrupt it, must be taken on the basis of individualised evaluation of the patient's thrombotic risk, and requires an specific management for both preoperative discontinuation and postoperative restart.

The recommendations about the perioperative management of antiplatelet therapy in these patients can be summarized as follows [2, 5]:

15.4.1.1 Aspirin

- In most cases it is recommended that a low dose of aspirin (75–100 mg) be maintained throughout the perioperative period. Only in cases of very high bleeding risk outweighing the thrombotic risk it is suggested to stop it before surgery (3-day window).
- In order to reduce the potential risk of bleeding, aspirin dose higher than 200 mg should be replace by 75 or 100 mg at least 5 days before surgery.
- The administration of the aspirin after surgery should be done as soon as possible. Main recommendation is to give it in the first 24 h after the end of surgery if the haemostatic competence of the patient is assured.

15.4.2 Clopidogrel and Prasugrel

- In most cases these drugs must be discontinued. They should be stopped the shortest time possible: 5 days for clopidogrel or 7 days for prasugrel. Thereafter, treatment should be restarted as soon as possible following surgery after ensuring haemostasis (1 or 2 days after surgery).
- In patients on clopidogrel as monotherapy and with moderate to high thrombotic risk, discontinue clopidogrel 5 days before surgery, and start aspirin 100 mg/day (unless contraindicated).
- Patients on dual therapy (aspirin + clopidogrel or prasugrel) have high thrombotic risk in vast majority of cases. The management is difficult, but, in general:
  - Maintain aspirin at 100 mg/day.
  - Maintain both drugs whenever bleeding risk allows, in consensus with the corresponding surgical team.
  - If clopidogrel or prasugrel must be stopped (moderate-high bleeding risk), stop them the shortest time possible: 5 days for clopidogrel or 7 days for prasugrel, maintaining aspirin if possible.

15.5 Is It Suitable the Thromboprophylaxis in Thoracic Surgery?

Venous thromboembolism (VTE) comprising deep venous thrombosis (DVT) and pulmonary embolism (PE) contribute to a high incidence of perioperative mortality. VTE is currently regarded as the result of the interaction between patient-related and setting-related risk factors. Patient-related predisposing factors are usually permanent, whereas setting-related predisposing factors are more often temporary. Patient-related predisposing factors include age, history of previous VTE, active cancer, neurological disease with extremity paresis, medical disorders causing prolonged bed rest (such as heart or acute respiratory failure) and congenital or acquired thrombophilia, hormone replacement therapy and oral contraceptive therapy [24–26]. Identifying patients at higher risk for perioperative VTE is crucial before instituting preventive measures that seek to decrease the incidence of symptomatic events without increasing the risk for bleeding complications [27].

During the perioperative period, VTE is a frequent and yet relatively preventable cause of post-operative morbidity and mortality. Although the benefits of thromboprophylaxis are broadly recognized in this context, the recent proposed objective is to offer a tailored, procedure-specific, patient-specific regimen, case-per-case decided.

15.5.1 Which Methods for Thromboprophylaxis Are Available?

Methods used for thromboprophylaxis in surgical patients include general measures, mechanical and pharmacological methods.

– *General measures* include mobilisation and leg exercises. Adequate hydration should be ensured in immobilised patients.
– *Mechanical methods* increase mean flow velocity in leg veins and reduce venous stasis. They include graduated compression stockings (GCS), intermittent pneumatic compression (IPC) devices and pneumatic foot pumps (PFP).
– *Pharmacological methods* are necessary when the thrombotic risk is moderate to high. They include low molecular weight heparins (LMWH) that are the most extended drugs used for thromboprophylaxis. Other drugs available for thoracic surgical patients when indicated are fondaparinux, unfractionated heparin (UFH) and anti-vitamin K drugs (VKAs) (warfarin/acenocoumarol).

15.5.2 Rationale for Thromboprophylaxis in Thoracic Surgery

The rationale for use of thromboprophylaxis in patients admitted to a hospital is based on [24–26]:

– *High prevalence of VTE* among hospitalized patients, because almost all of them have one or more risk factors for VTE. If no prophylaxis is given, the risk to develop any kind of VTE is highly variable, in dependence of the medical/surgical condition of the patient.
– *Adverse consequences* of un-prevented VTE, mainly symptomatic DVT or PE, fatal PE and post-thrombotic syndrome.
– *Efficacy of thromboprophylaxis*, with a good cost-effectiveness relation of pharmacological and mechanical methods.

In patients undergoing thoracic surgery the incidence of VTE remains unclear. It depends of the underlying disease (e.g. cancer), the type of procedure (e.g. thoracotomy vs. minimally invasive), the patient co-morbidities, the screening strategy and the prophylactic approach [28]. Although the incidence of VTE seems to be low in the general thoracic population (less tan 0.20%) [27], the incidence is higher in patients presenting with two or more of the following risk factors: advanced age, obesity, cancer and history of DVT [29]. Lung cancer patients undergoing thoracic surgery have two to threefold increased risk of VTE compared with those without surgery [30].

15.5.3 Which Recommendations for Thromboprophylaxis in Thoracic Surgery?

Based on the rationale describe above, all patients scheduled for thoracic surgery should be assessed on their thrombotic risk, balanced against their bleeding risk. The final decision about the optimal thromboprophylaxis protocol to be administrated should be made after the consideration of both risk factors.

Table 15.6 Suggested thromboprophylaxis in thoracic surgical patients

Patient group	Suggested thromboprophylaxis options	Suggested duration
Low risk for VTE (Caprini score 0–1)	Early deambulation	–
Moderate risk for VTE (Caprini score: 2–3) No high risk for bleeding	LMWH or UFH or IPC/GCS (preferably LMWH or IPC)	7–10 days (if pharmacological prophylaxis) or until discharge
High risk for VTE (Caprini score: 4 or more) No high risk for bleeding	LMWH (or UFH) IPC/GCS (preferably IPC) should be added to pharmacologic prophylaxis	7–10 days (in cancer patients, consider prolongation up to 4 weeks)
Moderate or high risk for VTE High risk for bleeding	IPC/GCS (preferably IPC) Initiate LMWH (or UFH) when bleeding risk diminishes	7–10 days (if pharmacological prophylaxis) or until discharge (in cancer patients, consider prolongation up to 4 weeks)

VTE venous thromboembolism, *LMWH* low molecular weight heparin, *UFH* unfractionated heparin, *IPC* intermittent pneumatic compression, *GCS* graduated compression stockings

But the problem is that only a few studies have compared different prophylactic strategies in patients undergoing thoracic surgery, and the evidence for strong recommendations is really low. Following last published guidelines [27] and mainly base on the application of stratification models of thrombotic risk factors [31], the summary of recommendations could be (see Table 15.6):

- Patients undergoing thoracic surgery in the absence of cancer could be considered at low risk of VTE and those with a diagnosis of cancer should be considered at high risk for VTE with an equally high bleeding risk.
- In the absence of evidence regarding patients undergoing minimally invasive procedure, it is suitable to stratify the VTE risk in each patient using a validated model such as Caprini score [31] which includes: age, type/duration of surgery, obesity, history of VTE or thrombophilia, presence of a central venous catheter and malignancy.
- In low-risk patients, it is suggested the use of mechanical prophylaxis using IPC (Grade 2C). In high-risk patients, it is suggested the use of pharmacological prophylaxis in addition to IPC (Grade 2B).

Some controversies haven been issued related with the moment of pharmacological thromboprophylaxis initiation. There are no differences reported in the literature in efficacy and safety between pre- or postoperative administration of the first dose of LMWH. Although the current tendency is to begin the thromboprophylaxis in the postoperative period (between 6 and 12 h after the end of surgery), it is possible the preoperative administration 12 h before surgery (this option is preferred in bedridden patients).

15.5.4 Thromboprophylaxis in the Perioperative Period: Implications for the Anaesthesiologist

The performance of regional anaesthesia, particularly epidural technique that is specially indicated in this kind of surgery for postoperative analgesia, seems safe in patients receiving anticoagulant drugs for thromboprophylaxis if there is an appropriate management based on safety intervals suited to the type of anaesthetic-analgesic technique to be carried out, and particularly to the characteristics of the drug [32, 33]. Nevertheless, the final decision to perform regional anaesthesia in patients receiving drugs that affect haemostasis will be taken after careful assessment of individual risks and benefits, mainly in patients receiving one anticlotting drug for thromboprophylaxis plus one antiplatelet drug for any other medical indication.

Main recommendations for the performance of neuraxial anaesthesia can be summarize as follows:

- Low dose Aspirin (up to 300 mg) is not a contraindication for the performance of a neuraxial block. It should be resumed as soon as possible after surgery (ideally not more than 24 h).
- If clopidogrel cannot be stopped 5 days before surgery (or prasugrel 7 days), the performance of an epidural technique is not recommended and the anaesthesiologist must have into account the "level of benefit" for the epidural technique. The reintroduction of this drugs should be after catheter removal.
- Prophylactic doses of a LMWH are safe if the delay between its administration and the performance of the neuraxial block is, at least, 10–12 h. If the first dose of LMWH is administrated after surgery, the delay between the epidural block and the LMWH administration should be 6–8 h. Finally, the epidural catheter should not be removed till 12 h has passed since the last dose of the administration of LMWH.

References

1. Llau JV, Ferrandis R. Antiagregantes y anticoagulantes en cirugía torácica. In: Granell M, editor. Anestesia y Reanimación en Cirugía Torácica. Madrid: Médica Panamericana; 2019. p. 16.
2. Vivas D, Roldan I, Ferrandis R, Marin F, Roldan V, Tello-Montoliu A, et al. Perioperative and periprocedural management of antithrombotic therapy: consensus document. Rev Esp Cardiol. 2018;71:553–64. https://doi.org/10.1016/j.recesp.2018.01.001.
3. Tafur A, McBane R, Wysokinski WE, Litin S, Daniels P, Slusser J, et al. Predictors of periprocedural bleeding among patients on chronic anticoagulation. J Thromb Haemost. 2012;10:261–7.
4. Omran H, Bauersachs R, Rübenacker S, Goss F, Hammeerstingl C. The HAS-BLED score predicts bleedings during bridging of chronic oral anticoagulation: results from the national multicenter BNK Online bRiDging REgistRy (BORDER). Thromb Haemost. 2012;108:65–73.
5. Sierra P, Gomez-Luque A, Llau JV, Ferrandis R, Casinello C, Hidalgo F. Recommendations for perioperative antiplatelet treatment in non-cardiac surgery. Working Group of the Spanish Society of Anaesthesiology-Resuscitation and Pain Therapy, Division of Haemostasis,

Transfusion Medicine, and Perioperative Fluid Therapy. Update of the Clinical practice guide 2018. Rev Esp Anestesiol Reanim. 2019;66:18–36.
6. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, et al. Perioperative management of antithrombotic therapy. Chest. 2012;141:e326S–50S.
7. Spyropoulos AC. Bridging of oral anticoagulation therapy for invasive procedures. Curr Hematol Rep. 2005;4:405–13.
8. Dunn A. Perioperative management of oral anticoagulation: when and how to bridge. J Thromb Thrombolysis. 2006;21:85–9.
9. Van Veen JJ, Makris M. Management of perioperative antithrombotic therapy. Anaesthesia. 2015;70(Suppl 1):58–67.
10. Siegal D, Yudin J, Kaatz S, Douketis JD, Lim W, Spyropoulos AC. Periprocedural heparin bridging in patients receiving vitamin K antagonists: systematic review and meta-analysis of bleeding and thromboembolic rates. Circulation. 2012;126:1630–9.
11. Wysokinski WE, Mc Bane RD II. Periprocedural bridging management on anticoagulation. Circulation. 2012;126:486–90.
12. Rechenmacher SJ, Fang JC. Bridging anticoagulation: primum non nocere. J Am Coll Cardiol. 2015;66:1392–403.
13. Steinberg BA, Peterson ED, Kim S, Thomas L, Gersh BJ, Fonarow GC, et al. Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). Circulation. 2015;131:488–94.
14. Douketis JD, Spyropoulos AC, Kaatz S, Becker RC, Caprini JA, Dunn AS, et al. Perioperative bridging anticoagulation in patients with atrial fibrillation. N Engl J Med. 2015;373:823–33.
15. Fenger-Eriksen C, Munster AM, Grove EL. New oral anticoagulants: clinical indications, monitoring and treatment of acute bleeding complications. Acta Anesthesiol Scand. 2014;58:651–9.
16. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016;37:2893–962.
17. Ferrandis R, Castillo J, De Andrés J, Gomar C, Gomez-Luque A, Hidalgo F, et al. The perioperative management of new direct oral anticoagulants: a question without answers. Thromb Haemost. 2013;110:515–22.
18. Levy JH, Faraoni D, Spring JL, Douketis JD, Samama CM. Managing new oral anticoagulants in the perioperative and intensive care unit setting. Anesthesiology. 2013;118:1466–74.
19. Faraoni D, Samama CM, Ranucci M, Dietrich W, Levy JH. Perioperative management o patients receiving new oral anticoagulants. Clin Lab Med. 2014;34:637–54.
20. Hidalgo F, Gómez-Luque A, Ferrandis R, Llau JV, De Andres J, Gomar C, et al. Perioperative management of direct oral anticoagulant in emergency surgery and bleeding. Haemostasis monitoring and treatment. Rev Esp Anestesiol Reanim. 2015;62:450–60.
21. Faraoni D, Levy JH, Albaladejo P, Samama CM. Updates in the perioperative and emergency management of non-vitamin K antagonist oral anticoagulants. Crit Care. 2015;19:203.
22. Albaladejo P, Bonhomme F, Blais N, Collet JP, Faraoni D, Fontana P, et al. Management of direct oral anticoagulants in patients undergoing elective surgeries and invasive procedures: updated guidelines from the French Working Group on Perioperative Hemostasis (GHIP) – September 2015. Anaesth Crit Care. 2017;36:73–6.
23. Llau JV, Ferrandis R, Sierra P, Gomez Luque A. Prevention of renarrowing of coronary ateries using drug-eluting stents in the perioperative period: an update. Vasc Health Risk Manag. 2010;6:1–13.
24. Scottish Intercollegiate Guidelines Network (SIGN). Prevention and management of venous thromboembolism. Edinburgh: SIGN; 2010.
25. The Royal College of Surgeons of England. Venous thromboembolism: reducing the risks. Guía NICE. Updated January 2010. London: The Royal College of Surgeons of England; 2010.
26. Gould MK, García DA, Wren SN, Karanicolas PJ, Arcelus JI, Heit JA, et al. Prevention of VTE in non-orthopedical surgical patients. Chest. 2012;141(2). Suppl):227–77.

27. Ahmed AB, Koster A, Lance M, Faraoni D. for the ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis. Cardiovascular and thoracic surgery. Eur J Anaesthesiol. 2018;35:84–9.
28. Di Nisio M, Peinemann F, Porreca E, Rutjes AW. Primary prophylaxis for venous thromboembolism in patients undergoing cardiac or thoracic surgery. Cochrane Database Syst Rev. 2015;(6):CD009658.
29. Gomez-Hernandez MT, Rodriguez-Perez M, Novoa-Valentin N, Jiménez-López N, Aranda-Alcaide JL, Varela-Simó G. Prevalence of venous thromboembolism in elective thoracic surgery. Arch Bronconeumol. 2013;49:297–302.
30. Tesselaar ME, Osanto S. Risk of venous thromboembolism in lung cancer. Curr Opin Pulm Med. 2007;13:362–7.
31. Caprini JA. Thrombosis risk assessment as a guide to quality patient care. Dis Mon. 2005;51:70–8.
32. Gogarten W, Vandermeulen E, Van Aken H, Kozek S, Llau JV, Samama CM. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. Eur J Anaesthesiol. 2010;27:999–1015.
33. Breivik H, Norum H, Fenger-Eriksen C, Alahuhta S, Vigfússon G, Thomas O, Lagerkranser M. Reducing risk of spinal haematoma from spinal and epidural pain procedures. Scand J Pain. 2018;18(2):129–50.

Prevention and Treatment of Infections

16

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16.1 Introduction

Nosocomial infections are common after lung surgery [1, 2]. The main infectious complications described after thoracic surgery include surgical site infection, nosocomial pneumonia, empyema, and less frequent, urinary tract infection or bacteraemia [3, 4].

The incidence varies depending on the geographical area and hospital from 2% to 24% [5–10]. The largest Italian cohort [7] of 3289 patients undergoing thoracic surgery showed 123 (3.7%) patients who developed a hospital acquired infection: pneumonia 1.9%, ventilator associated pneumonia 0.36%, surgical site infections 0.24% and exacerbations of chronic obstructive pulmonary disease 1.18%. The overall infective mortality was 3.25%. Infection development was statistically associated with smoking status and malnutrition [7]. In a smaller Italian cohort [6] of 1091 resected patients, 124 (11.4%) developed one or more infection: wound infection 3.2%, pneumonia 8.3% and empyema 1.9%. There were significant differences according to the type of surgery: wedge resection 4.8%, lobectomy 17.4% and pneumonectomy 35.0%. Multivariable analysis showed that male gender, diabetes, preoperative steroids, induction chemo/radiotherapy, missed antibiotic prophylaxis and resection type were independent risk factors for postoperative infections [6]. Video-Assisted Thoracoscopic Surgery (VATS) has a lower incidence of infections than open surgery [5, 9]. Other risk factors for infection after thoracic surgery includes: prior immunosuppression, prior infections, pre-operative stay >2 days,

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neoplasia, chronic obstructive pulmonary disease (COPD), duration of surgery and ICU admission [9, 11].

Infections are responsible for increased hospital mortality as well as increased costs and length of hospital stay.

16.2 Surgical Site Infections

Surgical Site Infections (SSI) compose up to 20% of all of healthcare-associated infections and is defined as wound infection that occurs after a surgical procedure at or near the surgical incision within 30 days of the procedure or within 90 days if prosthetic material is implanted at surgery [12]. A SSI may range from a spontaneously limited wound discharge within 7–10 days of an operation to a life-threatening postoperative complication. SSI are classified into incisional SSI, which can be superficial (involves only skin and subcutaneous tissue of incision) or deep (fascial and muscle layers); and organ/space SSI. Organ/space SSI affect the rest of the body other than the wall layers and account for one-third of all SSI but are associated with more than 90% of deaths related to SSI. Clinical criteria for defining SSI include one or more of the following: a purulent exudate draining from a surgical site, a positive fluid culture obtained from a surgical site that was closed primarily, a surgical site that is reopened in the setting of at least one clinical sign of infection (pain, swelling, erythema, warmth) and is culture positive or not cultured, and also if the surgeon makes the diagnosis of infection. Most surgical site infections are caused by contamination of an incision with microorganisms from the patient's own body during or after surgery [10]. They are associated with considerable morbidity and extended hospital stay. In addition, one third of wound infections are detected after hospital discharge [11] because patients are allowed home earlier following day case and fast-track surgery. The most frequently isolated microorganisms in SSI are Staph. aureus, coagulase-negative Staphylococci, Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* and 9% of SSIs are polymicrobial [5]. Diabetes mellitus, an American Society of Anesthesiology (ASA) score ≥3, preoperative white blood cell count and the number of blood products used perioperatively were found to be independent risk factors for SSI. Mortality rate and total length of hospital stay were significantly higher in patients with SSI [5, 24].

The risk of SSI can be predicted by the Surgical Site Infection Risk Score. The risk increases with patient factors (smoking, increased body mass index), certain comorbidities (peripheral vascular disease, metastatic cancer, chronic steroid use, recent sepsis), and operative characteristics (surgical urgency; increased ASA class; longer operation duration; infected wounds; general anaesthesia; performance of more than one procedure; and Current Procedural Terminology (CPT) score) [13].

Guidelines for the management of SSI were published by the Infectious Diseases Society of America (IDSA) in 2014 [14], by the WHO in 2016 [15], and by the CDC in 2017 [16]. Treatment recommendations include suture removal plus incision and drainage, and adjunctive systemic antimicrobial therapy only if systemic response (extensive erythema and induration, fever, tachycardia or leucocytosis) is present.

The best choice is a first-generation cephalosporin or an anti-staphylococcal penicillin for methicillin-sensitive Staph. aureus (MSSA). In the presence of risk factors for MRSA (nasal colonization, prior MRSA infection, recent hospitalization, or recent antibiotics) we may use vancomycin, linezolid, daptomycin, telavancin, or ceftaroline according to the local flora.

16.3 Prevention of Surgical Site Infections on Thoracic Surgery

16.3.1 CDC: OMS Recommendations

The measures used to prevent infection in surgical procedures have been promoted by the World Health Organization (WHO) [17, 18], the USA Centers for Disease Control and Prevention (CDC) [16, 19], and the English National Institute for Health and Care Excellence [12]. In addition to antibiotics, recommendations [17] include: the preoperative administration of oral or enteral multiple nutrient-enhanced nutritional formulas in underweight patients; a bath (full body) or shower, either with a plain or an antimicrobial soap, on at least the night before the operative day [16]; the perioperative intranasal applications of mupirocin 2% ointment [20] with or without a combination of chlorhexidine gluconate body wash in patients with known nasal carriage of *Staph. aureus*; the avoidance of hair removal or shaving and, if absolutely necessary, with the use of an electric clipper with a single-use head on the day of surgery [12]; surgical hand preparation either by scrubbing with a suitable antimicrobial soap and water or using a suitable alcohol-based hand rub before donning sterile gloves; sterile disposable non-woven or sterile reusable woven drapes and surgical gowns; and surgical site skin preparation with alcohol antiseptic solutions, based on chlorhexidine gluconate, unless contraindicated [17]. Further measures include the use of 80% fraction of inspired oxygen intraoperatively and, if feasible, in the immediate postoperative period for 2–6 h for adult patients with normal pulmonary function undergoing general anaesthesia with endotracheal intubation; the use of warming devices in the operating room and during the surgical procedure to maintain normothermia of the patient; intensive perioperative blood glucose control for both diabetic and non-diabetic adult patients using blood glucose target levels less than 200 mg/dL [16]; goal-directed fluid therapy intraoperatively; irrigation of deep or subcutaneous tissues of the incisional wound with an aqueous povidone-iodine solution before closure, particularly in clean and clean-contaminated wounds; triclosan-coated sutures [19]; standard interactive dressing on primarily closed surgical wounds [12], but prophylactic negative-pressure wound therapy on high-risk wounds; and early removal of wound drain when clinically indicated [18]. Perioperative oral hygiene has also proven useful in decreasing postoperative nosocomial infections [21]. Perioperative decontamination of the nasopharynx and/or oropharynx is a cheap strategy that can easily be carried out by the patients themselves. It reduces postoperative nosocomial infections: lower respiratory tract and deep surgical site infections, but not urinary tract infections [21].

16.3.2 Multimodal Strategy in Thoracic Surgery: Enhanced Recovery Thoracic Surgery

The enhanced recovery after surgery (ERAS) or fast track programs have also a preventive effect reducing nosocomial infections [22, 23]. An ERAS program is achieved through the introduction of multiple evidence-based recommendations for the optimal perioperative management of patients undergoing thoracic surgery that aim to diminish postoperative organ dysfunction while facilitating recovery [22]. Key recommendations, endorsed by the Enhanced Recovery after Surgery Society and the European Society for Thoracic Surgery, include preoperative counselling, nutritional screening, smoking cessation, prehabilitation for high-risk patients, avoidance of fasting, carbohydrate loading, avoidance of preoperative sedatives, venous thromboembolism prophylaxis, prevention of hypothermia, short-acting anaesthetics to facilitate early emergence, regional anaesthesia, nausea and vomiting control, opioid-sparing analgesia, euvolemic fluid management, minimally invasive surgery, early chest drain removal, avoidance of urinary catheters and early mobilization after surgery. A prospective, randomized controlled pilot study [23], comparing a conservative and fast track treatment regimen in patients undergoing lung resections, with differences between the two groups in preoperative fasting (6 h vs. 2 h) and analgesia (patient controlled analgesia vs patient controlled epidural analgesia) showed less pulmonary complications (pneumonia, atelectasis, prolonged air leak) in the fast track program. The rate of postoperative pulmonary complications was 35% in the conservative and 6.6% in the fast track group ($p = 0.009$). Overall morbidity was not significantly different (46% vs 26%, $p = 0.172$), and mortality was comparable in both groups (4% vs 3%) [23].

16.4 Antibiotic Prophylaxis in Thoracic surgery

Antibiotic prophylaxis is only one of the multiple measures described for the prevention of surgical infections which are a substantial burden to health-care systems in terms of patient morbidity, mortality and additional costs.

The efficacy of antibiotic prophylaxis to prevent surgical site infection, by reducing the burden of microorganisms at the surgical site during the operative procedure, has been clearly established [24, 25]. The recommendations for antibiotic prophylaxis include clean-contaminated procedures where an incision through the respiratory tract is entered under controlled conditions but with no contamination encountered [26]. Preoperative antibiotics are warranted if there is high risk of infection, as in contaminated wounds, or if there is high risk of deleterious outcomes should infection develop at the surgical site (such as in the setting of immune compromise) [27].

Antimicrobial prophylaxis should be administered only when indicated based on published clinical practice guidelines [28, 29] and timed such that a bactericidal concentration of the agents is established in the serum and tissues when the incision is made [16] (Table 16.1).

Table 16.1 Antibiotic prophylaxis in thoracic surgery

Type of surgery	Preferred antibiotic	Alternatives	Penicillin allergy
Thoracic Noncardiac procedures, including lobectomy, pneumonectomy, lung resection, and thoracotomy	Cefazolin	Ampicillin–sulbactam, Cefamandole, Cefuroxime.	Clindamycin, Vancomycin, Clindamycin + gentamycin
Video-assisted thoracoscopic surgery	Cefazolin	Ampicillin–sulbactam	Clindamycin, Vancomycin
Empyema or abscess	Cefazolin + metronidazole	Ampicillin–sulbactam	Clindamycin, Vancomycin + metronidazole
Lung transplantation	Cefazolin	Ampicillin–sulbactam, Vancomycin + cefotaxime, Cefepime	Clindamycin, Vancomycin, Clindamycin + gentamycin

Recommendations for prophylactic antibiotic therapy in thoracic surgery [28–30] for pneumonectomy/lobectomy include first-generation cephalosporins, such as cefazolin, which have good coverage for the most common pulmonary surgical site infections. The appropriate dosage for cefazolin is 2 g IV (child 30 mg/kg up to 2 g) prior to incision. Instead of cefazolin, other choices are cefamandole (1.5 g IV) or cefuroxime (1.5 g IV). In surgery for decortication or pleurectomy the use of cefazolin is also recommended. If anaerobic cover is required (empyema or abscess) then add metronidazole 500 mg IV infusion (child: 12.5 mg/kg), repeated 12 hourly for 2 more doses commencing 6 h after initial dose. In video-assisted thoracoscopic surgery (VATS) use also cefazolin 2 g IV [31].

The initial antimicrobial dose should be adequate based on the patient's weight. A single pre-operative dose is sufficient for most procedures, however repeat intra-operative doses are advisable for delayed or prolonged surgery, when the duration of the procedure exceeds two half-lives of the antimicrobial agent (e.g., more than 3 h for cefazolin), or if major blood loss occurs (i.e., >1500 mL), following fluid resuscitation.

We need to consider individual risk factors for every patient that may alter the need for prophylaxis, the drug choice or the dose (e.g. immune suppression, presence of prostheses, allergies, obesity, malnutrition, diabetes, infection at another site, available pathology or malignancy). Pre-existing infections (known or suspected), if present, requires the use of appropriate treatment regimen instead of prophylactic regimen for procedure. Doses should be scheduled to allow for re-dosing just prior to skin incision. If the patient has a history of methicillin-resistant *Staph aureus* (MRSA) or a penicillin allergy, then vancomycin 1 g IV can be used in place of cefazolin, and we can also use clindamycin plus gentamycin [10].

In MRSA risk patients (defined as history of MRSA colonisation or infection, or inpatient of hospital for more than the last 5 days), add vancomycin to cefazolin. Give vancomycin 1 g (1.5 g for patients >80 kg actual body weight) by IV infusion started 30–120 min before surgical incision and given at a recommended rate of 1 g per h (1.5 g over 90 min). Infusion can be completed after skin incision.

Drug administration should be timed ≤60 min before skin incision (optimal 30 min). Patients who receive prophylactic antibiotics within half to 2 h before the initial incision have lower rates of SSI than patients who receive antibiotics sooner or later than this window. So, the recommendations state that we must consider giving a single dose of antibiotic prophylaxis intravenously on starting anaesthesia [12] or within 120 min before incision, while considering the half-life of the antibiotic [17], using the local antibiotic formulary and always considering the potential adverse effects. Patients receiving antimicrobial prophylaxis are at relatively low risk for adverse drug events such as development of Clostridioides (formerly Clostridium) difficile [32] and postoperative infection due to drug-resistant organisms. For those operations for which the cephalosporins represent the most appropriate antimicrobials for prophylaxis, the medical history should be adequate to determine if the patient has a history of allergy or serious adverse antibiotic reaction.

The shortest effective period of prophylactic antimicrobial administration is not known and studies have demonstrated that post-surgical antibiotic administration is unnecessary. Furthermore, there were no proven benefits in multiple dose when compared to single-dose regimens. Post-operative antibiotics are NOT indicated unless infection is confirmed or suspected. If infection is suspected, consider modification of antibiotic regimen according to clinical condition and microbiology results. For clean and clean-contaminated procedures, additional prophylactic antimicrobial agent doses should not be administered after the surgical incision is closed in the operating room for the purpose of preventing infection, even in the presence of a drain [18]. Prophylactic antimicrobials should be discontinued in thoracic surgery within 24 h of the end of surgery. Topical antimicrobial agents should not be applied to the surgical incision [16].

Patients undergoing lung transplantation have a particular regimen of antibiotic prophylaxis [33]. The Infectious Diseases Society of America (IDSA) guidelines recommend a single first-generation cephalosporin for perioperative antibiotic prophylaxis in lung transplantation. An alternative approach would be vancomycin (particularly in centres with a high rate of MRSA) plus a third-generation cephalosporin or cefepime for 48–72 h.

16.5 Early Infection Diagnosis

A blood culture remains the "gold standard" in the diagnosis of bacteremia, although its limitations must be taken into account when interpreting the results. The sensitivity of blood cultures is influenced by many factors, including the characteristics of

the patient, the timing of the culture, the volume and source of blood, the number of cultures performed and the type of underlying infection.

16.5.1 Rapid Microbiological Diagnostic Tests

Since blood culture as a "gold standard" is slow and insufficiently sensitive, new techniques have been developed to detect bacteria and fungi in the blood. We currently have new sensitive and ultra-rapid technologies for surveillance and diagnosis of pneumonia along with improved understandings of host immune responses and the lung microbiome [34].

The techniques based on DNA demonstration, hybridization probes and methods based on the polymerase chain reaction (PCR) are aimed at the rapid identification of microorganisms in positive blood cultures and provide results within 2 h after the first sign of growth. Also the direct detection of microorganisms (or their genetic traces) in the blood using pangeneric or pathogen-specific PCR techniques has yielded promising results in different clinical scenarios [35–38].

However, like conventional blood cultures, new diagnostic techniques also have their limitations. The interpretation of the results is sometimes complicated, given the fact, that these molecular tests detect the DNA of the microorganisms more than to them as living pathogens, in addition to the risk of interference by contamination, the presence of "background" DNA in the blood and the lack of an ideal "gold standard" [39].

Another important limitation of molecular techniques in the detection and identification of bacteria is that antimicrobial sensitivity results can not always be simultaneously provided. For this reason, these techniques tend to be more a potentially useful tool that complements conventional blood cultures than a definitive method that would exempt their practice [38].

Recently, the use of "microchips" or "microarray" matrices based on DNA technology for rapid identification of bacteria in positive blood cultures has been shown to be highly sensitive and specific. In addition, these microchips make it easier to detect associated resistance genes [40]. Also, matrix-assisted laser desorption/ionization time-of-flight (MALDI - TOF) mass spectrometry is used to quickly identify microorganisms after isolation in solid culture media (agar) from clinical samples or positive blood culture subcultures (liquid media). The characteristic patterns of these proteins are used to reliably and accurately identify the genus and species isolated in 30 min. Recently studies have been published endorsing the use of MALDI-TOF directly from the blood culture bottle (without the need for prior agar subculture). This new application of the technique allows the identification of the causative agent of bacteremia or fungemia in 24–36 h after blood culture extraction, a time much less than that required by conventional identification methods [41].

In summary, all these quick-diagnosis genetic molecular techniques (with well-known manufacturing names, such as SeptiFast™, FilmArray™ or MagicPlex System™) are based on a real-time polymerase chain reaction and are capable of

detecting directly from a blood sample most of the infectious agents (bacteria and some fungi) that cause the bacteremia.

Among the proteomic techniques, the MALDI - TOF also allows the identification of microorganisms through the analysis of proteins from colonies or directly from samples, through the creation of a mass spectrum that is specific for each species. Both technologies are able to offer results in many cases in less than 6 h.

Importantly, although nucleic acid amplification testing (NAAT), mass spectrometry, and fluorescence in-situ hybridization (FISH) identification techniques can all rapidly identify pathogens in blood culture or respiratory samples in an hour or 2, NAAT and mass spectrometry are capable only of identifying presence of selected antibiotic resistance genes whereas the real-time multiplexed FISH-based microscopy ID/AST system (Accelerate Diagnostics, Tucson, Arizona, USA) is capable of evaluating antibiotic sensitivity and resistance against live pathogenic organisms from blood cultures or respiratory samples using automated phenotypic growth pattern analysis [34].

Since all of them are emerging and developing techniques, their real clinical value and the cost-effectiveness need to be evaluated; meanwhile, blood cultures remain the most important diagnostic tools for the diagnosis of bacteremia.

16.5.2 Exhaled Breath Biomarkers

The exhaled breath contains both volatile organic components (VOC) and non-volatile components. Using gas chromatography-mass spectrometry (GC-MS) analysis, a spectrum of VOCs has been identified (termed ‘exhalome’ [42], ‘volatilome’ [43], or ‘breathome’ [44]) that represent a highly innovative and compelling approach for informing precision medicine strategies. Exhaled breath analysis represents an organ-specific approach as a diagnostic tool for early detection of respiratory disorders. The collection process is non-invasive and has the potential to monitor therapy or diagnose diseases. In addition, breath analysis could generate novel therapeutic clinical trials and allows for rapid diagnosis, identification of the effectiveness of a new drug or detection of potential adverse effects. VOC-guided microbiological identification has been reported from ventilated ICU patients. VOC signatures were effective in differentiating colonized patients without VAP from those with VAP and were predictive of disease course. VOC exhalomes may thus inform precision treatment response monitoring [45].

16.5.3 Blood Biomarkers

As a result of septic disease, an extremely complex chain of events is developed, not only involving proinflammatory but also anti-inflammatory processes. Success of treatment is highly time-dependent. Consequently, the early diagnosis of sepsis and evaluation of its severity is vitally important [46]. The non-specificity of signs and symptoms of sepsis is a complicating factor for early diagnosis. However, blood

biomarkers can have an important place in this process indicating the presence or absence or severity of sepsis [47].

On the other hand, potential uses of biomarkers included roles in the prognostic, guiding antibiotic treatment, or even evaluating the response to therapy and recovery from sepsis. Clinically useful biomarkers need not only to provide additional information but also be available in a timely and cost-effective manner, as well as easy to be applied to clinical practice.

Many biomarkers have been proposed in sepsis detection. Most commonly used in septic disease included C reactive protein (CRP), procalcitonin (PCT), various cytokines (IL-6, IL-8, IL-10, TNF-a), adrenomedullin (ADM) and MRproADM, and triggering receptor expressed on myeloid cells 1 (TREM-1) [48].

C reactive protein (CRP) is a positive acute phase protein produced by the liver in response to stimulation by interleukin (IL)-6 whose hepatic synthesis starts 6–8 h after bacterial infection whereas others biomarkers start production between 1 and 5 h after bacterial aggression. Some studies reported a relationship between severity of bacteremia and CRP concentrations, but did not obtain significant results that correlated CRP and mortality [49]. Despite CRP is a rapid and inexpensive measurement, the time course of its concentrations is more useful than a single value, since it is not useful for discriminating septic from non-septic patients at an early stage of the disease. Studies that included patients with ventilator-associated pneumonia (VAP) or community-acquired pneumonia (CAP) did not observed differences in CRP concentrations at VAP diagnosis between survivors and non-survivors, but the risk of developing septic shock was higher when CRP increased between days 1 and 7 [50].

Procalcitonin (PCT) is a precursor of the hormone calcitonin and is synthesized physiologically by thyroid C cell. In bacterial infections, PCT is synthesized in various extrathyroidal neuroendocrine tissues, becoming a sign of inflammatory response [48]. Importantly, PCT levels start to rise 4 h after the onset of bacterial systemic infection, and peak between 8 and 24 h, being a useful and early diagnostic biomarker of sepsis. In surgical patients, PCT can increase particularly after major abdominal surgery, and in pancreatitis. However, PCT levels only increase transiently for 12–24 h after surgery before falling back to normal levels in the absence of infection [51]. Serum PCT levels have also been noted to increase with increasing severity of sepsis and organ dysfunction [52, 53]. The use of PCT as a guide for antibiotic therapy has been extensively studied outside the critical care environment and in last years in critical patients as well. Multiple trials have demonstrated significant decreases in antibiotic use without any apparent increase in harm in lower respiratory tract infection [54], community-acquired pneumonia [55] or showed non-significant difference in mortality and infection recurrence in critical patients [56]. Accordingly, PCT is one of the most employed blood biomarkers for sepsis diagnosis in clinical practice.

Adrenomedullin (ADM) is a peptide, produced in different tissues during physiologic and infectious stress with several functions including vasodilatory, anti-inflammatory and antimicrobial activity. Consequently, ADM is considered a "hormokine", with a hormone-like behaviour in non-inflammatory conditions,

produced by endocrine cells, and on the other hand, a cytokine-like behaviour in sepsis when it is hyper-expressed [57]. ADM measure is particularly complicate due to a rapid degradation and clearance from blood circulation. Preventing this, the mid-regional fragment of proadrenomedullin (MRproADM) is more stable and directly reflects levels of the rapidly degraded active ADM peptide. Recent studies have observed increased MR-proADM concentrations in the plasma of patients with community acquired pneumonia (CAP) and demonstrated that the performance of this biomarker to determine the risk of mortality in sepsis is influenced by disease severity, improving other standard biomarkers [58, 59].

Cytokines have been widely assessed as potential biomarkers of sepsis, but none of the cytokines studied has shown a sufficient specificity or sensitivity to be routinely employed in clinical practice [60]. Even knowing that levels of TNF and IL-10 increase within the first 24 h after infection, blood cytokine concentrations are rather erratic and do not have a clear time course compared to the sepsis one, which makes interpretation difficult [61]. Multiple studies found cytokines levels to be significantly higher in septic patients who died compared with survivors. Despite the results in which both IL-6 and IL-8 significantly predicted sepsis, only procalcitonin was significantly associated with diagnosis when combined with traditional markers of sepsis [48].

And last but not least, triggering receptor expressed on myeloid cells-1 (TREM-1) is another biomarker related to sepsis. TREM-1 is an inflammatory immunoglobulin superfamily member, expressed in neutrophils, monocytes and macrophages, producing an expanded inflammatory response. Soluble TREM-1 (sTREM-1) is a subtype of secreted TREM-1 that could be released into the blood or body fluids during infection, being useful not only to identify infection but also to graduate inflammation severity [62]. Recently, several systematic reviews and meta-analyses have shown the diagnostic value for infection of sTREM-1 in plasma, bronchoalveolar lavage fluid or pleural fluid [63]. In short, sTREM-1 has a moderate diagnostic significance in assessing infection in adult patients, not being a significant biomarker to predict mortality of infection. However, a panel of biomarkers including sTREM-1 is recommended to predict prognosis of an infection [64].

In summary, none of these biomarkers either alone or in combination have been reported to significantly enhance routine clinical and radiological diagnosis for infection and pneumonia.

16.5.4 Immune Dysregulation

Sepsis physiopathology is focused on immune dysregulation, and quantifying immunological dysfunction could be a successful tool to distinguish septic from uninfected patients early and efficiently. Transcriptomic analysis has demonstrated to be useful for evaluating immune alterations in sepsis. Numerous trials in last year have observed and studied these immune impairments in septic patients [65, 66]. The EXPRESS study, through microarrays processing, identified a gene expression pattern considered a marker of sepsis, characterised by the presence of up-regulated

group of genes in which interestingly were involved genes of innate immunity (neutrophil proteases and interleukin receptors) and those involved immunoglobulin synthesis, but also low expression genes related to events of adaptative immunity, such as antigen presentation (antigen presentation cells HLA-DR, and T CD4 lymphocytes) [67]. However, an important limitation of microarrays is the long time needed for analysis and provides just a semiquantitative measurement of gene expression, making microarrays difficult to be applied to clinical practice.

Gene expression quantification by quantitative real-time polymerase chain reaction (q RT-PCR) was the next step for fast identification of immune dysregulation, but still has limitations, providing relative quantification of gene expression [68, 69]. Consequently, absolute quantification of gene expression achieved by droplet digital PCR (ddPCR) is the next generation, offering better precision and reproducibility than q RT-PCR methods [70].

As evidenced of multiple trials, low expression of HLA-DRA at the very beginning of sepsis, has been independently associated with the risk of mortality, demonstrating a principal role of antigen presentation in infection, becoming HLA-DRA as a predictor of mortality of the disease [71, 72].

Recently, with the objective to improve early diagnosis of sepsis, new combinations of blood biomarkers and gene expression of immune dysfunction have been proposed as a promising tool, also for evaluating the degree of dysregulation in sepsis, as well as predicting mortality in this disease [73]. Almansa et al. [74] have demonstrated for the first time, using ddPCR, that combining quantification ratio of PCT/HLA-DRA is a useful tool for early diagnosis of sepsis, improving the sensitivity of PCT, preserving specificity.

16.5.5 Endothelium and Infection

Acute vascular endothelial dysfunction (ED) is a central event in the pathogenesis of sepsis, increasing vascular permeability, promoting activation of the coagulation cascade, tissue oedema and compromising perfusion of vital organs. As occurs in sepsis, aging and chronic ED promotes a pro-inflammatory, pro-oxidative and pro-coagulation status in the blood vessels, favouring vasomotor tone alterations, platelet activation and leukocyte adhesion and transmigration. In addition, aging and chronic diseases impair the regenerative ability of the endothelium. Aging and chronic ED thus contribute to generate a basal degree of organ failure [75].

In addition to aging and chronic disease, there are other factors such as critical illness, surgery, trauma or hypervolemia which induce ED preceding sepsis. Increasing evidence supports that this previous ED could facilitate the incidence of sepsis [76, 77].

When an aged individual with chronic disease shows signs of infection, monitoring ED could help to predict or detect early sepsis [78]. ED could be profiled “in vivo” using non-invasive image techniques like intravital microscopy or hand-held video images of sublingual microcirculation [79]. The other approach to evaluate ED is using biomarkers. Biomarkers of ED include markers of endothelial

glycocalyx degradation (heparan sulfate, chondroitin sulfate, hyaluronic acid and syndecan), markers of endothelial cell activation (endocan or Angiopoietin-2), cell adhesion molecules (selectins, ICAM-1 and VCAM-1), vasoactive peptides, coagulation inhibitors (thrombomodulin), vasoconstrictor and vasopressor molecules (endothelin), growth factors (vascular endothelial growth factor VEGF), and circulating endothelial cells as some of the most relevant [75, 80].

The best approach to cover the different features of endothelial injury is a multimarker strategy. Using coupled methods such as the ultra-high performance liquid chromatography together with mass spectrometry-based multiple reaction allows to simultaneously profile multiple endothelial biomarkers and could contribute to diagnose sepsis earlier [81, 82].

16.6 Nosocomial Infection

16.6.1 Pneumonia

Pneumonia is the most common infective respiratory complication after thoracic surgery [83]. It is an infection of the lower respiratory tract that involves the terminal airways: respiratory bronchioles, alveolar ducts, and alveoli. The infection develops when the sterility of the tracheobronchial tree is breached by the introduction of a virulent pathogen or a defect in the host immunologic defence. Pneumonia is diagnosed by new lung infiltrates plus clinical evidence of an infectious origin, which include the new onset of fever, purulent sputum, leucocytosis, and decline in oxygenation. Hospital-acquired pneumonia, or nosocomial pneumonia, is a lower respiratory infection that was not incubating at the time of hospital admission and that presents clinically 2 or more days after hospitalization. Ventilator-associated pneumonia (VAP) is defined as pneumonia that presents more than 48 h after endotracheal intubation.

Existing clinical and radiological-based risk criteria (CPIS, CURB65) alone or associated with conventional microbiological culture of tracheal aspirates or bronchoalveolar lavage (BAL) are widely used for diagnosis but consistently have been shown to provide a suboptimal approach [34].

There are three major limitations of the standard pneumonia definition: Many of the diagnostic criteria are very subjective, the definition correlates poorly with histological pneumonia, and 60% of clinically diagnosed nosocomial pneumonia episodes cannot be confirmed microbiologically [84].

In order to improve the diagnosis of VAP, epidemiological surveillance definitions have been proposed [84, 85]. However, although newer surveillance definitions are sensitive for pneumonia in the ICU including VAP, consistently under detect patients that are clinically shown to have bacterial VAP based on clinical diagnostic criteria and response to antibiotic treatment [86].

The most common source of postoperative pneumonia is aspirated gastric secretions, particularly in ventilated patients. Postoperative pneumonia after lung resection can also be caused by bacterial colonization of atelectatic lung. Postoperative

atelectasis after pulmonary surgery should be aggressively managed before it deteriorates into pneumonia [1]. Chest physiotherapy, pain control, bronchodilators, and early ambulation should be done for all patients, but pneumonia may develop regardless of these measures. Pneumonia is also described after bronchoscopy before surgery in patients with lung cancer, associated with central location of the tumour, age >70 years, and current smoking [87].

The aetiology and clinical manifestations of postoperative pneumonia depend on the environment where the disease is acquired and the host characteristics [88]. The aetiology includes germs typically responsible for community-acquired pneumonia and classically isolated from patients with COPD. Haemophilus species, Streptococcus species, and, to a much lesser extent, Pseudomonas, Staphylococcus and Serratia species are the most frequently identified pathogens [83]. Immunosuppressed patients are prone to atypical infections, including a variety of viral and fungal organisms [88]. Pathogens cultured from intraoperative bronchial samples are likely to be responsible for a significant percentage of postoperative pneumonia. The antibiotic prophylaxis based on a first or second-generation cephalosporin is usually effective in the prevention of wound infection and empyema, but it does not specifically target the respiratory pathogens found in these patients and is not optimal in several instances. A more adapted prophylaxis might be able to decrease the rate of in-hospital acquired pneumonia after thoracic surgery and should be evaluated.

In order to reduce the mortality associated with nosocomial pneumonia, specific programs for the prevention of this infection have been included in national campaigns [89].

Very recently, it has been reported that a multimodal intervention based on the simultaneous implementation of a evidence-based bundle measures reduces in more than 50% the incidence of ventilator-associated pneumonia and this beneficial was sustained longer after implementation [90] (Table 16.2).

The reported prevalence of pneumonia in post thoracotomy patients ranges from 2% to 22%, with a higher incidence in those who have undergone more extensive lung resections [3]. Risk factors for postoperative pneumonia include: age >75 years, BMI > 30 kg/m^2, ASA > 3, smoking history, COPD, extent of resection, presence of intraoperative bronchial colonization, and male sex [2, 83].

Patients with postoperative pneumonia requires non-invasive ventilation or reintubation more frequently than patients who did not develop pneumonia and is associated with longer intensive care unit and hospital stay [83]. Life-threatening pneumonia can be seen related to aspirated fluid in the presence of a bronchopleural fistula [1]. Pneumonia after pneumonectomy is associated with a 25% mortality rate and is the leading cause of postoperative mortality [4]. Patients with prolonged infection or who have suffered large volume aspiration are at risk for severe necrotizing bronchopneumonia or abscess formation. Lung abscess should be managed initially with appropriate medical therapy and/or percutaneous drainage [88].

Radiographic findings vary based on the type of bacteria colonizing the lung. Commonly, chest X-rays demonstrate patchy consolidation in a bronchopneumonic distribution, with lobar consolidations less commonly observed. Computed

tomography will typically demonstrate consolidation and ground-glass attenuation in the affected lung and is particularly useful in the evaluation of aspiration pneumonia caused by trans bronchial spill of fluid via a bronchopleural fistula, as it clearly delineates the fistula as the culprit in the infection [1].

Postoperative pneumonia should be aggressively treated with appropriate antibiotics after culture. Although prompt initiation of antibiotics is critical, all patients with suspected pneumonia should have a sampling done of lower respiratory tract secretions to better guide the therapy [88]. Treatment of pneumonia is based on an assessment of place of therapy (hospital ward or ICU), the presence of coexisting cardiopulmonary diseases, and the presence of modifying factors [88]. Management described by IDSA [91] includes: using clinical criteria to decide whether to initiate antibiotic therapy; a non-invasive sampling with semi quantitative cultures to diagnose the aetiology of pneumonia; the use of antibiogram data to decrease the unnecessary use of dual gram-negative and empiric MRSA antibiotic treatment; and a 7-day course of antimicrobial therapy regardless of microbial aetiology, as well as antibiotic de-escalation. Each hospital should generate local protocols according to antibiograms to guide the optimal choice of antibiotics. In patients with suspected VAP, IDSA recommends to include coverage for Staph aureus, Pseudomonas aeruginosa, and other gram-negative bacilli in all empiric regimens. If empiric coverage for MRSA is indicated, either vancomycin or linezolid is recommended. When empiric treatment that includes coverage for MSSA (and not MRSA) is indicated, the guidelines suggest a regimen including piperacillin-tazobactam, cefepime, levofloxacin, imipenem, or meropenem. Oxacillin, nafcillin, and cefazolin are preferred agents for treatment of proven MSSA, but are not necessary for the empiric treatment of VAP if one of the above agents is used. For patients with pneumonia due to Pseud. aeruginosa, the guidelines recommend that the choice of an antibiotic for definitive (not empiric) therapy be based on the results of antimicrobial susceptibility testing.

Table 16.2 Measures for ventilator-associated pneumonia prevention

Basic mandatory measures
Education and training in appropriate airway management
Strict hand hygiene with alcohol solutions before airway management
Control and maintenance of cuff pressure
Oral hygiene with chlorhexidine
Semirecumbent positioning. Avoidance of 0° supine positioning
Promoting procedures and protocols that safely avoid or reduce duration of mechanical ventilation
Avoidance of elective changes of ventilator circuits, humidifiers, and endotracheal tubes
Highly recommended measures
Selective decontamination of the digestive tract or selective oropharyngeal decontamination
Continuous aspiration of subglottic secretions
Short course (2–3 doses) of systemic antibiotics during intubation of patients with previous decreased consciousness

Adapted from Álvarez-Lerma et al. Prevention of Ventilator-Associated Pneumonia: The Multimodal Approach of the Spanish ICU "Pneumonia Zero" Program

16.6.1.1 Non-antibiotic Treatment of Infection

Taken into account the rise of antibacterial resistance and the challenges of common antibacterial agent discovery and development it would consider the potential role of non-conventional approaches Alternative non-antibiotic treatment strategies may provide an effective way for therapy. The more recent developments in this area consist in strategies targeting of bacterial virulence factors, the use of bacteriophages to kill bacteria, vaccination to prevent healthcare associated infections and manipulation of the microbiome to fight against infections [92] (Table 16.3).

The pathogens produce virulence factors that allow them to resist clearance by the host, to invade deeper tissues, and to damage host cells. Several innovative alternatives under development interact with virulence factors. They can be classified in agents that induce inhibition of toxins and secretion systems (chemical inhibitors or antibodies), methods designed to prevent biofilm formation and to disaggregate biofilms once formed (catheters coated with polymeric sulfobetaine, inhibitors of the pili biosynthesis reducing bacterial adhesion), and substances against the bacterial signalling and regulation acting against quorum sensing [92].

The main advantage of antivirulence strategies is that taking into account that virulence factor are specific of pathogens they do not affect the commensal flora.

Phages are viruses that only infect bacterial cells. They are specific for bacteria and even particular strains and species of bacteria, they do not infect human cells, and they have little or no effect on normal microbial flora. The high specificity is also and disadvantage, as cocktails of multiple phages are required to target multiple species and even most strains within a species [93].

Nowadays, some technological advances offer the possibility of customizing bacteriophages and improve their characteristics, particularly: expand the ability of bacteriophages to penetrate bacterial biofilms; enlarge their potency and effectiveness; adapt the spectrum of activities of bacteriophages to infections caused by numerous bacterial species and strains; and make them more stable and specific [94].

Table 16.3 Non-antibiotic strategies for infectious diseases

Anti-virulence strategies	– Inhibition of toxins and secretion systems – Targeting biofilms and adherence – Targeting signaling and regulation
Microbiome modulation	– Prebiotics – Probiotics – Faecal microbiota transplantation (FMT)
Vaccines	*Clostridium difficile, S aureus, P aeruginosa, monoclonal antibodies (mAbs)*
Bacteriophages and phage therapy	Phages Cocktails Customized phages • Ability to penetrate biofilms • High potency and effectiveness • Adapt the spectrum • Increase stability and specificity

In the last years, the prophylaxis of multidrug-resistant pathogen infections through the use of vaccines and passive immunization has growing the interest. Its application in high-risk patients will both prevent infections and reduce the use of antimicrobials and the consequent development of resistance. Actually, among the Gram-negative bacteria the vaccines against *P. aeruginosa* have presented a greater development, having already been concluded a phase 3 study [92].

In another way, the use of monoclonal antibodies has taken a big development in the last years. *C. difficile*, *S. aureus* and *P. aeruginosa* monoclonal Antibodies are currently in phase 2–3 clinical trials [95].

Human microbiota is the amount of microorganisms that are found in human body and contribute to regulate physiological functions. Alterations of this microbiome has been associated with many diseases like diabetes mellitus, asthma, inflammatory bowel disease (IBD), antibiotics-associated diarrhoea and cancer.

So far, the most important application of microbiome in medicine is in the sphere of treating recurrent infections caused by *C. Difficile*. The effect of prebiotics and probiotics in preserving normal microbiome and preventing the growth of pathogenic bacteria is actually in investigation [96].

In summary, alternatives to antibiotics may become important therapeutic options for bacterial infections on the near future.

16.6.2 Empyema

Empyema thoracis is defined as "pus in the chest" [97]. Postoperative empyema is an uncommon, but serious, infective complication. There is a 2–16% risk of empyema after lung cancer resection, with most authors reporting a risk of less than 5% [3]. Risk factors for empyema include malnutrition or underlying immunodeficiency syndromes, a completion pneumonectomy following prior lobectomy, right pneumonectomy, mediastinal lymphadenectomy, preoperative radiation therapy, and postoperative mechanical ventilation [4]. Empyema in the early post-operative period is typically attributed to residual pleural infection and/or intraoperative contamination [3]. It may be associated with persistent pleural effusion, air space, or bronchopleural fistula. Bronchopleural fistula is the main cause of post-pneumonectomy empyema, identified in over 80% of patients. When associated with a large bronchopleural fistula, mortality rates from empyema are especially high, reaching up to 71% [3, 4].

The presence of empyema should be considered if the patient has a pleural collection in association with fever, cough, or haemoptysis [4]. Serum C-reactive protein levels are typically elevated [4]. Useful investigations include sputum, blood and pleural fluid cultures, chest X-ray, and computed tomography. Although not routinely done, a positive chest tube tip culture strongly predicts postoperative empyema [98]. In postoperative empyema following lobar, segmental, or wedge resections, there may be thickening and increased enhancement of the visceral and parietal pleura, separated by an empyema or exudative effusion. This is referred to as the "split pleura sign" and has been documented in 68–86% of all empyema cases [3].

Multiple air–fluid levels may also be seen. In post pneumonectomy empyema, the radiographic features include rapid fluid filling and decreased air–fluid level in the pneumonectomy space, with contralateral mediastinal shift. Computed tomography images may demonstrate expansion of the pneumonectomy space with mass effect on the adjacent mediastinum, increased residual parietal pleural thickening and enhancement, and bronchopleural fistula if present [3].

The two key components of empyema treatment are to drain the infected pleural space and to treat the fistula. Appropriate antibiotic therapy is also required [4]. The American Association for Thoracic Surgery has published in 2017 guidelines for the management of empyema [97]. They recommend a prompt intervention to identify or rule out the presence of a bronchopleural fistula in post pneumonectomy empyema and provide drainage of pus with an aggressive surgical approach that includes antibiotics, serial debridement, closure of the fistula when present, and obliteration of the residual pleural space using vascularized tissue transposition. If a bronchopleural fistula is confirmed, they recommend closure of the fistula with a combination of primary closure and buttressing with a well-vascularized transposed soft-tissue pedicle. Transposition of the omentum is preferred over skeletal muscle flaps or mediastinal soft tissue, and this should be attempted after the purulent fluid has been drained completely and the pleural cavity has a surface of granulation tissue. In the absence of a bronchopleural fistula there is a general shift among practicing surgeons away from open thoracotomy to VATS for the surgical management of empyema [97].

16.6.3 Mediastinitis

Mediastinitis is a life-threatening infectious complication after thoracic surgery. It may result from contamination during surgery from the patient and the surgeon, as well as extension of infection from adjacent structures such as the oesophagus (i.e. due to oesophageal perforation), airways (e.g. due to tracheobronchial perforation) and lungs (e.g. pleural empyema). Mediastinitis incidence remains significant and ranges between 0.25% and 5% [38]. The European Association for Cardio-Thoracic Surgery has published in 2017 guidelines for the prevention and management of mediastinitis [99] that recommends: routine prophylactic topical mupirocin for 5 days; a shower or bath using soap, either the day before or on the day of surgery; a beta-lactam antibiotic as a single antibiotic completed within 1 h of the skin incision; or vancomycin with additional Gram-negative coverage for patients with beta-lactam allergy or with proven or suspected MRSA colonization; and glucose control with continuous IV insulin. Once a clinical diagnosis of mediastinitis is suspected or established, the cornerstones of treatment are surgical drainage, broad-spectrum antibiotic therapy after blood culture, and supportive care. Superficial median sternotomy infections with a stable sternum may be managed with local drainage. When deep mediastinal structures are involved, after debridement and drainage and antibiotics, various treatment options include simple closure, closure over drains, negative pressure wound therapy either as a destination or as a bridge prior to final

surgical closure, the use of bilateral pectoralis myocutaneous or omental flap closure in case of sternal instability or insufficient bone stock, and open management with delayed closure [99]. Sternal osteomyelitis is generally treated with antibiotics for 4–6 weeks.

References

1. Iyer A, Yadav S. Postoperative care and complications after thoracic surgery. In: Principles and practice of cardiothoracic surgery. Rijeka: InTech; 2013. Available from http://www.intechopen.com/books/principles-and-practice-of-cardiothoracic-surgery/postoperative-care-and-complications-after-thoracic-surgery.
2. Agostini P, Cieslik H, Rathinam S, Bishay E, Kalkat MS, Rajesh PB, et al. Postoperative pulmonary complications following thoracic surgery: are there any modifiable risk factors? Thorax. 2010;65(9):815–8.
3. Rotman JA, Plodkowski AJ, Hayes SA, de Groot PM, Shepard J-AO, Munden RF, et al. Postoperative complications after thoracic surgery for lung cancer. Clin Imaging. 2015;39(5):735–49.
4. Myles PS. Complications of thoracic surgery. In: Oxford textbook of cardiothoracic anaesthesia. Oxford: Oxford University Press; 2015. p. 415–24. Available from http://oxfordmedicine.com/view/10.1093/med/9780199653478.001.0001/med-9780199653478-chapter-37.
5. Ceken S, Simsek Yavuz S, Sensoy A, Imamoglu O. Epidemiology and risk factors for surgical site infections following thoracic surgery. Int J Clin Exp Med. 2016;9:12018.
6. Imperatori A, Nardecchia E, Dominioni L, Sambucci D, Spampatti S, Feliciotti G, et al. Surgical site infections after lung resection: a prospective study of risk factors in 1,091 consecutive patients. J Thorac Dis. 2017;9(9):3222–31.
7. Olivetti S, Lanza GV, Ruffini E, Oliaro A, Filosso PL. O-019healthcare associated infection after lung surgery. Interact Cardiovasc Thorac Surg. 2016;23(Suppl 1):i6.2–i6.
8. Zajac-Lenczewska I, Czarniak E, Skokowski J, Samet A. Infections in patients after thoracic surgery. Pneumonol Alergol Pol. 2003;71(1–2):36–42.
9. Nan DN, Fernández-Ayala M, Fariñas-Álvarez C, Mons R, González-Macías J, Carmen Fariñas M, et al. Infección nosocomial después de cirugía toracoscópica videoasisitida. Rev Esp Quimioter. 2011;24:217.
10. Sok M, Dragaš AZ, Eržen J, Jerman J. Sources of pathogens causing pleuropulmonary infections after lung cancer resection. Eur J Cardio Thoracic Surg. 2002;22(1):23–9.
11. Nan DN, Fernández-Ayala M, Fariñas-Álvarez C, Mons R, Ortega FJ, González-Macías J, et al. Nosocomial infection after lung surgery. Chest. 2005;128(4):2647–52.
12. NICE. Surgical site infections: prevention and treatment | Guidance and guidelines | NICE. London: NICE; 2008. Available from https://www.nice.org.uk/guidance/cg74.
13. van Walraven C, Musselman R. The surgical site infection risk score (SSIRS): a model to predict the risk of surgical site infections. PLoS One. 2013;8(6):e67167.
14. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJC, Gorbach SL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;59(2):e10–52.
15. WHO. WHO | Global guidelines on the prevention of surgical site infection. Geneva: WHO; 2017. Available from https://www.who.int/gpsc/ssi-guidelines/en/.
16. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention Guideline for the prevention of surgical site infection, 2017. JAMA Surg. 2017;152(8):784.
17. Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016;16(12):e276–87.

18. Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016;16(12):e288–303.
19. O'Hara LM, Thom KA, Preas MA. Update to the Centers for Disease Control and Prevention and the Healthcare Infection Control Practices Advisory Committee Guideline for the Prevention of Surgical Site Infection (2017): a summary, review, and strategies for implementation. Am J Infect Control. 2018;46(6):602–9.
20. Liu Z, Norman G, Iheozor-Ejiofor Z, Wong JK, Crosbie EJ, Wilson P. Nasal decontamination for the prevention of surgical site infection in Staphylococcus aureus carriers. Cochrane Database Syst Rev. 2017;5:CD012462.
21. Pedersen PU, Larsen P, Håkonsen SJ. The effectiveness of systematic perioperative oral hygiene in reduction of postoperative respiratory tract infections after elective thoracic surgery in adults: a systematic review. JBI Datab Syst Rev Impl Rep. 2016;14(1):140–73.
22. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, Gonzalez M, et al. Guidelines for enhanced recovery after lung surgery: recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). Eur J Cardio Thoracic Surg. 2019;55:91.
23. Muehling BM, Halter GL, Schelzig H, Meierhenrich R, Steffen P, Sunder-Plassmann L, et al. Reduction of postoperative pulmonary complications after lung surgery using a fast track clinical pathway. Eur J Cardio Thoracic Surg. 2008;34(1):174–80.
24. Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Am J Surg. 2005;189(4):395–404.
25. Anderson DJ, Sexton DJ. Antimicrobial prophylaxis for prevention of surgical site infection in adults. UpToDate. 2018:17–9.
26. Bassetti M, Righi E, Astilean A, Corcione S, Petrolo A, Farina EC, et al. Antimicrobial prophylaxis in minor and major surgery. Minerva Anestesiol. 2015;81(1):76–91.
27. Ierano C, Peel T, Ayton D, Rajkhowa A, Marshall C, Thursky K. Surgical antibiotic prophylaxis – the evidence and understanding its impact on consensus guidelines. Infect Dis Heal. 2018;23(3):179–88.
28. Scottish Intercollegiate Guidelines Network. Antibiotic prophylaxis in surgery. Edinburgh: Scottish Intercollegiate Guidelines Network; 2008. Available from www.sign.ac.uk/guidelines/published/numlist.html.
29. South Australian expert Advisory Group on Antimicrobial Resistance. Surgical antimicrobial prophylaxis clinical guideline. Adelaide, SA: SA Health; 2011. Available from https://www.sahealth.sa.gov.au/wps/wcm/connect/6bb523804358edbd883b9ef2cadc00ab/Surgical+Antimicrobial+Prophylaxis_v2.0_23112017.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-6bb523804358edbd883b9ef2cadc00ab-msq.2DQ.
30. Chang SH, Krupnick AS. Perioperative antibiotics in thoracic surgery. Thorac Surg Clin. 2012;22(1):35–45, vi.
31. Dhooria S, Sehgal IS, Prasad KT, Bal A, Aggarwal AN, Behera D, et al. A randomized trial of antimicrobial prophylaxis in patients undergoing medical thoracoscopy (APT). Respiration. 2017;94(2):207–15.
32. Kirkwood KA, Gulack BC, Iribarne A, Bowdish ME, Greco G, Mayer ML, et al. A multiinstitutional cohort study confirming the risks of Clostridium difficile infection associated with prolonged antibiotic prophylaxis. J Thorac Cardiovasc Surg. 2018;155(2):670–678.e1.
33. Anesi JA, Blumberg EA, Abbo LM. Perioperative antibiotic prophylaxis to prevent surgical site infections in solid organ transplantation. Transplantation. 2018;102(1):21–34.
34. Douglas SI. New diagnostic methods for pneumonia in the ICU. Curr Opin Infect Dis. 2016;29:197–204.
35. Peters RP, van Agtmael MA, Danner SA, et al. New developments in the diagnosis of bloodstream infections. Lancet Infect Dis. 2004;4(12):7517–60.
36. Westh H, Lisby G, Breysse F, et al. Multiplex real - time PCR and blood culture for identification of bloodstream pathogens in patients with suspected sepsis. Clin Microbiol Infect. 2009;15(6):544–51.

37. Lehmann LE, Alvarez J, Hunfeld KP, et al. Potential clinical utility of polymerase chain reaction in microbiological testing for sepsis. Crit Care Med. 2009;37(12):3085–90.
38. Klouche M, Schröder U. Rapid methods for diagnosis of bloodstream infections. Clin Chem Lab Med. 2008;46(7):888–908.
39. Nikkari S, McLaughlin IJ, Bi W, et al. Does blood of healthy subjects contain bacterial ribosomal DNA? J Clin Microbiol. 2001;39(5):1956–9.
40. Tissari P, Zumla A, Tarkka E, et al. Accurate and rapid identification of bacterial species from positive blood cultures with a DNA - based microarray platform: an observational study. Lancet. 2010;375(9710):224–30.
41. Huang A, Newton D, Kunapuli A, Gandhi T, Washer L, Curtis J, Collins D, Nagel J. Impact of rapid organism identification via matrix - assisted laser desorption/ionization time - of - flight combined with antimicrobial stewardship team intervention in adult patients with bacteremia and candidemia. Clin Infect Dis. 2013;57:1237–45.
42. Martinez-Lozano Sinues P, Zenobi R, Kohler M. Analysis of the exhalome: a diagnostic tool of the future. Chest. 2013;144:746–9.
43. Amann A, Costello Bde L, Miekisch W, et al. The human volatilome: volatile organic compounds (VOCs) in exhaled breath, skin emanations, urine, feces and saliva. J Breath Res. 2014;8:034001.
44. van der Schee MP, Paff T, Brinkman P, et al. Breathomics in lung disease. Chest. 2015;147:224–31.
45. Schnabel R, Fijten R, Smolinska A, et al. Analysis of volatile organic compounds in exhaled breath to diagnose ventilator-associated pneumonia. Sci Rep. 2015;5:17179.
46. Moore LJ, Moore FA. Early diagnosis and evidence-based care of surgical sepsis. J Intensive Care Med. 2013;28(2):107–17.
47. Pierrakos C, Vincent JL. Sepsis biomarkers: a review. Crit Care. 2010;14(1):R15.
48. Kibe S, Adams K, Barlow G. Diagnostic and prognostic biomarkers of sepsis in critical care. J Antimicrob Chemother. 2011;66(Suppl 2):ii33–40.
49. Coelho L, Povoa P, Almeida E, Fernandes A, Mealha R, Moreira P, et al. Usefulness of C-reactive protein in monitoring the severe community-acquired pneumonia clinical course. Crit Care. 2007;11(4):R92.
50. Hillas G, Vassilakopoulos T, Plantza P, Rasidakis A, Bakakos P. C-reactive protein and procalcitonin as predictors of survival and septic shock in ventilator-associated pneumonia. Eur Respir J. 2010;35(4):805–11.
51. Lindberg M, Hole A, Johnsen H, Asberg A, Rydning A, Myrvold HE, et al. Reference intervals for procalcitonin and C-reactive protein after major abdominal surgery. Scand J Clin Lab Invest. 2002;62(3):189–94.
52. Giamarellos-Bourboulis EJ, Mega A, Grecka P, Scarpa N, Koratzanis G, Thomopoulos G, et al. Procalcitonin: a marker to clearly differentiate systemic inflammatory response syndrome and sepsis in the critically ill patient? Intensive Care Med. 2002;28(9):1351–6.
53. Giamarellos-Bourboulis EJ, Raftogiannis M. The immune response to severe bacterial infections: consequences for therapy. Expert Rev Anti Infect Ther. 2012;10(3):369–80.
54. Schuetz P, Christ-Crain M, Thomann R, Falconnier C, Wolbers M, Widmer I, et al. Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial. JAMA. 2009;302(10):1059–66.
55. Christ-Crain M, Stolz D, Bingisser R, Muller C, Miedinger D, Huber PR, et al. Procalcitonin guidance of antibiotic therapy in community-acquired pneumonia: a randomized trial. Am J Respir Crit Care Med. 2006;174(1):84–93.
56. Nobre V, Harbarth S, Graf JD, Rohner P, Pugin J. Use of procalcitonin to shorten antibiotic treatment duration in septic patients: a randomized trial. Am J Respir Crit Care Med. 2008;177(5):498–505.
57. Andaluz-Ojeda D, Nguyen HB, Meunier-Beillard N, Cicuendez R, Quenot JP, Calvo D, et al. Superior accuracy of mid-regional proadrenomedullin for mortality prediction in sepsis with varying levels of illness severity. Ann Intensive Care. 2017;7(1):15.

58. Andaluz-Ojeda D, Cicuendez R, Calvo D, Largo E, Nogales L, Munoz MF, et al. Sustained value of proadrenomedullin as mortality predictor in severe sepsis. J Infect. 2015;71(1):136–9.
59. Bello S, Lasierra AB, Minchole E, Fandos S, Ruiz MA, Vera E, et al. Prognostic power of proadrenomedullin in community-acquired pneumonia is independent of aetiology. Eur Respir J. 2012;39(5):1144–55.
60. Andaluz-Ojeda D, Bobillo F, Iglesias V, Almansa R, Rico L, Gandia F, et al. A combined score of pro- and anti-inflammatory interleukins improves mortality prediction in severe sepsis. Cytokine. 2012;57(3):332–6.
61. Harbarth S, Holeckova K, Froidevaux C, Pittet D, Ricou B, Grau GE, et al. Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis. Am J Respir Crit Care Med. 2001;164(3):396–402.
62. Su L, Feng L, Song Q, Kang H, Zhang X, Liang Z, et al. Diagnostic value of dynamics serum sCD163, sTREM-1, PCT, and CRP in differentiating sepsis, severity assessment, and prognostic prediction. Mediators Inflamm. 2013;2013:969875.
63. Wu Y, Wang F, Fan X, Bao R, Bo L, Li J, et al. Accuracy of plasma sTREM-1 for sepsis diagnosis in systemic inflammatory patients: a systematic review and meta-analysis. Crit Care. 2012;16(6):R229.
64. Su L, Liu D, Chai W, Liu D, Long Y. Role of sTREM-1 in predicting mortality of infection: a systematic review and meta-analysis. BMJ Open. 2016;6(5):e010314.
65. Benjamin TM, et al. Genome-wide transcription profiling of human sespis: a systematic review. Crit Care. 2010;14(6):R237.
66. Xiao W, Mindrinos MN, Seok J, Cuschieri J, Cuenca AG, Gao H, et al. A genomic storm in critically injured humans. J Exp Med. 2011;208(13):2581–90.
67. Almansa R, Heredia-Rodriguez M, Gomez-Sanchez E, Andaluz-Ojeda D, Iglesias V, Rico L, et al. Transcriptomic correlates of organ failure extent in sepsis. J Infect. 2015;70(5):445–56.
68. Cajander S, Backman A, Tina E, Stralin K, Soderquist B, Kallman J. Preliminary results in quantitation of HLA-DRA by real-time PCR: a promising approach to identify immunosuppression in sepsis. Crit Care. 2013;17(5):R223.
69. Cajander S, Tina E, Backman A, Magnuson A, Stralin K, Soderquist B, et al. Quantitative real-time polymerase chain reaction measurement of HLA-DRA gene expression in whole blood is highly reproducible and shows changes that reflect dynamic shifts in monocyte surface HLA-DR expression during the course of sepsis. PLoS One. 2016;11(5):e0154690.
70. Hindson CM, Chevillet JR, Briggs HA, Gallichotte EN, Ruf IK, Hindson BJ, et al. Absolute quantification by droplet digital PCR versus analog real-time PCR. Nat Methods. 2013;10(10):1003–5.
71. Cazalis MA, Friggeri A, Cave L, Demaret J, Barbalat V, Cerrato E, et al. Decreased HLA-DR antigen-associated invariant chain (CD74) mRNA expression predicts mortality after septic shock. Crit Care. 2013;17(6):R287.
72. Monneret G, Lepape A, Voirin N, Bohe J, Venet F, Debard AL, et al. Persisting low monocyte human leukocyte antigen-DR expression predicts mortality in septic shock. Intensive Care Med. 2006;32(8):1175–83.
73. Winkler MS, Rissiek A, Priefler M, Schwedhelm E, Robbe L, Bauer A, et al. Human leucocyte antigen (HLA-DR) gene expression is reduced in sepsis and correlates with impaired TNFalpha response: a diagnostic tool for immunosuppression? PLoS One. 2017;12(8):e0182427.
74. Almansa R, Martin S, Martin-Fernandez M, Heredia-Rodriguez M, Gomez-Sanchez E, Aragon M, et al. Combined quantification of procalcitonin and HLA-DR improves sepsis detection in surgical patients. Sci Rep. 2018;8(1):11999.
75. Bermejo-Martin JF, Martin-Fernandez M, Lopez-Mestanza C, Duque P, Almansa R. Shared features of endothelial dysfunction between sepsis and its preceding risk factors (aging and chronic disease). J Clin Med. 2018;7:400.
76. Wang J, Wu A, Wu Y. Endothelial glycocalyx layer: a possible therapeutic target for acute lung injury during lung resection. Biomed Res Int. 2017;2017:5969657.

77. Vassiliou AG, Mastora Z, Orfanos SE, Jahaj E, Maniatis NA, Koutsoukou A, Armaganidis A, Kotanidou A. Elevated biomarkers of endothelial dysfunction/activation at ICU admission are associated with sepsis development. Cytokine. 2014;69:240–7.
78. Colbert JF, Schmidt EP. Endothelial and microcirculatory function and dysfunction in sepsis. Clin Chest Med. 2016;37:263–75.
79. Ince C, Mayeux PR, Nguyen T, Gomez H, Kellum JA, Ospina-Tascón GA, Hernandez G, Murray P, De Backer D. ADQI XIV Workgroup. The endothelium in sepsis. Shock. 2016;45:259–70.
80. Xing K, Murthy S, Liles WC, Singh JM. Clinical utility of biomarkers of endothelial activation in sepsis—a systematic review. Crit Care. 2012;16:7.
81. Walczak M, Suraj J, Kus K, Kij A, Zakrzewska A, Chlopicki S. Towards a comprehensive endothelial biomarkers profiling and endothelium-guided pharmacotherapy. Pharmacol Rep. 2015;67:771–7.
82. Reddy B Jr, Hassan U, Seymour C, Angus DC, Isbell TS, White K, Weir W, Yeh L, Vincent A, Bashir R. Point-of-care sensors for the management of sepsis. Nat Biomed Eng. 2018;2:640–8.
83. Schussler O, Alifano M, Dermine H, Strano S, Casetta A, Sepulveda S, et al. Postoperative pneumonia after major lung resection. Am J Respir Crit Care Med. 2006;173(10):1161–9.
84. Klompas M, Magill S, Robicsek A, Strymish JM, Kleinman K, Evans RS, Lloyd JF, Khan Y, Yokoe DS, Stevenson K, Samore M, Platt R, CDC Prevention Epicenters Program. Objective surveillance definitions for ventilator-associated pneumonia. Crit Care Med. 2012;40(12):3154–61.
85. Klompas M. Complications of mechanical ventilation-the CDC's new surveillance paradigm. N Engl J Med. 2013;368(16):1472–5.
86. Boyer AF, Schoenberg N, Babcock H, et al. A prospective evaluation of ventilator-associated conditions and infection-related ventilator-associated conditions. Chest. 2015;147:68–81.
87. Takiguchi H, Hayama N, Oguma T, Harada K, Sato M, Horio Y, et al. Post-bronchoscopy pneumonia in patients suffering from lung cancer: development and validation of a risk prediction score. Respir Investig. 2017;55(3):212–8.
88. Yuh DD. Johns Hopkins textbook of cardiothoracic surgery. New York, NY: McGraw-Hill Companies; 2014. 1443 p. Available from https://accesssurgery.mhmedical.com/content.aspx?sectionid=55166007&bookid=963.
89. Berwick DM, Calkins DR, McCannon CJ, et al. The 100,000 lives campaign: setting a goal and a deadline for improving health care quality. JAMA. 2006;295:324–7.
90. Álvarez-Lerma F, Palomar-Martínez M, Sánchez-García M, Martínez-Alonso M, Álvarez-Rodríguez J, Lorente L, Arias-Rivera S, García R, Gordo F, Añón JM, Jam-Gatell R, Vázquez-Calatayud M, Agra Y. Prevention of ventilator-associated pneumonia: the multimodal approach of the Spanish ICU "Pneumonia Zero" Program∗. Crit Care Med. 2018;46(2):181–18891.
91. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63(5):e61–111.
92. Ruiz J, Castro I, Calabuig E, Salavert M. Non-antibiotic treatment for infectious diseases. Rev Esp Quimioter. 2017;30(Suppl. 1):66–71.
93. Hauser AR, Mecsas J, Moir DT. Beyond antibiotics: new therapeutic approaches for bacterial infections. Clin Infect Dis. 2016;63:89–95.
94. Nobrega FL, Costa AR, Kluskens LD, Azeredo J. Revisiting phage therapy: new applications for old resources. Trends Microbiol. 2015;23:185–91.
95. Rello J, Krenn CG, Locker G, Pilger E, Madl C, Balica L, et al. A randomized placebo-controlled phase II study of a Pseudomonas vaccine in ventilated ICU patients. Crit Care. 2017;21:22.
96. Saha S, Tomaro-Duchesneau C, Tabrizian M, Prakash S. Probiotics as oral health biotherapeutics. Expert Opin Biol Ther. 2012;12:1207–20.

97. Shen KR, Bribriesco A, Crabtree T, Denlinger C, Eby J, Eiken P, et al. The American Association for Thoracic Surgery consensus guidelines for the management of empyema. J Thorac Cardiovasc Surg. 2017;153(6):e129–46.
98. Yamauchi Y, Isaka M, Maniwa T, Takahashi S, Kurai H, Ohde Y. Chest tube tip culture as a predictor of postoperative infection in lung cancer operations. Ann Thorac Surg. 2013;96:1796–802.
99. Abu-Omar Y, Kocher GJ, Bosco P, Barbero C, Waller D, Gudbjartsson T, et al. European Association for cardio-thoracic surgery expert consensus statement on the prevention and management of mediastinitis. Eur J Cardio Thoracic Surg. 2017;51(1):10–29.

The Role of Ultrasound (US) in Thoracic Surgery

17

Stefaan Bouchez and Patrick F. Wouters

17.1 Introduction

For several decades, pioneers have emphasized the vast potential of ultrasound-based technology in the field of anesthesia and critical care, not only as an imaging technique that enhances the safety and efficacy of many technical invasive procedures, but also as a non-invasive monitoring tool for the bedside evaluation of vital organ function and anatomy [1–3]. Today the number of anesthesiologists and intensivists who embrace ultrasound and incorporate it in their daily clinical practice is increasing rapidly.

US-guided technical procedures will not be discussed here as such information is available in excellent dedicated literature [4, 5]. This chapter will focus on the value of ultrasound as a bedside tool to monitor vital organ function and anatomy in patients undergoing thoracic surgery. The two primary applications of US for this purpose are echocardiography and lung US.

17.2 Echocardiography in Thoracic Surgery and Chest Trauma

Perioperative echocardiography is considered an essential part of cardiac anesthesia where it plays an undisputed role in intraoperative decision making and evaluation of surgical results. Outside the cardiac theatre, however, the place of perioperative

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echocardiography is less well defined. Pertinent practice guidelines state that echocardiography should be used: (1) when the nature of the planned surgery or the patient's cardiovascular pathology might result in severe hemodynamic, pulmonary, or neurologic compromise and (2) when unexplained life-threatening circulatory instability persists despite corrective therapy [6]. Such conditions are frequently encountered in thoracic anesthesia, and yet there is wide practice variation today. In fact, the decision to use echocardiography during non-cardiac surgery rather depends on the individual anesthesiologist's level of competence and experience with the technique. This indicates that there is an urgent need for structured echocardiography training programs if the potential benefits of this monitoring tool are expected to extend beyond cardiac anesthesia practice [7]. In a consensus paper from the ASA and SCA Reeves et al. emphasize the significant role of basic perioperative echocardiography and define its scope as an "intraoperative monitoring technique focusing on cardiac causes of hemodynamic or ventilatory instability, including ventricular size and function, valvular anatomy and function, volume status, pericardial abnormalities and complications from invasive procedures, as well as the clinical impact or etiology of pulmonary dysfunction" [8]. The authors clearly delineate the knowledge and training requirements, as well as the indications and scope of a basic echocardiographic exam, distinct from the advanced (cardiac-diagnostic) level, and with value in its own right.

In thoracic anesthesia, the unique ability of echocardiography to monitor right ventricular function is of particular interest. Lung surgery exposes patients to conditions associated with increased RV afterload such as hypoxia, hypercapnia, one lung ventilation and pulmonary artery clamping [9]. As RV pump function is very sensitive to increases in afterload, RV dysfunction is a frequent cause of hemodynamic instability in this setting. A rapid differential diagnosis is important to enable specific and rapid treatment. Routine use of echocardiography in non-transplant thoracic surgery for this purpose is not recommended, but lung transplantation is a clear indication for intraoperative transesophageal echocardiography [10]. Pneumonectomy is also associated with profound changes in RV volume- and pressure load. For subjects with reduced cardiovascular reserve, pneumonectomy imposes a significant risk and such patients could benefit from continuous intraoperative echocardiography as well. Finally, patients with known or suspected pulmonary arterial hypertension are at increased risk for perioperative RV failure. This subgroup should be monitored with echocardiography during and after any type of intermediate risk surgery.

The quantification of RV function has become a topic of intense research. Several new indices have been proposed but the majority is sensitive to error or requires advanced interpretation [11]. We recommend a pragmatic, fast and rather simple approach that can easily be integrated in a basic echo exam and consists of only two consecutive measurements: (1) a comparison of Left and Right chamber dimensions and (2) measurement of the long axis displacement of the tricuspid annulus during systole. Both can be obtained in the standard 4-chamber view (mid-esophageal for TEE, apical for TTE) and allow a semiquantitative appreciation of RV function, provided that the imaging plane is optimally aligned with regard to the heart's long axis (no foreshortening) and positioned midway the anteroposterior diameter (Fig. 17.1).

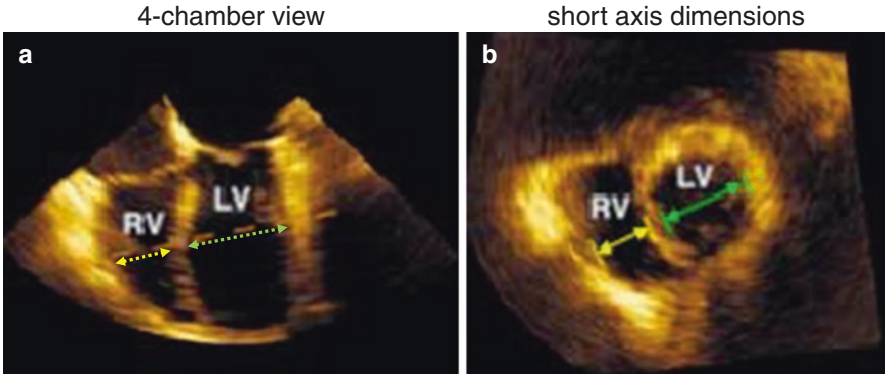

Fig. 17.1 Measurement of short axis dimensions of right ventricle (yellow line) and left ventricle (green line) at midventricular level in (**a**) 4-chamber and (**b**) short axis view, respectively. A size ratio of 2/3 for the RV/LV diameter indicates Normal RV function

Primary RV dysfunction is always associated with enlargement of the RV cavity. As the pericardial space is restricted, RV dilation goes at the expense of LV size. The most reliable sign of RV enlargement is therefore an increase in the size ratio of the RV versus the LV. In normal conditions, the RV size is smaller than the LV and its dimensions never exceed 2/3 of the corresponding LV dimension. The semi-quantitative appreciation of relative proportions is simple and shows a high interobserver agreement. For a quantitative assessment, the short axis diameter of the RV is measured as the distance from the RV free wall to the RV septal site, and compared to the short axis diameter of the LV, i.e. the distance from the LV free wall to the LV septal site at a corresponding level midway the apex and basis of the heart on a line perpendicular to the long axis.

The second measurement of RV function is based on the fact that RV systolic deformation occurs primarily along its long axis, producing a piston-like displacement of the tricuspid annulus towards a nearly immobile apex. The absolute distance travelled by the tricuspid annulus during systolic ejection is termed "Tricuspid Annular Plane Systolic Excursion (TAPSE)" and is considered a very reliable, though load sensitive, measurement of right ventricular ejection. Normal distances vary from 1.5 to 2.5 cm and lower values apply for mechanically ventilated patients. A decrease below 1.5 cm when combined with an increase in RV/LV size ratio above 2/3 indicates a reduction in right ventriculo-vascular coupling, i.e. a functional decline in RV performance. During surgery, this is almost invariably associated with an acute increase in RV afterload.

Apart from monitoring RV function, other specific advantages of echocardiography during noncardiac thoracic surgery include the ability to detect lesions that can predict adverse outcomes (aortic atheromata), to provide guidance in the placement of extracorporeal membrane oxygenation cannulas [12] and for hemodynamic management in ECMO patients, and to diagnose patent foramen ovale in unexplained hypoxia. The use of echocardiography for such purposes requires significant experience however. While transesophageal echocardiography is considered the only

possible modality for the anesthesiologist to image the heart during surgery, Kratz et al. recently demonstrated that transthoracic echocardiography is also feasible. In a patient positioned in lateral decubitus they achieved access to the subcostal window from where the 4-chamber subcostal view and measurements of caval vein diameter can be obtained [13].

In the postoperative setting, basic echocardiography offers the same value as discussed for the intraoperative scenario. The ability to use the transthoracic modality lowers the threshold for using it in the Post Anesthesia and Intensive Care Unit even more. The information obtained is non-continuous however and its value determined primarily by the proficiency of its user.

17.3 Perioperative Lung Ultrasound (PoLUS)

Lung ultrasound provides a representation of the lung based on real-time dynamic 2D imaging and artifacts from the interplay between ultrasonic waves and air, lung tissue, pleura, fluids and bone. It has gained much attention in recent years for its value in clinical perioperative practice for screening, diagnosis and as a monitoring tool [14–17]. Lung ultrasound is non-invasive, readily available in most operating rooms and intensive care settings and reduces the need for X-rays.

17.3.1 Equipment

A micro-convex probe with an emission frequency of 5–7 MHz is preferred for optimal ultrasound visualization of the lung, however, virtually all probe types can be used. As lung ultrasound relies on the visualization of natural images with many artifacts, all filters on the echo-device, such as harmonics or dynamic noise filters which are designed to attenuate artifacts and optimize image quality, should be inactivated. Most vendors have created default settings for lung ultrasound which turn off these filters automatically.

17.3.2 Recommended Scanning Regions (Fig. 17.2)

The exam should be performed in a standardized and comprehensive way with the patient in supine or semi-recumbent position. It is recommended to scan the anterior, anteromedial and posterior zones of the lung [18]. The anterior points are referred to as upper BLUE, the anteromedial points as lower BLUE and the posterior points as ‘posterolateral alveolar and/or pleural syndrome point’, or PLAPS point. The number of scan-points can be extended as needed e.g. to identify the exact location of the lung point in pneumothorax.

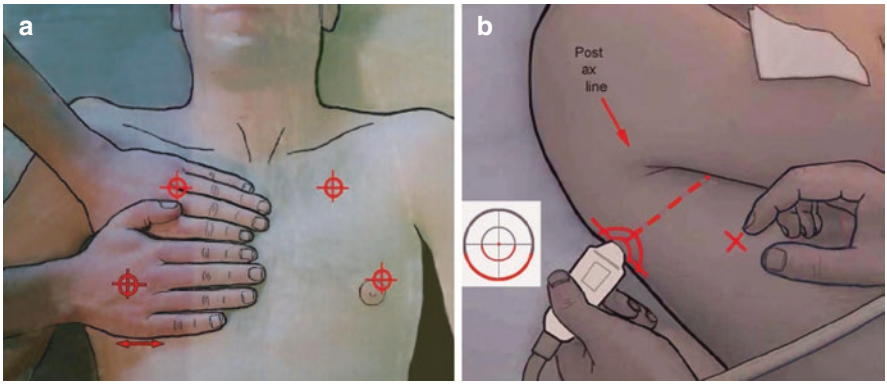

Fig. 17.2 (**a**) The upper hand is applied with the little finger touching the lower border of the clavicle. The finger tips touch the midline. The lower hand is applied below the first one. The thumbs do not count. The upper BLUE-point is at the middle of the hand (root of the middle and ring fingers). The lower BLUE-point is in the middle of the palm of the lower hand. This definition allows avoiding the heart. The lower edge of the lower hand indicates the phrenic line, i.e., the end of the lung [18]. (**b**) The probe indicates the PLAPS-point, in the horizontal continuation with the lower BLUE-point (dotted line), as posterior as possible to the posterior axillary line with the patient remaining supine. The PLAPS-point is therefore located slightly above the diaphragm (right index) [18]

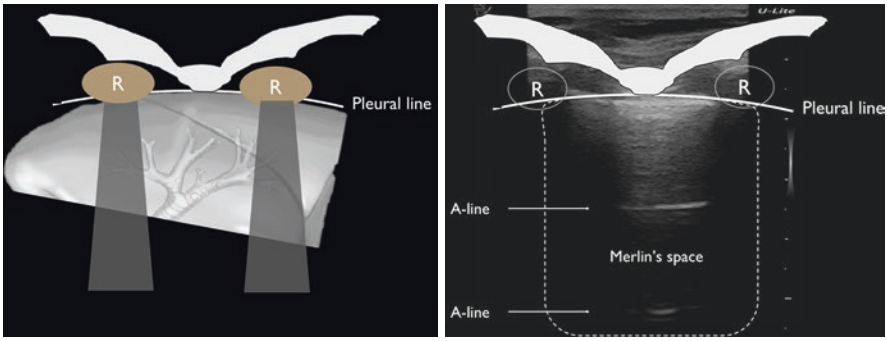

Fig. 17.3 BAT-sign. Pleural line below the two ribs (R). The BAT-sign resembling a bat flying towards the reader, is formed by the two ribs and the pleural line (belly of the bat). The dotted area on the right side represents Merlin's space. Two A-lines are detectable in Merlin's space

17.3.3 Terminology: The Lung Ultrasound Alphabet

17.3.3.1 BAT-Sign with Identification of the Pleural Line (Fig. 17.3)

The identification of the pleural line is fundamental in lung ultrasound. The pleural line is a hyperechoic horizontal line about 5 mm below the rib line (virtual line between two ribs) in standard adult patients. The pattern created by the two ribs and the pleural line resembles the image of a bat. The two ribs serve as a landmark for

the location of the pleural line to avoid confusion with other hyperechoic structures in the image. For this reason, the scanning plane should be longitudinal at the level of the BLUE-points. The space between the pleural line and the acoustic shadows of the ribs is called Merlin's space [14, 19].

17.3.3.2 A-lines

When ultrasound waves encounter a tissue-air interface, they are reflected back to the probe creating a repetition of artifacts within Merlin's space (reverberation artifacts). The distances between these artifacts, called A-lines (Fig. 17.3), are similar and equal to the distance between the skin and the pleural line. The A-lines indicate the presence of air in the thoracic cage and are present in normal lungs but also in pneumothorax [20, 21]. The presence of A-lines rules out excessive fluid in the scanning field and has been considered indicative for a pulmonary occlusion pressure below 18 mmHg, hence clearance for volume therapy in case of a low blood pressure [21–23].

17.3.3.3 Lung Sliding and Lung Pulse

In normal conditions, the visceral pleura slides freely over the parietal pleura during a respiratory cycle. This sliding motion causes a subtle sparkling of the hyperechoic pleural line in a real time 2D ultrasound image (Video 17.1). The presence of lung sliding indicates normal pleural mechanics and precludes a pneumothorax. When ventilation is stopped, lung sliding ceases, however, the pleural line will show micro-oscillations caused by cardiac pulsations that are transmitted over the lung towards the pleura. This phenomenon is called the lung-pulse and also serves as a sign to exclude pneumothorax [14] (Video 17.2).

17.3.3.4 M-Mode Signs: The Seashore, Stratosphere Sign and T-Lines (Fig. 17.4)

M-mode echography is used to explore temporal changes in the reflection pattern of tissue under the probe along a very narrow line of interrogation (the cursor line). For LUS, the cursor line is placed in the center of the BAT-sign. The resulting M-mode view is a composite image with a typical pattern consisting of (1) near-field reflections generated by immobile subcutaneous tissue which results in series of horizontal lines and (2) far-field reflections from lung tissue which move continuously during a respiratory cycle. The former resembles the smoothly lined image of a "sea" while the latter shows a granular pattern like a "shore", hence the "sea-shore sign" [14] observed in normal lungs.

When there is no lung sliding and no lung pulse in ventilated lungs, the M-mode image will consist only of horizontal lines. This image is referred to as the stratosphere sign. Typically, a pneumothorax will produce a stratosphere sign.

In the absence of ventilation, M-mode imaging will also produce a stratosphere-like image. However, in the absence of pneumothorax, cardiac pulsations will be visible at the pleural line (lung pulse) and show as little crackles in the horizontal lines of an M-mode image. The crackles are called T-lines and rule out pneumothorax [14].

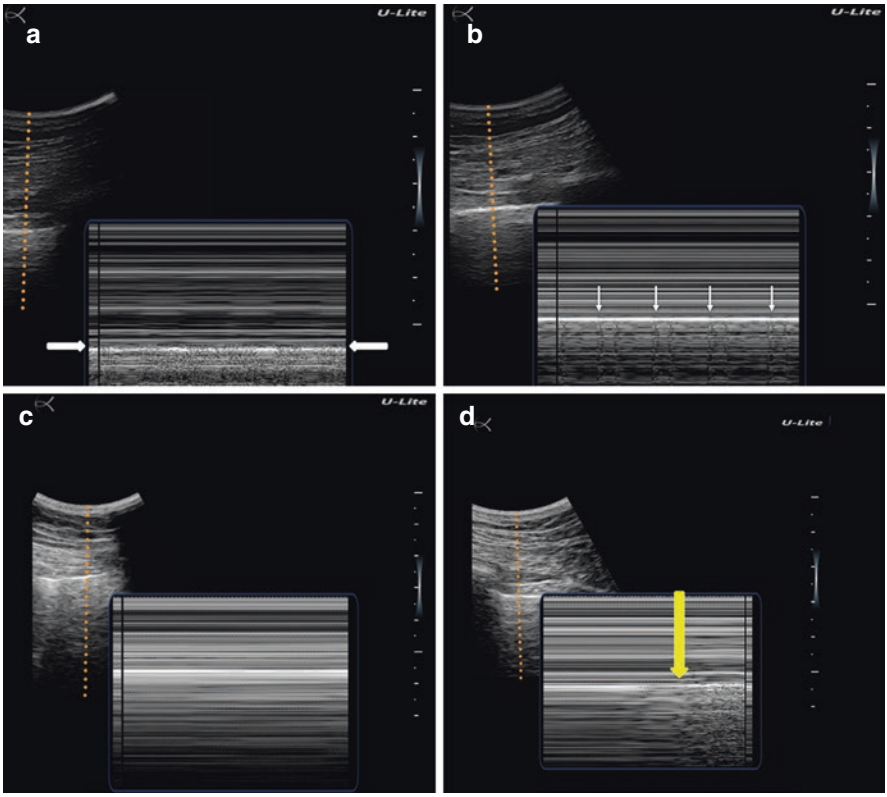

Fig. 17.4 (**a**) Seashore sign. M-mode through the center of the BAT-sign. The white arrows indicate the pleural line. The area above the pleural line shows horizontal lines resembling the waves of the sea, while the area below the pleural line has a sandy pattern generated by lung sliding. (**b**) T-lines. M-mode through the center of the BAT-sign when ventilation is stopped and no lung sliding is present. The cardiac pulsations are transmitted to the pleural line which creates 'crackles' in Merlin's space (arrows). These are called T-lines. (**c**) Stratosphere sign. In M-mode, the abolition of lung sliding creates a pattern exclusively made of horizontal lines and is called the stratosphere sign. (**d**) Lung point. M-mode at the level of the lung point. The point where the lung is detached from the thorax in a pneumothorax. In M-mode it is the point where the stratosphere sign stops and the seashore sign appears again

17.3.3.5 The Lung Point

In the presence of a pneumothorax, the exact location where visceral and parietal pleural membranes separate is called the "lung point" (Video 17.3 and Fig. 17.4). The presence of a lung point is 100% specific for the diagnosis of pneumothorax. The position of the lung point also provides information on the size and the location of the pneumothorax [3, 14].

17.3.3.6 B-Lines and Lung Rockets

B-lines are also ultrasound artifacts arising from the pleural line (Fig. 17.5). They require the presence of thickened, fluid-filled interlobular septa surrounded with aerated alveoli to appear. B-lines are hyperechoic comet-tail artifacts distal from the pleural line. They move with lung sliding and make A-lines disappear. B-lines resemble sunrays shining through the clouds. The clinical impact is determined by the number of B-lines present: one or two B-lines within one intercostal space can be perfectly normal, especially at the level of a lung fissure. More than two B-lines are called "lung rockets". The presence of lung rockets at the anterior BLUE-points indicates a volume-overload. An interstitial syndrome ('wet lungs') is defined as three or more B-lines present in one intercostal view at the BLUE-points. Posterior B-lines and lung rockets are often observed in supine, ventilated patients [14].

17.3.3.7 The Tissue-Like Sign

A massive lobular consolidated lung (hepatization of the lung) reflects ultrasound as effectively as solid tissue (the tissue-like sign). Analogous to pleural fluid, a consolidated lung is found most frequently at the level of the PLAPS-point [14] (Fig. 17.6).

17.3.3.8 Pleural Fluid

Pleural fluid appears transparent to ultrasound (black on a 2D echographic image) and is best visualized at the level of the PLAPS-point. The amount of pleural fluid is best appreciated by scanning longitudinally at the PLAPS-point with the diaphragm as a reference. Quantification can be done using a transversal view at the PLAPS-point [14, 24, 25] (Fig. 17.6). This image resembles a CT-like image and is obtained by turning the probe 90° from the longitudinal towards the transversal position.

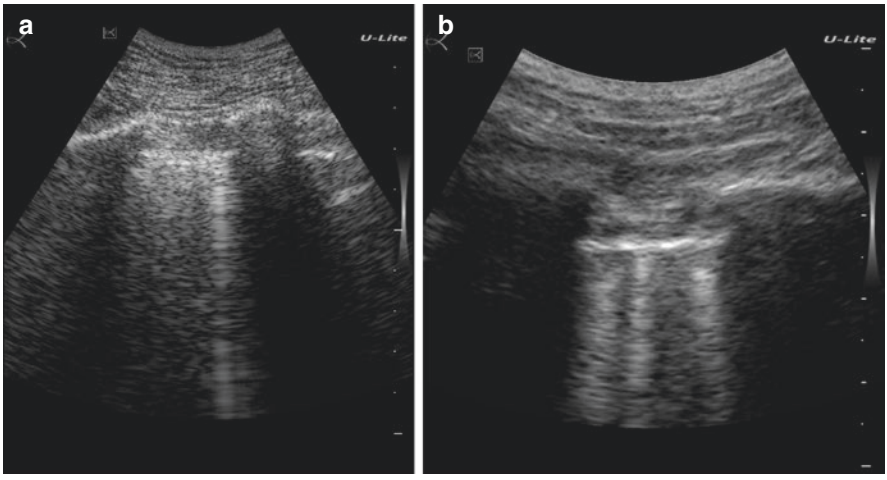

Fig. 17.5 B-lines. (**a**) One B-line is present between two ribs. (**b**) Three B-lines are simultaneously visible between two ribs resembling 'wet' lungs or interstitial syndrome (Lung rockets)

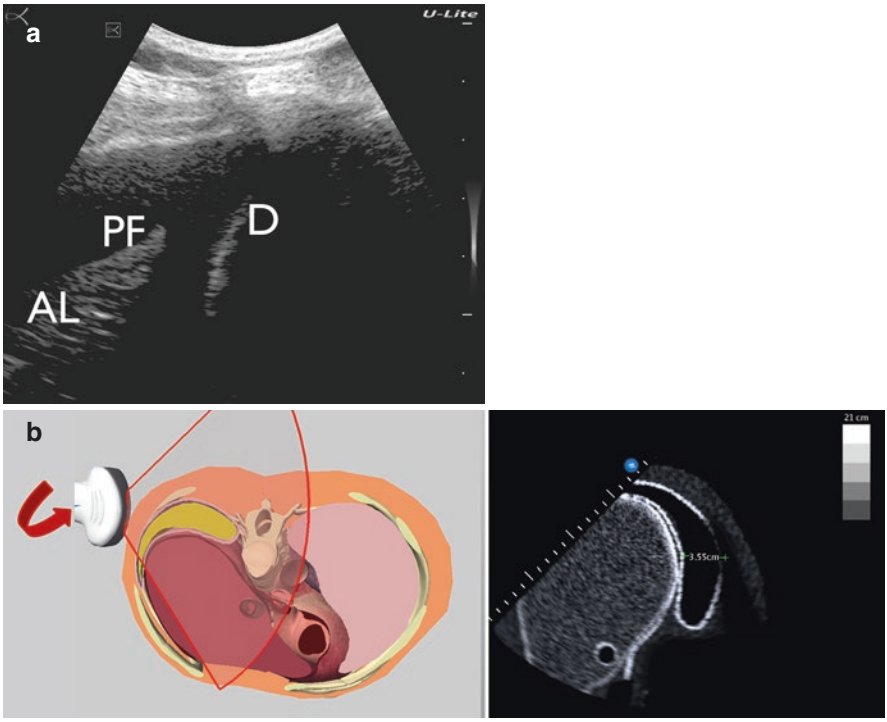

Fig. 17.6 (**a**) Tissue-like sign. Atelectatic lung (AL) surrounded by pleural fluid (PF) at the level of the diaphragm (D). The atelectatic lung resembles tissue like the liver (hepatization of the lung). (**b**) Pleural fluid. Simulator Image (Vimedix®). Transversal view through the thoracic cage at the PLAPS-point (CT-like image). It's preferably used to measure and estimate the amount of pleural fluid

17.3.4 Clinical Applications

17.3.4.1 One-Lung Ventilation and Airway Instrumentation

Lung ultrasound can be used to verify one-lung ventilation after placement of a double lumen tube or bronchial blocker. It is inferior to fiber-optic bronchoscopy but may outperform auscultation, particularly with reduced lung sounds or in noisy environments. Two dynamic ultrasound signs are required to confirm absence of ventilation following the bronchial occlusion test: (1) abolition of lung sliding, with disappearance of the normal seashore sign in the M-mode image and (2) the presence of a lung pulse. If both lung sliding and lung pulse are absent, a pneumothorax is suspected.

The probe is positioned at the upper BLUE points and the test is performed with tidal volumes of 5 ml/kg and PEEP of 5 mmHg. Larger tidal volumes may cause false positive lung sliding in the non-ventilated lung due to transmission of excessive volume shifts from the ventilated lung [26–29].

17.3.4.2 Pneumothorax

Pneumothorax results in the disappearance of lung sliding. This is a sensitive, but not a very specific sign because ARDS and pneumonia can also abolish lung sliding if extensive pleural adhesions are present. ARDS and pneumonia will also show B-lines, however, and these are incompatible with pneumothorax as they are generated from the intact pleura. When lung sliding is detected in a nondependent lung, pneumothorax can be excluded.

If absence of lung sliding and lung pulse is confirmed and pneumothorax is suspected, the probe is shifted from the BLUE-points to a more lateral position until the lung point is found. The lung point is pathognomonic for pneumothorax and has a specificity of 100%. Sensitivity is not 100% because major pneumothorax showing complete lung retraction will not generate a lung point [3].

17.3.4.3 Fluid Administration/Lung Edema

Excessive fluid resuscitation can result in volume overload, particularly in patients with impaired cardiopulmonary reserve. Lung ultrasound can pick up early signs of volume overload: the presence of three or more B-lines between two ribs at the anterior BLUE-points is indicative of interstitial edema. In the context of volume resuscitation, such a finding could provide an argument to stop fluid therapy and initiate diuretics, vasodilators or inotropic support.

On the other hand, when a patient is hypotensive and lung ultrasound shows lung sliding at the level of the anterior BLUE-points, accompanied by A-lines and in the absence of B-lines, fluid therapy can be started safely. If hypotension persists and is unresponsive to fluid resuscitation, echocardiography can be used to exclude other causes of hemodynamic instability such as right ventricular dysfunction, cardiac tamponade or sepsis. The FALLS protocol by Lichtenstein uses an applicable algorithm which can also be used perioperatively [22].

17.3.4.4 Atelectasis/Lung Expansion

Ultrasound has the ability to detect atelectasis in its early stage of development. This is striking when the whole lung is involved as occurs in upper bronchial obstruction due to foreign body aspiration, or in single lung intubation. As there is no peripheral expansion of lung tissue *(a-tele-ectasis)*, lung sliding is immediately abolished even when the lung is still aerated, and the lung pulse becomes clearly visible (sensitivity of 90%) [27]. In a later stage, alveolar gas is resorbed and consolidation appears. The consolidation may initially still include partially absorbed gas particles, which are called static air bronchograms. In a later state the air bronchograms will disappear and complete consolidation ensues. The process of atelectasis can be reverted by lung recruitment maneuvers. Lung ultrasound can be used to assess the effectiveness of such a recruitment maneuver and to adjust ventilation parameters to prevent atelectasis. For this purpose, the ultrasound probe is placed in the most dependent part of the atelectatic lung, usually the PLAPS-point. When the lung is re-inflated during the recruitment maneuver, the consolidation-pattern will vanish, and B lines will appear just before the lung image recovers its normal pattern with A-lines and lung sliding (the A-profile). The pressure required to expand the atelectatic lung (as observed

with ultrasound) is the opening pressure. After lung recruitment, PEEP level should be readjusted to prevent re-atelectasis. Airway pressures and PEEP can be decreased in a stepwise approach until B-lines reappear. The phase where B-lines reappear is defined as the lung closing pressure. PEEP level should be selected 2 cm H_2O above this closing pressure during ongoing ventilation [30].

Lung ultrasound can also be used to evaluate post-surgical lung expansion after thoracic surgery [31]. The reappearance of lung sliding at both upper and lower BLUE-points, serves as an indicator of adequate lung expansion. Digital chest drains provide complementary information for this evaluation. The presence of lung sliding indicates that both parietal and visceral pleura are in contact and there is no air in between. An air leak value of 0 ml/min makes the possibility of a pneumothorax then very unlikely [32]. The incorporation and correct application of lung ultrasound in this way, can significantly reduce the need for chest radiographs in thoracic surgery departments.

17.3.4.5 Pleural Fluid and Thoracentesis

Pleural effusions are located in the dependent areas so scanning should occur at the location of the PLAPS point. An anechoic (black) space at the PLAPS point usually indicates the presence of pleural fluid. However, blood, pus etc. have different echogenicity and the fluid on echo seems similar to plankton (Plankton sign).

Safe thoracentesis should be performed immediately after the ultrasound-based localization. A 15 mm inspiratory interpleural distance is considered to be a safe distance [33] (Fig. 17.6).

Different methods have been published for estimating the amount of pleural fluid using US. One popular method is to measure the distance between the pleural line and the lung line at expiration. This distance is multiplied by 10 if it is <20 mm and multiplied by 20 if the distance is equal or greater than 20 mm. While in general, lung ultrasound is performed longitudinally, for this particular purpose the probe should be turned 90° to scan transversally. It produces a CT-like image and facilitates measurement of the distances [24].

17.3.4.6 Diaphragmatic Function

Direct injury to the phrenic nerve from mechanical trauma following thoracic surgery has been described to produce diaphragmatic dysfunction. Patients with preexisting pulmonary dysfunction may not even tolerate a unilateral diaphragmatic paralysis [34] and experience difficulties to wean from mechanical ventilation. Ultrasound signs and measurements have been described to evaluate diaphragmatic function. Ultrasound measurements of the diaphragm are obtained from still B-mode images and from M-mode tracings. Diaphragmatic thickness, the change in muscle thickness and diaphragmatic excursion can be measured to assess its function (Fig. 17.7). Ultrasound assessment of thickness is best performed with a high frequency transducer at the anterior axillary line between the seventh and ninth rib. The thickness should be >20 mm and the change in thickness between inspiration an expiration should be more than 20% in normal diaphragmatic function. Diaphragm thickening <20% is proposed to be consistent with paralysis.

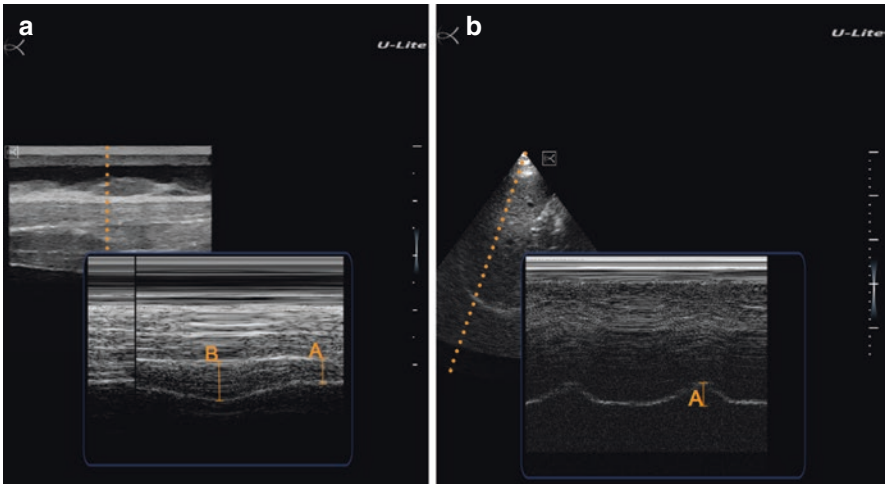

Fig. 17.7 (**a**) Measurement of diaphragmatic thickness and change of thickness during normal breathing using a linear probe. (**b**) Evaluation of diaphragmatic excursion using a curvilinear probe

For ultrasound evaluation of diaphragmatic excursion, a lower frequency probe is needed because it allows greater penetration depth. Excursion greater than 2.5 cm in adults has been proposed as a cut off for excluding severe diaphragm dysfunction. Excursion represents one of the most clinically useful markers of diaphragm function [35, 36].

17.4 Conclusion

Ultrasound-based imaging has definitely evolved to become an indispensable tool in the daily practice of anesthesia and perioperative medicine. It facilitates many technical procedures which were previously performed using "blind" external landmark techniques, but US also provides a unique approach to monitor vital organ function and anatomy. Echocardiography and Lung Ultrasound are the primary applications for this purpose. In thoracic surgery the use of basic echocardiography and lung ultrasound offers specific advantages over other monitoring tools but there is large practice variation today. Clearly, structured teaching programs and a certification process are needed to further implement and standardize the use of US in our specialism and exploit its full potential on a larger scale.

References

1. Konstadt SN, Thys D, Mindich BP, Kaplan JA, Goldman M. Validation of quantitative intraoperative transesophageal echocardiography. Anesthesiology. 1986;65(4):418–21.
2. Jensen MB, Sloth E. Echocardiography for cardiopulmonary optimization in the intensive care unit: should we expand its use? Acta Anaesthesiol Scand. 2004;48(9):1069–70.

3. Lichtenstein DA, Menu Y. A bedside ultrasound sign ruling out pneumothorax in the critically ill: lung sliding. Chest. 1995;108(5):1345–8.
4. Reusz G, Csomos A. The role of ultrasound guidance for vascular access. Curr Opin Anaesthesiol. 2015;28(6):710–6.
5. Barrington MJ, Uda Y. Did ultrasound fulfill the promise of safety in regional anesthesia? Curr Opin Anaesthesiol. 2018;31(5):649–55.
6. Thys DM. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Anesthesiology. 2010;112(5):1084–96.
7. Mahmood F, Matyal R, Skubas N, Montealegre-Gallegos M, Swaminathan M, Denault A, et al. Perioperative ultrasound training in anesthesiology: a call to action. Anesth Analg. 2016;122(6):1794–804.
8. Reeves ST, Finley AC, Skubas NJ, Swaminathan M, Whitley WS, Glas KE, et al. Basic perioperative transesophageal echocardiography examination: a consensus statement of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. Anesth Analg. 2013;117(3):543–58.
9. Wink J, de Wilde RBP, Wouters PF, van Dorp ELA, Veering BT, Versteegh MIM, et al. Thoracic epidural anesthesia reduces right ventricular systolic function with maintained ventricular-pulmonary coupling. Circulation. 2016;134(16):1163–75.
10. Evans A, Dwarakanath S, Hogue C, Brady M, Poppers J, Miller S, et al. Intraoperative echocardiography for patients undergoing lung transplantation. Anesth Analg. 2014;118(4):725–30.
11. Ashes C, Roscoe A. Transesophageal echocardiography in thoracic anesthesia: pulmonary hypertension and right ventricular function. Curr Opin Anaesthesiol. 2015;28(1):38–44.
12. Sullivan B, Puskas F, Fernandez-Bustamante A. Transesophageal echocardiography in noncardiac thoracic surgery. Anesthesiol Clin. 2012;30(4):657–69.
13. Kratz T, Holz S, Steinfeldt T, Exner M, dell'Orto MC, Kratz C, et al. Feasibility and impact of focused intraoperative transthoracic echocardiography on management in thoracic surgery patients: an observational study. J Cardiothorac Vasc Anesth. 2018;32(2):848–52.
14. Lichtenstein DA. Lung ultrasound in the critically ill. Ann Intensive Care. 2014;4(1):1.
15. Lichtenstein D, van Hooland S, Elbers P, Malbrain MLNG. Ten good reasons to practice ultrasound in critical care. Anaesthesiol Intens Ther. 2014;46(5):323–35.
16. Via G, Storti E, Gulati G, Neri L, Mojoli F, Braschi A. Lung ultrasound in the ICU: from diagnostic instrument to respiratory monitoring tool. Minerva Anestesiol. 2012;78(11):1282–96.
17. Diaz-Gomez JL, Ripoll JG, Ratzlaff RA, Tavazzi G, Via G, Mookadam F, et al. Perioperative lung ultrasound for the cardiothoracic anesthesiologist: emerging importance and clinical applications. J Cardiothorac Vasc Anesth. 2017;31(2):610–25.
18. Lichtenstein DA, Mezière GA. The BLUE-points: three standardized points used in the BLUE-protocol for ultrasound assessment of the lung in acute respiratory failure. Crit Ultrasound J. 2011;3(2):109–10.
19. Miller A. Practical approach to lung ultrasound. BJA Educ. 2016;16(2):39–45.
20. Lichtenstein DA, Mezière GA. Relevance of lung ultrasound in the diagnosis of acute respiratory failure*: the BLUE protocol. Chest. 2008;134(1):117–25.
21. Lichtenstein DA, Mezière GA, Lagoueyte J-F, Biderman P, Goldstein I, Gepner A. A-lines and B-lines: lung ultrasound as a bedside tool for predicting pulmonary artery occlusion pressure in the critically ill. Chest. 2009;136(4):1014–20.
22. Lichtenstein DA. BLUE-protocol and FALLS-protocol: two applications of lung ultrasound in the critically ill. Chest. 2015;147(6):1659–70.
23. Lichtenstein D, Mézière G, Biderman P, Gepner A, Barré O. The comet-tail artifact. Am J Respir Crit Care Med. 2012;156(5):1640–6.
24. Eibenberger KL, Dock WI, Ammann ME, Dorffner R, Hörmann MF, Grabenwöger F. Quantification of pleural effusions: sonography versus radiography. Radiology. 1994; 191(3):681–4.

25. Bouhemad B, Zhang M, Lu Q, Rouby J-J. Clinical review: bedside lung ultrasound in critical care practice. Crit Care. 2007;11(1):205.
26. Ponsonnard S, Gardet E, Bertin F, Marsaud JP, Fuzier R, Nathan N. Value of lung sonography to control of right-sided double lumen endotracheal tube location: 1AP2-1. Eur J Anaesthesiol. 2012;29:8.
27. Lichtenstein DA, Lascols N, Prin S, Mézière G. The "lung pulse": an early ultrasound sign of complete atelectasis. Intensive Care Med. 2003;29(12):2187–92.
28. Saporito A, Piccolo Lo A, Franceschini D, Tomasetti R, Anselmi L. Thoracic ultrasound confirmation of correct lung exclusion before one-lung ventilation during thoracic surgery. J Ultrasound. 2013;16(4):195–9.
29. Hu W-C, Xu L, Zhang Q, Wei L, Zhang W. Point-of-care ultrasound versus auscultation in determining the position of double-lumen tube. Medicine. 2018;97(13):e9311.
30. Tusman G, Acosta CM, Costantini M. Ultrasonography for the assessment of lung recruitment maneuvers. Crit Ultrasound J. 2016;8(1):8.
31. Bouhemad B, Brisson H, Le-Guen M, Arbelot C, Lu Q, Rouby J-J. Bedside ultrasound assessment of positive end-expiratory pressure-induced lung recruitment. Am J Respir Crit Care Med. 2011;183(3):341–7.
32. Chavarín A, Mier JM, Fibla JJ, Izquierdo-Vidal C, Molins L. The use of transthoracic ultrasound for the assessment of lung expansion combined with digital air leak measurement in thoracic surgery patients. Interact Cardiovasc Thorac Surg. 2013;17:S58.
33. Lichtenstein D, Hulot JS, Rabiller A, Tostivint I, Meziere G. Feasibility and safety of ultrasound-aided thoracentesis in mechanically ventilated patients. Intensive Care Med. 1999;25(9):955–8.
34. Sengupta S. Post-operative pulmonary complications after thoracotomy. Ind J Anaesth. 2015;59(9):618–26.
35. Sarwal A, Walker FO, Cartwright MS. Neuromuscular ultrasound for evaluation of the diaphragm. Muscle Nerve. 2013;47(3):319–29.
36. Dubé B-P, Dres M, Mayaux J, Demiri S, Similowski T, Demoule A. Ultrasound evaluation of diaphragm function in mechanically ventilated patients: comparison to phrenic stimulation and prognostic implications. Thorax. 2017;72(9):811–8.

Changes in Classical Monitoring: Hemodynamic Monitoring, New Devices, NIRS, etc.

18

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18.1 Hemodynamic Monitoring

In perioperative medicine, hemodynamic management aims at an optimization of perfusion pressure and oxygen delivery (DO_2) in order to maintain or restore adequate cellular metabolism. For complex patients in the operating room or in the intensive care unit, many questions regarding their hemodynamic management cannot be answered with simple clinical examination. In particular, arterial pressure allows only a rough estimation of CO. Until recently, the measurement of advanced hemodynamic variables required invasive hemodynamic monitoring. Advanced cardiovascular monitoring typically consists of invasive blood pressure and central venous pressure (CVP), CO monitoring, and other parameters such as central venous or mixed oxygen saturation ($ScvO_2/SvO_2$) will provide very valuable information for the management of the hemodynamically unstable patients, as it will be able to influence the different variables that influence the DO_2 to the tissues (see Fig. 18.1).

Hemodynamic monitoring represents a functional tool that may be used to derive estimates of performance and physiological reserve that may in turn direct treatment. Many methods have been developed to carry out advanced cardiovascular monitoring, some invasive, others semi-invasive and even recently non-invasive (see Table 18.1). They have in common, that allow us to obtain data of the hemodynamics very reliable to be able to carry out a good handling of the patients.

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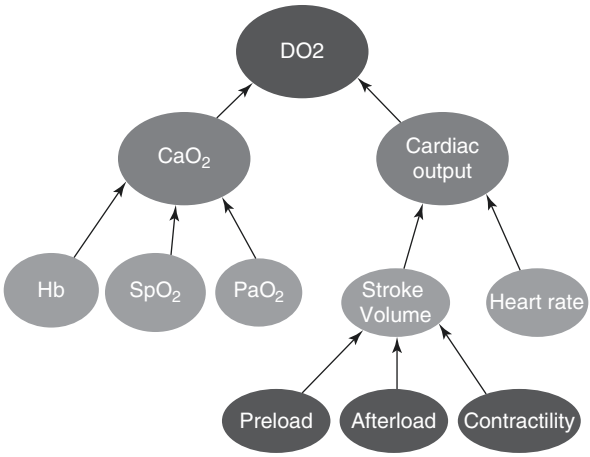

Fig. 18.1 Contributors to oxygen delivery. DO_2; oxygen delivery. CaO_2; arterial oxygen content, Hb: hemoglobin. SaO_2; arterial Hb saturated with oxygen. PaO_2; Partial pressure of oxygen in mmHg

18.1.1 Invasive Monitoring

18.1.1.1 Pulmonary Artery Catheter

For decades, the main method of advanced cardiovascular monitoring has been transcardiac thermodilution (TC-TD) through the insertion of a pulmonary artery (PA) catheter, however, it has fallen out of favor as it was shown not to improve outcome or to be potentially harmful, leading in in a drastic reduction in its use. Unlike TP-TD devices, the PA catheter provides a direct estimation of pulmonary artery resistance. Right ventricular failure and severe pulmonary hypertension represent specific indications for the PA catheter. Nevertheless, errors in the measurement of CO resulting from tricuspid regurgitations must be kept in mind, even though it seems to exist mostly for severe regurgitations. Also, the PA catheter measures both CVP and pulmonary artery pressure (PAP) and pulmonary artery occlusion pressure (PAOP), allowing the estimation of right and left cardiac functions, while TP-TD only estimates the global cardiac function. Another strong advantage of the PA catheter is that it directly measures continuous SvO_2. Probably, the best isolated indicator of the adequacy of global oxygen transport.

18.1.1.2 Transpulmonary Thermodilution Methods

The TP-TD technique emerged in the early 2000s. The approach of TP-TD is quite different from PA catheterisation in many respects. TP-TD is a technique that provides a full haemodynamic assessment through CO and other indices. Through the analysis of the thermodilution curve recorded at the tip of an arterial catheter after the injection of a cold bolus in the venous circulation, TP-TD intermittently measures CO. This measure allows the calibration of pulse contour analysis. This provides continuous and real time monitoring of CO, which is not possible with the PA catheter. It is more direct than the PA catheter, but does not allow the distinct estimation of right and left cardiac function. The PiCCO (*Pulsion Medical Systems, Munich, Germany*) and the Volume View (*Edwards LifeSciences, Irvine, United*

Table 18.1 Non-invasive and invasive monitoring

Invasiveness	Method		Monitor
Invasive	Transcardiac thermodilution (TC-TD)		Pulmonary artery catheter Vigileo® (Edwards)
Minimally invasive	Pulmonary thermodilution (P-TD)	Calibration by TDTP	PiCCO® (Pulsion) VolumeView™ (Edwards)
	Transpulmonary thermodilution (TP-TD)	Calibration by dilution of Lithium	PulseCO® (LiDCO)
	Pulse-wave contour Analysis	Calibration by P-TD	PiCCO® PulseCO® (LiDCO) VolumeView™ (Edwards)
		Calibration 3 or 4 times by P-TD	Modelflow (TNO/BMI)
		No external calibration required	FloTrac®/Vigileo® (Edwards) MostCare® (Vygon) LiDCOrapid® (LiDCO) ProAQT® (Pulsion)
Non-invasive			Modelflow-Nexfin® (FMS, Amsterdam, The Netherlands) Clearsight® (Edwards, integrated in EV1000 clinical platform)
		Calibration based non-invasive blood pressure	LiDCOrapid^{v2} CNAP™ module (LiDCO)
	Bioimpedance		Lifegard®, TEBCO®, HOTMAN®, BioZ®, ECOM
	Bioreactance		NICOM®
	Fick principle (CO_2 rebreathing)		NICO®
	Transthoracic Doppler Esophageal Doppler*		USCOM® CardioQ™
Echocardiography	Transthoracic Echo and transesophageal Echo*		

*non invasive methods

States of America) devices measure CO but also provide several other valuable pieces of haemodynamic information. They both estimate the end-diastolic volume of the four cardiac cavities, which is a marker of cardiac preload. Intrathoracic blood volume (ITBV)—volume in heart + pulmonary vessels—and global end-diastolic volume (GEDV)—all four chambers—are better indicators or preload than central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) and not influenced by mechanical ventilation. Extravascular lung water (EVLW)—water content in lungs—can be assess with both devices and, let us know quantify the volume of pulmonary oedema, and pulmonary vascular permeability, which quantifies the degree of a pulmonary capillary leak, being very helpful for guiding fluid strategy. The LiDCO system, use lithium as the indicator. A set dose of lithium

is injected into the venous system via either the central venous access or peripheral cannula. This flows through the heart with the normal flow of blood and then down the arterial system to where the lithium selective sensor is attached to the arterial line. Blood is pumped out of the arterial line through the use of a roller pump past the lithium selective sensor and the level of lithium in the arterial sample is measured over time. So in theory the longer it takes for the lithium in the blood to reach the sensor over a given time the lower the cardiac output, and the faster the flow of blood to the sensor the higher the CO. The system requires a minimum of 12 h between calibration and more frequently (e.g. 8 hourly) if any concerns regarding its accuracy.

18.1.2 Minimally Invasive Monitoring

Minimally invasive monitoring is based on varied physiologic principles and can be used for several hemodynamic trends. Different techniques are commercially available and in the recent years they have proven adequate in replacing the PA catheter under certain clinical conditions. The minimally invasive hemodynamic monitoring techniques are based in pulse wave analysis, Doppler measurement techniques and partial carbon dioxide rebreathing using the applied Fick's principle. Pulse wave analysis, also referred to as 'pulse contour analysis', is based on the principle that the stroke volume (SV) can be tracked continuously by analysis of the arterial pressure waveform. Because the arterial pressure waveform is the result of an interaction between SV and the vascular structure, resistance, compliance and characteristic impedance have to be considered.

Different mathematical models are used today in order to assess SV/CO in the commercially available pulse wave analysis morphology devices. The methods and systems available on the market for analyzing pulse wave morphology are the following: PiCCO® plus (Pulsion Medical Systems, Munich, Germany), PulseCO® (LiDCO Ltd, London, UK), Modelflow (TNO/BMI), MostCare® (Vygon) and FloTrac®/Vigileo® (Edwards Life-sciences, Irvine, USA).

Strong clinical outcomes data support the use of these devices in patients undergoing major surgical procedures although these studies generally do not target thoracic surgical procedures specifically. The predictive ability of respiratory variation (for measuring fluid responsiveness) is controversial in both one lung and low tidal volume ventilation. EVLW measurements are well validated, predict postoperative lung function, but require the use of TP-TD.

18.1.2.1 Non-invasive Monitoring: *Bioimpedance and Bioreactance*

Devices using bioimpedance include NCCOM (Bomed Medical, Irvine, CA, USA), BioZ (Cardiodynamics, San Diego, CA, USA), NICCOMO (MEDIS, Limenau, Germany), ICON (Osypka Cardiotronic, Berlin, Germany), ICG (Philips Medical Systems, Andover, MA, USA), NICOMON (Larsen and Toubro Ltd., Mumbai, India), the CSM3000 (Cheers Sails Medical, Shenzhen, China), and PHYSIOFLOW (Manatec Biomedical, Paris, France). The NICaS system (NI Medical, Petah-Tikva, Israel) uses the same principles but applied to the whole

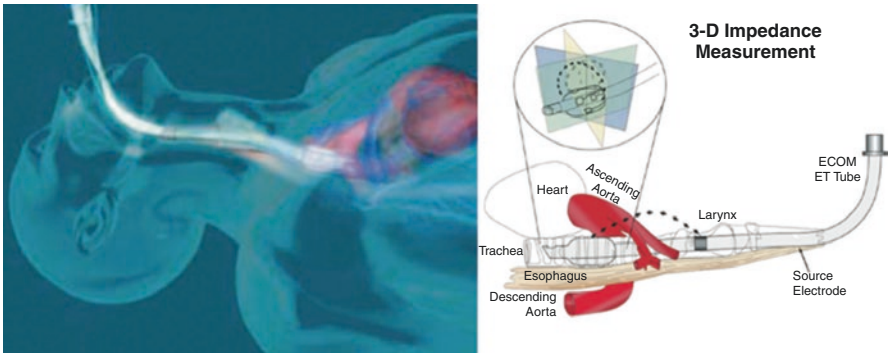

Fig. 18.2 ECOM system device. Non-invasive hemodynamic monitoring. The transmitting and receiving electrodes are located on the cuff of an endotracheal tube

body. In the ECOM system (Ecom Medical, San Juan Capistrano, CA, USA), the transmitting and receiving electrodes are located on the cuff of an endotracheal tube, therefore close to the ascending aorta, in order to minimize the impact of analogous signals from other cardiac structures (see Fig. 18.2). Bioreactance is used by two products from the same company NICOM and Starling (Cheetah medical, Wilmington, DE, USA).

Bioimpedance and bioreactance have the strong advantage of being totally non-invasive and low costs. Literature on bioimpedance includes hundreds of articles, results are somewhat contradictory. At least a third of the publications failed to assess bioimpedance as a reliable mean to assess CO. Focusing on positive articles, most of them took place outside from an ICU setting most often in situations where the absolute value of CO has less importance than relative changes. Moreover, total body impedance is less accurate than localized thoracic impedance. Finally, even though last iterations of this technology seem more advanced (such as electrical velocimetry), results are not quite as clear either. As of today, bioimpedance is not consensually viewed as accurate enough to estimate CO. Bioreactance on the other hand has scarcer documentation. Theoretical superiority of bioreactance over bioimpedance was hinted in small sample studies set. Concerns may be raised about decrease in accuracy during low-flow state and when electrocauterization was performed.

18.1.2.2 Applied Fick's Principles: Partial CO_2 Rebreathing (NICO® System)

NICO® system use Fick's principle applied to CO_2 for CO measurement. CO_2 analysis is performed using a mainstream infrared and airflow sensor. This technique may be applied in intubated mechanically ventilated patients under sedation only, with minimal alterations in gas exchange and minimal dead space, and also with hemodynamic stability. Validation studies of this technique compared to PA catheter are limited; however, they indicate a reasonably good correlation. In conclusion, it is not a replacement of PA catheter, but it seems a feasible technique as an alternative in certain patients, such as those undergoing thoracic surgery.

18.1.2.3 Doppler Techniques

Doppler technology can be used to get SV/CO, and other derived parameters. Different Doppler probes are available in the market (ODM II, Abbott, Maidenhead, UK; Cardio-Q/Medicina TECO, Deltex Medical Ltd, Chichester, UK; HemoSonic100, Arrow, Reading, USA). CO is typically calculated from measured aortic blood flow and aortic cross-sectional area obtained either from nomograms or by M-mode ultrasound quantification (HemoSonic 100). Determination can also be performed in the descending aorta, in which adequate characteristic flow signals can be obtained as a result of the close proximity to the oesophagus and the aorta. However, validation studies in the last few years have revealed inconsistent results. Limited accuracy may result from signal detection failure, the assumption of fixed regional blood flow or the use of nomograms to determine aortic cross-sectional area. Therefore, the value of this minimally invasive technique may be limited in clinical practice. However, Doppler devices may be used in specific situations by skilled observers. Based on the ability to reliably track SV changes over time, early goal-directed therapy in a perioperative setting may be a typical indication.

In conclusion, hemodynamic monitoring in perioperative patients has transitioned away from invasive devices (e.g. PA catheter) and towards noninvasive monitoring modalities. For patients undergoing thoracic surgery, SV and CO may be measured with arterial waveform analysis, esophageal Doppler, and bioreactance-based devices, which are based on different underlying principles that affect their performance characteristics. These devices have been used to improve outcomes in patients undergoing major surgery but in general clinical studies of non-invasive CO monitoring devices do not focus on thoracic surgical patients specifically.

18.2 Near-Infrared Spectroscopy (NIRS)

18.2.1 NIRS History

In 1800, along with the discovery of infrared lights, the NIRS has evolved over the years [1]. Herschel, after drawing a rainbow with the help of a prism, measured the heating effects of different lights and noticed that the effect of heating from blue to red increased [2]. Developments related to distribution regions, spectrum width and usage areas of near infrared light were investigated until 1900s [1–3]. In the 1950s, interest in infrared lights and electromagnetic spectrum was greatly increased [4]. But almost all current use of NIRS is based on the work of Karl Norris [5–7]. For this reason, Norris was accepted as the first researcher of near infrared spectroscopy and the article, which is of historical importance, was published in the "Journal of Near Infrared Spectroscopy" [5, 7]. In early periods, NIRS used such as agriculture, industry, livestock, environment, textile areas. Following the announcement of NIRS in the medical field by Jobsis [8], the pioneers of the NIRS practice are Delphy et al. from London [9]. His studies on the measurement of the oxygenation status of premature infants brains, have reached far reaching conclusions. And even later, in the operating room, NIRS was recommended to be

a routine monitoring method [10]. Although articles have been put forward to evaluate the oxygenation through real-time, easy, noninvasive method, the commercial NIRS systems have not been established until the first one was made by Japanese Hamamatsu in 1989 [11]. Near infrared spectroscopy delay entered the medical field due to the complexity of the samples investigated. In addition to complexity, intense water absorption forming a major component of bio-liquids is another problem. To overcome these problems, good reproducibility should be ensured for spectra and a high signal-to-noise ratio. This was achieved by the Fourier-transform spectroscopy (FFT). The spectroscopic analysis of human blood with FFT was the beginning of a new period [12].

18.2.2 Principle and Limitations of NIRS

Near infrared light wave (650–1000 nm) penetrates into biological tissues better than visible light, light absorption is low and can be detected in tissue up to 8 cm. However, due to the high absorption of visible light (450–700 nm) wave spectrum, it cannot penetrate more than 1 cm in the tissue. Therefore, the first studies on NIRS were made in the transluminal newborn head [13]. The diffusion of light from biological tissue depends on reflection, absorption and scattering. A NIRS device consists of a source (sources) that emits two or more wavelengths of light in the near infrared light range (650–1000 nm) and a detector at a distance The specific wavelength-forming diodes (light emitting diodes), and the photodiodes, which are usually made of silicone, that can measure the transmission/absorption ratio, are adhered to the measuring zone. The diode-photodiode distance is recommended to be 5 cm for proper penetration [14, 15]. The loss of light depends on absorption and scattering. The absorption of light can be measured by Beer-lambert's law (Fig. 18.3).

The light is absorbed by chromophore with different absorbency, such as water, melanin, lipid, myoglobin, oxy-deoxyhemoglobin and cytochrome oxidase. This allows spectroscopic separation because these absorbents absorb different wavelengths. The scattering of light constitutes 80% of attenuation, which is the biggest problem of NIRS measurements. Most clinical spectrophotometers are continuous waveform devices using modified Beer Lambert's law to calculate changes in chromophore concentrations [16]. Mathematically, it can be defined as [chromophore concentration = absorption rate/distance from light in tissue × chromophore extinction coefficient]. In NIRS measurements, at least two different wavelengths should be used to make the comparison of chromophore concentrations. Since photons are subject to breakage, reflection and scattering in tissues, the distance between the light source and the detector cannot be measured directly. To overcome this situation, manufacturers have developed spatial resolution spectroscopy (currently most commonly used), frequency dependent spectroscopy and time-dependent spectroscopy techniques. As the devices use different techniques and algorithms, the measured values may differ between devices [17]. Since oxy and deoxy Hb show absorption differences in light at wavelengths between 700 and 850 nm, these two

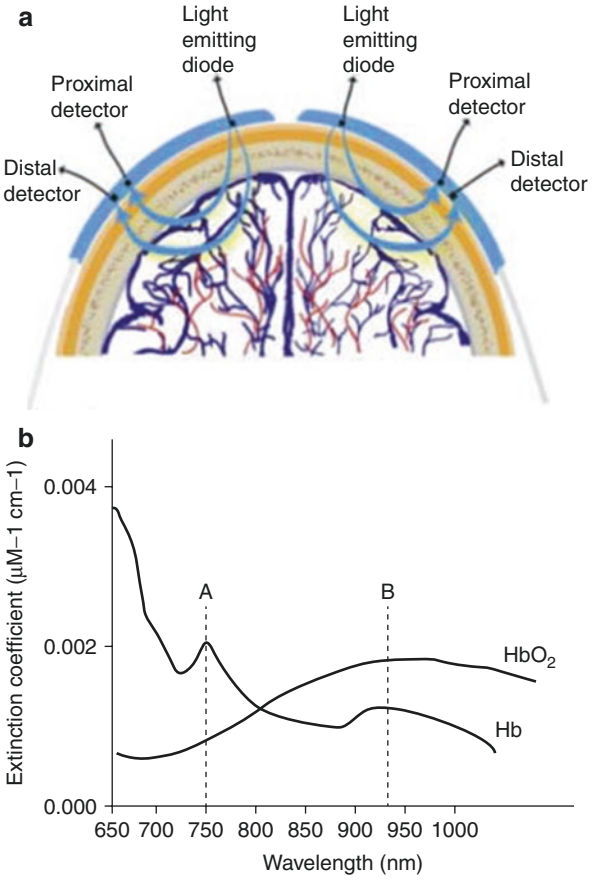

Fig. 18.3 Basic principles of the NIRS technology

wavelengths are commonly used in measurements [18]. While two wavelengths are used in the first produced devices, the accuracy of the measurements is increased by using multiple wavelengths in current devices. NIRS devices do not perform plethysmographic measurements such as pulse oximeters, i.e. they are not pulsatility-dependent and cannot distinguish arterial flow. The measured oxygen saturation corresponds to mixed blood saturation (25–30% arterial, 70–75% venous). Capillary is neglected because it constitutes less than 2% volume. Therefore, NIRS regional hemoglobin oxygen saturation measurements often represent the saturation of the venous portion of the tissue [16, 18, 19]. Since the baseline values vary greatly among individuals, monitoring of the change of baseline values over time is clinically more important [20]. Therefore, NIRS is a trend monitor, the oximeter values being below 40%, or more than 25% of baseline changes may be predictive of cerebral ischemia [21].

The most important limitation of NIRS is that the measurements obtained do not reflect pure brain oxygen saturation due to signals originating from extracranial tissues. To overcome this, algorithms are used to extract scalp data using two detectors

[22]. Another limitation is the difference of the basal values between individuals, therefore it is recommended to use as a trend monitor. In some cases, such as hemodilution, hematoma, and arteriovenous shunting, measurements are still varied. In cases that increase the diode-photodiode distance, such as tissue edema, measurements which do not match the reality can be observed [23, 24]. Changes in skin pigmentation may lead to false readings [25]. NIRS cannot recognize the etiology of low oxygenation values and cannot differentiate between embolism or hypoperfusion. It can only give information about the region (mostly frontal) to which it is adhered, cannot make global evaluations [23–25].

18.2.3 Cerebral Autoregulation and NIRS

The brain is one of the most metabolically active organs, responsible for 20% of the body's resting energy consumption despite weighing only 2% of the total body mass. In order to maintain normal brain function, the cerebral blood flow must be meticulously regulated. Cerebral autoregulation is an important mechanism that maintains stable cerebral blood supply, despite changes in mean arterial blood pressure (MAP). The cerebral autoregulation mechanism is effective between 50 and 150 mmHg MAP values. Within this MAP range, vasomotor tonus offers cerebrovascular resistance, therefore cerebral blood flow remains relatively constant [26]. The regulation of vascular resistance is believed to have individual upper and lower thresholds. These thresholds might differ in pediatric, septic or hypertensive patients [27–29]. Transcranial Doppler ultrasound and near infrared spectroscopic techniques (NIRS) are used for evaluating cerebral blood flow and oxygenation. It is also believed that NIRS monitoring gives information about cerebral autoregulation [28, 30]. TCD has some limitations, especially it measures only middle cerebral artery blood flow and cannot give microvascular flow changes. NIRS has a sensitivity specific to blood flow changes in the microvascular bed, so it can be obtained information about dynamic cerebral autoregulation [26]. Moreover, monitoring cerebral autoregulation with NIRS, exhibited moderate but significant correlation with previously validated TCD based methods in patients with acute neurological injury [31]. It is founded that an association between impaired cerebrovascular autoregulation, measured by near-infrared spectroscopy, and delirium in the early postoperative period after cardiac surgery [32]. As a result, the NIRS technique continues to strengthen its position as a noninvasive, easy and rapid assessment method in the evaluation of cerebral autoregulation.

18.2.4 In Assessing Tissue Perfusion with NIRS and Changes in the Presence of Comorbidities

As a result of imbalance between oxygen demand and supply, tissue perfusion deterioration begins at the cellular level, then leads to dysfunction and damage in tissue and organ levels. In addition to mandatory functions such as growth,

membrane transport and repair, the cell also requires oxygen for facultative functions such as specialized tasks, biosynthetic activities and electrolyte/protein transport. The adequacy of oxygenation is determined by cardiac output, hemoglobin level, partial arterial oxygen pressure, oxygen affinity of hemoglobin, local microcirculatory regulation parameters. Global markers such as mixed/central venous oxygen saturation and lactate levels are used in critically ill patients with impaired tissue oxygen presentation. Techniques such as direct visualization of the microvascular bed (videomicroscopy) are used in direct perfusion assessment. Although NIRS is the leading method to evaluate microcirculation indirectly, techniques such as sublingual capnometry, gastric tonometry and tissue oxygen electrodes are also used [33]. Although StO_2 measured by NIRS has been evaluated in many vital organs, the skeletal muscle StO_2 value is considered to be an early potential detector of hypoperfusion due to the nonvital peripheral organ [34]. Although the thenar region, which is less affected by individual changes such as edema and adipose tissue, is shown as a safe measurement site, safe measurement has also been obtained from the forearm, masseter, deltoid and knee regions [33, 35]. In the large patient series, basal StO_2 values evaluated in the thenar region were found to be $87 \pm 6\%$, i.e. close to mixed venous oxygen saturation [36]. A decrease in StO_2 is expected when there is a decrease in oxygen supply to the tissue or an increase demand, but it is likely that there will be no change in StO_2 when the supply and demand decrease together. The idea that the area of forearm rather than the thenar region is more ideal suggests that a cold vasodilatation of the hands may lead to misdiagnosis, although perfusion deterioration (vasoconstriction) is expected in the case of hypothermia [37]. The relationship between hypothermia and NIRS is quite complex. Reduced tissue oxygen consumption with hypothermia are expected to increase in NIRS, however in reality the condition is more complicated. The vasoconstriction and deterioration of autoregulatory mechanisms associated with hypothermia, severely affect blood flow to the tissue. Moreover, there is a myocardium that needs to fight with increased vascular resistance due to hypothermia. Myocardial depressant effect of hypothermia also adversely affects cardiac functions, such as increased vascular resistance. In addition, gas solubility and hemoglobin oxygen affinity changes also contribute to impaired tissue oxygenation. With all therapeutic interventions, hypothermia has both advantages and disadvantages for various organs. After hypothermia period, the NIRS values rise over basal levels in the re-warming phase. This is indicative of vascular reactivity deterioration and the associated luxury perfusion, which both may be harmful [38]. A little-known feature for NIRS is that it can evaluate tissue temperature depending on the temperature of the water absorption spectrum. This unique feature of NIRS has been shown in human infants as shown in animals [39]. The relationship between hypothermia and NIRS seems to require longer research.

Compared to normal healthy individuals, patients with comorbidity have lower baseline NIRS values [40]. In the presence of diabetes mellitus, low basal cerebral and tissue NIRS values are seen and thought to be due to microangiopathy [41]. Diabetic patients have been shown to have more tissue oxygen desaturation with exercise, and it has been suggested that NIRS is useful for the detection of this

condition [42]. Similarly, hypertension, which is among the microangiopathic diseases, also shows impaired basal tissue oxygenation levels [43]. In such patients, it is difficult to compensate for developing desaturation and requires a long time.

18.2.5 Assessment of Anemia-Transfusion Threshold, Cardiac Output, Oxygenation

In addition to the microcirculatory vascular factors that affect tissue oxygenation locally, the decrease in NIRS values is expected in case of decreased oxygen carrier hemoglobin. The main determinants of global oxygen delivery to tissue are the oxygen content of the blood and cardiac output. In clinical practice, only the hemoglobin level is tested and the transfusion threshold is determined, however tissue oxygen delivery is often not considered. However, the organism has the capacity to compensate for the hemoglobin decrease to a certain level. By assessing tissue oxygenation, it may be possible to avoid the harmful effects of unnecessary transfusion. NIRS, which can monitor tissue oxygenation rapidly and continuously, can guide to determine the transfusion threshold [44, 45]. In chronic anemia that develops over a long period of time, a decrease in NIRS values may not be observed since the organism provides the necessary compensation [46]. On the contrary in cases of acute hemorrhage, blood loss and volume loss may occur together, hemoglobin value may be measured incorrectly normal, due to hemoconcentration. But in fact there is considerable tissue oxygenation disorder. These examples indicate that the transfusion decision, which should be considered twice, should be done by evaluating the tissue oxygenation adequacy instead of purely quantitative measurements. NIRS has been shown to be a reliable guide in hemoglobin/myoglobin changes and may determine the need for transfusions [44, 47–49].

Clinical and laboratory markers of inadequate cardiac output occur as mottling in the skin, decreased urine output, peripheral coldness, delayed capillary filling time, tachycardia, increased serum lactate, decreased in central venous oxygen saturation and acidosis. However, objective cardiac output measurement requires complicated technologies such as indicator dilution, Fick method, bioimpedance, Doppler. NIRS is a noninvasive and early-warning marker in such cases, acts as a proxy of central venous oxygen saturation [50, 51]. Reductions in tissue oxygen saturation show positive correlations with cardiac output [51]. During cardiac surgery, there is a strong correlation between NIRS and central venous oxygen saturation in pediatric and adult patients. These results show that the dependence of cerebral oxygen saturation on the local tissue blood flow represented by CO is a reliable trend monitor [51, 52].

Tissue oxygenation is severely impaired under pathological conditions such as cancer, diabetes, coronary artery disease, stroke, and these are also associated with a decrease in PO_2, i.e., hypoxia. In perioperative conditions without comorbidities, hypoxia often develops without any warning and the patient may not be aware of it. It is also possible to easily detect hypoxia that can develop in the perioperative period with NIRS [50, 51]. Similarly, it can detect acute hypoxia during intensive

exercise in healthy subjects [53]. In children with congenital heart disease with chronic hypoxia, tissue oxygenation values determined by NIRS were within normal limits [54]. In such cases, hemoglobin increases in the long term, oxygenation is provided at the normal level, but if there is an acute decrease in hemoglobin and/or cardiac output, there will be sudden decreases in NIRS. As a result, if to the body is given enough time to compensate for some pathologies, it adjusts hypoxia, anemia, cardiac output and microcirculation, and tries to provide normal oxygen delivery. However, it is useful to detect reductions in oxygen delivery in a severe and acute clinical setting with a trend monitor such as NIRS.

18.2.6 One-Lung Ventilation and NIRS

One-lung ventilation (OLV) is performed in thorax and other surgeries to eliminate lung movement and increase visualization in the surgical field. During the OLV, intrapulmonary shunt develops due to ventilation/perfusion imbalance and this may impair systemic and cerebral oxygenation. Although potential hypoxaemia associated with OLV is tried to be eliminated by various methods, overt hypoxia is observed in 5–10% of patients [55]. To prevent OLV-associated hypoxia and hypercarbia, apply PEEP to dependent and non-dependent lungs, low tidal volume + PEEP instead of high volumes, raising FiO_2, intermittent ventilation of the dependent lung, decrease peak airway pressures, pressure-controlled ventilation modes, avoiding excessive hemodilution strategies are used. Studies using NIRS to determine hypoxia that may develop during OLV revealed that low rSO_2 was observed during OLV, and this was an independent risk factor for cognitive dysfunction [56, 57]. The main determinant of cerebral blood flow is $PaCO_2$ rather than PaO_2. While hypoxia during OLV may affect the brain, conditions such as $PaCO_2$ increase/decrease will also affect cerebral hypoxia by regulating brain blood flow. The reason why there is no significant decrease in cerebral oxygenation in OLV cases where normocapnia can be provided is this physiological autoregulation mechanism. Similarly, cerebral hypoxia is not observed in OLV cases where peripheral oxygen saturation is above 90% [58]. Considering that anesthesia decreases the cerebral metabolic rate, these changes appear to be tolerable in many cases. However, it would be difficult to tolerate cerebral and systemic hypoxia in patients with OLV who have problems with comorbidity, anemia, low cardiac reserve or cerebrovascular disease, which may be a nuisance in these compensation mechanisms, and this will prepare the step for morbidity. Therefore, monitoring of both systemic and cerebral tissue oxygenation is very important in critically ill patients. OLV application time is also a risk factor for cerebral desaturation. Prolongation of duration will increase oxidative stress, strengthen the inflammatory response, increase the severity of hypoxia, reduce tolerance [59]. Therefore, keeping the OLV duration short, applying lung protective mechanical ventilator strategies, optimizing the patients' comorbidities, anemia and cardiorespiratory functions during preoperative preparation, and enabling early intervention by closely monitoring the hypoxia that may develop in the perioperative period will be the correct approaches. In cases where the intrathoracic pressure

increases, mean arterial pressure and cardiac output are decreased and this has been suggested to decrease frontal lobe oxygenation detected by NIRS. Frontal lobe oxygenation decreases by >10% in patients with a mean arterial pressure reduction of more than 15 mmHg [60]. In cases where intraabdominal pressure increases, changes in NIRS values are observed [61]. In elderly and obese patients, desaturation with intraabdominal insufflation is more common, and thus, monitoring these patients with NIRS is an important component of perioperative care [62].

The limitations of technology are overcome by human experience and interpretation.

References

1. Wheeler OH. Near infrared spectra. A neglected field of spectral study. J Chem Educ. 1960;37:234–6.
2. Herschel W. Experiments on the refrangibility of the invisible rays of the sun. Phil Trans R Soc Lond. 1800;90(Pt II):284–92.
3. Goddu RF, Delker D. Spectra-structure correlations for the near-infrared region. Anal Chem. 1960;32:140–1.
4. Whetsel KB. NIR News. 1991;2(5):10–1.
5. Norris KH, Barnes RF, Moore JE, Shenk JS. Predicting forage quality by infrared reflectance spectroscopy. J Anim Sci. 1976;43:889–97.
6. Norris KH, Hart JR. Proceedings of the 1963 International Symposium on Humidity and Moisture, vol. 4. New York, NY: Reinhold Publishing; 1965. p. 19–25.
7. Norris KH, Hart JR. Direct spectrophotometric determination of moisture content of grain and seeds. J Near Infr Spectrosc. 1996;4:23–9.
8. Jobsis FF. Noninvasive infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. Science. 1977;198:1264–7.
9. Cope M, Delpy DT. System for long-term measurement of cerebral blood and tissue oxygenation on newborn infants by near infra-red transillumination. Med Biol Eng Comput. 1988;26:289–94.
10. Wallon J, Yan SH, Tong J, Meurens M, Haot J. Identification of breast carcinomatous tissue by near-infrared reflectance spectroscopy. Appl Spectrosc. 1994;48(3):190–3.
11. Quaresima V, Ferrari M. Medical near infrared spectroscopy: a prestigious history and a bright future. NIR News. 2016;27(1):10–3.
12. Hall W, Pollard A. Near-infrared spectrophotometry: a new dimension in clinical chemistry. Clin Chem. 1992;38:1623–31.
13. Brazy JE, Lewis DW, Mitnisk MH, Jöbsis FF. Noninvasive monitoring of cerebral oxygenation in preterm infants: preliminary observation. Pediatrics. 1985;75:217–25.
14. Ohmae E, Ouchi Y, Oda M, Suzuki T, Nobesawa S, Kanno T, et al. Cerebral hemodynamics evaluation by near-infrared time-resolved spectroscopy: correlation with simultaneous positron emission tomography measurements. Neuroimage. 2006;29(3):697–705.
15. Germon TJ, Evans PD, Barnett NJ, Wall P, Manara AR, Nelson RJ. Cerebral near infrared spectroscopy: emitter-detector separation must be increased. Br J Anaesth. 1999;82(6):831–7.
16. Pellicer A, Bravo MC. Near-infrared spectroscopy: a methodology-focused review. Semin Fetal Neonatal Med. 2011;16(1):42–9.
17. Thavasothy M, Broadhead M, Elwell C, Peters M, Smith M. A comparison of cerebral oxygenation as measured by the NIRO 300 and the INVOS 5100 near-infrared spectrophotometers. Anaesthesia. 2002;57(10):999–1006.
18. Steppan J, Hogue CW Jr. Cerebral and tissue oximetry. Best Pract Res Clin Anaesthesiol. 2014;28(4):429–39.

19. McCormick PW, Stewart M, Goetting MG, Balakrishnan G. Regional cerebrovascular oxygen saturation measured by optical spectroscopy in humans. Stroke. 1991;22(5):596–602.
20. Denault A, Deschamps A, Murkin JM. A proposed algorithm for the intraoperative use of cerebral near-infrared spectroscopy. Semin Cardiothorac Vasc Anesth. 2007;11(4):274–81.
21. Butterworth JF, Mackey DE, Wasnick JD. Morgan & Mikhail's clinical anesthesiology. New York, NY: McGraw-Hill; 2013. p. 123–42.
22. Murkin JM, Arango M. Near-infrared spectroscopy as an index of brain and tissue oxygenation. Br J Anaesth. 2009;103(Suppl 1):i3–13.
23. Yoshitani K. Comparison of changes in jugular venous bulb oxygen saturation and cerebral oxygen saturation during variations of haemoglobin concentration under propofol and sevoflurane anaesthesia. Br J Anaesth. 2005;94(3):341–6.
24. Yoshitani K, Kawaguchi M, Miura N, Okuno T, Kanoda T, Ohnishi Y, et al. Effects of hemoglobin concentration, skull thickness, and the area of the cerebrospinal fluid layer on near-infrared spectroscopy measurements. Anesthesiology. 2007;106(3):458–62.
25. Cooper RJ, Selb J, Gagnon L, Phillip D, Schytz HW, Iversen HK, et al. A systematic comparison of motion artifact correction techniques for functional near-infrared spectroscopy. Front Neurosci. 2012;6:147.
26. Kainerstorfer JM, Sassaroli A, Tgavalekos KT, Fantini S. Cerebral autoregulation in the microvasculature measured with near-infrared spectroscopy. J Cereb Blood Flow Metab. 2015;35:959–66.
27. Kooi EMW, Verhagen EA, Elting JWJ, Czosnyka M, Austin T, Wong FY, Aries MJH. Measuring cerebrovascular autoregulation in preterm infants using near-infrared spectroscopy: an overview of the literature. Expert Rev Neurother. 2017;17(8):801–18.
28. Demir A, Balcı E, Karadeniz U. Quick evaluation of cerebral autoregulation limits with near infrared spectroscopic techniques in the intraoperative period. Turk J Anaesthesiol Reanim. 2018;46(4):316–8.
29. Carrie MG, Rosenblatt K, Lara LR, Winters B, Nyquist P, Hogue C. Near-infrared spectroscopy (NIRS) to monitor cerebral autoregulation in sepsis: a potential method to individualize resuscitation endpoints. Am J Respir Crit Care Med. 2016;193:A7037.
30. Moerman A, De Hert S. Recent advances in cerebral oximetry. Assessment of cerebral autoregulation with near-infrared spectroscopy: myth or reality? F1000 Res. 2017;6:1615.
31. Rivera-Lara L, Geocadin R, Zorrilla-Vaca A, Healy R, Radzik BR, Palmisano C, Mirski M, Ziai WC, Hogue C. Validation of near-infrared spectroscopy for monitoring cerebral autoregulation in comatose patients. Neurocrit Care. 2017;27(3):362–9.
32. Chan B, Aneman A. A prospective, observational study of cerebrovascular autoregulation and its association with delirium following cardiac surgery. Anaesthesia. 2019;74:33. https://doi.org/10.1111/anae.14457.
33. Mesquida J, Gruartmoner G, Espinal C. Skeletal muscle oxygen saturation (StO2) measured by near-infrared spectroscopy in the critically ill patients. Biomed Res Int. 2013;2013:502194. https://doi.org/10.1155/2013/502194.
34. Taylor DE, Simonson SG. Use of near-infrared spectroscopy to monitor tissue oxygenation. New Horiz. 1996;4(4):420–5.
35. Bartels SA, Bezemer R, de Vries FJ, Milstein DM, Lima A, Cherpanath TG, van den Meiracker AH, van Bommel J, Heger M, Karemaker JM, Ince C. Multi-site and multi-depth near-infrared spectroscopy in a model of simulated (central) hypovolemia: lower body negative pressure. Intensive Care Med. 2011;37(4):671–7.
36. Crookes BA, Cohn SM, Bloch S, et al. Can near-infrared spectroscopy identify the severity of shock in trauma patients? J Trauma. 2005;58(4):806–16.
37. Bezemer R, Karemaker JM, Klijn E, Martin D, Mitchell K, Grocott M, Heger M, Ince C. Simultaneous multi-depth assessment of tissue oxygen saturation in thenar and forearm using near-infrared spectroscopy during a simple cardiovascular challenge. Crit Care. 2009;13(Suppl 5):S5.
38. Absalom AR, Scheeren TWL. NIRS during therapeutic hypothermia: cool or hot? Resuscitation. 2013;84:720–1.

39. Holper L, Mitra S, Bale G, Robertson N, Tachtsidis I. Prediction of brain tissue temperature using near-infrared spectroscopy. Neurophotonics. 2017;4(2):021106. https://doi.org/10.1117/1.NPh.4.2.021106.
40. Scheeren TWL, Schober P, Schwarte LA. Monitoring tissue oxygenation by near infrared spectroscopy (NIRS): background and current applications. J Clin Monit Comput. 2012;26:279–87.
41. Rooke TW, Osmundson PJ. The influence of age, sex, smoking, and diabetes on lower limb transcutaneous oxygen tension in patients with arterial occlusive disease. Arch Intern Med. 1990;150:129–32. https://doi.org/10.1001/archinte.150.1.129.
42. Gustafsson P, Crenshaw AG, Edmundsson D, Toolanen G, Crnalic S. Muscle oxygenation in Type 1 diabetic and non-diabetic patients with and without chronic compartment syndrome. PLoS One. 2017;12(10):e0186790.
43. Tzanis G, Dimopoulos S, Manetos C, Koroboki E, Manios E, Vasileiadis I, Zakopoulos N, Nanas S. Muscle microcirculation alterations and relation to dipping status in newly diagnosed untreated patients with arterial hypertension-a pilot study. Microcirculation. 2017;24(7) https://doi.org/10.1111/micc.12384.
44. Cem A, Serpil UO, Fevzi T, Murat O, Umit G, Esin E, Pinar U, Sahin S, Hasan K, Cem A. Efficacy of near-infrared spectrometry for monitoring the cerebral effects of severe dilutional anemia. Heart Surg Forum. 2014;17(3):E154–9.
45. Leal-Noval SR, Arellano-Orden V, Muñoz-Gómez M, Cayuela A, Marín-Caballos A, Rincón-Ferrari MD, García-Alfaro C, Amaya-Villar R, Casado-Méndez M, Dusseck R, Murillo-Cabezas F. Red blood cell transfusion guided by near infrared spectroscopy in neurocritically ill patients with moderate or severe anemia: a randomized, controlled trial. J Neurotrauma. 2017;34(17):2553–9.
46. Yuruk K, Bartels SA, Milstein DM, Bezemer R, Biemond BJ, Ince C. Red blood cell transfusions and tissue oxygenation in anemic hematologyoutpatients. Transfusion. 2012;52(3):641–6.
47. Chiu AS. Application of TR-NIRS in healthy and diseased children during exercise. 2017. UC Irvine. ProQuest ID: Chiu_uci_0030D_14746. Merritt ID: ark:/13030/m5tr0xch.
48. Mintzer JP, Parvez B, La Gamma EF. Regional tissue oxygen extraction and severity of anemia in very low birth weight neonates: a pilot NIRS analysis. Am J Perinatol. 2018;15:1411. https://doi.org/10.1055/s-0038-1660458.
49. Saito-Benz M, Sandle ME, Jackson PB, Berry MJ. Blood transfusion for anaemia of prematurity: current practice in Australia and New Zealand. J Paediatr Child Health. 2019;55:433. https://doi.org/10.1111/jpc.14222.
50. Desmond FA, Namachivayam S. Does near-infrared spectroscopy play a role in paediatric intensive care? BJA Educ. 2016;16(8):281–5.
51. Schramm P, Tzanova I, Hagen F, Berres M, Closhen D, Pestel G, Engelhard K. Cerebral oxygen saturation and cardiac output during anaesthesia in sitting position for neurosurgical procedures: a prospective observational study. Br J Anaesth. 2016;117(4):482–8.
52. Ranucci M, Isgro G, De la Torre T, et al. Near-infrared spectroscopy correlates with continuous superior vena cava oxygen saturation in paediatric cardiac surgery patients. Paediatr Anaesth. 2008;18:1163–9.
53. Subudhi AW, Dimmen AC, Roach RC. Effects of acute hypoxia on cerebral and muscle oxygenation during incremental exercise. J Appl Physiol (1985). 2007;103(1):177–83.
54. Kussman BD, Laussen PC, Benni PB, McGowan FX Jr, McElhinney DB. Cerebral oxygen saturation in children with congenital heart disease and chronic hypoxemia. Anesth Analg. 2017;125(1):234–40.
55. Stéphan A, Laroche S, Davis S. Learning deficits and dysfunctional synaptic plasticity induced by aggregated amyloid deposits in the dentate gyrus are rescued by chronic treatment with indomethacin. Eur J Neurosci. 2003;17(9):1921–7.
56. Yamada N, Nagata H, Sato Y, Tomoyasu M. Effects of propofol or sevoflurane on cerebral regional oxygen saturation (rSO2) during one-lung ventilation. Masui. 2008;57(11):1388–97.
57. Li XM, Li F, Liu ZK, Shao MT. Investigation of one-lung ventilation postoperative cognitive dysfunction and regional cerebral oxygen saturation relations. J Zhejiang Univ Sci B. 2015;16(12):1042–8.

58. Végh T, Szatmári S, Juhász M, László I, Vaskó A, Takács I, Szegedi L, Fülesdi B. One-lung ventilation does not result in cerebral desaturation during application of lung protective strategy if normocapnia is maintained. Acta Physiol Hung. 2013;100(2):163–72.
59. Misthos P, Katsaragakis S, Milingos N, Kakaris S, Sepsas E, et al. Postresectional pulmonary oxidative stress in lung cancer patients. The role of one-lung ventilation. Eur J Cardiothorac Surg. 2005;27:379–82.
60. Pedersen LM, Nielsen J, Østergaard M, Nygård E, Nielsen HB. Increased intrathoracic pressure affects cerebral oxygenation following cardiac surgery. Clin Physiol Funct Imaging. 2012;32(5):367–71.
61. Kemerci PU, Demir A, Aydınlı B, Güçlü ÇY, Karadeniz Ü, Çiçek ÖF, Taşoğlu İ, Özgök A. 10 cm H2O PEEP application in laparoscopic surgery and cerebral oxygenation: a comparative study with INVOS and FORESIGHT. Surg Endosc. 2016;30(3):971–8.
62. Ružman T, Mraović B, Šimurina T, Gulam D, Ružman N, Miškulin M. Transcranial cerebral oxymetric monitoring reduces brain hypoxia in obese and elderly patients undergoing general anesthesia for laparoscopic cholecystectomy. Surg Laparosc Endosc Percutan Tech. 2017;27(4):248–52.

Part IV

Specific Surgical Situations

Lung Transplantation: Justification for a Paradigm Change

19

Nandor Marczin, Rosalba Romano, and Marco Scaramuzzi

19.1 Introduction

Lung transplantation (LTx) represents a spectrum of complex and invasive surgeries ranging from single, bilateral sequential, and lobar to heart-lung transplantation and other combined procedures including kidney and liver [1]. The end-stage pulmonary diseases, the impact of the respiratory condition on the pulmonary vasculature and right and left ventricles (cor pulmonale), their systemic co-morbidities, and the frequently poor general condition of the recipient, together with the challenging surgery and severe alterations of cardiopulmonary physiology required for different stages of the surgery, make the intraoperative management supremely challenging [2, 3]. Current clinical management during the intraoperative period is evolving both regarding multidisciplinary interdependence and novel technologies ranging from surgical advances to monitoring, therapeutic repertoire, and extracorporeal circulatory and respiratory support. This multidisciplinary nature demands new attitudes from our specialty not only in terms of superspecialisation and expertise in

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anaesthetic technologies but taking major new roles in multidisciplinary team efforts and communications.

The reality of the current era of transplantation is that recipients are increasingly of higher risk patients, donors are frequently suboptimal or coming from the "extended criteria" donor pool and the surgical procedures are becoming more complex with less invasive strategies without the use of cardiopulmonary bypass (CPB) requiring expert management of difficult one lung ventilation, significant pulmonary hypertension and circulatory challenges for prolonged period of time. Despite these adverse conditions, survival is improving especially considering early postoperative survival. However, we cannot rest as severe primary graft dysfunction (PGD) remains too prevalent and nonpulmonary complications are nearly ubiquitous and they negatively impact on long term patient survival and quality of life.

For these reasons, the international community of lung transplant anaesthetists continue to strive towards constant quality improvement and critical appraisal of our management goals. There is increasing activities in many relevant international organisations to formalise these dialogues, survey our practices and to attempt to arrive at a consensus. The recent ISHLT consensus project on PGD is a good example framework in this direction. Indeed, currently, there is a seven-society coordination towards the first international consensus on anaesthesia and intensive care management of lung transplantation.

This chapter focuses on selected areas of paradigm changes in lung transplantation including (a) anaesthesia mission (b) ex vivo lung perfusion (c) potentially modifiable intraoperative risk factors (d) posttransplant ventilation strategies and (e) some novel understanding of basic inflammatory aspects of lung injury in the setting of lung transplantation.

19.2 Lung Transplant Anaesthesia Mission

19.2.1 Preoperative Paradigms

Traditionally our specialty has mainly focussed on technical conduct of anaesthesia towards successful completion of surgery and delivering the patient to the intensive care unit. We have generally learnt about the emergency transplant procedure in the middle of the night and first met our patient in the anaesthetic room who was listed for transplantation by respiratory physicians and surgeons. We have made tremendous progress in some aspects of monitoring, airway management and lung isolation and ensured adequate pain control. Surgery for bilateral sequential lung transplantation routinely involved using CPB and we have followed a few straightforward management principles after bypass such as fluid restriction and vasoconstriction as haemodynamic principles. Generally, patients were of a relatively young age, with only lung failure and organ donors were young usually due to tragic road traffic accidents and brain injury.

This landscape has changed dramatically towards older recipient ages with multiple comorbidities and prevalence of frailty. Listing rarely follows absolute

indications and contraindications but requires careful assessment that a relatively high-risk patient would still benefit from transplantation compared to conventional medical treatment, and that the patient has a reasonable chance to survive the lung transplant surgery, to reduce his/her disability and to improve their health related quality of life. This requires input from different specialties and it is increasingly recognised that anaesthesia and intensive care input is paramount for patients with relative contraindications to LTx as part of these multidisciplinary teams. Since the relative contraindications and the complexity of these candidates invariably represent higher recipient risks for adverse transplant outcomes these should be recognised and must be negated by various perioperative risk reduction strategies. Among others, these may require anesthetic expertise to safely avoid CPB and to facilitate minimally invasive approaches, familiarity with advanced blood conservation techniques, cutting-edge pulmonary vasodilator and inotropic treatments and with protective ventilation strategies. Similarly, intensive care proficiency in mechanical respiratory and circulatory support is paramount in bridging critically ill recipients for lung transplantation or managing severe postoperative PGD in complex patients.

Such trend calls for a broader preoperative role for anesthetists and intensivists towards an extended, more holistic and comprehensive anesthesia/intensive care with more active involvement in recipient evaluation, listing and preoperative assessment. There would be significant benefits by such paradigm change to the multidisciplinary team. Firstly, the anesthesiologists and intensivists would be furnished with all available information at the time of listing to plan an optimal perioperative patient journey and the transplant physicians and surgeons would be assisted with anesthetic and intensive care insights into exact risks that may compromise outcomes. Such dialogue could lead to better identification of modifiable risk factors and strategies for preoperative optimization and perioperative risk reduction. Therefore we would advocate a role beyond evaluating the technical feasibility of anesthetic, to play a more integral part in the multidisciplinary team as comprehensive perioperative physicians contributing to patient assessment and to planning the perioperative care. Indeed, there is a trend in this direction as for instance, regulatory bodies in the UK, have now recognised the presence of named anesthesiologists and intensivists as one of the important quality measures of transplant MDT discussions.

19.2.2 Donor Management Paradigms and Ex Vivo Lung Perfusion

We have recently reviewed this area in details [4]. Relevant to the current theme of this monograph, we have advocated significant paradigm change in critical care management of the potential donor, for improving retrieval practices and for more intellectual involvement of our specialties in organ preservation, ex vivo evaluation and reconditioning and the need for leap advance in our efficiency in converting unacceptable allografts to suitable donor organs. As one of the practice points we have recommended that cardiothoracic anesthesia and critical care should take

greater responsibility for donor injury and ownership for better monitoring, evaluation and management of the organ donor. We have also suggested that the anesthetic and critical care community should be more closely involved in research developments to mobilize further multidisciplinary expertise and investigative talent from our specialties.

19.2.3 Intra and Postoperative Paradigms

As part of an extended and truly perioperative medicine approach anesthesia occupies a strategic place to plan and coordinate collaborative strategies across the continuum of patient care with a focus on the intraoperative and postoperative activities. Indeed, in their inspirational editorial a decade ago, Evers and Miller called for anesthesia to take ownership of the substantial perioperative morbidity and mortality associated with modern surgery as a core a anesthesia mission [5]. Adapting such strategy for anaesthetic mission for lung transplantation thus requires a better understanding of the exact perioperative complications contributing to overall morbidity burden and mortality and identifying the intraoperative and intensive care strategies that may prevent or attenuate these adverse events.

The most important cause of early morbidity and mortality after lung transplantation is PGD, a form of acute lung injury characterized by severe hypoxemia and infiltrates in the lung allograft that develops within 72 h after LTx [1, 2, 6–11]. This syndrome occurs in 10–30% of lung transplant recipients who require prolonged mechanical ventilation, ICU and hospital stay associated with reduced survival. Moreover, PGD also impacts on long term outcomes as PGD scores correlate with higher risk of chronic rejection and the development of bronchiolitis obliterans syndrome.

The development of PGD appears to be multifactorial reflecting the summation of injury inflicted upon the donor lung by the transplant process including donor-related factors and ischaemic events during preservation prior to implantation. However the role of intraoperative factors, especially conditions of reperfusion and consequences of intensive care management are being increasingly recognised with potential further damage to the lung allograft with additional assaults [6, 10, 12, 13]. Substantial current evidence points to surgical and anaesthetic factors suggesting that some of these could be mitigated by appropriate intraoperative management strategies [6–8, 10, 11, 14]. Therefore focussing anaesthesia mission on preservation of the pulmonary allograft quality, taking stronger ownership for the development of PGD and deploying our technical capabilities to effectively control modifiable intraoperative risk factors of PGD has a major potential to improve early postoperative and longer-term outcomes.

As LTx is one of the most invasive and extensive surgical procedures, the recipient's body is subjected to severe physiological, cellular, and molecular stresses from the combined effects of anaesthesia, one-lung ventilation, pneumonectomy, and surgical trauma that may compromise perfusion and O_2 delivery to systemic organs [15–19]. This may lead to single or multi-organ dysfunction, especially in high-risk

patients with significant comorbidities and already compromised organ function with limited reserves.

A recent study by the Pittsburgh group revealed that more than 90% of patients had a complication after LTx and demonstrated that the presence of any complication was negatively correlated with long-term survival. Those with the greatest negative impact included renal, cardiac, hepatic, and vascular complications [15, 16]. Such significant appreciation of a "ripple effect" by which non allograft related perioperative complications negatively affect long-term survival provides the anaesthetist with an opportunity to employ preventative measures and/or to improve treatment strategies for specific complications.

For instance, postoperative AKI is multifunctional and mainly relates to intra- and postoperative adverse events (e.g., prolonged episodes of hypotension, low flow, hypoxemia, nephrotoxic drug and concurrent rhabdomyolysis). Importantly, patients with preexisting renal dysfunction are much more vulnerable to develop perioperative AKI and these recurring injuries due to multiple hits may progress towards chronic kidney disease, a significant long term posttransplant complication. Such recognition has major implications to preoperative assessment, risk stratification, optimization and intra-operative risk minimization strategies. Moreover, anaesthesia and intensive care could facilitate a perioperative renal protection plan aiming to reduce the likelihood or to attenuate the severity of postoperative AKI by minimising renal insults such as prolonged hypotension, renal hypoperfusion, hypoxemia and administration of nephrotoxic drugs.

Thus, perioperative anaesthetic management should guarantee not only safe completion of the transplant surgery but go beyond towards improving the quality of the allograft, preventing extrapulmonary complications thereby reducing total burden of postoperative complications. Unfortunately, some of the management principles to protect the allograft and to preserve systemic organ function are conflicting, and priorities need to be decided and principles compromised according to the exact clinical situation.

19.3 Ex Vivo Lung Perfusion (EVLP)

EVLP is one of the most significant advances of the last two decades in lung transplantation. Steen and colleagues originally developed EVLP to allow better clinical and physiological assessments of donor lungs in the Donation after Cardiac Death (DCD) setting [20, 21]. Subsequently, it has been recognized that EVLP might facilitate better recovery from donors, preserve lung injury, and help recondition lungs that were initially considered unsuitable for transplantation. Clinical experience from Lund, Toronto, Harefield, and others indicate that perioperative and mid-term outcomes of transplantation of EVLP-reconditioned lungs are comparable to standard lung transplantation [22–26]. However, the conversion rate of evaluated allografts to transplantation and success of these transplants is not universal. Most UK experience indicated an approximately 60% progress to transplantation [24]. The first multicentre study to evaluate the clinical value of *ex vivo* lung perfusion in

the UK, that involved all lung transplant centres, was terminated due to increased adverse signals in transplant recipients following implantation of *ex vivo* reconditioned lungs [27]. These results indicate that further work is needed to better define the acceptance criteria for EVLP evaluation and more rigorous decision making in accepting these lungs for transplantation. Regardless of such setbacks, there are current, large studies evaluating the role of *ex vivo* lung and heart perfusion and safely expanding the donor pool for successful lung transplantation.

The Transmedics group has expanded EVLP evaluation to the donor hospital and provides continuous machine perfusion during transit between the donor and implanting hospitals. Initial results using the integrated and portable Organ Care System (OCS) Lung device suggest that the technology allows favourable organ preservation and transplantation [28, 29]. Final results of the INSPIRE multi-centre trial have recently been published demonstrating the efficacy and safety of this novel technology. A significant reduction of PGD grade 3 within the first 72 h was demonstrated in patients receiving lungs after normothermic OCS preservation compared to static cold storage [30]. It remains to be elucidated if these observations translate into earlier recovery and improved long-term outcomes after lung transplantation.

Both the current static EVLP technology and the portable OCS platform involve careful ventilation and perfusion protocols with specific algorithms for evaluating lung performance on these systems. The consensus membership strongly feel that anaesthetists and intensivists should be an integral part of the EVLP team in order to maximise expertise for optimal ventilation and perfusion strategies along with assessment of specific and global lung functions to facilitate decision making regarding transplantation.

19.4 Intraoperative Management Strategies to Prevent PGD and Nonpulmonary Complications

Lung injury associated with transplantation can be conceptualised as a sequential series of haemodynamic, metabolic, and inflammatory insults. It starts with pulmonary manifestations of critical illness and side effects of medical management preceding brain death. The sequence continues with the neurogenic effects of coning followed by suboptimal preservation during the period of ischaemia, and finally, reperfusion injury and early post-implantation management [31–33].

The recent update on the International Society of Heart and Lung Transplantation (ISHLT) consensus project on PGD has recommended minor changes in PGD definitions, and the mechanism and treatment review has comprehensively addressed donor, recipient, and procedure related aspects [6, 34, 35]. Here, we expand on perioperative issues with a focus on the potentially modifiable factors and components.

Potentially modifiable intraoperative risk factors include the recipient perioperative pulmonary arterial hypertension, use of (CPB), an elevated inspired concentration of oxygen (FiO_2) and oxidative stress during and following allograft reperfusion,

injurious mechanical ventilation, and fluid management especially the transfusion of large-volumes of blood products [10]. Therefore, modifying surgical approaches towards less invasive strategies and avoiding CPB, limiting hydrostatic forces, hyperoxia, oxidative stress, and employment of protective ventilation strategies may attenuate degree of PGD. Some centres routinely practice controlled reperfusion and there is potential for utilisation of antioxidants.

19.4.1 Trend Away from Clamshell Towards Minimally Invasive LTx (MILT)

Depending on the recipient's condition, single lung-, bilateral-lung, or heart-lung transplantation may be indicated [1, 36]. Heart-lung transplantation is now reserved only for patients with irreversible pulmonary disease who have coexisting and uncorrectable cardiac failure. This combined procedure is now performed with decreasing frequency as more options are available for managing heart failure. Currently, the more commonly used surgical procedure is bilateral, sequential single-lung transplant (BSSLT). Replacing two lungs generally offers longer survival and better quality of life for the patient [1, 37, 38].

Bilateral sequential lung transplants are commonly performed via a transverse thoracosternotomy, popularly called a clamshell incision [39]. Motivated by reducing the invasiveness of the clamshell incision, there has been a move to use sternum-sparing sequential anterolateral or posterolateral thoracotomies with videoscopic assist [40–45]. These incisions are believed to achieve better cosmetic results and postoperative wound healing.

The minimally invasive approach is gaining momentum as there are perceived and single centre observations regarding perioperative benefits, reduction in wound infections, and better functional recovery following transplantation. However, there is paucity of data on the impact of minimally invasive lung transplantation on warm ischemia time, early graft function, and physiologic perturbations intraoperatively with potential impact upon systemic organ function (renal, CNS, hepatic) and will need all to be addressed in the future.

We have successfully introduced the MILT procedure in our program [44]. In our experience the surgical approach provides acceptable exposure to critical surgical areas facilitating safe dissection of recipient and implantation of the donor lungs. Interestingly, total surgical time was less in MILT suggesting that the surgical technique does not prolong the overall procedure duration and perhaps facilitates speed of chest closure due to less bleeding complications. Indeed, a significant fraction of MILT surgery was completed without the use of blood products. In those who required transfusion, the MILT group required significantly less plasma, platelet and specific hemostasis products. There was also trend for less red blood cell usage both intraoperatively and in the intensive care unit. However, in some patients, we encountered major vascular bleeding during the MILT surgery, which required conversion of the procedure to CPB. In this subset, the blood transfusion requirement was actually higher that the other groups.

In our experience MILT has been successfully applied to a broad spectrum of patients suggesting that MILT can be considered for most lung pathologies. However severe pulmonary hypertension represents unique challenges for both off pump BSLT and MILT and we prefer elective bypass for transplantation for PPH.

Compared to the traditional clamshell approach duration of mechanical ventilation and overall ICU stay were shorter with MILT. However, both CS and MILT was associated with similar kinetics and magnitude of leucocytosis and CRP increase. We have also observed beneficial effects of MILT on evolution of lung function. In our study lung function improved steadily over the first year after transplantation with the CS reaching approx. 80% predicted FEV1 and FVC after 6 months. MILT has provided consistently superior lung function during the first year time period after transplantation. The bilateral thoracotomies may have favorable impact on chest wall and lung mechanics in early postoperative periods.

Minimally invasive transplantation represents unique challenges both to surgeons and anesthetists. For instance, during the minimally invasive approach, the heart is not directly visible so continuous transesophageal (TOE) evaluation of heart function is essential [44, 46]. In addition, surgical manipulations of the hilum and heart are more pronounced requiring the anesthesiologist to be vigilant and in constant communication with the surgeon. Finally, vascular anastomoses need to be secured prior to inflating the lung, and there is higher risk for shunt circulation, hypoxia, and catastrophic blood loss [44, 46]. While these challenges dictate a more involved anaesthesia requirement and constant anaesthetic vigilance, the observed clinical benefits warrant such anaesthetic dedication and commitment.

19.4.2 Role of Cardiopulmonary Bypass (CPB)

In the recent study by the Lung Transplant Outcomes Group covering the period of 2002–2010 in ten leading transplant centres with more than 1200 LT recipients, the use of CPB represented the strongest risk (OR 3.4) for the development of severe PGD at 48 or 72 h [10]. Thus, safe avoidance of CPB during LT may represent the single most influential aspect to reduce postoperative morbidity of LT recipients. Our consensus has maintained this priority and provides clear management strategies at various critical parts of the operation to control the factors that would trigger the controlled or emergent institution of CPB. However, we also recommend that timely and safe institution of CPB is important to prevent systemic organ dysfunction due to severe and ongoing cardiorespiratory instability [17, 44, 47]. We have also recommended that veno-arterial (V-A) ECMO should be considered as alternative mechanical support in appropriate situations [46, 48–52].

19.4.3 Management of Pulmonary Hypertension

Clamping of the Pulmonary Artery is the single most significant event regarding cardiovascular and systemic organ function during LTx [46, 52, 53]. Occluding the right or left PA significantly decreases the vascular cross-sectional area, which increases the pulmonary vascular pressure and may lead to abrupt RV pressure

overload with acute RV dysfunction and failure, essentially independent of preoperative existing RV hypertrophy. This in turn compromises organ function with dire consequences for postoperative recovery and outcomes. Moreover, it may necessitate mechanical support, which in turn will compromise allograft function and contribute to PGD. Thus, the entire anesthetic period from induction to PA clamping is required in preparation for this event to optimise hemodynamics, fluid status, attenuate pulmonary vasoconstriction, and maintain RV contractility by ensuring adequate perfusion pressure, preload, and afterload.

Cardiopulmonary function during One Lung Ventilation (OLV) and one-lung perfusion (OLP) for transplantation is significantly different from similar situations during pneumonectomy for cancer resection. In the latter situation, patients are carefully selected with appropriate ventilatory reserve and generally without significant PH. During lung transplantation, OLV needs to support homeostasis with end stage lung disease and significant primary or secondary pre-existing PH with cardiopulmonary remodelling. Successful OLV and OLP will require careful optimisation of RV preload. Hypovolaemia will reduce cardiac output whereas fluid overload will lead to RV overdistension, myocardial ischaemia, tricuspid regurgitation, and further decrease of forward flow.

RV afterload should be optimised by complimentary strategies including non-specific means and active pharmacological therapy with pulmonary vasodilators [54, 55]. Among non-specific measures, hypoxemia, hypercapnia, acidosis, and hypothermia, light anesthesia should be all considered. In addition, pulmonary vasodilators—especially those with pulmonary selectivity—should be up and running. Selective pulmonary vasodilators decrease PVR and maintain MAP and RV perfusion pressure, while also helping with V/Q matching and reducing shunts [56–60]. Figure 19.1 demonstrates our regular strategy for administration of inhaled pulmonary vasodilators including iNO and Iloprost.

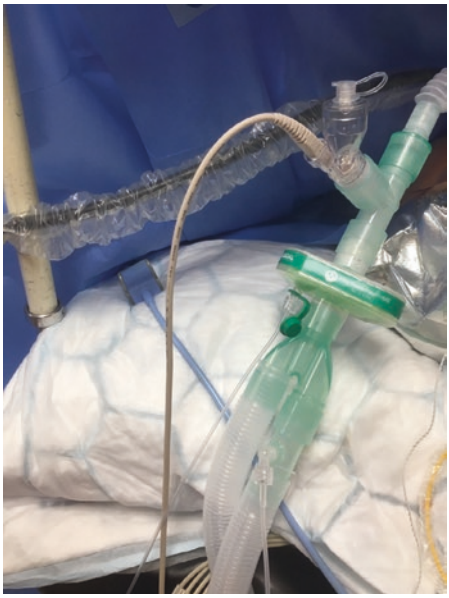

Fig. 19.1 Combined administration of inhaled pulmonary vasodilator inhaled nitric oxide (shown is measurement port to monitor exact delivery of inhaled nitric oxide in the distal inhalation limb of the ventilation circuit but proximal to humidifying filter) and ultrasonically nebulised Iloprost as the authors standard preoptimisation strategy for pulmonary vascular and right ventricular support therapy

Intravenous vasodilators could be useful in case of dominance of pulmonary vasoconstriction; however, systemic vasodilation, and thereby reduction in perfusion pressures to the RV, kidneys, and brain should be taken into consideration, monitored, and protected by additional means.

19.4.4 Controlled Reperfusion

There is strong animal experimental data to suggest that rapid reperfusion is harmful by causing stress failure of ischaemic lung microvasculature. In addition, small and large animal preparations indicate that limiting the initial reperfusion pressure for a short period of time has beneficial effects on subsequent allograft function and the development of PGD [61, 62]. Hence, the concept of controlled reperfusion is being increasingly recognised in clinical transplantation. Lick and colleagues from Texas have demonstrated that controlled reperfusion of the transplanted lung with white cell-filtered, nutrient-enriched blood has given excellent results [63]. They have collected 1.5 l arterial blood in a cardiotomy reservoir, and a modified blood/preservation perfusate was infused into the transplant pulmonary artery for 10 min at a low perfusion rate of 200 mL/min and low pressure (less than 20 mmHg), immediately before removal of the vascular clamp. Schnickel et al. has expanded such experience with the modified reperfusion technique and demonstrated low incidence of severe primary graft dysfunction and favourable short-term outcomes [64]. While these specific and complex reperfusion protocols have not been tested in large RCTs and are not practiced routinely, attempts should be made to control reperfusion conditions. As this has been taken up widely, the PA clamp can be reduced gradually by the surgeon while blood flow is slowly introduced to the new lung over a 10–15 min period. A combination of anaesthetic techniques including permissive systemic hypotension and use of vasoactive agents to maintain low PAP and pulmonary blood flow in order to reduce microvascular stresses for the first 10 min of reperfusion.

19.4.5 Hyperoxia and Oxygen Toxicity

Given that oxidative stress is a principle mechanism of reperfusion injury, hyperoxia has been long considered a major contributing factor for the development of acute lung injury and detrimental to early graft function [65–69]. The strongest clinical insights into these adverse events come from the study of Diamond et al. who investigated the effect of pre-reperfusion FiO_2 on subsequent development of grade 3 PGD at 48 and 72 h [10]. Increased FiO_2 during allograft reperfusion was strongly associated with development of severe PGD, independent of transplant type, bypass use, and pretransplant diagnosis. If the FiO_2 was kept below 40%, the predicted risk of grade 3 PGD was 12%. However, in the group that received higher than 40%, the risk increased to 18%, a relative risk increase of 30%. While higher FiO_2 may reflect patient needs during the surgical procedure, especially in the

setting of minimally invasive transplantation. Diamond and colleagues have highlighted different intraoperative practice patterns and preferences among the participant institutions, which represent a potentially modifiable factor in protecting allograft quality [10].

19.4.6 Antioxidant Treatment

There is major discrepancy between the strong conclusion of experimental studies regarding oxidative stress, the reported beneficial effects of antioxidants, and clinical applications [70]. Despite some real benefits of antioxidant treatment in renal transplants, there has been little clinical effort in lung transplantation to fully evaluate antioxidant treatment [70–73]. Our recent survey indicated that there is only a minority of centres who routinely administer antioxidative drugs for reperfusion injury ascorbic acid (6.7%; n = 5), acetylcysteine (6.7%; n = 5) [74]. This is in contrast with the recent clear demonstration that severe PGD was associated with increased plasma levels of lipid peroxidation products such as F2-isoprostanes and isofuranes, with even higher levels of these biomarkers in the setting of hyperoxia at reperfusion or in recipients of lungs from donors with smoke exposure [75]. Other important information suggests that the antioxidant capacity of lung transplant recipients is compromised before transplants and remains lower following transplantation with evidence of increased oxidative stress both in the lungs and plasma long after implantation [76].

Inhaled NO has been advocated as master reperfusion treatment, but most studies have not shown true benefit in preventing and treating reperfusion injury. We have recently provided a detailed analysis of the LT literature regarding the current status of iNO [59]. Both the European recommendations for inhaled NO or the recent ISHLT PGD consensus groups could not make a strong case for inhaled NO as a reperfusion therapy but appreciated the potential roles of iNO as rescue therapy for severe PGD [35, 77]. The only clinical study showing significant reduction in PGD by inhaled NO was the Valencia study, but those utilized lower iNO concentrations throughout the implant procedures and the effect could be related to hemodynamic management rather than true reperfusion effect [78]. Also, inhaled NO may promote free radical formation, negate any potential benefits and potentially injure the vulnerable allograft.

19.4.7 Intravenous Fluid Therapy

Judicious administration of intravenous fluid at induction of anesthesia and at critical stages of high-risk hypotension is justified. However, the benefits of fluid loading should be balanced with potential detrimental effects of intravascular fluid overload on one-lung perfusion and right ventricular performance as well as its contribution to interstitial and alveolar oedema following lung reperfusion [79]. Evidence of appropriate volume loading of the left and right ventricles should be

sought by transoesophageal echocardiography (TEE) aiming for adequate renal perfusion but avoiding overload to limit the risk of pulmonary oedema.

Large volumes of intravenous crystalloid infusions should increase pulmonary filtration forces, and colloids should reduce fluid filtration by increasing vascular oncotic pressure. However, in the face of increased permeability, the situation may be more complex with colloids contributing to interstitial oedema and reduction of gas exchange. Indeed, single centre results indicate that increasing volume of intraoperative colloid was associated with impaired gas exchange following transplant, reduced rate of tracheal extubation, and a trend for prolonging duration of stay in ICU [19]. It should be noted, that the colloid used was Gelofusine®, B. Braun, Australia, which has a small molecular weight (30,000 Da), and the findings may not be generalised for higher weight colloids such as human albumin with molecular weight of 65,000 Da.

Indeed, another large single centre study found no association between the non-blood components of fluid therapy (crystalloids and colloids) and grade-3 PGD, while there was a positive association between the total amount of fluids administered and development of severe PGD [80]. In this investigation, the odds for development of grade-3 PGD increased by 13% for each additional liter of fluid, and particularly, patients with grade-3 PGD were given a significantly higher volume of red blood cells than patients with lower grades of PGD. In a multi-institutional collaboration, the Lung Transplant Outcomes Group also reported a significant association between blood transfusions and PGD development with the conclusion that transfusing more than a liter of blood being associated with a twofold increase in the incidence of PGD [10]. Furthermore, a meta-analysis also concluded that transfusion of red blood cells and plasma was associated with PGD development [81].

These observations have major implications to intravenous fluid therapy. While this remains the cornerstone of intraoperative management of lung transplantation and is required for hemodynamic stability and organ perfusion, excessive fluid administration, infusion of low molecular weight colloids such as gelatins and allogenic blood transfusion may augment lung injury and predispose to primary graft dysfunction. The fluid and transfusion restriction however, should be balanced by the requirement of maintaining perfusion pressure and cardiac output especially towards preserving renal homeostasis.

19.5 Protective Ventilation

Mechanical ventilation (MV) is crucial in the intraoperative and early postoperative management of lung transplant recipients. Despite this, the intense research on mechanical ventilation in general intensive care units and in patients suffering from ARDS has only been partially translated to the special setting of LT [82–89]. Thus, many fundamental aspects remain unknown. There are only limited studies directly observing perioperative ventilation techniques in human lung transplantation, and the influence of different ventilation strategies on clinical outcomes currently remains largely unknown. Importantly, lung transplant recipients were excluded

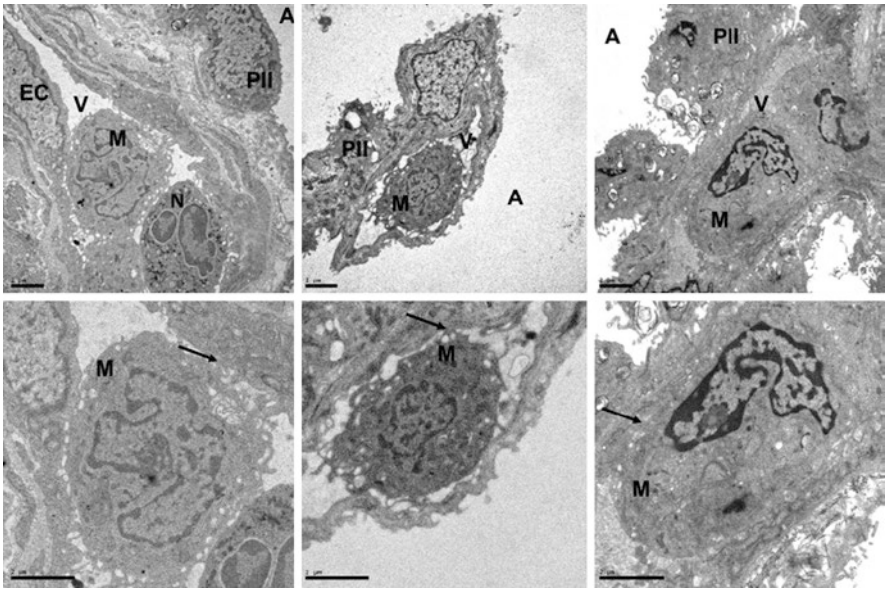

Fig. 19.2 Electron micrographs showing intravascular monocyte in pre-implantation lung biopsies. From three different lung. Samples were obtained at the end of the cold ischaemia, prior to implantation. Despite the flushing at the time of the retrieval, monocytes (M), with typical horseshoe-like nuclei, and neutrophils (N), with bi-lobed nuclei, are seen within the pulmonary vasculature with various grades of monocyte–endothelial (EC) interactions (arrows), including multiple connections with the ECs consistent with tethering and manifest adhesion

from the original and subsequent ARDS trials. As a consequence, institutional policies, reports from single centres, and broader surveys derive their recommendations as an extrapolation from results from the ARDS field and emerging experience from other perioperative settings [50, 74, 82, 83, 89–93] (Fig. 19.2).

In both situations, the message has been to employ protective, rather than injurious ventilation settings, although the strengths and details of such recommendations vary [94, 95]. The general message for the last decade has been low tidal volume ventilation with appropriate PEEP to reduce cyclic opening and closing of lung units to avoid volutrauma and barotrauma [88]. Lately, it has become clear that the benefits of low tidal volume can only be realised when the low tidal volume conferred low driving pressures, as the latter parameter is now believed to be the major factor determining lung injury and cause of poor outcomes [96]. Similar analysis also revealed driving pressure but not tidal volume or PEEP as the principle mediating factor of postoperative complications in a large meta-analysis of individual patient data undergoing various forms of general and thoracic surgery [97]. These ventilator strategies are just beginning to emerge in LT [90, 98].

For instance, investigators from Iowa and Maryland advocated lung-protective MV with low tidal volumes (≤6 mL/kg predicted body weight) and positive end-expiratory pressure for the LT-recipient. They have recommended that the tidal

volume should be standardized for donor body ideal weight as a parameter reflecting of actual allograft size, rather than based on recipient characteristics. However, the report of Diamond et al. showed that tidal volumes at the time of reperfusion were not a risk factor for the development of subsequent PGD [10].

A systematic review of the LT ventilation literature of the new millennium has failed to make recommendations for optimal ventilation strategies for lung transplantation and mainly cited perioperative studies from general cardiac and thoracic surgery. Thakuria et al. have advocated taking driving pressure into consideration, either by limiting inflation pressures or increasing PEEP [90, 98]. Moreover, the only RCT regarding intraoperative ventilation strategies has utilized low tidal volume ventilation and also explored a lung open concept strategy in a pilot setting. Verbeek et al. demonstrated that intraoperative open-lung protective ventilation strategies based on stepwise recruitment, PEEP, and pressure-controlled ventilation with tidal volume based on ideal recipient body weight calculation are achievable and safe in patients undergoing lung transplantation and appear to be associated with a reduced duration of mechanical ventilation and improved oxygenation in the acute implantation period [99].

Therefore perioperative protective ventilation strategies represent a major new paradigm change for lung Tx anaesthesia. Intraoperative ventilation practice should avoid injurious large tidal volumes, high inspiratory pressures, and low PEEP strategies and should employ lung protective and open concept ventilation strategies.

19.6 Novel Mechanisms of Lung Injury: Monocytes and Cytokines

Current mechanistic and translational scientific basis of lung injury includes ischaemic structural and functional damage to the microvascular endothelium and alveolar epithelium, inflammatory activation of alveolar cells, circulating and resident leukocytes, proinflammatory cytokine imbalance, and increased oxidative stress [100] [11] [27, 46, 101, 102]. There is strong evidence to suggest that inflammatory genetic alterations are already present at the end of the ischaemic period in lungs that subsequently suffer from PGD [103]. Furthermore, reperfusion sets into motion programmed cell death cascades with up to 30% lung cells exhibiting signs of apoptosis prior to chest closure [104].

For the last few years we have embarked to investigate basic inflammatory mechanisms of lung injury associated with LTx. On the basis of previous studies at Imperial College where marginated and activated monocytes contribute to endotoxin and ventilator induced lung injury, we hypothesised that donor lung-marginated, intravascular monocytes, exposed directly to the I/R-induced vascular stress and in close contact with the pulmonary capillary endothelium, would play a key role in development of transplant-related I/R lung injury, and thus PGD. We investigated this hypothesis using a mouse isolated perfused lung (IPL) model of transplant-related early I/R injury, combined with intravascular monocyte depletion and repletion treatments. We then evaluated numbers and phenotypes of

mononuclear phagocytes within pre-implantation lungs and studied their relationships with post-implantation gas exchange and PGD severity in human lung transplantation.

We have demonstrated that intravascular monocytes retained in the IPL model become activated and contribute significantly to the development of I/R lung injury. The clinical significance of these observations was supported by our pilot study with human donor lungs, where monocyte numbers and their expression of surface activation markers were associated with reduced postoperative gas exchange and development of PGD in recipients. Figure 19.1 demonstrate marginated passenger leukocytes following harvesting, flushing but before reperfusion of human lung allografts. As a substantial intravascular population with immediate exposure to and interactions with donor and recipient environments, donor-derived passenger monocytes could represent a novel therapeutic target to improve the quality and function of lung allografts.

These monocytes may also contribute to lung injury in the EVLP platform. Our collaboration with other LTx centres during the DEVELOP-UK trial and the translational studies with Newcastle University has shed some novel lights on the cytokine theory of lung injury [27, 105]. We have analysed longitudinal samples of perfusate, bronchoalveolar lavage, and tissue from 42 human donor lungs undergoing clinical EVLP assessments for markers of inflammation and tissue injury. Levels were compared according to EVLP success i.e. acceptance for clinical transplantation and stratified according to post-transplant outcomes.

The most effective markers to differentiate between in-hospital survival and non-survival post-transplant were perfusate interleukin (IL)-1β (area under the curve = 1.00, $p = 0.002$) and tumour necrosis factor-α (area under the curve = 0.95, $p = 0.006$) after 30 min of EVLP. These exciting data provide tremendous insights into the cytokine debate regarding acute lung injury. We have clearly demonstrated that donor lungs develop a detectable pro-inflammatory signature in perfusate during EVLP and that these cytokines and discriminate lungs that are accepted or rejected for transplantation and also relate to clinical outcomes after transplantation.

These observations contribute substantially to current understanding of the development of lung injury with important clinical and therapeutic potential. They indicate that more should be done in attenuating donor passenger leukocyte retention and activation. Furthermore, the cytokine data during human EVLP provides solid foundations for targeted pharmacological treatments towards blocking the IL-1β and TNF pathways.

References

1. Chambers DC, Cherikh WS, Goldfarb SB, Hayes D Jr, Kucheryavaya AY, Toll AE, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: thirty-fifth adult lung and heart-lung transplant report-2018; focus theme: multiorgan transplantation. J Heart Lung Transplant. 2018;37(10):1169–83.
2. Stehlik J, Chambers DC, Zuckermann A, Mehra MR, Khush KK. Increasing complexity of thoracic transplantation and the rise of multiorgan transplantation around the world: insights

from the International Society for Heart and Lung Transplantation Registry. J Heart Lung Transplant. 2018;37(10):1145–54.
3. Myles PS, Weeks AM, Buckland MR, Silvers A, Bujor M, Langley M. Anesthesia for bilateral sequential lung transplantation: experience of 64 cases. J Cardiothorac Vasc Anesth. 1997;11(2):177–83.
4. von Dossow V, Costa J, D'Ovidio F, Marczin N. Worldwide trends in heart and lung transplantation: guarding the most precious gift ever. Best Pract Res Clin Anaesthesiol. 2017;31(2):141–52.
5. Evers AS, Miller RD. Can we get there if we don't know where we're going? Anesthesiology. 2007;106(4):651–2.
6. Snell GI, Yusen RD, Weill D, Strueber M, Garrity E, Reed A, et al. Report of the ISHLT working group on primary lung graft dysfunction, Part I: definition and grading-a 2016 consensus group statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2017;36(10):1097–103.
7. Christie JD, Bellamy S, Ware LB, Lederer D, Hadjiliadis D, Lee J, et al. Construct validity of the definition of primary graft dysfunction after lung transplantation. J Heart Lung Transplant. 2010;29(11):1231–9.
8. Christie J, Keshavjee S, Orens J, Arcasoy S, DePerrot M, Barr M, et al. Potential refinements of the International Society for Heart and Lung Transplantation primary graft dysfunction grading system. J Heart Lung Transplant. 2008;27(1):138.
9. Christie JD, Carby M, Bag R, Corris P, Hertz M, Weill D, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction part II: definition. A consensus statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2005;24(10):1454–9.
10. Diamond JM, Lee JC, Kawut SM, Shah RJ, Localio AR, Bellamy SL, et al. Clinical risk factors for primary graft dysfunction after lung transplantation. Am J Respir Crit Care Med. 2013;187(5):527–34.
11. Suzuki Y, Cantu E, Christie JD. Primary graft dysfunction. Semin Respir Crit Care Med. 2013;34(3):305–19.
12. Kotloff RM, Thabut G. Lung transplantation. Am J Respir Crit Care Med. 2011;184(2):159–71.
13. Diamond JM, Wigfield CH. Role of innate immunity in primary graft dysfunction after lung transplantation. Curr Opin Organ Transplant. 2013;18:518.
14. Cantu E, Diamond JM, Suzuki Y, Lasky J, Schaufler C, Lim B, et al. Quantitative evidence for revising the definition of primary graft dysfunction after lung transplant. Am J Respir Crit Care Med. 2018;197(2):235–43.
15. Chan EG, Bianco V III, Richards T, Hayanga JW, Morrell M, Shigemura N, et al. The ripple effect of a complication in lung transplantation: evidence for increased long-term survival risk. J Thorac Cardiovasc Surg. 2016;151(4):1171–9.
16. Kinaschuk K, Nagendran J. Improving long-term survival by preventing early complications after lung transplantation: can we prevent ripples by keeping pebbles out of the water? J Thorac Cardiovasc Surg. 2016;151(4):1181–2.
17. Mohite PN, Sabashnikov A, Patil NP, Garcia-Saez D, Zych B, Zeriouh M, et al. The role of cardiopulmonary bypass in lung transplantation. Clin Transplant. 2016;30(3):202–9.
18. Marczin N, Royston D, Yacoub M. Pro: lung transplantation should be routinely performed with cardiopulmonary bypass. J Cardiothorac Vasc Anesth. 2000;14(6):739–45.
19. McIlroy DR, Pilcher DV, Snell GI. Does anaesthetic management affect early outcomes after lung transplant? An exploratory analysis. Br J Anaesth. 2009;102(4):506–14.
20. Steen S, Sjoberg T, Pierre L, Liao Q, Eriksson L, Algotsson L. Transplantation of lungs from a non-heart-beating donor. Lancet. 2001;357(9259):825–9.
21. Steen S, Liao Q, Wierup PN, Bolys R, Pierre L, Sjoberg T. Transplantation of lungs from non-heart-beating donors after functional assessment ex vivo. Ann Thorac Surg. 2003;76(1):244–52; discussion 252.
22. Ingemansson R, Eyjolfsson A, Mared L, Pierre L, Algotsson L, Ekmehag B, et al. Clinical transplantation of initially rejected donor lungs after reconditioning ex vivo. Ann Thorac Surg. 2009;87(1):255–60.

23. Cypel M, Yeung JC, Liu M, Anraku M, Chen F, Karolak W, et al. Normothermic ex vivo lung perfusion in clinical lung transplantation. N Engl J Med. 2011;364(15):1431–40.
24. Zych B, Popov AF, Stavri G, Bashford A, Bahrami T, Amrani M, et al. Early outcomes of bilateral sequential single lung transplantation after ex-vivo lung evaluation and reconditioning. J Heart Lung Transplant. 2012;31(3):274–81.
25. Wallinder A, Ricksten SE, Hansson C, Riise GC, Silverborn M, Liden H, et al. Transplantation of initially rejected donor lungs after ex vivo lung perfusion. J Thorac Cardiovasc Surg. 2012;144(5):1222–8.
26. Aigner C, Slama A, Hotzenecker K, Scheed A, Urbanek B, Schmid W, et al. Clinical ex vivo lung perfusion--pushing the limits. Am J Transplant. 2012;12(7):1839–47.
27. Andreasson ASI, Borthwick LA, Gillespie C, Jiwa K, Scott J, Henderson P, et al. The role of interleukin-1beta as a predictive biomarker and potential therapeutic target during clinical ex vivo lung perfusion. J Heart Lung Transplant. 2017;36(9):985–95.
28. Warnecke G, Moradiellos J, Tudorache I, Kuhn C, Avsar M, Wiegmann B, et al. Normothermic perfusion of donor lungs for preservation and assessment with the Organ Care System Lung before bilateral transplantation: a pilot study of 12 patients. Lancet. 2012;380(9856):1851–8.
29. Methangkool E, Mahajan A, Gao G, Chua JH. Anesthetic management of bilateral lung transplantation from donor lungs managed by the organ care system. J Cardiothorac Vasc Anesth. 2014;28(4):1133–6.
30. Warnecke G, Van Raemdonck D, Smith MA, Massard G, Kukreja J, Rea F, et al. Normothermic ex-vivo preservation with the portable Organ Care System Lung device for bilateral lung transplantation (INSPIRE): a randomised, open-label, non-inferiority, phase 3 study. Lancet Respir Med. 2018;6(5):357–67. https://doi.org/10.1016/S2213-2600(18)30136-X. Epub 2018 Apr 9.
31. Meyer DM, Bennett LE, Novick RJ, Hosenpud JD. Effect of donor age and ischemic time on intermediate survival and morbidity after lung transplantation. Chest. 2000;118(5):1255–62.
32. Gammie JS, Stukus DR, Pham SM, Hattler BG, McGrath MF, McCurry KR, et al. Effect of ischemic time on survival in clinical lung transplantation. Ann Thorac Surg. 1999;68(6):2015–9; discussion 2019–20.
33. Ueno T, Snell GI, Williams TJ, Kotsimbos TC, Smith JA, Rabinov M, et al. Impact of graft ischemic time on outcomes after bilateral sequential single-lung transplantation. Ann Thorac Surg. 1999;67(6):1577–82.
34. Gelman AE, Fisher AJ, Huang HJ, Baz MA, Shaver CM, Egan TM, et al. Report of the ISHLT working group on primary lung graft dysfunction Part III: mechanisms: a 2016 consensus group statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2017;36(10):1114–20.
35. Van Raemdonck D, Hartwig MG, Hertz MI, Davis RD, Cypel M, Hayes D Jr, et al. Report of the ISHLT working group on primary lung graft dysfunction Part IV: prevention and treatment: a 2016 consensus group statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2017;36(10):1121–36.
36. Yusen RD, Edwards LB, Dipchand AI, Goldfarb SB, Kucheryavaya AY, Levvey BJ, et al. The Registry of the International Society for Heart and Lung Transplantation: thirty-third adult lung and heart-lung transplant report-2016; focus theme: primary diagnostic indications for transplant. J Heart Lung Transplant. 2016;35(10):1170–84.
37. Black MC, Trivedi J, Schumer EM, Bousamra M II, van Berkel V. Double lung transplants have significantly improved survival compared with single lung transplants in high lung allocation score patients. Ann Thorac Surg. 2014;98(5):1737–41.
38. Villavicencio MA, Axtell AL, Osho A, Astor T, Roy N, Melnitchouk S, et al. Single- versus double-lung transplantation in pulmonary fibrosis: impact of age and pulmonary hypertension. Ann Thorac Surg. 2018;106(3):856–63.
39. Macchiarini P, Ladurie FL, Cerrina J, Fadel E, Chapelier A, Dartevelle P. Clamshell or sternotomy for double lung or heart-lung transplantation? Eur J Cardiothorac Surg. 1999;15(3):333–9.

40. Taghavi S, Birsan T, Seitelberger R, Kupilik N, Mares P, Zuckermann A, et al. Initial experience with two sequential anterolateral thoracotomies for bilateral lung transplantation. Ann Thorac Surg. 1999;67(5):1440–3.
41. Meyers BF, Sundaresan RS, Guthrie T, Cooper JD, Patterson GA. Bilateral sequential lung transplantation without sternal division eliminates posttransplantation sternal complications. J Thorac Cardiovasc Surg. 1999;117(2):358–64.
42. Bittner HB, Lehmann S, Binner C, Garbade J, Barten M, Mohr FW. Sternum sparing thoracotomy incisions in lung transplantation surgery: a superior technique to the clamshell approach. Innovations. 2011;6(2):116–21.
43. Venuta F, Rendina EA, De Giacomo T, Ciccone AM, Moretti M, Mercadante E, et al. Bilateral sequential lung transplantation without sternal division. Eur J Cardiothorac Surg. 2003;23(6):894–7.
44. Marczin N, Popov AF, Zych B, Romano R, Kiss R, Sabashnikov A, et al. Outcomes of minimally invasive lung transplantation in a single centre: the routine approach for the future or do we still need clamshell incision? Interact Cardiovasc Thorac Surg. 2016;22(5):537–45.
45. Fischer S, Struber M, Simon AR, Anssar M, Wilhelmi M, Leyh RG, et al. Video-assisted minimally invasive approach in clinical bilateral lung transplantation. J Thorac Cardiovasc Surg. 2001;122(6):1196–8.
46. Marczin N, Lakshminarasimhan Kuppurao I, Wright G, Simon AR. Anaesthesia for lung transplantation. In: Alston RP, Myles PS, Ranucci M, editors. Oxford textbook of cardiac anaesthesia. Oxford: Oxford University Press; 2015.
47. Taka H, Miyoshi K, Kurosaki T, Douguchi T, Itoh H, Sugimoto S, et al. Lung transplantation via cardiopulmonary bypass: excellent survival outcomes from extended criteria donors. Gen Thorac Cardiovasc Surg. 2019;67:624.
48. Moreno Garijo J, Cypel M, McRae K, Machuca T, Cunningham V, Slinger P. The evolving role of extracorporeal membrane oxygenation in lung transplantation: implications for anesthetic management. J Cardiothorac Vasc Anesth. 2019;33:1995. https://doi.org/10.1053/j.jvca.2018.10.007. pii: S1053-0770(18)30933-9.
49. Hayes D Jr, Tobias JD, Tumin D. Center volume and extracorporeal membrane oxygenation support at lung transplantation in the lung allocation score era. Am J Respir Crit Care Med. 2016;194(3):317–26.
50. Sellers D, Cassar-Demajo W, Keshavjee S, Slinger P. The evolution of anesthesia for lung transplantation. J Cardiothorac Vasc Anesth. 2017;31(3):1071–9.
51. Slinger P. Anaesthetic management for lung transplantation. Transpl Med. 2012;24:27–34.
52. Kachulis B, Mitrev L, Jordan D. Intraoperative anesthetic management of lung transplantation patients. Best Pract Res Clin Anaesthesiol. 2017;31(2):261–72.
53. Rosenberg AL, Rao M, Benedict PE. Anesthetic implications for lung transplantation. Anesthesiol Clin North America. 2004;22(4):767–88.
54. McGlothlin D, Ivascu N, Heerdt PM. Anesthesia and pulmonary hypertension. Prog Cardiovasc Dis. 2012;55(2):199–217.
55. Strumpher J, Jacobsohn E. Pulmonary hypertension and right ventricular dysfunction: physiology and perioperative management. J Cardiothorac Vasc Anesth. 2011;25(4):687–704.
56. Fischer LG, Van Aken H, Burkle H. Management of pulmonary hypertension: physiological and pharmacological considerations for anesthesiologists. Anesth Analg. 2003;96(6):1603–16.
57. Rex S, Busch T, Vettelschoss M, de Rossi L, Rossaint R, Buhre W. Intraoperative management of severe pulmonary hypertension during cardiac surgery with inhaled iloprost. Anesthesiology. 2003;99(3):745–7.
58. Humbert M, Guignabert C, Bonnet S, Dorfmuller P, Klinger JR, Nicolls MR, et al. Pathology and pathobiology of pulmonary hypertension: state of the art and research perspectives. Eur Respir J. 2019;53(1) https://doi.org/10.1183/13993003.01887-2018.
59. Benedetto M, Romano R, Baca G, Sarridou D, Fischer A, Simon A, et al. Inhaled nitric oxide in cardiac surgery: evidence or tradition? Nitric Oxide. 2015;49:67–79.
60. Rabanal Llevot JM, Cimadevilla Calvo B, Cifrian Martinez JM, Ruisanchez Villar C, Mons LR. Effect of nebulised iloprost combined with inhaled nitric oxide and oral sildenafil on lung

transplant patients. Therapeutic efficacy in pulmonary hypertension during surgery. Rev Esp Anestesiol Reanim. 2012;59(3):142–9.
61. Halldorsson A, Kronon M, Allen BS, Bolling KS, Wang T, Rahman S, et al. Controlled reperfusion after lung ischemia: implications for improved function after lung transplantation. J Thorac Cardiovasc Surg. 1998;115(2):415–24; discussion 424–5.
62. Fiser SM, Kron IL, Long SM, Kaza AK, Kern JA, Cassada DC, et al. Controlled perfusion decreases reperfusion injury after high-flow reperfusion. J Heart Lung Transplant. 2002;21(6):687–91.
63. Lick SD, Brown PS Jr, Kurusz M, Vertrees RA, McQuitty CK, Johnston WE. Technique of controlled reperfusion of the transplanted lung in humans. Ann Thorac Surg. 2000;69(3):910–2.
64. Schnickel GT, Ross DJ, Beygui R, Shefizadeh A, Laks H, Saggar R, et al. Modified reperfusion in clinical lung transplantation: the results of 100 consecutive cases. J Thorac Cardiovasc Surg. 2006;131(1):218–23.
65. Liu YY, Li LF, Fu JY, Kao KC, Huang CC, Chien Y, et al. Induced pluripotent stem cell therapy ameliorates hyperoxia-augmented ventilator-induced lung injury through suppressing the Src pathway. PLoS One. 2014;9(10):e109953.
66. Sutsko RP, Young KC, Ribeiro A, Torres E, Rodriguez M, Hehre D, et al. Long-term reparative effects of mesenchymal stem cell therapy following neonatal hyperoxia-induced lung injury. Pediatr Res. 2013;73(1):46–53.
67. Zhang H, Zhang P, Han C, Zhou F, Li L, Liu W. Treatment of hyperoxic acute lung injury with stem cell transplantation in murine models: a brief review. Undersea Hyperb Med. 2016;43(4):437–45.
68. Bhandari V, Choo-Wing R, Lee CG, Zhu Z, Nedrelow JH, Chupp GL, et al. Hyperoxia causes angiopoietin 2-mediated acute lung injury and necrotic cell death. Nat Med. 2006;12(11):1286–93.
69. Kallet RH, Matthay MA. Hyperoxic acute lung injury. Respir Care. 2013;58(1):123–41.
70. Christofidou-Solomidou M, Muzykantov VR. Antioxidant strategies in respiratory medicine. Treat Respir Med. 2006;5(1):47–78.
71. Erne BV, Jungraithmayr W, Buschmann J, Arni S, Weder W, Inci I. Effect of N-acetylcysteine on acute allograft rejection after rat lung transplantation. Ann Thorac Surg. 2013;95(3):1021–7.
72. Yamada Y, Iskender I, Arni S, Hillinger S, Cosgun T, Yu K, et al. Ex vivo treatment with inhaled N-acetylcysteine in porcine lung transplantation. J Surg Res. 2017;218:341–7.
73. Rega FR, Wuyts WA, Vanaudenaerde BM, Jannis NC, Neyrinck AP, Verleden GM, et al. Nebulized N-acetyl cysteine protects the pulmonary graft inside the non-heart-beating donor. J Heart Lung Transplant. 2005;24(9):1369–77.
74. Tomasi R, Betz D, Schlager S, Kammerer T, Hoechter DJ, Weig T, et al. Intraoperative anesthetic management of lung transplantation: center-specific practices and geographic and centers size differences. J Cardiothorac Vasc Anesth. 2018;32(1):62–9.
75. Diamond JM, Porteous MK, Roberts LJ II, Wickersham N, Rushefski M, Kawut SM, et al. The relationship between plasma lipid peroxidation products and primary graft dysfunction after lung transplantation is modified by donor smoking and reperfusion hyperoxia. J Heart Lung Transplant. 2016;35(4):500–7.
76. Williams A, Riise GC, Anderson BA, Kjellstrom C, Schersten H, Kelly FJ. Compromised antioxidant status and persistent oxidative stress in lung transplant recipients. Free Radic Res. 1999;30(5):383–93.
77. Germann P, Braschi A, Della Rocca G, Dinh-Xuan AT, Falke K, Frostell C, et al. Inhaled nitric oxide therapy in adults: European expert recommendations. Intensive Care Med. 2005;31(8):1029–41.
78. Moreno I, Vicente R, Mir A, Leon I, Ramos F, Vicente JL, et al. Effects of inhaled nitric oxide on primary graft dysfunction in lung transplantation. Transplant Proc. 2009;41(6):2210–2.
79. Myles PS, Snell GI, Westall GP. Lung transplantation. Curr Opin Anaesthesiol. 2007;20(1):21–6.

80. Geube MA, Perez-Protto SE, McGrath TL, Yang D, Sessler DI, Budev MM, et al. Increased intraoperative fluid administration is associated with severe primary graft dysfunction after lung transplantation. Anesth Analg. 2016;122(4):1081–8.
81. Liu Y, Liu Y, Su L, Jiang SJ. Recipient-related clinical risk factors for primary graft dysfunction after lung transplantation: a systematic review and meta-analysis. PLoS One. 2014;9(3):e92773.
82. Thakuria L, Davey R, Romano R, Carby MR, Kaul S, Griffiths MJ, et al. Mechanical ventilation after lung transplantation. J Crit Care. 2016;31(1):110–8.
83. Barnes L, Reed RM, Parekh KR, Bhama JK, Pena T, Rajagopal S, et al. Mechanical ventilation for the lung transplant recipient. Curr Pulmonol Rep. 2015;4(2):88–96.
84. Guldner A, Kiss T, Serpa Neto A, Hemmes SN, Canet J, Spieth PM, et al. Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. Anesthesiology. 2015;123(3):692–713.
85. Lohser J, Slinger P. Lung injury after one-lung ventilation: a review of the pathophysiologic mechanisms affecting the ventilated and the collapsed lung. Anesth Analg. 2015;121(2):302–18.
86. Schultz MJ, Abreu MG, Pelosi P. Mechanical ventilation strategies for the surgical patient. Curr Opin Crit Care. 2015;21(4):351–7.
87. Senturk M, Slinger P, Cohen E. Intraoperative mechanical ventilation strategies for one-lung ventilation. Best Pract Res Clin Anaesthesiol. 2015;29(3):357–69.
88. Serpa Neto A, Hemmes SN, Barbas CS, Beiderlinden M, Biehl M, Binnekade JM, et al. Protective versus conventional ventilation for surgery: a systematic review and individual patient data meta-analysis. Anesthesiology. 2015;123(1):66–78.
89. Beer A, Reed RM, Bolukbas S, Budev M, Chaux G, Zamora MR, et al. Mechanical ventilation after lung transplantation. An international survey of practices and preferences. Ann Am Thorac Soc. 2014;11(4):546–53.
90. Thakuria L, Reed A, Simon AR, Marczin N. Mechanical ventilation after lung transplantation. Chest. 2017;151(2):516–7.
91. Slinger PD. Optimizing one-lung ventilation: moving beyond tidal volume. J Cardiothorac Vasc Anesth. 2018;32(6):2673–5.
92. Marseu K, Slinger P. Perioperative lung protection. Korean J Anesthesiol. 2017;70(3):239–44.
93. Marseu K, Slinger P. Peri-operative pulmonary dysfunction and protection. Anaesthesia. 2016;71(Suppl 1):46–50.
94. Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, et al. An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine clinical practice guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med. 2017;195(9):1253–63.
95. Chiumello D, Brochard L, Marini JJ, Slutsky AS, Mancebo J, Ranieri VM, et al. Respiratory support in patients with acute respiratory distress syndrome: an expert opinion. Crit Care. 2017;21(1):240. https://doi.org/10.1186/s13054-017-1820-0.
96. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med. 2015;372(8):747–55.
97. Neto AS, Hemmes SN, Barbas CS, Beiderlinden M, Fernandez-Bustamante A, Futier E, et al. Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. Lancet Respir Med. 2016;4(4):272–80.
98. Fuehner T, Kuehn C, Welte T, Gottlieb J. ICU Care Before and After Lung Transplantation. Chest. 2016;150(2):442–50.
99. Verbeek GL, Myles PS, Westall GP, Lin E, Hastings SL, Marasco SF, et al. Intra-operative protective mechanical ventilation in lung transplantation: a randomised, controlled trial. Anaesthesia. 2017;72(8):993–1004.

100. Shah RJ, Bellamy SL, Localio AR, Wickersham N, Diamond JM, Weinacker A, et al. A panel of lung injury biomarkers enhances the definition of primary graft dysfunction (PGD) after lung transplantation. J Heart Lung Transplant. 2012;31(9):942–9.
101. de Perrot M, Liu M, Waddell TK, Keshavjee S. Ischemia-reperfusion-induced lung injury. Am J Respir Crit Care Med. 2003;167(4):490–511.
102. Tatham KC, O'Dea KP, Romano R, Donaldson HE, Wakabayashi K, Patel BV, et al. Intravascular donor monocytes play a central role in lung transplant ischaemia-reperfusion injury. Thorax. 2018;73(4):350–60.
103. Ray M, Dharmarajan S, Freudenberg J, Zhang W, Patterson GA. Expression profiling of human donor lungs to understand primary graft dysfunction after lung transplantation. Am J Transplant. 2007;7(10):2396–405.
104. Fischer S, Cassivi SD, Xavier AM, Cardella JA, Cutz E, Edwards V, et al. Cell death in human lung transplantation: apoptosis induction in human lungs during ischemia and after transplantation. Ann Surg. 2000;231(3):424–31.
105. Fisher A, Andreasson A, Chrysos A, Lally J, Mamasoula C, Exley C, et al. An observational study of donor ex vivo lung perfusion in UK lung transplantation: DEVELOP-UK. Health Technol Assess. 2016;20(85):1–276.

Extracorporeal Life Support (ECMO) in Thoracic Surgery

20

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20.1 Introduction

Extracorporeal membrane oxygenation (ECMO) has been available for decades as a support treatment for severe cardiopulmonary disease; however, its use was initially associated with high complication rates and poor results. ECMO has evolved in design, technology, patient selection, cannulation techniques, devices and management, leading to extend its indications with promising results [1]. After CESAR study publication [2] an improvement in survival in adults suffering from acute respiratory distress syndrome (ARDS) randomized to ECMO compared with conventionally treated patients was reported.

New centrifugal pumps and heparin-coated circuits also led to a radical change in ECMO practice. Nowadays ECMO offers a long lasting support for several days or weeks with limited inflammatory reaction, less bleeding, less platelet dysfunction and reduced circuit malfunctions (Picture 20.1).

The objective of the ECMO devices is to provide respiratory and/or cardiocirculatory support.

Cardiopulmonary bypass (CPB) was used during thoracic surgery, but now more centers replaced CPB by ECMO for patients with respiratory and/or cardiac failure [3]. Several CPB-associated complications were reported, including increased need for blood products due to complete heparinization, risk of potential tumour cell spilling through the suction and reservoir system (open system) and systemic inflammatory response.

There are two types of ECMO: venovenous (VV) ECMO for respiratory failure and/or veno-arterial (VA) ECMO when there is also a hemodynamic compromise.

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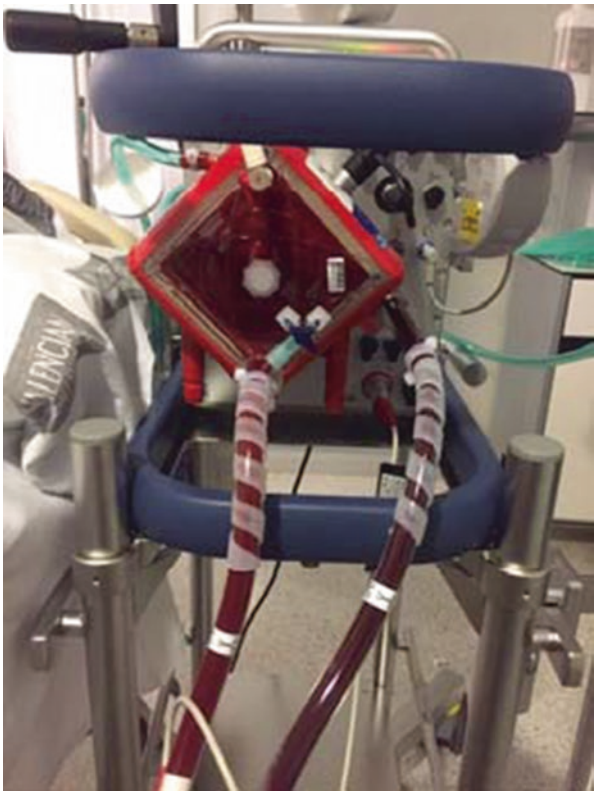


Picture 20.1 ECMO console

The VV ECMO is the most frequently used in thoracic surgery [4–6]. The most frequent surgeries with ECMO are airway surgery (tracheal resection, bronchial resection), resection advanced thoracic tumours, thoracic emergencies, difficult or impossible one lung ventilation, lung transplantation (LTx) and acute respiratory distress syndrome (ARDS).

In thoracic surgery ECMO is a well-established alternative to one lung ventilation, where intraoperative ECMO can ensure protective lung ventilation strategy and good surgical exposure. ECMO to facilitate recovery (bridge to recovery), in LTx (bridge to transplantation), change to other devices or configuration (bridge to bridge) or change of strategy (bridge to decision).

In the postoperative course VV ECMO has been mainly used in the ARDS context and in the severe primary graft failure [7]. It has also been reported that ECMO improves survival in pneumonectomy ARDS [8].

VA ECMO is performed for cardiocirculatory support with or without respiratory failure.

20.2 Configuration

20.2.1 VV ECMO

Allows oxygenation and carbon dioxide (CO_2) removal. Blood is drained from the inferior vena cava (IVC) or right atrium (RA), passing through a centrifugal pump and the oxygenator membrane and returns to the patient. Once in the RA, oxygenated and decarboxylated blood is mixed and ejected by the right ventricle (RV) to the pulmonary circulation. VV ECMO does not directly support the heart; however, severe hypoxemia/hypercarbia improvement, decreases pulmonary vascular resistance, decreases RV afterload and can enhance RV performance. In addition, the onset of VV ECMO usually results in a reduction in airway pressures, which also improves RV afterload.

20.2.2 VA ECMO

It offers cardiocirculatory support with or without respiratory failure. Peripheral VA ECMO should not be used as a first-line strategy in case of isolated lung failure. Blood is drained from the RA and reinfused into the aorta, thus decreases pulmonary venous return to the left atrium and left ventricle volume and pressure are reduced, promoting myocardial rest, improving coronary flow and therefore myocardial recovery.

20.3 Cannulation

Seldinger technique is usually preferred for venous cannulation while arterial cannulation depends on the anatomy, center experience and cannulation site [9–11].

20.3.1 VV ECMO

20.3.1.1 Two Cannula VV ECMO

- Femoro-jugular: blood is drained from the IVC through a cannula introduced in the femoral vein and is then advanced until the inferior cavoatrial junction. Blood is reinfused into the RA through a cannula inserted into the internal jugular vein, the tip advances to the superior cavoatrial junction.
- Femoro-femoral: The blood is drained from the IVC through a femoral venous cannula and is reinfused through a cannula introduced into the femoral vein (usually contralateral) and advanced into the RA. The drainage cannula is usually multi-perforated.

20.3.1.2 Single Cannula VV ECMO

Single cannula technique offers lower probability of recirculation, reduced risk of catheter-related infection, less bleeding and the ability to mobilize the patient. Optimal cannula positioning must be controlled with transesophageal echocardiography (TEE) or fluoroscopy. The echocardiographic guide and cannula visualization is essential for a safe cannulation. Ventricular rupture and cannula displacement are the main severe complications of this technique.

20.3.2 VA ECMO

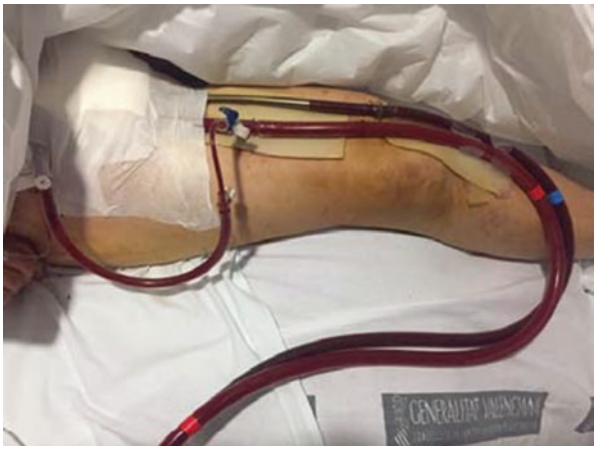
20.3.2.1 Central Cannulation (Sternotomy)

Often used in postcardiotomy cardiogenic shock or intraoperative cardiorespiratory support instead of conventional CPB. Venous cannula drains blood from RA and arterial cannula reinfuses oxygenated blood into the ascending aorta. Less heparin requirement and less systemic inflammation prevents bleeding and transfusion. No venting and the impossibility for cardioplegic arrest are VA ECMO main disadvantages.

20.3.2.2 Peripheral Cannulation

It can be performed through percutaneous or surgical access. Femoral access is of choice due to its accessibility. A multi-perforated cannula through the femoral vein (preferably the right femoral vein) is inserted and advanced to the cavoatrial junction. The arterial cannula (16–20 Fr) is inserted into the femoral artery with the tip of the cannula in iliac artery or aorta. Since the femoral arterial cannula can compromise limb perfusion, an additional arterial cannula (~10 Fr) should be inserted in order to perfuse the extremity (Picture 20.2).

When femoral vessels are not suitable for cannulation, subclavian artery by direct cannulation or vascular graft interposition is feasible. The subclavian arterial



Picture 20.2 Peripheral VA ECMO with limb perfusion cannula

cannulation and jugular venous cannulation, also offers the advantage of early mobilization and active rehabilitation.

20.4 ECMO in Thoracic Surgery

20.4.1 Airway Surgery

During tracheal resection surgery, ventilation strategy and airway management are crucial. Thoracic surgery frequently requires selective ventilation with right or left, double lumen tubes. In this scenario intraoperative hypoxemia can occur and conventional strategies used to prevent this complication (continuous positive airway pressure, alveolar recruitment, etc.) can impair surgical exposure. Selective ventilation could be impossible during tracheo-bronchial surgery, especially when the left main bronchus is involved [12]. Ventilation can be achieved by a high-frequency jet-ventilation catheter, by a fine probe of 5–6 mm crossing through the anastomosis or by a sterile probe inserted by the surgeon into the distal trachea. Complications of jet-ventilation include lung barotrauma and ventilation issues. In these procedures VV ECMO is an alternative to mechanical ventilation allowing better visualization and offering oxygenation and CO_2 clearance [13, 14] (Table 20.1).

20.4.2 Difficult or Impossible One Lung Ventilation (OLV)

OLV in pulmonary disease can result impossible. Pulmonary wedge resections supported with VV ECMO have been reported in post pneumonectomy patients [15, 16].

Table 20.1 ECMO indications [1–4]

	Peripheral VV ECMO	Peripheral VA ECMO	Central VA ECMO
Trauma	Yes	Yes	No
Lung resection	Yes	Yes	Yes
Volume reduction	Yes	No	No
PA surgery	Yes	Yes	No
Bridge Ltx	Yes	No	No
PH bridge Ltx	No	Yes	Yes
Ltx/intrao	No	Yes	Yes
Ltx/PGD	Yes	Yes	No

LTx lung transplantation, *PA* pulmonary artery, *PH* pulmonary arterial hypertension, *PGD* primary graft dysfunction, *INTRAO* intraoperative

20.4.3 Mediastinal Masses

Large masses occupying the anterior mediastinum have the potential to cause compression of the trachea, great vessels and RA. In the awake patient, the negative pressure generated by inspiration reduces this effect. This situation is abolished by muscle relaxants, and positive pressure ventilation can precipitate central airway obstruction or catastrophic reduction of cardiac output and cardiopulmonary arrest. The VA ECMO configuration warrants cardiorespiratory assistance before general anesthesia is initiated [17, 18].

20.4.4 Advanced Surgical Resections

Locally advanced thoracic tumors resection may occasionally be complex or even impossible to resect using conventional ventilation [19]. Lung tumor resection and reconstruction of superior or inferior vena cava, left atrium, distal aorta, and carina has been described with VA ECMO support. Cannulation sites may vary according to the planned resection.

20.4.5 Thoracic Emergencies

ECMO has been used outside the thoracic operating room during resuscitation maneuvers allowing rapid improvement of tissue oxygenation and hemodynamic stability. The choice of VV versus VA ECMO in emergency circumstances depends on the need for oxygenation versus the need for concomitant hemodynamic support. ECMO has been described as a lifesaving emergency treatment until hemodynamic stabilization. Severe pulmonary embolism, complex broncho-esophageal fistula, tracheal stenosis, thoracic severe trauma and hemoptysis control are different situations in pulmonary scenario that may require emergent ECMO [20–22].

20.4.6 Lung Transplantation (LTx)

Perioperative management in lung transplantation has evolved in the last decade and the use of ECMO has become a regular approach. ELSO database [1990–2016] reported that 1066 lung transplant recipients and/or patients were supported with ECMO in the perioperative period with an overall ECLS survival to hospital discharge of 65% [23].

ECMO can be used at different stages: (1) bridge to LTx; (2) intraoperative support (3) after LTx.

20.4.6.1 Bridge to Ltx

The role of ECMO in this context has been controversial. Some centers considered the use of ECMO in terminal respiratory failure a contraindication. However,

considering the recent technological improvements some authors estimated that 4–6 weeks until the right donor is found is a safe and reasonable period. In this scenario, both VV ECMO and VA ECMO are used, depending on the hemodynamic situation and the presence of pulmonary hypertension. Polymethylpentene (PMP) oxygenators and new centrifugal pumps have allowed the reduction of failure and technical problems during their handling. Thus, the requirements for blood transfusions have been significantly reduced, thereby improving the exchange of gases, reducing the frequency of oxygenator failure and improving the safety of the devices. In addition, the incorporation of the heat exchanger and the lower ECMO priming volumes have undoubtedly improved the results [24–26].

The use of VV ECMO in awake, non-intubated spontaneously breathing patients was first described for respiratory deterioration in patients awaiting lung transplantation. These patients are the ideal candidates for an awake ECMO approach given their usual single organ dysfunction, their fragile heart–lung equilibrium, and the potential great benefit from the maintenance of preoperative physical rehabilitation.

The role of ECMO as bridge to LTx is double: (1) restitute the oxygen delivery and CO_2 clearance; (2) keep the patient in good conditions (awake, mechanical ventilation weaning, ambulatory ECMO) for better LTx outcomes. Except for patients suffering from terminal pulmonary hypertension, the best ECMO strategy to bridge patients to LTx is the single-site VV ECMO using the Avalon Elite™ cannula. Many patients with hypercapnic respiratory failure can be bridged with pumpless AV ECMO or low flow VV ECMO. Those with significant hypoxia will require full flow VV or if hemodynamically unstable, peripheral VA ECMO.

Concerning the pulmonary hypertension patient, VV ECMO should be avoided. Indeed VV ECMO would significantly increase the RV preload and would promote a life-threatening right dysfunction. In this situation VA ECMO or the pulmonary artery-left atrium (PA-LA) Novalung® can be used [27].

20.4.6.2 Intraoperative support

Lung transplant surgery is characterized by hemodynamic and respiratory compromise [28]. In the last decade ECMO has gradually supplanted CPB. CPB is known to increase transfusion rate, in addition to increase the levels of cytokines impairing lung function and aggravating the ischemia-reperfusion syndrome. VA ECMO decreases the requirement for dialysis, the risk of bleeding, the need of transfusions, the rates primary graft dysfunction (PGD), and critical care unit and hospital length stay [29, 30].

Central or peripheral VA ECMO can be used during LTx as an intraoperative support. In case of bilateral or single right LTx, the central aortic and atrial cannulations can be performed through a Clamshell incision or a right hemi-clamshell incision, respectively. In case of left single LTx, it is possible to cannulate the aorta according to a central mode and a femoral vein percutaneously. Peripheral VA ECMO has the advantage to be kept in the postoperative period if needed. Patients bridged to lung transplantation on VV-ECMO can occasionally be supported with VV ECMO support during their transplant or combined with VA ECMO support.

20.4.6.3 Postoperative Period

Complications such as PGD, hyperacute rejection and hemodynamic alterations are the main causes of respiratory failure. ECMO is considered an adequate system to provide cardiorespiratory support in patients with pulmonary dysfunction after transplantation once conventional treatments are not effective. According to the International Society for Heart and Lung Transplantation, PGD is responsible for one third of postoperative mortality (30 days) and 15% of deaths during the first 3 months in patients who underwent LTx leading to a significant increase in postoperative morbidity.

PGD represents a multifactorial complication that develops within 72 h after LTx. PGD is defined by the presence of bilateral lung edema in absence of heart dysfunction or overloading status. ECMO is indicated in severe and refractory PGD [31]. An increase in capillary permeability, as an expression of the damage due to the ischemia of the implanted lung is the main mechanism of PGD. The edema is influenced by several factors: degree of preservation, time of ischemia, previous neurogenic edema, surgical trauma, hydration of the recipient, interruption of pulmonary lymphatic drainage, etc. Pulmonary venous drainage stenosis or thrombosis must be also ruled out [32, 33].

The advantages of veno-venous cannulation compared with veno-arterial cannulation have been described in numerous studies (Table 20.2). Double or single-cannula VV ECMO have both several advantages and drawbacks. Double-cannula VV ECMO will allow a better oxygenation in case of high level of O_2 requirements whereas the single cannula VV ECMO will be compatible with an ambulatory strategy [34].

20.4.7 Acute Respiratory Distress Syndrome (ARDS)

The ARDS is the most severe form of lung injury and the largest indication of ECMO in thoracic surgery. ECMO is indicated in severe and refractory ARDS in association with the protective ventilation strategy. The main goals are to ascertain gas exchanges and promote lung recovery by resting the lungs. VV ECMO is of choice in severe and refractory adult respiratory failure. Although there are several criteria, the ELSO recommends initiation of ECMO when the PaO_2/FiO_2 is $\leq$100 on

Table 20.2 Differences between VV ECMO and VA ECMO [34]

VA ECMO	VV ECMO
Cardiac support	No cardiac support
Arterial and venous cannulation (related complications)	Venous cannulation
Decreases pulmonary artery pressure/supports RV.	Pulmonary blood flow is maintained
Higher PO_2 with lower perfusion rates	Higher perfusion rates are needed
Higher heparin need and neurological complications	Less anticoagulation needed
LV dilation or Harlequin syndrome	Recirculation

FiO_2 >90% and/or score in the Murray scale 3–4 and/or hypercapnia with pH <7.2 despite optimal mechanical ventilation or plateau pressure >30 cm H_2O [35, 36].

20.5 Management

20.5.1 Monitoring

Proper monitoring prevents increases in morbidity and mortality [37]. Echography plays a key role in the assistance of the patient with ECMO. Especially, echocardiography can help during the daily management of ECMO, as well as at the time of cannulation for optimal cannula placement. Echocardiography is essential to evaluate ventricular and lung recovery and timing of weaning.

20.5.2 Anticoagulation

Systemic anticoagulation remains an important component in ECMO management. The goal of anticoagulation is to balance therapeutic doses to prevent circuit thrombus with minimization of bleeding complications.

Activated clotting time (ACT), activated partial thromboplastin time (APTT), anti-factor Xa levels and thromboelastography (TEG) have all been utilized to measure level of anticoagulation. ELSO guidelines provide details about possible anticoagulation.

Cannulation may start if ACT is ≥250 s for both central and peripheral cannulation (bolus of heparin 1–1.5 mg/kg). After finishing the surgical intervention protamine may be added. In special situations, such as heparin-induced thrombocytopenia, bivalirudin or argatroban can be used as anticoagulant agents [38, 39].

May ECMO be continued in the intensive care unit, a continuous infusion of heparin will be used (2 mg/kg/day) in order to approach ACT 160–180 s. Individualized and continuous follow-up should be carried out (every 2 h) and the anticoagulation should be adjusted to the specific circumstances (bleeding risk, thrombus risk). The heparin should not be administered or should be stopped if the thoracic drain is greater than 100 ml/h. In case of hemorrhage, traumatic brain injury, severe chest trauma with major risk of bleeding, it is possible not to use heparin until the risk of bleeding has decreased.

Hemoglobin threshold to receive red cells depends on the patient diagnose and situation but generally is accepted to transfuse if hemoglobin ≤8 g/dl, in case of platelets if the count $\leq 50 \times 10^9$/L, and fresh frozen plasma if the international normalization ratio ≥1.5 or in case of coagulopathy, or both [40, 41].

If the required dose of heparin is high (>20 U/kg/h), levels of antithrombin III (ATIII) must be measured; fresh frozen plasma or recombinant ATIII is indicated if ATIII ≤50% and high requirement of heparin is found. In order to prevent thrombus formation, in VA ECMO weaning or low flow VV ECMO (ECMO <1.5 l/min) ACT should remain above 200 s.

20.5.3 Ventilation

Once the assistance with ECMO has begun and adequate SaO_2 has been achieved, ventilator settings should be adjusted avoiding plateau pressure ≥30 cm H_2O. Hypercarbia should be cautiously treated due to rapid changes in pH. Alveolar recruitment during the acute phase of ARDS should be avoided and once stability is achieved spontaneous ventilation must be promoted.

20.5.4 Hemodynamic

Mean arterial pressures should be in range of 65 mmHg. In VA ECMO pressure pulse can be diminished depending on the left ventricular function, fluid status and centrifuge velocity. Aortic valve opening must be regularly achieved in order to avoid left ventricular dilation. In VV ECMO hemodynamics depends on the patient's cardiac function and vascular resistance.

20.5.5 Other Monitoring

Limb ischemia signs due to limb cannula thrombosis, circuit inspection, infection signs, neurological complications, oxygenator thrombus.

20.5.6 Weaning

VV ECMO weaning must be considered if pulmonary compliance and clinical status improved (mechanical ventilation with Fio_2 <50%, PEEP <5 cm H_2O, plateau pressure <30 cm H_2O, with TV > 4 mL/kg). Sweep gas flow can be progressively decreased and close off in the presence of constant ECMO blood flow. We will proceed with VA ECMO weaning if cardiac function is restored. In VA ECMO gas sweep must never be stopped and if ECMO flows are decreased ventilation should be increased.

20.6 Complications

Depending on the scenario ECMO exhibits high rate of complications with an incidence of 32–40%. These complications are shown in Table 20.3.

Cannulation issues are common and should be minimized by careful evaluation and monitoring. Seldinger technique and venous cannulation allow preventing vessel injuries and risk of bleeding. Echography offers information in terms of vessel size, enhancing cannula size choice and therefore ECMO flow and reduces cannulation complications.

Table 20.3 Complications

	Peripheral VV ECMO	Peripheral VA ECMO	Central VA ECMO
Bleeding	+	++	+++
Vessel damage	+	+++	++
Air/thrombo emboli	+	+++	+++
Limb ischemia	+	+++	+
Harlequin	+	+++	+
Recirculation	+++	+	+
Neurological complication	++	+++++	+++++
Infection	++	++	+++

VA-ECMO disadvantages include risk of arterial injury, bleeding, embolism, limb ischemia and cardiac thrombus.

In peripheral VA ECMO Harlequin syndrome can occur [42]. When cardiac function improves but pulmonary function is still altered, ECMO oxygenated blood will preferentially perfuse the inferior part of the body and the ejected blood from the native heart will perfuse the upper body (coronary arteries and cerebral circulation). This complication can be solved changing to VV ECMO mode, changing the arterial cannula to axillary artery or performing central cannulation.

Neurological complications such as intracranial bleeding, ischemic stroke and brain edema are critical. Sedatives must be interrupted in a daily manner in order to check for neurological damage. Other complications include, renal failure, infections, hemolysis, heparin induced thrombocytopenia or gastrointestinal bleeding [43–46].

If refractory hypoxemia occurs and high oxygen saturation in the drainage cannula (drained blood looks highly oxygenated), blood recirculation should be ruled out (infused oxygenated blood) into the atrium recirculates continuously through the system.

20.7 Conclusions

VV or VA ECMO offer circulatory/respiratory support in the postoperative period and in surgical procedures.

VV ECMO is less invasive that VA ECMO, ECMO is an essential tool in thoracic surgery, lung transplantation and refractory cardiorespiratory failure.

ECMO exhibits high complication and mortality rates. Monitoring and careful indication is essential in ECMO management.

References

1. Squiers JJ, Lima B, DiMaio JM. Contemporary extracorporeal membrane oxygenation therapy in adults: fundamental principles and systematic review of the evidence. J Thorac Cardiovasc Surg. 2016;152:20–32.

2. Peek GJ, Clemens F, Elbourne D, et al. CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure. BMC Health Serv Res. 2006;6:163.
3. Machuca TN, Collaud S, Mercier O, et al. Outcomes of intraoperative extracorporeal membrane oxygenation versus cardiopulmonary bypass for lung transplantation. J Thorac Cardiovasc Surg. 2015;149:1152–7.
4. McRae K, de Perrot M. Principles and indications of extracorporeal life support in general thoracic surgery. J Thorac Dis. 2018;10(Suppl 8):S931–46.
5. Reeb J, Olland A, Renaud S, Collange O, et al. Extracorporeal life support in thoracic surgery: what are the indications and the pertinence? Rev Mal Respir. 2017;34(8):802–19.
6. Abrams D, Brodie D, Arcasoy SM. Extracorporeal life support in lung transplantation. Clin Chest Med. 2017;38(4):655–66.
7. Sharma NS, Hartwig MG, Hayes D Jr. Extracorporeal membrane oxygenation in the pre and post lung transplant period. Ann Transl Med. 2017;5(4):74.
8. Reeb J, Olland A, Pottecher J, et al. Extracorporeal membrane oxygenation for acute respiratory distress syndrome after pneumonectomy. Ann Thorac Surg. 2017;103(3):881–9.
9. Jayaraman AL, Cormican D, Shah P, et al. Cannulation strategies in adult veno-arterial and veno-venous extracorporeal membrane oxygenation: techniques, limitations, and special considerations. Ann Card Anaesth. 2017;20(Suppl 1):S11–8.
10. Reeb J, Olland A, Renaud S, et al. Vascular access for extracorporeal life support: tips and tricks. J Thorac Dis. 2016;8(Suppl 4):S353–63.
11. Ko M, dos Santos PR, Machuca TN, et al. Use of single-cannula venous-venous extracorporeal life support in the management of life-threatening airway obstruction. Ann Thorac Surg. 2015;99:63–5.
12. Hoetzenecker K, Klepetko W, Keshavjee S, et al. Extracorporeal support in airway surgery. J Thorac Dis. 2017;9:2108–17.
13. Owada-Ozaki Y, Matsumura Y, Suzuki H. VV-ECMO during subsequent segmentectomy after right pneumonectomyJ. Surg Case Rep. 2018;2018(8):1–3.
14. Ghanim B, Hötzenecker K, Klikovits T, et al. Extracorporeal membrane oxygenation support for complex tracheo-bronchial procedures. Eur J Cardiothorac Surg. 2015;47(2):250–5; discussion 256.
15. Gillon SA, Toufektzian L, Harrison-Phipps K, et al. Perioperative extracorporeal membrane oxygenation to facilitate lung resection after contralateral pneumonectomy. Ann Thorac Surg. 2016;101:e71–3.
16. Oey IF, Peek GJ, Firmin RK, et al. Post-pneumonectomy video-assisted thoracoscopic bullectomy using extra-corporeal membrane oxygenation. Eur J Cardiothorac Surg. 2001;20:874–6.
17. Redwan B, Ziegeler S, Freermann S, et al. Intraoperative veno-venous extracorporeal lung support in thoracic surgery: a single-centre experience. Interact Cardiovasc Thorac Surg. 2015;21:766–72.
18. Asai T. Emergency cardiopulmonary bypass in a patient with a mediastinal mass. Anaesthesia. 2007;62:859–60.
19. Lang G, Taghavi S, Aigner C, et al. Extracorporeal membrane oxygenation support for resection of locally advanced thoracic tumors. Ann Thorac Surg. 2011;92(1):264–70.
20. Yusuff HO, Zochios V, Vuylsteke A. Extracorporeal membrane oxygenation in acute massive pulmonary embolism: a systematic review. Perfusion. 2015;30(8):611–6.
21. Machuca TN, Cypel M, Keshavjee S. Cardiopulmonary bypass and extracorporeal life support for emergent intraoperative thoracic situations. Thorac Surg Clin. 2015;25:325–34.
22. Willms DC, Mendez R, Norman V, et al. Emergency bedside extracorporeal membrane oxygenation for rescue of acute tracheal obstruction. Respir Care. 2012;57:646–9.
23. Extracorporeal Life Support Organization. ECLS Registry report. Ann Arbor, MI: ELSO; 2016. Available from http://www.elso.org/.
24. Sauer CM, Yuh DD, Bonde P. Extracorporeal membrane oxygenation use has increased by 433 % in adults in the United States from 2006 to 2011. ASAIO J. 2015;61(1):31–6.

25. Hayanga AJ, Aboagye J, Esper S, et al. Extracorporeal membrane oxygenation as a bridge to lung transplantation in the United States: an evolving strategy in the management of rapidly advancing pulmonary disease. J Thorac Cardiovasc Surg. 2015;149:291–6.
26. Hoetzenecker K, Donahoe L, Yeung JC, et al. Extracorporeal life support as a bridge to lung transplantation-experience of a high volume transplant center. J Thorac Cardiovasc Surg. 2018;155:1316–28.
27. de Perrot M, Granton JT, McRae K, et al. Impact of extracorporeal life support on outcome in patients with idiopathic pulmonary arterial hypertension awaiting lung transplantation. J Heart Lung Transplant. 2011;30(9):997–1002.
28. Nicoara A, Anderson-Dam J. Anesthesia for lung transplantation. Anesthesiol Clin. 2017;35(3):473–89.
29. Magouliotis DE, Tasiopoulou VS, Svokos AA, et al. Extracorporeal membrane oxygenation versus cardiopulmonary bypass during lung transplantation: a meta-analysis. Gen Thorac Cardiovasc Surg. 2018;66(1):38–47.
30. Bermudez CA, Shiose A, Esper SA, et al. Outcomes of intraoperative venoarterial extracorporeal membrane oxygenation versus cardiopulmonary bypass during lung transplantation. Ann Thorac Surg. 2014;98(6):1936–42; discussion 1942–3.
31. Fischer S, Bohn D, Rycus P, et al. Extracorporeal membrane oxygenation for primary graft dysfunction after lung transplantation: analysis of the Extracorporeal Life Support Organization (ELSO) registry. J Heart Lung Transplant. 2007;26(5):472–7.
32. Fuehner T, Kuehn C, Welte T, et al. ICU care before and after lung transplantation. Chest. 2016;150(2):442–50.
33. Shah RJ, Diamond JM. Primary graft dysfunction (PGD) following lung transplantation. Semin Respir Crit Care Med. 2018;39(2):148–54.
34. Reeb J, Olland A, Renaud S, Lejay A, et al. Vascular access for extracorporeal life support: tips and tricks. J Thorac Dis. 2016;8(Suppl 4):S353–63.
35. Tautz E, Wagner D, Wiesemann S, et al. Treatment of a broncho-esophageal fistula complicated by severe ARDS. Infection. 2019;47:483. https://doi.org/10.1007/s15010-018-1247-9.
36. Martucci G, Panarello G, Bertani A, et al. Veno-venous ECMO in ARDS after post-traumatic pneumonectomy. Intensive Care Med. 2013;39(12):2235–6.
37. Douflé G, Ferguson ND. Monitoring during extracorporeal membrane oxygenation. Curr Opin Crit Care. 2016;22:230–8.
38. Pieri M, Agracheva N, Bonaveglio E, et al. Bivalirudin versus heparin as an anticoagulant during extracorporeal membrane oxygenation: a case-control study. J Cardiothorac Vasc Anesth. 2013;27:30–4.
39. Young G, Yonekawa KE, Nakagawa P, et al. Argatroban as an alternative to heparin in extracorporeal membrane oxygenation circuits. Perfusion. 2004;19:283–8.
40. Esper SA, Levy JH, Waters JH, et al. Extracorporeal membrane oxygenation in the adult: a review of anticoagulation monitoring and transfusion. Anesth Analg. 2014;118:731–43.
41. Raiten JM, Wong ZZ, Spelde A, et al. Anticoagulation and transfusion therapy in patients requiring extracorporeal membrane oxygenation. J Cardiothorac Vasc Anesth. 2017;31:1051–9.
42. Frenckner B, Broman M, Broomé M. Position of draining venous cannula in extracorporeal membrane oxygenation for respiratory and respiratory/circulatory support in adult patients. Crit Care. 2018;22:163.
43. Aubron C, DePuydt J, Belon F, et al. Predictive factors of bleeding events in adults undergoing extracorporeal membrane oxygenation. Ann Intensive Care. 2016;6:97.
44. Mazzeffi M, Greenwood J, Tanaka K, et al. Bleeding, transfusion, and mortality on extracorporeal life support: ECLS working group on thrombosis and hemostasis. Ann Thorac Surg. 2016;101:682–9.
45. Lorusso R, Gelsomino S, Parise O, et al. Neurologic injury in adults supported with veno-venous extracorporeal membrane oxygenation for respiratory failure: findings from the extracorporeal life support organization database. Crit Care Med. 2017;45:1389–97.
46. Biffi S, Di Bella S, Scaravilli V, et al. Infections during extracorporeal membrane oxygenation: epidemiology, risk factors, pathogenesis and prevention. Int J Antimicrob Agents. 2017;50:9–16.

Thoracic Surgery in Patients with Previous Lung Resection

21

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21.1 Introduction

More patients who have had previous lung cancer surgery, now can be expected to present for repeat lung cancer surgery. Lung cancer is the leading cause of cancer mortality in both sexes because exists an high prevalence of smoking in our societies [1]. The survival rate after lung cancer surgery is increasing because of improvements in surgical techniques and multidisciplinary therapy [2]. It is estimated that 5–10% of patients surviving lung cancer resection develop a second lung primary within 5 years. Most cancer centers have developed consistent follow-up protocols for patients after initial surgery so that the chance of detecting a second primary when it is still resectable is higher [3].

Some anatomic changes appear after lung resection, including expansion of the remaining lung to fill the thoracic cavity, upward displacement of the hemidiaphragm, and a lateral shift of the mediastinum, occur to varying degrees, depending

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on the size and site of the resected lung [4]. Accordingly, such bronchial displacement can more often occur after an upper than a lower lobectomy because bronchial angulation frequently results from upward displacement of the remaining lower lobe. Further, angulation of the remaining bronchus, defined as changes in the bronchial angle, is much greater after a left than right upper lobectomy, due to the much longer left main bronchus [5–7]. Therefore, deformity of the residual bronchus after a lobectomy is observed most predominantly after a left upper lobectomy [8].

One lung ventilation (OLV) is a greater challenge to the anesthesiologist when the ventilated lung has previously been submitted to resection [9]. OLV is then replaced by an even more challenging scenario: one lobe, or at most two-lobe ventilation. There are no controlled studies describing respiratory mechanics in these patients. Sporadic communications reporting gas exchange have been published [9–11]. The one lung ventilation of patients undergoing thoracic surgery who have undergone previous surgery in this lung can be very difficult due to the rapid onset of hypoxemia due to low pulmonary reserve. In this context, lobe collapse using bronchial blockers through a single lumen tube or a double lumen tube becomes important, allowing the collapse of the lobe undergoing surgery by blocking the entrance of a specific bronchial branch while the remaining lobes of the lung being operated could be normally ventilated [12].

After lung resection, a series of cardiopulmonary changes and adaptations are expected to occur in the remaining lung tissue, and are a function, in part, of the size of lung resection. Reduced exercise tolerance after pulmonary resection is related to pulmonary hypertension [13]. Following lung resection, exercise tolerance can decrease due to pulmonary hypertension and hypoxemia, which may not be evident at rest [10].

The principles involved in preanesthetic assessment of these patients are essentially the same as for patients presenting for first-time lung surgery. The respiratory system needs to be evaluated in terms of cardiopulmonary fitness, lung mechanical function, and lung parenchymal function. These parameters decrease after the second pulmonary resection in proportion to the amount of functioning lung removed at surgery. The postoperative mechanical function of the lungs in these patients would be expected to be above the levels associated with high risk (predicted postoperative $FEV_{1.0}$ >30–40%). These patients also should have documented exercise tolerance (formal exercise testing, 6-min walk test, or exercise oximetry) and parenchymal function (predicted postoperative lung diffusing capacity for carbon monoxide >40%) that meet minimal criteria for operability [14].

21.2 Respiratory Mechanics After Lung Resection

Loss of pulmonary tissue appears to be the most important (but not the only) problem after the lung resection. As a result of the lung tissue loss, the pleural pressure become even "more subatmospheric" (from approx. −6.5 cm H_2O preoperatively, to up to −10–12 cm H_2O), which is more elaborated in fibrotic/restrictive lungs [15]. This change causes a change in the balance of pleural and pulmonary water and

consequently an increased risk of pulmonary edema [16]. The respiratory work increases, forcing the patients to have a "rapid shallow breathing" pattern. Although the relative ratio of functional residual capacity (FRC) / vital capacity (VC) increases to up to 45–60%, both tissue loss and increased "work of breathing" are associated with a decrease in lung compliance exceeded by 10–15% the one expected from the resected mass.

Generally, early postoperative pulmonary pathophysiology can be explained by three factors: reduced lung volumes, impaired ventilation and impaired gas exchange [17, 18] (Fig. 21.1).

Indications of early re-thoracotomy are usually also the challenges for the anaesthetic strategy. Knowing the possible pathways of the pathophysiology can be helpful to deal with these challenges: Postresectional pulmonary edema may have several mechanisms: It is simple to argue that the same cardiac output flows through a decreased vascular bed; but there are also more sophisticated pathways such as damage of the glycocalyx, increased (more negative) intrapleural pressure, local hypoxia

Pathophysiology of lung function after thoracic surgery

Reduced lung volumes	Impaired ventilation	Impaired gas exchange
Resection of lung parenchyma		Ventilation–perfusion mismatch
	Functional residual capacity	
	Forced vital capacity	
Atelectasis	Diaphragm dysfunction	Atelectasis
Pleura effusions	Dysfunction of intercostal muscle	Lung edema
Restriction of thorax	Resistance	Cardiac output
Lung edema	Minute volume ventilation	Mixed venous oxygen partial pressure
Secret retention		Minute volume ventilation

Fig. 21.1 Pathophysiology of lung function after thoracic surgery

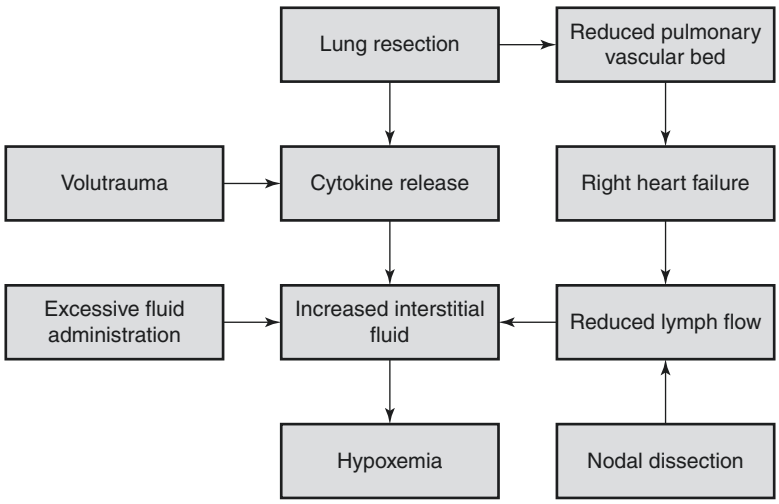

Fig. 21.2 Postresectional pulmonary edema mechanisms

in lung tissue, and impaired lymphatic drainage (Fig. 21.2). As quoted by Slinger, "(with IV fluids), we can make the lung injury worse, but we don't cause it" [19].

Changes in respiratory functions recover after some period; but depending on the amount of lung resection (pneumonectomy >> lobectomy ≫ segmental resection) this period can be longer than 12 months—of course, assuming that there would be no complications or recurrence [20].

21.3 Airway Anatomy Changes After Lung Resection

Some anatomic changes in the lower airway appear after lung resection, including expansion of the remaining lung to fill the thoracic cavity, upward displacement of the hemidiaphragm, and a lateral shift of the mediastinum, occur to varying degrees, depending on the size and site of the resected lung [4]. Bronchial stenosis or obstruction (BSO) may occur as an acquired lesion secondary to other conditions but is rare after chest surgery. BSO after upper lobectomy probably occurs due to upward movement of the remaining lobe(s) with torsion or deformation of the bronchus. The diagnosis of BSO can be confirmed at the time of bronchoscope or computed tomography (CT) scan by the findings of a kinked lobar bronchus [21]. Occasionally, patients with severe bronchial kinking may require endobronchial stenting to relieve the symptoms and signs of endobronchial stenosis [22].

Chest radiograph and CT scan preoperative assessment must be mandatory in patients with a previous lung resection because most tracheobronchial distortions that cause problems during placement of endobronchial tubes or blockers can be seen on the preoperative imaging [11].

Accordingly, such bronchial displacement can more often occur after an upper than a lower lobectomy because bronchial angulation frequently results from upward displacement of the remaining lower lobe. Further, angulation of the remaining bronchus, defined as changes in the bronchial angle, is much greater after a left than right upper lobectomy, due to the much longer left main bronchus [5–7]. Therefore, deformity of the residual bronchus after a lobectomy is observed most predominantly after a left upper lobectomy [8]. The remaining bronchus may produce deformation even if lung lobar torsion does not occur. Arai et al. described endoscopic and pathological study on deformation of the remaining bronchus after left upper lobectomy. They asserted that deformation of the remaining bronchus after upper lobectomy was observed most predominantly in cases of left upper lobectomy [23].

Moreover, Pinstein et al. reported that torsion of the right middle lobe may occur following right upper lobectomy when the middle lobe twists on its narrow pedicle in a clockwise rotation. In the postoperative state, other possible radiographic misinterpretations include atelectasis of the superior segment of the right lower lobe or simple atelectasis of the right middle lobe [24]. After right upper lobectomy, the orifice of the middle lobe bronchus is round in some cases, but is deformed in others. When the orifice was semicircular before right upper

lobectomy, deformation of the orifice of the right middle lobe bronchus was common after right upper lobectomy [25].

Brooks described that lung lobar torsion of the right middle lobe after upper lobectomy is the most common, but it can occur in all lobes [26]. Arai et al. [23] reported bronchial deformation of the left lower lobe bronchus after left upper lobectomy. Wong et al. [27] reported 28 cases of lobar torsion after lung resection; 16 (57%) of these 28 cases involved middle lobe torsion after right upper lobectomy. The others involved left upper lobe torsion after left lower lobectomy, and right lower lobe torsion after right upper lobectomy. There are published articles on left lower lobe torsion after left upper lobectomy, as well as right lower lobe torsion after right upper lobectomy [24].

21.4 Lung Isolation/Separation in Patients with Previous Lung Resections

Some anatomic changes in the lower airway appear after lung resection. This is the reason because all intubation procedures should be performed under bronchoscopic guidance to prevent airway trauma.

Sometimes patients with a reduced lung volume reserve, especially after a lobectomy or pneumonectomy, could suffer an important hypoxemia, hypercapnia and a barotrauma because very often they present a dangerous high airway pressure. Often the usual preoperative lung test don't assess enough about the probability that the anesthesiologist will have some intraoperative difficulties related with gases exchange and mechanical ventilation [28].

In patients with a previous upper left lobectomy scheduled for a right lung resection, the left-sided double lumen tubes are the most often device used by some authors (12–18 patients), but sometimes others devices as right double-lumen tubes or bronchial blockers inserted in the right side are the best option (6–18 patients). The presence of remarkable bronchial angulation, characterized by a combination of a wide (>140°) angle between the trachea and left main bronchus and a narrow (<100°) angle between the left main and lower bronchi critically affected left-sided DLT insertion [29].

Anesthesiologists can also select right-sided DLT for post left upper lobectomy (LUL) patients in the second lung surgery if their anatomy of right upper branch is within normal range. If the second surgery is the left lung surgery, we have to take care whether the lateral hole of right sided DLT fit right upper branch for adequate one lung ventilation, however it is easier to use right DLT in second right lung surgery because fitness of lateral hole is related only to collapsing of right upper lobe in surgical field.

Additional device can be recommended for bronchial anatomical change for such a post LUL patients particularly who undergo second right lung surgery. Specific left-sided DLT with a flexible wire-reinforced tip and a narrow bronchial cuff (Silbroncho®, Fuji Systems, Tokyo, Japan) may be adaptable for almost all

bronchial anatomical change of the post lung surgery patients. Kawagoe et al. also reported that the ventilation failure soon after left jack-knife positioning in the post lingula-sparing left upper lobectomy patient, who underwent robotic right upper lobectomy was solved by exchanging Left DLT to "Silbroncho® tube" [30].

Selective lobar blockade is an alternative technique to achieve lobar collapse in patients who have had a previous right or left lobectomy/pneumonectomy and require thoracic surgery. In patients with previous bronchial resection, recognition of tracheobronchial anatomy with the bronchoscope is mandatory to increase the successful placement and function of lung isolation devices. The advantages of a selective lobar blockade are to avoid total lung collapse and only block the lobe(s) in which surgery takes place and to improve intraoperative oxygenation [31]. Anesthesiologists have to be prepared to solve this problem with several strategies using different airway devices as double lumen tubes, bronchial blockers even the combination of double lumen tube and bronchial blockers. Sometimes we have to collapse only the lobes being operated using bronchial blockers introduced through a tracheal tube [11, 12, 32] or a double lumen tube [12, 29, 33] guided by bronchoscope (Fig. 21.3a, b).

Selective lobe blockade in the patients who needs right upper lobe blockade may be more difficult to perform than any other lobe due to its anatomical location though it is effective to avoid hypoxemia during OLV. The kind of bronchial blocker and anesthesiologist who perform this procedure should be selected carefully. In the case which needs partial blockade of right upper lobe, the interesting method had been reported that right-sided DLT can obstruct on right upper lobe branch with its bronchial cuff instead of bronchial blocker [34].

At first time we should check the correct DLT position in supine position using a bronchoscope and after that we must to assess if some critical desaturation became after starting the OLV. Arterial gas analysis should have been utilized at this point as a predictor for gas exchange during intraoperative OLV, and a different approach for lung isolation could have been planned at that time. In patients with a lower lung reserve a selective endobronchial blocker insertion prior to turning the patient on lateral decubitus should have been considered to avoid a severe hypoxemia has been proposed by some authors [12, 28] because they consider it as a convenient maneuver when anesthesiologist would suspect that this patient could suffer a respiratory failure during OLV.

21.5 Perioperative Mechanical Ventilation in Patients with Previous Lung Resections

As a general rule, mechanical ventilation has its two targets also in patient with previous lung resections: Maintenance adequate oxygenation/gas exchange AND protection of the lung. However, both can be very challenging in this patient group. "Protective" ventilation with low TV, PEEP and recruitment manoeuvre can be difficult to perform and can remain sometimes inadequate: As a "lobar

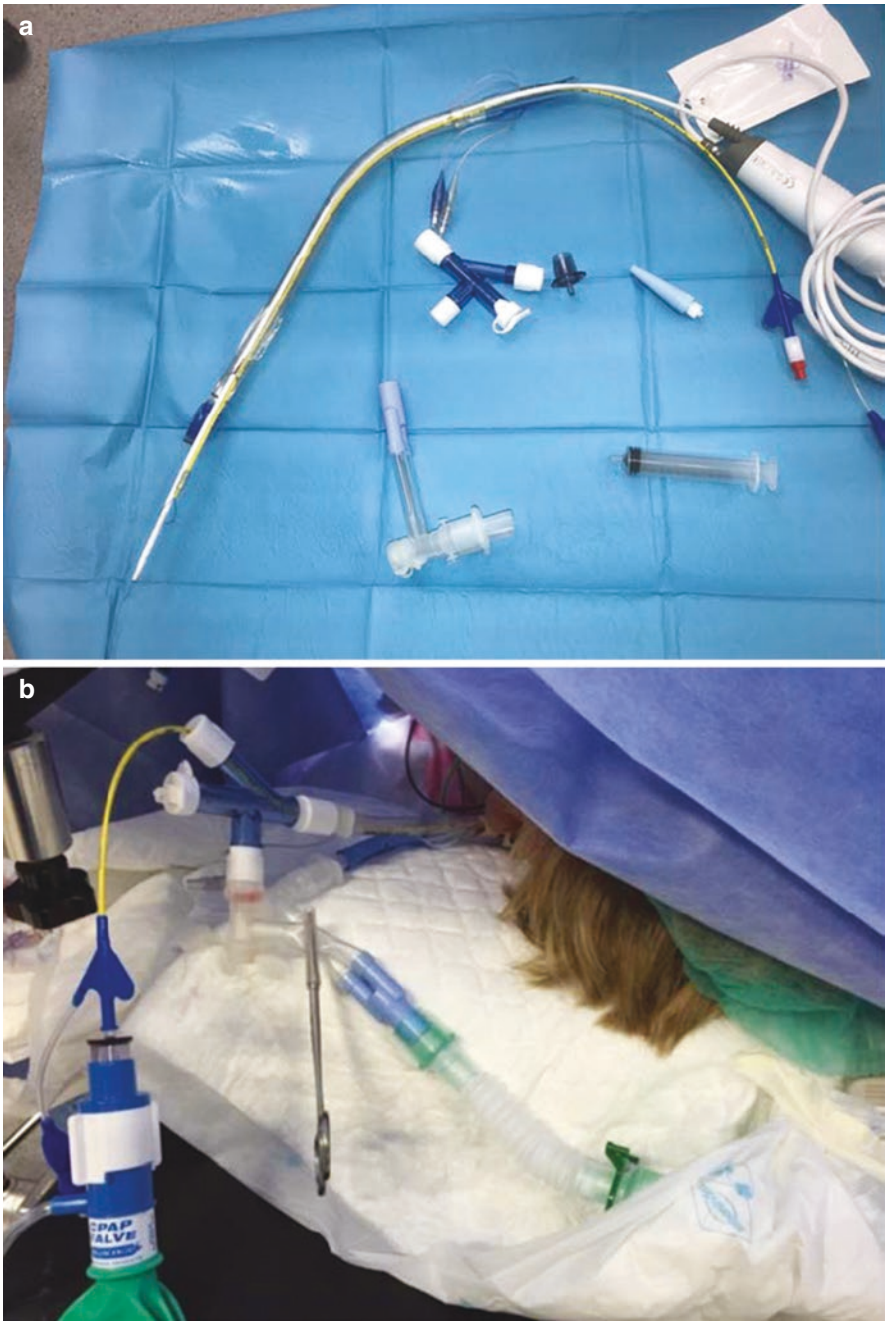

Fig. 21.3 (**a**, **b**) Use of bronchial blockers introduced through the tracheal lumen of a left double-lumen tube applying CPAP

blockade"—explained above—is usually indicated, even the lowest tidal volumes can be associated with inacceptable driving pressures due to the small amount of ventilated tissue (leading to lung injury), and/or these low tidal volumes can be associated with insufficient oxygenation.

In these cases, some rescue methods can be life saving:

- **Hypercapnic ventilation:** the decrease in VT can be compensated by an increase in frequency, but the price of shorter inspiration can be high ventilation pressures, and the price of shorter expiration can be air-trapping and auto-PEEP. More importantly, mild hypercapnia can be 'permitted' in many cases [35] and can even be 'therapeutic' for several hours [36]. There is still no sufficient evidence regarding the effects of therapeutic hypercapnia, but 'permissive hypercapnia' can protect the lung and improve the tissue oxygenation as a result of the increased cardiac output and right-shift of the O_2-saturation curve [37]. It has been shown in a comparative study that during OLV, hypercapnia (pCO_2 = 60–70 mmHg) improved respiratory function after OLV in lobectomy patients, reduced peak and plateau pressures and increased dynamic compliance. Hypercapnia also inhibited local and systematic inflammation by reducing serum and bronchoalveolar lavage fluid inflammatory mediators [38].

  However, hypercapnia enhances hypoxic pulmonary vasoconstriction; thus, permissive hypercapnia is contraindicated in pulmonary hypertension (which is more frequent in post-thoracotomy patients). In the remaining population, permissive hypercapnia can be considered as a rational part of PLV.
- **High frequency ventilation:** Ventilation avoiding high driving pressures can be achieved using high frequency ventilation (HFV) [39]. There are different ways (with different nomenclature !) to achieve HFV: in many of them, the VT is less than the dead space, but gas exchange is possible by combining different factors, such as convection, diffusion, and others. The types of HFV differ in setting (such as in frequency or pressure) and during perioperative ventilation in thoracic anaesthesia, it can be applied to both lungs or only to the non-dependent lung/lobe or even only to the dependent lung. However, there are no RCT that examine the effects of HFV in post-thoracotomy patients.
- **Extracorporeal ventilatory assistance:** (extracorporeal lung assist [ECLA]): Extracorporeal methods can be found in another chapter in this book. Regarding patients with previous lung resection, the so-called "ultraprotective ventilation" can be helpful both in intraoperative and postoperative period to achieve sufficient oxygenation and/or gas exchange. Iglesias et al. have shown in two studies (an animal study) [40] and a clinical study [41]. There are some evidence because ECLA help to decrease the TV to very low amounts to avoid high pressures during ALI in postoperative period; the resulting survival rate was much higher than usual (100% in the animal study, and 86% (six of seven patients) in clinical setting). For the intraoperative ventilation, in ten patients, apneic oxygenation could be applied successfully with the help of ECLA [42]. One of the author's experiences is a child with a previous right pneumonectomy who had to be reoperated

because of the metastases in the left mediastinum. The ECLA was initiated before the operation and continued for 24 h after the operation, and the device was removed 18 h after the extubation.

21.6 Hemodynamic Changes After Lung Resection and Perioperative Hemodynamic Management

Lung resection induces hemodynamic adaptative responses with the right ventricle being the focus of most studies. Its scant muscular mass makes it sensitive to changes in afterload, so increases in pulmonary arterial pressure (PAP) generate more overload and progressively change the morphology of the right ventricle, producing its dysfunction.

This increase in PAP appears as a result of the resection itself, changes in the position of the heart and great vessels after pneumonectomy [43] and pulmonary hypoxic vasoconstriction in COPD patients with FEV1<50% [44]. Pneumonia and respiratory distress syndrome, although transient, can worsen pulmonary hypertension (PHT). Small sample size and varying methodology in published studies make it difficult to draw conclusions and to determine the exact role of each of the mechanisms involved in right ventricle dysfunction after lung resection [43, 45–48].

Lung resection reduces the vascular bed. If the vascular compliance is normal and the volume of lung resected is a lobe or less, the right ventricle will adapt to the changes in the afterload during the first two postoperative days and at the end of the first week systolic and diastolic function will be normal, with minimal changes in PAP [46, 49–51].

After pneumonectomy PAP increases in the first two postoperative days and continues to be elevated 4 years after surgery. Right ventricle ejection fraction (RVEF) decreases, so maintaining systolic volume against an increased afterload depends on the capacity of the right ventricle to dilate. Heart rate at rest increases to compensate for this [43, 46–48, 50, 52]. As PAP increase it is not enough to induce right ventricle hypertrophy, an increase in afterload might not be the only mechanism involved in right ventricle dysfunction [43, 53]. Forty percent of patients have mild to moderate PHT after pneumonectomy, regardless of the side of the resection [46, 47, 50, 54].

On the other hand, there are few studies looking at the left ventricle function after lung resection [45, 48, 51, 52]. It seems that left ventricle ejection fraction lowers after lobectomy and pneumonectomy, but remains over 55% [52].

The detection of these hemodynamic changes also depends on the method of study: pulmonary artery catheter has been overcome by echocardiography. Even bidimensional and Doppler echocardiography are giving way to newer and more sensitive technologies, such as strain and speckle tracking echocardiography, that allow for detection of subclinic dysfunction when bidimensional and Doppler echocardiography are still normal [55]. Speckle tracking echocardiography reveals there might also be ventricle dysfunction in lobectomies, but there are very few studies and they just assess early postoperative period [49, 52].

Preoperative Plasma B-Type natriuretic peptide (BNP) levels in plasma help in grading the risk of postoperative cardiovascular complications [56]. BNP also increases during the first week after lung resection, suggesting its participation in the adaptative response [57]. Increases in BNP are significantly higher in patients who develop atrial fibrillation after surgery [58].

Following lung resection, exercise tolerance can decrease due to pulmonary hypertension and hypoxemia, which may not be evident at rest [10, 46, 47]. Other potential changes after pneumectomy include decrease in lung diffusion capacity, and elevation in right heart pressure during exercise [10]. Reduced stroke volume index after pneumectomy could be due to impaired filling of the left ventricle secondary to reduced pulmonary blood volume. The same occurs after lobectomy, although less significantly [13, 59].

21.7 Conclusions

Nowadays thoracic anesthesiologists have a challenge in patients with a previous lung resection and it's very important to assess very well the anatomic airway changes and the cardiopulmonary fitness, lung mechanical function, and lung parenchymal function.

Some airway anatomic changes appear after lung resection that require a previous Chest radiograph and CT scan preoperative assessment to choose the best airway devices including DLT, bronchial blockers or both to perform a lung isolation or a selective lobar blockade guided by bronchoscope to avoid tracheobronchial damage during these techniques and to obtain a successful airway isolation.

On the other hand, it is necessary to apply protective ventilation to these patients and also, if anesthesiologists need it, they should be ready to use other methods to improve the exchange of gases such as high frequency ventilation and extracorporeal ventilatory assistance, among others.

Moreover, it's necessary to apply a protective ventilation but if anesthesiologists needed have to be ready to use other methods to improve the gases exchange as high frequency ventilation and extracorporeal ventilatory assistance among others.

References

1. Feinstein MB, Bach PB. Epidemiology of lung cancer. Chest Surg Clin North Am. 2000;10:653–61.
2. Sawabata N, Miyaoka E, Asamura H, et al. Japanese lung cancer registry study of 11,663 surgical cases in 2004: demographic and prognosis changes over decade. J Thorac Oncol. 2011;6:1229–35.
3. Naunheim KS, Virgo KS. Postoperative surveillance following lung cancer resection. Chest Surg Clin North Am. 2001;11:213–25.
4. Nonaka M, Kadokura M, Yamamoto S, et al. Analysis of the anatomic changes in the thoracic cage after a lung resection using magnetic resonance imaging. Surg Today. 2000;30:879–85.
5. Matsuoka H, Nakamura H, Nishio W, et al. Division of the pulmonary ligament after upper lobectomy is less effective for the obliteration of dead space than leaving it intact. Surg Today. 2004;34:498–500.

6. Ueda K, Tanaka T, Hayashi M, et al. Clinical ramifications of bronchial kink after upper lobectomy. Ann Thorac Surg. 2012;93:259–65.
7. Seok Y, Cho S, Lee JY, et al. The effect of postoperative change in bronchial angle on postoperative pulmonary function after upper lobectomy in lung cáncer patients. Interact Cardiovasc Thorac Surg. 2014;18:183–8.
8. Usuda K, Sagawa M, Akikawa H, et al. Do Japanese thoracic surgeons think that dissection of the pulmonary ligament is necessary after an upper lobectomy? Surg Today. 2010;40:1097–9.
9. Ruiz Neto PP. One-lobe ventilation or the hazard of bilateral upper lobectomy (Letter). J Cardiothorac Anesth. 1989;3:254–5.
10. Nishimura H, Haniuda M, Morimoto M, Kubo K. Cardiopulmonary function after pulmonary lobectomy in patients with lung cancer. Ann Thorac Surg. 1993;55:1477–84.
11. Hagihira S, Maki N, Kawaguchi M, Singer P. Selective bronchial blockage in patients with previous contralateral lung surgery. J Cardiothorac Vasc Anesth. 2002;16:638–42.
12. Morales J, Granell M, Biosca E, Guijarro R, Arnau A, de Andrés J. Right lobar isolation by different methods in two patients with previous left lung resection. J Cardiothorac Vasc Anesth. 2017;31:S53.
13. Heerdt PM. Cardiovascular adaptation to lung resection. In: Kaplan JA, Slinger PD, editors. Thoracic anesthesia. 3rd ed. Philadelphia, PA: Churchill Livingstone Inc; 2003. p. 423–35.
14. Slinger PD, Johnston MR. Preoperative assessment for pulmonary resection. J Cardiothorac Vasc Anesth. 2000;14:202–11.
15. Miserocchi G, Beretta E, Rivolta LL. Respiratory mechanics and fluid dynamics after lung resection surgery. Thorac Surg Clin. 2010;20:345–57.
16. Salito C, Bovio D, Orsetti G, Salati M, Brunelli A, Aliverti A, et al. Effect of lung resection on pleuro-pulmonary mechanics and fluid balance. Respir Physiol Neurobiol. 2016;221:35–40.
17. Furrer M, Rechsteiner R, Eigenmann V, Signer C, Althaus U, Ris HB. Thoracotomy and thoracoscopy: postoperative pulmonary function, pain and chest wall complaints. Eur J Cardiothorac Surg. 1997;12(1):82–7.
18. Kozian A, Schilling T, Strang C, Hachenberg T. Anesthetic considerations in patients with previous thoracic surgery. Curr Opin Anaesthesiol. 2006;19(1):26–33.
19. Slinger PD. Postpneumonectomy pulmonary edema: good news, bad news. Anesthesiology. 2006;105:2–5.
20. Keenan RJ, Landreneau RJ, Maley RH Jr, Singh D, Macherey R, Bartley S, et al. Segmental resection spares pulmonary function in patients with stage I lung cancer. Ann Thorac Surg. 2004;78(1):228–33.
21. Kadokura M. Bronchial deformation associated with lobectomy. Ann Thorac Cardiovasc Surg. 2015;21:301–4.
22. Van Leuven M, Clayman JA, Snow N. Bronchial obstruction after upper lobectomy: kinked bronchus relieved by stenting. Ann Thorac Surg. 1999;68(1):235–7.
23. Arai T, Hirata M, Inagaki K, et al. Endoscopic and pathological study on deformation of the residual bronchus after upper lobectomy of the left lung. J Jap Soc Broncho. 1986;8:33–40.
24. Pinstein ML, Winer-Muram H, Eastridge C, et al. Middle lobe torsion following right upper lobectomy. Radiology. 1985;155:580.
25. Nonaka M, Kadokura M, Tanio N, et al. Bronchofiberscopic analysis for middle lobe bronchial deformity associated with right upper lobectomy. Jap J Chest Surg. 1998;12:474–81.
26. Brooks JW. 25 Complications following pulmonary lobectomy. In: Cordel AR, Ellison RG, editors. Complications of intrathoracic surgery. Boston, MA: Little Brown and Company; 1979. p. 235–45.
27. Wong PS, Goldstraw P. Pulmonary torsion: a questionnaire survey and a survey of the literature. Ann Thorac Surg. 1992;54:286–8.
28. Ruiz P, Kovarik G. Lung mechanics and gas exchange in one-lung ventilation following contralateral resection. Can J Anaesth. 2005;52(9):986–9.
29. Kawagoe I, Hayashida M, Suzuki K, Kitamura Y, Oh S, Satoh D, et al. Anesthetic management of patients undergoing right lung surgery after left upper lobectomy: selection of tubes for one-lung ventilation (OLV) and oxygenation during OLV. J Cardiothorac Vasc Anesth. 2016;30(4):961–6.

30. Kawagoe I, Hayashida M Satoh D, Suzuki K, Inada E. Ventilation failure after lateral jackknife positioning for robot-assisted lung cancer surgery in a patient after lingula-sparing left upper lobectomy. JA Clin Rep. 2018;4:51.
31. Campos J. Update on selective lobar blockade during pulmonary resections. Curr Opin Anaesthesiol. 2009;22:18–22.
32. Campos JH, Ledet C, Moyers JR. Improvement of arterial oxygen saturation with selective lobar bronchial block during hemorrhage in a patient with previous contralateral lobectomy. Anesth Analg. 1995;81:1095–6.
33. Cruz P, Orozco HD, Garutti I, Hernández G. Selective lobar blockade with a Coopdech blocker combined with a double-lumen endotracheal tube for lung metastases resection by laser. Rev Bras Anestesiol. 2018;68(2):200–4.
34. Morikawa T, Sugiura H, Kaji M, et al. Availability of lobe-selective bronchial blockade for video-assisted thoracic surgery. An initial experience with three cases. Surg Endosc. 2002;16:327–30.
35. Hickling KG, Walsh J, Henderson S, Jackson R. Low mortality rate in adult respiratory distress syndrome using low-volume, pressure-limited ventilation with permissive hypercapnia: a prospective study. Crit Care Med. 1994;22(10):1568–78.
36. Kavanagh BP, Laffey JG. Hypercapnia: permissive and therapeutic. Minerva Anestesiol. 2006;72:567–76.
37. Akça O. Carbon dioxide and tissue oxygenation: is there sufficient evidence to support application of hypercapnia for hemodynamic stability and better tissue perfusion in sepsis? Intensive Care Med. 2008;34(10):1752–4.
38. Gao W, Liu D, Li D, Cui G. Effect of therapeutic hypercapnia on inflammatory responses to one-lung ventilation in lobectomy patients. Anesthesiology. 2015;122:1235–52.
39. Ishiyama T, Iwashita H, Shibuya K, Terada Y, Masamune T, Nakadate Y, et al. High-frequency jet ventilation during video-assisted thoracoscopic surgery in a patient with previous contralateral pneumonectomy. J Clin Anesth. 2013;25(1):55–7.
40. Iglesias M, Jungebluth P, Petit C, et al. Extracorporeal lung membrane provides better lung protection than conventional treatment for severe postpneumonectomy noncardiogenic acute respiratory distress syndrome. J Thorac Cardiovasc Surg. 2008;135:1362–71.
41. Iglesias M, Martinez E, Badia JR, Macchiarini P. Extrapulmonary ventilation for unresponsive severe acute respiratory distress syndrome after pulmonary resection. Ann Thorac Surg. 2008;85:237–44.
42. Wiebe K, Poeling J, Arlt M, et al. Thoracic surgical procedures supported by a pumpless interventional lung assist. Ann Thorac Surg. 2010;89:1782–7.
43. Smulders SA, Holverda S, Vonk-Noordegraaf A, et al. Cardiac function and position more than 5 years after pneumonectomy. Ann Thorac Surg. 2007;83:1986–92.
44. Ryu JH, Krowka MJ, Pellikka PA, et al. Pulmonary hypertension in patients with interstitial lung diseases. Mayo Clin Proc. 2007;82:342–50.
45. Pedoto A, Amar D. Right heart function in thoracic surgery: role of echocardiography. Curr Opin Anaesthesiol. 2009;22:44–9.
46. Venuta F, Sciomer S, Andreetti C, et al. Long term Doppler echocardiographic evaluation of the right heart after major lung resections. Eur J Cardiothorac Surg. 2007;32:787–90.
47. Foroulis CN, Kotoulas CS, Kakouros S, et al. Study on the late effect of pneumonectomy on right heart pressures using Doppler echocardiography. Eur J Cardiothorac Surg. 2004;26:508–14.
48. Kowalewski J, Brocki M, Dryjanski T, et al. Right ventricular morphology and function after pulmonary resection. Eur J Cardiothorac Surg. 1999;15:444–8.
49. Henning JS, Kalverkamp S, Rashad Z, Autschbach R, Spillner JW, et al. Is systolic ventricular function reduced after thoracic nos-cardiac surgery? A propensity matched echocardiographic analysis. Ann Thorac Cardiovasc Surg. 2018;24:238–46.
50. Okada M, Ota T, Okada M, et al. Right ventricular dysfunction after major pulmonary resection. J Thorac Cardiovasc Surg. 1994;108:503–11.

51. Amar D, Burt ME, Roistacher N, Reinsel RA, Ginsberg RJ, Wilson RS. Value of perioperative Doppler echocardiography in patients urdergoing major lung resections. Ann Thorac Surg. 1996;61:516–20.
52. Wang Z, Yuan J, Chu W, Kou Y, Xijun Z. Evaluation of left and right ventricular myocardial function after lung resection using speckle tracking echocardiography. Medicine. 2016;95(31):e4290. https://doi.org/10.1097/MD.0000000000004290.
53. Reed CE, Spinale FG, Crawford FA. Effect of pulmonary resection on right ventricular function. Ann Thorac Surg. 1992;53:578–82.
54. Deslauriers J, Ugalde P, Miro S, Ferland S, Bergeron S, et al. Adjustments in cardiorespiratory function after pneumonectomy: results from the pneumonectomy project. J Thorac Cardiovasc Surg. 2011;141:7–15.
55. Ashes C, Roscoe A. Transesophageal echocardiography in thoracic anesthesia: pulmonary hypertension and right ventricular function. Curr Opin Anaesthesiol. 2015;28:38–44.
56. Ryding A, Kumar S, Worthington A, Burgess D. Prognostic value of brain natriuretic peptide in noncardiac surgery. Anesthesiology. 2009;111:311–9.
57. Tayama K, Takamori S, Mitsuoka M, Hayashi A, Tamura K, Mifune H, Shirouzu K. Natriuretic peptides after pulmonary resection. Ann Thorac Surg. 2002;73:1582–6.
58. Nojiri T, Maeda H, Takeuchi Y, Funakoshi Y, Kimura T, et al. Predictive value of B-type natriuretic peptide for postoperative atrial fibrillation following pulmonary resection for lung cancer. Eur J Cardiothorac Surg. 2010;37:787–91.
59. Vainshelboim B, Fox BD, Saute M, et al. Limitations in exercise and functional capacity in long-term postpneumonectomy patients. J Cardiopulm Rehabil Prev. 2015;35:56–64.

Anesthesia for Esophageal Surgery

22

Tamás Végh

22.1 Conceptual Hypothesis

Surgical procedures of the esophagus are very unique and difficult in terms of surgery, anesthesia, and postoperative care. Anesthesia for esophagectomy is a great challenge for the anesthesiologist, who is facing with the problem of patient selection, preoperative preparation, ventilatory strategy, accurate fluid management and pain management. The reason is that esophagus passes through three regions of the body, so surgical procedure may be performed in the cervical, thoracic, and abdominal region or in more than one region in same time. Perioperative care of patients undergoing esophageal resection is one of the most complex process in anesthesia.

In the last 10–15 years therapeutic strategies of esophageal cancer did not changed, nevertheless new surgical approaches and anesthesia techniques have been developed.

The most common reason for esophagectomy is cancer; however, it can also be a result of Barrett's esophagus, hiatus hernia, achalasia, stricture, rupture of the esophagus, or congenital conditions.

The two most common types of esophageal cancer are squamous cell carcinoma, originating in the thoracic part of the esophagus, and adenocarcinoma, which arises from the glandular cells lining in the distal part of the esophagus and at the esophagogastric junction.

The preferred treatment for esophageal cancer is surgery. However, for many patients, surgery is combined with chemotherapy, radiation therapy, or hormone therapy. These nonsurgical treatments may be administered before surgery (neoadjuvant therapy) or after surgery (adjuvant therapy) [1–5].

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22.2 Types of Esophagectomy

22.2.1 Traditional Approaches

Esophagectomy is a high-risk procedure, and the complication rate is high due to the anatomic challenges of the procedure. Esophagectomy may be done using either of two main types of techniques: open and minimal invasive method. In the standard, open technique, the surgeon operates through one or more large incisions in the neck, chest, or abdomen.

The choice of surgical approach depends upon the tumor location, submucosal extension, adherence to the surrounding tissues, the conduit to be used to restore gastrointestinal continuity, and the extent of lymphadenectomy [6] (Table 22.1).

Although the gastric interposition is most commonly used as a conduit for reconstruction following esophagectomy, the jejunum or the colon can also be used as the conduit. These conduits are resistant to the effects of gastric acid, and they have a shape similar to the native esophagus [19–21].

22.2.2 New Approaches

The laparoscopic techniques allows esophagectomy to be performed by minimally invasive approach. Minimally invasive approaches exist for transhiatal techniques as well as for the Ivor Lewis procedure, and the tri-incisional version combining thoracoscopic/laparoscopic mobilization with the cervical incision/anastomosis. Aim of minimal invasive approach is to reduce the thoracotomy and abdominal incision size, reduce blood loss, minimize inflammatory response, and finally improve postoperative outcomes. The most common approach for minimally invasive esophagectomy allows for completion of the classic Ivor Lewis operation through the use of multiple port sites (can be as many as 9–10) in the thoracic and abdominal region. Usually the thoracic portion of the procedure is performed using a VATS approach with the patient in left lateral decubitus position, however recently a surgical approach utilizing the prone position for the right VATS portion of esophageal mobilization has been described. Advantages of the prone position include improved visualization and reduced need for lung retraction due to effects of gravity, fewer port sites, better ergonomics for the surgeon, shorter learning curve compared to lateral decubitus approaches, ability to perform procedure using two lung ventilation, and theoretical oxygenation improvements. Disadvantages are the longer positioning period, limited access to the airway, difficulty converting to open thoracotomy in emergency, and lack of uniform surgical method. However, prone positioning appeared to be feasible and safe, there are no evidences on better outcome.

Robotic surgical techniques is also a new technique for use in minimally invasive esophagectomy, which is commonly done as a hybrid approach coupled with laparoscopic techniques [22–25].

Table 22.1 Traditional types of esophagectomy

Resection name	Indication	Surgical resection	Disadvantages
Cervical esophageal resection	Carcinoma of the cervical esophagus	Removal of portions of the pharynx, the larynx, the thyroid gland, and portions of the proximal esophagus. This one-stage, three-phase operation requires cervical, abdominal, and thoracic incisions, and a permanent terminal tracheostomy [7, 8]	
Transhiatal esophagectomy	Cervical, thoracic, and esophagogastric junction cancers	Upper midline laparotomy incision and a left neck incision, typically without a thoracotomy. The thoracic esophagus is bluntly dissected through the diaphragmatic hiatus superiorly and via the neck inferiorly. A cervical anastomosis is created most often with a gastric pull-up approach [9, 10]	Inability to perform a full thoracic lymphadenectomy
Ivor-Lewis transthoracic esophagectomy	Cancers in the lower third of the esophagus	Laparotomy with a right thoracotomy and an intrathoracic esophagogastric anastomosis allowing a full thoracic lymphadenectomy	Leak occurring at the intrathoracic anastomosis is associated with high morbidity and mortality [11–13]
Modified Ivor-Lewis transthoracic esophagectomy	Tumors of the gastroesophageal junction	Left thoracoabdominal incision with a gastric pull-up and an esophagogastric anastomosis in the left side of the chest	High incidence of complications [14]
Tri-incisional esophagectomy		Transthoracic total esophagectomy, a lymphadenectomy and cervical esophagogastric anastomosis [15, 16]	
Esophagogastric junction resection	Esophageal cancers at the esophagogastric junction or intra-abdominal esophagus	An esophagectomy with partial gastrectomy or an extended gastrectomy, with or without thoracotomy [17, 18]	

22.3 Preoperative Preparation and Patient Selection for Minimally Invasive and Robotic Esophagectomy

Preoperative selection and patient preparation did not changed in the last decades and are crucial for esophagectomy because an esophageal resection results in a large physiologic insult to the patient. Although the mortality from esophagectomy has decreased in the last decades, adequate patient selection is an important issue of that reduction in mortality by identifying high-risk patients in whom the procedure would be too hazardous. During the preoperative evaluation, anesthesiologists have to consider many factors, including age, cardiac and pulmonary function, nutritional status, general health, medications, neoadjuvant therapy, tumor stage, and blood transfusion.

Some issue must be considered in terms of minimally invasive and robotic esophagectomy. In case of prior coronary artery bypass grafting with a patent internal thoracic artery conduit in proximity of the operative field, proper planning for minimally invasive and/or robotic esophagectomy is essential. Preoperative imaging studies are crucial in delineating the course of the internal mammary artery graft to avoid iatrogenic damage leading to cardiac ischemia. As with any thoracic operation that has the potential to jeopardize an internal mammary artery conduit, appropriate preparations should be made, including ensuring the availability of cardiac surgery, depending upon the anticipated risk.

Inflammation and lesions with dense adhesions including calcified lymph nodes, are challenging to excise and present a higher risk of damage to adjacent structures. Damage of major vessels can lead to excess bleeding or loss of ventilatory control, requiring conversion to thoracotomy. Inflammatory lung changes also create edema and fibrosis, making it difficult to divide the lung or judge whether an anatomic margin is sufficiently remote from the lesion. Inflammation causing fibrothorax can limit viewing and working space in the pleural cavity.

Anatomic chest wall deformities or an elevated hemidiaphragm can limit optimal positioning or optimal access into the thorax and should be identified when considering video-assisted thoracoscopic surgery. Robotic surgery particularly requires adequate space within the pleural cavity to allow optimal visualization and manipulation of the arms and instruments.

Manipulation of the thoracoscope and instruments through the chest wall will be easier in patients with normal or slender body habitus. Dissection may become difficult in obese patients as more adipose tissue obscures the normal planes between structures. Intra-abdominal obesity also elevates the diaphragm and reduces volume of the thoracic cavity. Robotic surgery has advantage in obese patient: the robotic arms fulcrum the instruments around a fixed point such that once the trocars are in place, the thickness of the chest wall does not affect their mobility.

However, robotic esophagectomy requires prolonged one-lung ventilation (OLV) time and obese patients usually have reduced tolerance to OLV and are encouraged to try to lose weight before the surgery. Very young patients are also not suitable for robot-assisted thoracic surgery due to their small body size and short height, which make them unfit for OLV.

Pulmonary function testing, blood gas analysis and chest X-ray can all help determine whether a patient can tolerate the prolonged OLV. Under the resting state air inhalation conditions, if conditions such as hypercapnia ($PaCO_2$ >50 mmHg), hypoxemia (PaO_2 <65 mmHg), chronic obstructive pulmonary disease (COPD), bronchospasm, asthma, or severe emphysema are detected, then the patient cannot tolerate OLV and the hypercapnia, hypoxemia and pleural positive impact caused by continuous CO_2 infusion. Therefore, these patients are not suitable for this type of surgery. Patients with moderate COPD should go through hormone and physical therapy with bronchodilators or adrenocorticotropic steroids and wait until their lung functions are improved before being considered for robot-assisted thoracic surgery. Those patients who have long smoking histories must quit smoking a few weeks prior to the surgery [26–28].

22.4 Anesthesia for Minimal Invasive and Robotic Esophagectomy

22.4.1 Induction, Maintenance, Ventilation

Minimal invasive and robotic esophagectomy is a new challenge to surgeons and anesthesiologists. The surgeon performs surgical procedures in a small space, which requires high stability of the respiratory cycle and demands regular communication and cooperation between the anesthesiologist and the surgeon. The anesthesiologist should pay attention to the impacts of prolonged operation on the circulation, oxygenation during OLV, intrathoracic pressure caused by CO_2 pneumothorax and the surgical procedure and should actively respond should these abnormalities occur. The focus of anesthesia management is to maintain the respiratory function and hemodynamic stability.

The induction of anesthesia is usually performed by intravenous induction (propofol or etomidate), while the narcotic analgesics include the most commonly used sufentanil. The muscle relaxants have a very wide range of choices, rocuronium is most commonly used. Other drugs can be used appropriately based on the patient's condition.

Mobilization of the esophagus is usually performed in the right chest either with the patient positioned in the left decubitus or prone position. As surgery is performed with thoracoscope, an inadequately collapsed lung or lobe could disturb surgery and this is important when considering the method used to achieve lung isolation. Some practical points should be discussed regarding robotic surgery for esophagectomy. Access to the patient's airway and endotracheal tube is limited, securing and positioning the endotracheal tube is crucial. If any emergency develops, it may be necessary to undock the robot and potentially reposition the patient in order to access the airway, or chest.

After successful muscle relaxation, lung isolation can be provided through a left or right double lumen tube or a single lumen tracheal tube and bronchial blocker. Right-sided double-lumen tubes are perceived to be less reliable than left-sided

tubes, because there is a greater chance of occluding the opening to the upper lobe of the right bronchus that arises a shorter distance from the carina than on the left. Intubating the bronchus opposite the side of surgery may reduce the likelihood of intraoperative tube displacement and because most techniques of minimal invasive and robotic esophagectomy involve access to the right chest, a left-sided double-lumen tube is preferable. If a bronchial blocker is chosen, this will have to be placed on the right side as the right lung must be collapsed; however, the blocker cuff may occlude the opening to the right upper lobe impairing its collapse. Although sometimes use of bronchial blocker may be necessary (e.g. in cases of difficult intubation), author suggests that during minimal invasive and robotic esophagectomy use of left-sided double-lumen tube is the best choice. Whichever method of lung isolation is selected, a fibre-optic bronchoscope should be used to confirm correct positioning both after intubation and after moving the patient before surgery. However, a new generation of double lumen tubes with integrated high-resolution camera is also available. It helps visualizing the carina continuously, which could reduce the need for a routine fiber-optic bronchoscopy and intraoperative displacement can be diagnosed immediately and corrected.

Anesthesia can be maintained by continuous intravenous infusion of propofol and remifentanil, or targeted controlled infusion of propofol with a final plasma concentration of 1–1.5 μg/mL and remifentanil with a final plasma concentration of 5–10 ng/mL with guidance of bispectral index (BIS) while the anesthetic depth can be controlled by adjusting the concentration of sevoflurane inhalation. Muscle relaxants can be injected intermittently and intravenously according to the requirements of muscle relaxation. Thirty minutes before the completion of surgery, inhalation of anesthetics should be discontinued, and the intravenous anesthetic propofol and narcotic analgesic remifentanil infusion rates are gradually should be decreased as guided by the hemodynamic parameters to maintain the proper depth of anesthesia. Meanwhile, a single intravenous injection of sufentanil (5–15 μg) or a non-steroidal anti-inflammatory analgesic can be performed. At the end of the surgery, intravenous infusions of anesthetics and narcotic analgesics are stopped. Because this anesthesia method adopts intravenous infusion or injection of the drugs at the induction and awakening stages while adopting a combined intravenous and inhalational application of the drugs in the maintenance stage, it is also called “the sandwich technique”. This anesthesia technique can ensure early extubation and rapid patient recovery. Anesthesia for robotic esophagectomy should appropriately limit the uses of opioids, benzodiazepines and muscle relaxants. The application of midazolam to maintain anesthesia intraoperatively is not recommended to facilitate early postoperative extubation. Remifentanil can provide hemodynamic stability and has a better inhibitory effect on the stress response than the traditionally used opioids. In addition, remifentanil has no delay of postoperative respiratory depression and no need of prolonged postoperative ventilator support and, thus, is more reasonable for use in maintaining anesthesia in robot-assisted thoracic surgery than fentanyl or sufentanil.

There are other factors during the anesthesia which have influence on postoperative period after esophagectomy. Although the incidence of anastomotic complications

decreased in the last decades, anastomotic complications and perfusion of the conduit are important issues after esophagectomy, as it has been accounted for 37% of all hospital death after esophagectomy. Thoracic anastomoses have lower leak rate than cervical anastomoses but have higher morbidity and mortality.

One of the factors that are playing role in the incidence of anastomotic leaks is conduit ischemia. Appropriate tissue oxygenation depends on several variables: vascular anatomy and tone and blood oxygen tension. How can anesthesiologist improve blood supply of the conduit? Thoracic epidural anesthesia and the use of prostaglandins have influence on gastric vasomotor tone; the use of intravenous nitroglycerin and venous bloodletting can reduce venous congestion. Systemic hypotension may impair gastric tube perfusion and must be treated. The use of vasoconstrictors in normovolemic condition has no detrimental effect on gastric blood flow, and the use of short-acting vasopressors as phenylephrine or ephedrine is safe and not associated with postoperative anastomotic leak. Norepinephrine may be a better option than phenylephrine as it more readily preserves cardiac output and produces less splanchnic vasoconstriction and a lesser rise in lactate concentrations than phenylephrine. The notion of completely avoiding vasopressor boluses or infusions is unfounded and likely results in excess fluid administration, a known precipitant of morbidity. However, vasopressor infusions are rarely necessary intraoperatively even when providing epidural anesthesia; although, they are almost universally required during the first postoperative night. It is recommended to use low-dose norepinephrine infusions during the first postoperative night to counteract the epidural sympathectomy and avoid overhydration. We have to note, that before the use of vasopressors hypovolemia should always be excluded.

Another important anesthesia technique which has influence on postoperative outcome and complication is ventilation during esophagectomy. Minimal invasive and robotic esophagectomy often requires prolonged one-lung ventilation. It has been demonstrated that lung-protective ventilation with small tidal volume and with the use of moderate PEEP provides sufficient oxygenation during OLV and resulted in reduced inflammatory response after esophagectomy, improved lung function, and earlier extubation These findings have recently been reconfirmed in a randomized control trial comparing protective ventilation with tidal volumes of 5 ml/kg and positive end-expiratory pressure (PEEP) during three-hole minimally invasive esophagectomy, which demonstrated reduced PPC when compared with tidal volumes of 8 ml/kg and no PEEP. Additionally, continuous positive airway pressure (CPAP) applied to the collapsed lung during the intrathoracic stage of esophagectomy reduces local inflammation in the collapsed lung and may therefore be a strategy to further reduce lung injury. These strategies, coupled with mild permissive hypercapnea and attempts to limit the duration of OLV, should now be routine for OLV during the intrathoracic portion of esophagectomy procedures. A PEEP level of 5 cm H_2O has been shown to be insufficient during OLV in patients with relatively normal lung function. Individualized PEEP levels should therefore be determined by optimizing dynamic lung compliance in a PEEP titration study after a recruitment maneuver.

Minimal invasive and robotic esophagectomy often requires continuous blowing of CO_2 into the ipsilateral chest. This artificial pneumothorax used to reduce the incidence of air embolism while facilitating lung collapse, revealing the surgical field. The pressure of this artificial pneumothorax is usually 5–12 mmHg. CO_2 can absorb to the blood causing increased CO_2 levels in the blood. OLV also can lead to accumulation of CO_2 and this elevated CO_2 level may have a significant impact on a severely ill patient. On other hand, artificial pneumothorax may sometimes lead to tension pneumothorax, giving rise to significantly decreased venous return and hypotension. During the surgery, the air blowing pressure, airway pressure, exhaled tidal volume and central venous pressure should be monitored in real time. Central venous pressure monitoring helps to assess the impact of artificial CO_2 pneumothorax, while direct monitoring of the pleural cavity pressure can avoid excessive pressure-induced tension pneumothorax. Anesthesiologists must consider that CO_2 pneumothorax can reduce cardiac output by 10–30% due to increased vena cava pressure induced by the increased intrathoracic pressure, increased venous resistance, retention in the venous blood, and others. The reduction in reflux is proportional to the decrease of the cardiac output. OLV induces lung V/Q imbalance, increases pulmonary artery pressure and also reduces cardiac output; CO_2 pneumothorax elevates mediastinal pressure, inhibits systolic and diastolic functions and accelerates the accumulation of CO_2 in the body, leading to acidosis, which is manifested by decreased blood pressure and high heart rate. The blood pressure can be raised by rapid fluid replacement and vasopressor application via appropriate uses of phenylephrine or dopamine. Some believe that appropriately controlling the infusion amount can reduce exudate in the surgical field and can make it easier to operate; in the absence of massive bleeding, infusion of excessive liquid is indeed unnecessary [29–41].

22.4.2 Fluid Management

Fluid management is also crucial for all thoracic surgeries including esophagectomy. Association between excess perioperative fluid therapy combined with hypoalbuminemia, which is common in patients undergoing esophagectomy, and respiratory complication after esophagectomy is well established. Hypervolemia precipitates acute lung injury and anastomosis leak. However, restrictive fluid management can lead to hypovolemia resulting ischemia in conduit. Determining which patients require more volume remains a challenge as commonly proposed mechanisms of stroke volume variation and pulse pressure variation are not predictive of fluid responsiveness after abdominothoracic esophagectomy and have not been validated in the open chest setting. Correspondingly, goal-directed fluid therapy only achieved a level C recommendation in a recent evidence-based guideline for esophagectomy [17, 18]. While intuitively intriguing, the role of noninvasive cardiac output monitors in the absence of supportive evidence at present is likely limited to optimization at the start of the operation prior to commencement of the intrathoracic portion. On the basis of the above, it appears reasonable to provide maintenance

fluids of 2–3 ml/kg/h and replace blood losses with an appropriate volume of crystalloid or colloid to achieve a total intraoperative fluid volume of at least 3 ml/kg/h but not exceeding 10 ml/kg/h. It means, that anesthesiologists should consider a restrictive fluid administration in the first 24 h (<20 ml/kg, less than 2 L crystalloid and less than 1 L albumin intraoperatively with less than 3 L of total amount of crystalloids in the first 24 h) Therefore, close monitoring of intravascular volume status is required, along with invasive hemodynamic monitoring (arterial blood pressure, central venous pressure, thermodilution techniques) and urine output.

Routine monitoring should include pulse oximetry, noninvasive blood pressure monitoring, and electrocardiography. Since many patients presenting for esophageal surgery have comorbid disease of the cardiovascular and respiratory systems, consideration should be given to invasive monitors where appropriate. With the exception of patients with advanced cardiovascular or pulmonary disease, routine intraoperative monitors will generally suffice for those patients presenting for endoscopic and minimally invasive procedures limited to the abdominal cavity. Transthoracic approaches to the esophagus generally mandate a more aggressive approach to monitoring. An indwelling arterial catheter for continuous measurement of systemic arterial blood pressure is the standard of care for these procedures.

Surgical manipulation of thoracic and mediastinal structures can profoundly affect determinants of cardiac performance including venous return and cardiac filling and may contribute to the development of dysrhythmias, all of which can compromise cardiac output and hemodynamic status. In addition, many of these procedures require lung isolation and OLV, a ventilation strategy which substantially limits arterial oxygenation. Surgical dissection can lead to unexpected bleeding, occasionally massive in nature. Point of care testing of arterial blood samples can aid in the assessment and maintenance of adequate arterial oxygenation, acid base status, as well as hemoglobin and electrolyte concentrations.

Euthermia can be achieved by use of commercially available forced warm air heating blankets and fluid warmers.

Special attention must be made during positioning of the patient, as the heavy robot is typically located directly over the patient in order to dock correctly and strict attention must be made to pad all exposed pressure points. In lateral decubitus position slightly greater arm extension may needed, thus placing the brachial plexus as risk [42–46].

22.4.3 Blood Administration

Regardless of the specific approach (transthoracic versus transhiatal), esophagectomy with lymphadenectomy represents a major operation with a mean operative blood loss of 3–500 ml approximately. The use of neoadjuvant chemotherapy can cause bone marrow suppression and anemia in patients undergoing esophagectomy. All of these factors require consideration of administration of blood transfusion in the perioperative period. Nevertheless, there are evidences that blood transfusion

may worsen the oncologic outcome, though these reports were uncontrolled. Patients who received blood transfusion have had larger tumors, more sever medical conditions. Therefore, the relationship between cancer recurrence and death has not been clearly proven.

The ideal perioperative hemoglobin level is not clear. Keeping the hemoglobin level above 100 g/l is poorly supported with evidences. Recently, in hemodynamically stable patients, the transfusion trigger is 70 g/l. There are evidences that the use of allogenic blood transfusion decreases survival and increases the incidence of cancer recurrence, compared with the use of autologous transfusion [47, 48].

22.4.4 Analgesia

Effective analgesia after esophagectomy is a challenging issue in anesthesia. Analgesia for thoracic procedures has been discussed extensively in another chapter of this book. However, it is important to remember that sympathetic activation caused by surgical procedure and pain manifests as tachycardia, hypertension, and increased contractility, all of which result in increased myocardial oxygen consumption. As it has been noted, most of the patients undergoing esophagectomy have cardiovascular coexisting diseases, especially ischemic heart disease (IHD). These patients' response to surgical stress differs from that of healthy patients. Sympathetic stimulation caused by pain may constrict post-stenotic coronary arteries and reduce blood supply to the subendocardium. The difference in oxygen delivery and demand presents as postoperative myocardial ischemia. The selective sympathectomy using thoracic anesthesia in patients with IHD can dilate constricted coronary vessels, reduce heart rate, and improve cardiac function by reducing preload and afterload and optimizing myocardial oxygen delivery. The sympathectomy of thoracic epidural analgesia causes vasodilatation in mesenteric vessels and has been shown to improve bowel function by reducing the duration of postoperative ileus, enhancing bowel blood. The increase in bowel motility from unopposed parasympathetic activity is not associated with any significant increase in anastomotic dehiscence.

In patients in whom thoracic epidural analgesia is contraindicated, there are several alternative methods. Using intercostal nerve block a catheter is placed in a paravertebral space just below the level of incision. Effectiveness of this method is mostly similar to epidural analgesia. Intravenous opioids and nonsteroid analgesics can work synergistically and can reduce postoperative pain [49–54].

22.5 Postoperative Care After Esophagectomy: Enhanced Recovery After Esophagectomy

The enhanced recovery after surgery (ERAS) program, also known as fast track surgery, is a patient-centered, surgeon-led system combining anesthesia, nursing, nutrition and psychology, which was initiated in the 1990s. However, ERAS developed relatively late in esophagectomy (2014) due to its surgical complexity and high morbidity of postoperative complications. Recently, use of minimally invasive

technique, attention to organ function protection concepts and improvement of gastric conduit and anastomosis techniques allows enhanced recovery program after esophagectomy. ERAS can minimize stress response, reduce postoperative pulmonary complications, and improve patient outcome, decrease hospital stay and reduce hospital costs [55].

22.5.1 Timing of Extubation and Supplemental Oxygen Therapy

Timing of extubation is a crucial issue after esophagectomy. Basically there are two concepts of extubation after esophagectomy: prolonged ventilation and early extubation. Before the introduction of thoracic epidural analgesia, studies suggested prolonged postoperative ventilation up to 2 days. However, prolonged ventilation has not been shown to decrease incidence of postoperative pulmonary complications. Moreover, there are disadvantages of this approach: sedation-related side effects, risk of aspiration, and weaning problems.

Use of thoracic epidural analgesia and shorter operative time, early extubation has been advocated to reduce mortality, morbidity, and cost after esophagectomy. Early extubation may reduce intensive stay and cost, decreases postoperative respiratory complications, and does not increase the risk of reintubation.

However, there are conditions that could require prolonged ventilation: bleeding, hemodynamic instability, respiratory insufficiency, and neurologic impairment.

After extubation supplemental oxygen administration should be used either by face mask or nasal cannula (1–6 l/min) for maintaining of oxygen saturation above 90%. Supplemental oxygen has advantages after esophagectomy: decreased incidence of postoperative nausea and vomiting, improved wound healing, maintenance of adequate cardiac and central nervous function, and decreased incidence of arrhythmias. There are data that low oxygen delivery after esophagectomy is associated with the risk of complications [56–58].

22.5.2 Deep Vein Thrombosis Prophylaxis

Postoperatively, a majority of thoracic surgery patients are not able to move because of pain, respiratory distress, and age. The lack of ambulation can result in a blood stasis in lower extremities; this increases the contact time between blood and vein wall irregularities, helping a blood clot formation. The incidence of deep venous thrombosis in patients in medical and surgical intensive care units is about 10–30%. Prophylaxis with mechanical (compression stockings are applied to both lower extremities) and pharmacological methods (heparin shots are given subcutaneously twice a day) has been shown to be effective and safe in most types of surgery and should be routinely implemented. Both subcutaneous, low-dose unfractionated heparin (LDUH) and low molecular-weight heparin (LMWH) have been shown to reduce the risk of venous thrombosis. Low-dose unfractionated heparin use does not interfere with epidural catheter placement or removal. However, LMWH should be held for 12–24 h before epidural placement or removal, to decrease the risk of

hematoma formation. The use of LMWH for 2–3 weeks after hospital discharge in patients undergoing major cancer surgery may reduce the incidence of asymptomatic deep venous thrombosis. Until patients are ambulating independently, they should keep the stockings on when in bed. Encourage early ambulation as well as leg and ankle exercises. Early mobilization of patients includes getting them out of bed to a chair the first postoperative day and three times each day thereafter [59, 60].

22.5.3 Management of Drainage Tubes

Chest tubes are indwelling catheters placed into the pleural space to evacuate air and fluids and maintain a physiological negative pleural pressure. Air collects at the less dependent part (apically or retrosternal, depending on patient's position), and fluid collects at the lower part of the chest cavity. That's why most guideline recommends the use of two chest tubes.

However, chest tubes can impair patient mobilization, cause pain, and increase the risk of infection. Early chest tube removal improves lung function after thoracic surgical procedures. It also reduces pain, allows early mobilization of the patient, and results in shorter hospital stay. Therefore, early chest drain removal represents an important element of ERAS protocol in esophageal surgery.

In the absence of air leak (50 ml/min in 12 h or less than 20 ml/min in 8 h), most postoperative chest tube removal protocol is based on quantity and quality of secretions. If bleeding, chylothorax, or empyema does not exist, the normal daily pleural secretion is about 350 ml. Most surgeons remove chest drains if the daily secretion is less than 300 ml.

If an air leak exists, a digital drainage system with continuous suction with (minus 15 cm H_2O) is recommended. If air leak reach less than 50 ml/min in 12 h or 20 ml/min in 8 h, chest tubes are removable.

As chest tubes are playing major role in postoperative pain, their early removal appears to accelerate postoperative recovery [61, 62].

Digital drainage systems have several advantages over a traditional water seal: they are light, compact and have a built-in suction pump so there is no need to attach to wall suction, favoring early patient mobilization and able to objectively display the volume of air leak. There are evidences, that digital systems are associated with reduced chest tube time, length of stay, air leak duration and costs. The use of digital drainage systems is therefore to be recommended as they remove variability in clinical decision-making and facilitate early mobilization while positively influencing patient outcomes.

22.5.4 Physiotherapy

Early mobilization and physiotherapy are intuitive components of ERAS and are meant to counteract the deleterious effects of immobilization. Postoperative immobility is associated with increased morbidity and length of stay following esophagectomy.

Therefore, patients should be mobilized as soon as possible, and certainly within 24 h of surgery, to avoid the deleterious effects of bed rest.

Respiratory complications are frequent after esophagectomy. The benefits of physiotherapy in the perioperative period have been shown by numerous studies. It has been showed that preoperative physiotherapy (e.g., inspiratory muscle training) for two or more weeks before cardiac surgery reduced the incidence of pulmonary complications. Preoperative physiotherapy is also feasible for patients undergoing esophagectomy to preserve respiratory muscle strength.

There are two main types of breathing exercises: active cycles of breathing and using incentive spirometry. Both techniques aim to re-expand the lung with maximum sustained and fractional inspiration and clear airways with assisted cough. For both types of exercises, patients must be in upright position either in bed or chair. During active cycle of breathing, patients must place hand over upper abdomen and take slow deep breaths and hold for 3–5 s and repeat four to five times. After this cycle, the patient has to huff as this maneuver helps move phlegm to clear. Using incentive spirometer, patient inhales from the spirometer and holds breath as long as it is possible. This should be practiced up to 10 breaths per h. It is important to mobilize patients as soon as possible after esophagectomy to prevent postoperative complications such as pneumonia and deep vein thrombosis. At the first day, the aim is to sit in chair that can help to improve lungs by increasing the depth of each breath. By the second postoperative day, patients should aim to walk with assistance on the ward and increase gradually the exercise tolerance. Due to the wound and chest drains, patients may be reluctant to move arm on the operated side. It is important to practice shoulder mobility to prevent joint stiffness [63–65].

22.5.5 Pain Management

For adequate physiotherapy and early mobilization correct pain management is indispensable. Thoracic epidural analgesia is considered the gold standard technique for pain control after thoracic surgery and an essential part of ERAS protocols after esophagectomy. In comparison with conventional analgesia techniques, TEA provides superior analgesia for postthoracotomy pain, attenuates surgical stress response, having a positive impact on postoperative recovery. However, TEA has several disadvantages including hypotension, urinary retention, and muscular weakness. It can be overcome by performing thoracic paravertebral block (PVB). Recent meta-analysis and systematic reviews confirmed that PVB provides comparable analgesia to the TEA, but with statistically significant lower incidence of side effects, suggesting PVB as analgesic technique for major thoracic surgery [66].

22.6 Conclusions

Although complications reduced in the last decades, esophageal resection remains one of the most high risk procedure. Perioperative care for esophageal surgery is a very complex process, which has key elements as fluid management, lung protective

ventilatory strategy with low tidal volume, pain management using epidural and perioperative physiotherapy. Multidisciplinary team work, careful patient selection and well trained anesthesiologist are the key elements of improvement of outcome.

References

1. Mariette C, Piessen G, Triboulet JP. Therapeutic strategies in esophageal carcinoma: role of surgery and other modalities. Lancet Oncol. 2007;8(6):545–53.
2. Holmes RS, Vaughan TL. Epidemiology and pathogenesis of esophageal cancer. Semin Radiat Oncol. 2007;17(1):2–9.
3. Hirst J, Smithers BM, Gotley DC, Thomas J, Barbour A. Defining cure for esophageal cancer: analysis of actual 5-year survivors following esophagectomy. Ann Surg Oncol. 2011;18(6):1766–74.
4. Miyata H, Yamasaki M, Kurokawa Y, et al. Multimodal treatment for resectable esophageal cancer. Gen Thorac Cardiovasc Surg. 2011;59(7):461–6.
5. Narsule CK, Montgomery MM, Fernando HC. Evidence-based review of the management of cancers of the gastresophageal junction. Thorac Surg Clin. 2012;22(1):109–21.
6. Lagarde SM, Vrouenraets BC, Stassen LP, van Lanschot JJ. Evidence-based surgical treatment of esophageal cancer: overview of high-quality studies. Ann Thorac Surg. 2010;89(4):1319–26.
7. Daiko H, Hayashi R, Saikawa M, et al. Surgical management of carcinoma of the cervical esophagus. J Surg Oncol. 2007;96(2):166–72.
8. Peracchia A, Bonavina L, Botturi M, Pagani M, Via A, Saino G. Current status of surgery for carcinoma of the hypopharynx and cervical esophagus. Dis Esophagus. 2001;14(2):95–7.
9. Macha M, Whyte RI. The current role of transhiatal esophagectomy. Chest Surg Clin N Am. 2000;10(3):499–518.
10. Hulscher JB, Tijssen JG, Obertop H, van Lanschot JJ. Transthoracic versus transhiatal resection for carcinoma of the esophagus: a meta-analysis. Ann Thorac Surg. 2001;72(1):306–13.
11. Müller JM, Erasmi H, Stelzner M, Zieren U, Pichlmaier H. Surgical therapy of esophageal carcinoma. Br J Surg. 1990;77(8):845–57.
12. Mathisen DJ, Grillo HC, Wilkins EW Jr, Moncure AC, Hilgenberg AD. Transthoracic esophagectomy: a safe approach to carcinoma of the esophagus. Ann Thorac Surg. 1988;45(2):137–43.
13. Visbal AL, Allen MS, Miller DL, Deschamps C, Trastek VF, Pairolero PC. Ivor Lewis esophagogastrectomy for esophageal cancer. Ann Thorac Surg. 2001;71(6):1803–8.
14. Krasna MJ. Left transthoracic esophagectomy. Chest Surg Clin N Am. 1995;5(3):543–54.
15. Swanson SJ, Sugarbaker DJ. The three-hole esophagectomy. The Brigham and Women's Hospital approach (modified McKeown technique). Chest Surg Clin N Am. 2000;10(3):531–52.
16. Swanson SJ, Batirel HF, Bueno R, et al. Transthoracic esophagectomy with radical mediastinal and abdominal lymph node dissection and cervical esophagogastrostomy for esophageal carcinoma. Ann Thorac Surg. 2001;72(6):1918–24.
17. Ito H, Clancy TE, Osteen RT, Swanson RS, et al. Adenocarcinoma of the gastric cardia: what is the optimal surgical approach? J Am Coll Surg. 2004;199(6):880–6.
18. Schiesser M, Schneider PM. Surgical strategies for adenocarcinoma of the esophagogastric junction. Recent Results Cancer Res. 2010;182:93–106.
19. Davis PA, Law S, Wong J. Colonic interposition after esophagectomy for cancer. Arch Surg. 2003;138(3):303–8.
20. Akiyama H, Miyazono H, Tsurumaru M, Hashimoto C, Kawamura T. Use of the stomach as an esophageal substitute. Ann Surg. 1978;188(5):606–10.
21. Foker JE, Ring WS, Varco RL. Technique of jejunal interposition for esophageal replacement. J Thorac Cardiovasc Surg. 1982;83(6):928–33.
22. Santillan AA, Farma JM, Meredith KL, Shah NR, Kelley ST. Minimally invasive surgery for esophageal cancer. J Natl Compr Canc Netw. 2008;6(9):879–84.

23. Biere SS, van Berge Henegouwen MI, Maas KW, et al. Minimally invasive versus open esophagectomy for patients with esophageal cancer: a multicentre, open-label, randomised controlled trial. Lancet. 2012;379(9829):1887–92.
24. Bartels K, Fiegel M, Stevens Q, Ahlgren B, Weitzel N. Approaches to perioperative care for esophagectomy. J Cardiothorac Vasc Anesth. 2015;29(2):472–80.
25. van der Sluis PC, van Hillegersberg R. Robot assisted minimally invasive esophagectomy (RAMIE) for esophageal cancer. Best Pract Res Clin Gastroenterol. 2018;36-37:81–3.
26. Akutsu Y1, Matsubara H. Perioperative management for the prevention of postoperative pneumonia with esophageal surgery. Ann Thorac Cardiovasc Surg. 2009;15(5):280–5.
27. Donington JS. Preoperative preparation for esophageal surgery. Thorac Surg Clin. 2005;15(2):277–85.
28. Herbella FAM, Zamuner M, Patti MG. Esophagectomy perianesthetic care from a surgeon's point of view. SOJ Anesthesiol Pain Manag. 2014;1(1):1–7.
29. Carney A, Dickinson M. Anesthesia for esophagectomy. Anesthesiol Clin. 2015;33:143–63.
30. Lee JR. Anesthetic considerations for robotic surgery. Korean J Anesthesiol. 2014;66(1):3–1131.
31. Campos HJ. An update on robotic thoracic surgery and anesthesia. Curr Opin Anaesthesiol. 2010;23:1–6.
32. Zhang Y, Wang S, Sun Y. Anaesthesia for robotic thoracic surgery. Ann Transl Med. 2015;3(5):71.
33. Durkin C, Schisler T, Lohser J. Current trends in anesthesia for esophagectomy. Curr Opin Anesthesiol. 2017;30:30–5.
34. Steenwyk B, Lyerly R 3rd. Advancements in robotic-assisted thoracic surgery. Anesthesiol Clin. 2012;30(4):699–708.
35. Veelo DP, Geerts BF. Anaesthesia during esophagectomy. J Thorac Dis. 2017;9(Suppl 8):S705–12.
36. Lohser J, Slinger P. Lung injury after one-lung ventilation: a review of the pathophysiologic mechanisms affecting the ventilated and collapsed lung. Survey Anesthesiol. 2016;60:98–9.
37. Shen Y, Zhong M, Wu W, et al. The impact of tidal volume on pulmonary complications following minimally invasive esophagectomy: a randomized and controlled study. J Thorac Cardiovasc Surg. 2013;146:1267–74.
38. Verhage RJ, Boone J, Rijkers GT, et al. Reduced local immune response with continuous positive airway pressure during one-lung ventilation for esophagectomy. Br J Anaesth. 2014;112:920–8.
39. Ferrando C, Mugarra A, Gutierrez A, et al. Setting individualized positive endexpiratory pressure level with a positive end-expiratory pressure decrement trial after a recruitment maneuver improves oxygenation and lung mechanics during one-lung ventilation. Anesth Analg. 2014;118:657–65.
40. Michelet P, D'Journo XB, Roch A, Doddoli C, Marin V, Papazian L, Decamps I, Bregeon F, Thomas P, Auffray JP. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. Anesthesiology. 2006;105(5):911–9.
41. Végh T, Juhász M, Szatmári S, Enyedi A, Sessler DI, Szegedi LL, Fülesdi B. Effects of different tidal volumes for one-lung ventilation on oxygenation with open chest condition and surgical manipulation: a randomised cross-over trial. Minerva Anestesiol. 2013;79(1):24–32.
42. Ashes C, Slinger P. Volume management and resuscitation in thoracic surgery. Curr Anesthesiol Rep. 2014;4:386–96.
43. Chau EH, Slinger P. Perioperative fluid management for pulmonary resection surgery and esophagectomy. Semin Cardiothorac Vasc Anesth. 2014;18(1):36–44.
44. Kita T, Mammoto T, Kishi Y. Fluid management and postoperative respiratory disturbances in patients with transthoracic esophagectomy for carcinoma. J Clin Anesth. 2002;14(4):252–6.
45. Casado D, López F, Martí R. Perioperative fluid man-agement and major respiratory complications in patients undergoing esophagectomy. Dis Esophagus. 2010;23(7):523–8.
46. Raphael J, Regali LA, Thiele RH. Hemodynamic monitoring in thoracic surgical patients. Curr Opin Anaesthesiol. 2017;30(1):7–16.

47. Motoyama S, Okuyama M, Kitamura M, et al. Use of autologous instead of allogeneic blood transfusion during esophagectomy prolongs disease-free survival among patients with recurrent esophageal cancer. J Surg Oncol. 2004;87(1):26–31.
48. Hébert PC, Wells G, Blajchman MA. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med. 1999;340(6):409–17.
49. Clemente A, Carli F. The physiological effects of thoracic epidural anesthesia and analgesia on the cardiovascular, respiratory and gastrointestinal systems. Minerva Anestesiol. 2008;74(10):549–63.
50. Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. Br J Anaesth. 2011;107(6):859–68.
51. Sentürk M, Ozcan PE, Talu GK, et al. The effects of three different analgesia techniques on long term postthoracotomy pain. Anesth Analg. 2002;94(1):11–5.
52. Komatsu R, Makarova N, Dalton JE, et al. Association of thoracic epidural analgesia with risk of atrial arrhythmias after pulmonary resection: a retrospective cohort study. J Anesth. 2015;29(1):47–55.
53. Hanna MN, Murphy JD, Kumar K, Wu CL. Postoperative pain management in the elderly undergoing thoracic sur-gery. Thorac Surg Clin. 2009;19(3):353–61.
54. Kingma BF, Visser E, Marsman M, Ruurda JP, van Hillegersberg R. Epidural analgesia after minimally invasive esophagectomy: efficacy and complication profile. Dis Esophagus. 2019;32(8):1.
55. Parise P, Ferrari C, Cossu A, et al. Enhanced recovery after surgery (ERAS) pathway in esophagectomy: is a reasonable prediction of hospital stay possible? Ann Surg. 2019;270:77.
56. Shackford SR, Virgilio RW, Peters RM. Early extubation versus prophylactic ventilation in the high risk patient: a comparison of postoperative management in the prevention of respiratory complications. Anesth Analg. 1981;60(2):76–80.
57. Caldwell MT, Murphy PG, Page R, Walsh TN, Hen-nessy TP. Timing of extubation after esophagectomy. Br J Surg. 1993;80(12):1537–9.
58. Robertson SA, Skipworth RJ, Clarke DL, Crofts TJ, Lee A, de Beaux AC, Paterson-Brown S. Ventilatory and intensive care requirements following esophageal resection. Ann R Coll Surg Engl. 2006;88(4):354–7.
59. Rollins KE, Peters CJ, Safranek PM, Ford H, Baglin TP, Hardwick RH. Venous thromboembolism in esophago-gastric carcinoma: incidence of symptomatic and asymptomatic events following chemotherapy and surgery. Eur J Surg Oncol. 2011;37(12):1072–7.
60. Thodiyil PA, Walsh DC, Kakkar AK. Thromboprophylaxis in the cancer patient. Acta Haematol. 2001;106(1–2):73–80.
61. Zardo P, Busk H, Kutschka I. Chest tube management: state of the art. Curr Opin Anaesthesiol. 2015;28(1):45–9.
62. Coughlin SM, Emmerton-Coughlin HM. Malthaner. Management of chest tubes after pulmonary resection: a systematic review and meta-analysis. Can J Surg. 2012;55(4):264–70.
63. Nakatsuchi T, Otani M, Osugi H, Ito Y, Koike T. The necessity of chest physical therapy for thoracoscopic esophagectomy. J Int Med Res. 2005;33(4):434–41.
64. Lunardi AC, Cecconello I, Carvalho CR. Postoperative chest physical therapy prevents respiratory complications in patients undergoing esophagectomy. Rev Bras Fisioter. 2011;15(2):160–5.
65. Overend TJ, Anderson CM, Lucy SD, Bhatia C, Jonsson BI, Timmermans C. The effect of incentive spirometry on postoperative pulmonary complications: a systematic review. Chest. 2001;120(3):971–8.
66. Feltracco P, Bortolato A, Barbieri S, Michieletto E, Serra E, Ruol A, Merigliano S, Ori C. Perioperative benefit and outcome of thoracic epidural in esophageal surgery: a clinical review. Dis Esophagus. 2018;31(5)

Tracheal and Bronchial Surgery: HJFV

23

Radu Stoica and Ioan Cordos

Abbreviations

3D	Tridimensional
BIS	Bispectral index
DLT	Double lumen tube
ECMO	Extracorporeal membrane oxygenation
EEG	Electroencephalogram
ETT	Endotracheal tube
HFJV	High frequency jet ventilation
ILTS	Idiopathic laryngotracheal stenosis
MPR	Multiplanar reconstruction
PEEP	Positive end-expiratory pressure
PIP	Peak inspiratory pressure
PITS	Post-intubation tracheal stenosis
TIVA	Total intravenous anesthesia
TEF	Tracheoesophageal fistulas
VE	Virtual bronchoscopy

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23.1 Introduction

Any tracheal segment, from the cricoid cartilage to the carina, if it measures less than half the length of the trachea, can be safely resected by a trained team of surgeons and anesthetists [1, 2]. Carinal resections may be accompanied by the partial resection of the main bronchus, with or without lobectomy or pneumonectomy. There are differences in anesthetic techniques, depending on the type of resection: whether proximal, median or carinal, with bronchial reconstruction. Ventilation is different from the other types of anesthesia in thoracic surgery. And it is not only about the interference with the main way of ensuring the gas exchange during the general anesthesia. Having specific technical equipment and materials, acquiring the appropriate skills by the anesthetic team and, not least, a perfect coordination of the anesthetic and surgical times are mandatory.

23.2 Etiology: Post-tracheostomy Tracheal Stenoses Are on the Rise

Prolonged tracheal intubation is, by tradition, the main cause of laryngotracheal stenosis [3], whose incidence has taken an obvious downward trend since the introduction of the low pressure endotracheal tubes [4]. The incidence of these types of lesions, varying between 6% and 21%, is difficult to assess, given that stenotic lesions may take months or even years to develop after the moment of intubation [5]. *The increasingly large number of critical patients with classical or percutaneous tracheostomy makes it likely to become the first cause of benign laryngotracheal stenosis to require surgical resection* [6, 7]. Tracheobronchial resections for other benign stenoses are less frequent (below 1%), the most highly cited being the tracheal infections (bacterial, tuberculosis etc.), idiopathic and collagen vascular diseases [8]. The tumoral pathology is much more diverse, including primary or secondary tumors of the large airways, with a 0.2% incidence of respiratory malignant lesions [9], like in tumoral extensions, mostly in the lung or the thyroid. Table 23.1 illustrates a comparison between the etiology of 901 cases at the Massachusetts General Hospital in 28 years [10] and of the 284 cases of tracheobronchial resection performed at the Marius Nasta Institute of Pulmonology from Bucharest (Romania) in the past 18 years.

23.3 Does the Surgery of the Large Airways Require Special Equipment?

During anesthesia predictable or unpredictable situations may occur that make gas exchanges difficult to achieve. The decisions and reactions of the anesthetic and surgical teams must be quick and optimal, while all technical devices should be available in the operating room (Table 23.2). Aside from the usual equipment needed in thoracic surgery for general anesthesia (including fiberbronchoscope,

Table 23.1 Etiology of tracheal stenoses operated at the Massachusetts General Hospital (28 years) and at the National Institute of Pulmonology Bucharest (18 years)

Massachusetts General Hospital 1975–2003 (901 patients)	National Institute of Pulmonology Bucharest 2000–2017 (284 patients)
Post-intubation tracheal stenosis (PITS): 589 patients Tumors: 208 patients Idiopathic laryngotracheal stenosis (ILTS): 83 patients Tracheoesophageal fistulas (TEF): 21 patients	PITS 185 – Subglottic 69 – Tracheal 116 Primitive neoplasia 31 – Thyroid invasion 21 – Lung 7 – Metastatic 3 Benign tumors or ILT 7 – TEF 14 – Post-traumatic 2 – Post-tuberculosis 3 – Other 11

Table 23.2 Additional equipment needed in the operating room in tracheobronchial resections

- Flexible, wired tracheal tubes of different sizes and lengths (for unilateral bronchial intubation)
- ETT connectors and extenders for "cross-field" intubation
- Laryngeal masks
- High frequency jet ventilator (HFJV) with separate plugs for oxygen and air
- Jet ventilator catheters
- EZ-blocker [13]
- Equipment for interventional bronchology (tracheoscopes, connectors, etc.)
- "Rescue therapy":
  - Second ventilator (rare situations of independent lung ventilation)
  - Extracorporeal assist device (ECMO)

high-flow oxygen anesthesia machine, double lumen tubes, flexible wires endotracheal tube, etc.), the equipment for High Frequency Jet Ventilation (HFJV) is mandatory. The centers specialized in such interventions should be equipped with an extracorporeal assist device for oxygenation for a potential "rescue therapy", preferably the device for extracorporeal membrane oxygenation (ECMO), with staff trained to apply this method [11]. A second anesthesia or ventilation machine may be needed, rarely, during carinal resections when one-lung ventilation fails to provide sufficient oxygenation [12].

23.4 General Anesthesia: Always Necessary?

General anesthesia, whether intravenous or with inhalation, sometimes combined or used successively, is indicated in most cases and used in all centers with experience in tracheal surgery [14, 15]. Total intravenous anesthesia (TIVA) infusion is commonly used during HFJV and apneic episodes. The inhalational substances are the usual ones (mainly Sevoflurane), just like the intravenous ones (propofol, etomidate, ketamine, short acting opioids and muscle relaxants), so the choice and administration thereof

are at the discretion of the anesthetist. When the surgical approach is performed by thoracotomy, a regional technique may be added on (epidural or paravertebral analgesia) which helps with both faster recovery and earlier extubation at the end of the surgery [16]. Basic monitoring is applied [17], usually supplemented by a left radial arterial catheter to avoid interferences due to interception of the innominate artery. If the surgery is major or the cardiovascular conditions require it, a central venous catheter may be placed if it does not interfere with the operating field. Inserting a gastric tube, to be suppressed before extubation, is helpful in detecting the esophagus during the tracheal dissection. Given the potential periods with poor ventilation (hypoxemia, permissive hypercapnia, apnea) when the administration of the intravenous medication should be better titrated, as well as the need for early extubation, the monitoring of the depth of anesthesia with an EEG bispectral index (BIS) and the neuromuscular one may be added [18, 19].

Is tracheal surgery possible with awake anesthesia only, without intubation? There are reports of isolated cases of tracheal resection, especially in the subglottic area, without intubation or any moment of positive ventilation [20, 21]. The local-regional anesthesia techniques have been either intravenous sedation combined with cervical plexus local anesthesia [20], or sedation and local anesthesia with ropivacaine [21], the spontaneous ventilation being initially provided with laryngeal mask and low-flow oxygen. The most relevant study is the one published by Macchiarini et al. in 2010 [22] that looks prospectively at the clinical feasibility of resections in the subglottic area or in the median trachea under cervical epidural anesthesia with ropivacaine, with mild sedation, with the patient awake and breathing spontaneously. Of 21 patients, only one was converted to general anesthesia, with a high level of patient satisfaction.

In centers with experience in tracheobronchial surgery, general anesthesia remains the primary option, both in terms of patient safety throughout the procedure and of surgical comfort.

Extracorporeal circulation, most commonly ECMO, may be an alternative to the conventional procedures especially in pediatric surgery [23, 24] or as "rescue therapy" in patients that, during the tracheobronchial resections, may suffer critical situations where conventional methods cannot provide proper ventilation [25, 26], such as major tracheal trauma or complex carinal resections [27]. A meta-analysis published in 2017 by Schieren et al. presents only 25 cases of tracheal resections with new forms of extracorporeal support out of a total of 759 patients [28]. There are no standardized recommendations regarding the extracorporeal support methods in complex tracheobronchial resections, causing them to be used only on rare occasions.

23.5 Prepping the Patient for Anesthesia: What Information Do We Need?

The patients to be subject to tracheal and bronchial resections get to the anesthesia after going through a series of specialist consultations including, usually, the pulmonologist, the bronchoscopist, the radiologist and the thoracic surgeon, as well as other physicians, in case of significant comorbidities.

Before deciding on the anesthetic strategy, several key questions must be answered.

1. *Is it a respiratory emergency or not?* Most cases are not emergencies, but in situations with imminent suffocation, the primary objective is freeing the airways through an interventional bronchoscopy maneuver (partial resection of the lesion, dilation etc.) or tracheostomy, followed by the actual resection as a second step [29, 30].
2. *What is the site, the extent of the lesion and the degree of stenosis?* This is valuable information, as it helps establish the ventilatory strategy and the succession of the anesthetic maneuvers from induction until the end of the intervention. Usually, the patient is investigated by the pulmonologist from a clinical and respiratory function perspective (Table 23.3). The symptomatology may develop insidiously or acutely, the obvious signs (wheezing or stridor) occurring usually when the adult's trachea narrows down to 5–6 mm (an approximately 70% reduction in diameter). Interpreting the respiratory function tests, especially the peak inspiratory and expiratory flows, may point to the presence and, to a certain extent, the degree of obstruction and the site: intrathoracic, extrathoracic or whether it is fixed (flow-volume curves) [31].

   The bronchoscopic examination is extremely important [32]. It assesses the degree of stenosis and, in most cases, its extent, the appearance and nature of the lesions by biopsy and the possibility of initially ventilating the patient with or without the dilation prior to induction. The appearance, mobility and distance between the vocal cords and the lesion are equally relevant [33]. If the patient has a tracheostomy tube, then the bronchoscopic assessment of the lesion is done both at transglottic level and through the tracheal orifice.

Table 23.3 Clinical and functional signs of tracheobronchial stenoses

History
– a history of prolonged intubation
– progressive dyspnea at increasingly smaller efforts
Clinical examination
– cough, hoarseness
– increased dyspnea in forced inspiration (extrathoracic stenosis) or in forced expiration (intrathoracic stenosis)
– suprasternal retractions
– wheezing, stridor
– cyanosis
Respiratory function tests
– flow-volume curves: flattening the inspiratory limb in variable extrathoracic obstruction, flattening the expiratory limb in variable intrathoracic obstruction, flattening of both limbs in fixed obstruction
– Midpoint maximal inspiratory flow is FIF50% <100 L/min
– FEF50% > 1/FIF50%
– FEV1/PEFR > 10 mL/L/min
– FEV1/FEV0.5 > 1.5

FIF50%: midpoint maximal expiratory flow. FEF50%: midpoint maximal inspiratory flow. FEV1: forced expiratory volume in 1 s. PEFR: peak expiratory flow rate. FEV0.5: forced expiratory volume in 0.5 s

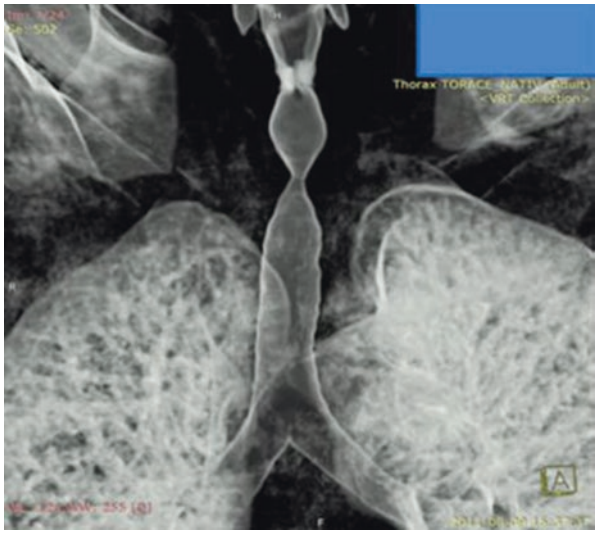

Fig. 23.1 3D-CT double tracheal stenosis

The modern X-ray examination supplements and enhances the precision of the preoperative assessment of the tracheobronchial stenoses. The axial CT (computer tomography) scan, but especially the spiral CT with multiplanar reconstruction (MPR) and tridimensional (3D) images, as well as the virtual bronchoscopy (VE) improve the diagnosis accuracy. The matching between the preoperative assessment of stenosis severity and extent using these means and the actual one, resected during the surgery, is more than 95% [34, 35]. 3-D CT is very helpful in the stenosis of the main bronchus, where the fibrobronchoscope cannot pass, like in the case of double stenoses after prolonged intubation and tracheostomy (Fig. 23.1).

In case of esotracheal fistulas, the esophageal endoscopy completes the mandatory preoperative investigation [36].

3. *Other investigations*. Mortality due to other comorbidities may be higher than the one secondary to the actual surgery [37]. The patient with tracheobronchial stenosis is subject to the usual preoperative investigations in thoracic surgery, with a special remark for cardiac assessment. Aside from a routine ECG, patients with coronary risk factors (elderly, history, smokers), may require specific cardiological treatment following more complex investigations. Other comorbidities (diabetes, kidney failure, neurological, liver and others) must be evaluated and treated by specialist consultations.

23.6 The Anesthetic Technique Varies by Lesion Site: Optimizing the Anesthetic Steps with the Surgical Moments

The anesthetic and surgical team has all the investigations related to the type, degree, site and extent of the stenotic lesions. The surgeon describes the extension of the resection and the way he plans to achieve the reconstruction of the airways. He also

Table 23.4 Tracheobronchial surgery. Surgical and anesthetic strategy

Surgical	Anesthetic
Stenotic lesion: site, severity, extent, pathology *Surgical approach:* cervical, cervico-sternotomy, sternotomy, laterothoracic *Extent of resection*: laryngotracheal, tracheal, carinal, pneumonectomy with carina, main bronchus *Tracheobronchial reconstruction*: laryngotracheal (thyro-tracheal or crico-tracheal), tracheo-tracheal, tracheobronchial (sleeve with or without preservation of the pulmonary parenchyma), carina reconstruction *Anesthetic requirements for surgical comfort*: "cross-field ventilation", HFJV, succession of the ventilation techniques	*Position of the patient* at induction and during the intervention *Anesthetic medication* at induction and intraoperative. *Monitoring requirements* *Initial ventilation*: preoperative dilation of the stenosis (HFJV), intubation with transstenotic ETT or with ETT above the stenosis, laryngeal mask, tracheostomy, intubation with double lumen tube. *Ventilatory needs during the intervention*: providing ETT and connectors for "cross-field ventilation", HFJV with accessories. *Vulnerabilities*: *How is the patient ventilated at the most challenging moments during surgery*. *Is a form of "rescue therapy"* (ECMO) *possible/necessary*?

outlines the most delicate moments of the intervention when he needs intraoperative comfort to perform the anastomosis of the airways. Table 23.4 summarizes the main issues subject to discussion prior to the surgical intervention.

Always be ready for a difficult airway management!

23.6.1 Upper Tracheal Stenosis (Non-critical Subglottic)

Proximal resections are interventions that require the removal of stenosis located in the upper third of the trachea, with or without cricoid cartilage involvement. The approach usually consists of Kocher cervicotomy. Sometimes, during the preoperative preparation, the patient undergoes a dilation session to facilitate ventilation. The endotracheal tube cannot always go beyond the obstacle.

Step 1. After the anesthetic induction, ventilation can be performed:

- with a flexometallic (wired) tube, suprastenotic (fixed in the stenosis) (Fig. 23.2a).
- with a transstenotic flexometallic tube, possibly after preoperative bronchoscopic dilation, which is the most convenient option.
- on a preexisting tracheostoma (in case of very tight or complete subglottic stenosis)
- more rarely, on a laryngeal mask when the stenosis is tight and very high and cannot be ventilated with the abovementioned methods [38].

Comments. Before severing the trachea below the stenosis, pediatric ETTs with an inside diameter of 4–4.5 mm may be inserted, under acceptable ventilatory conditions for a short while [39].

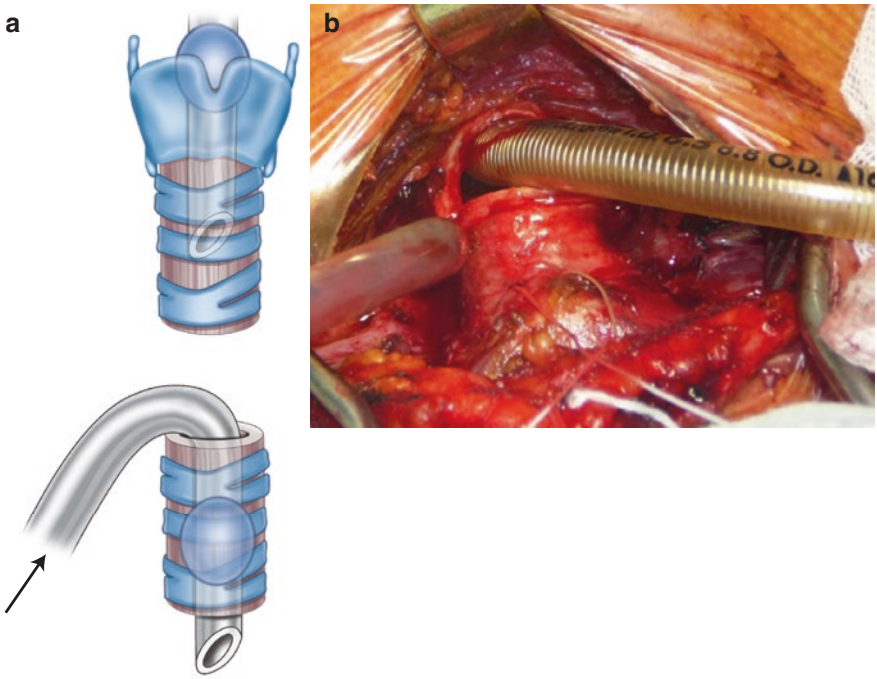

Fig. 23.2 (**a**) "Cross-field" ETT (**b**) "Cross-field" ETT with wired ETT "pending" above the stenosis

Step 2. After sectioning the distal trachea below the stenosis, the ventilation can be performed:

- by having the surgeon place in the distal trachea a flexometallic ETT connected to the anesthetic circuit through an extension, for "cross-field" ventilation (Fig. 23.2a, b). In case of initial ventilation via the tracheostomy tube, it is suppressed.
- by introducing an HFJV catheter in the distal trachea through the initial ETT, which is "pending" above the stenosis, or through LMA [40].
- by passing the initial flexometallic tube in the distal trachea after resection of the stenotic section
- to make the sutures, there can be periods of apnea after ventilation with oxygen 100%.

Comments. ETT temporarily positioned between the cords, for the initial ventilation in upper stenoses, can be extubated during the surgical maneuvers. The patient is re-intubated after completing the posterior part of the crico-tracheal anastomosis, in order to ensure ventilation until the end of the intervention regardless of how the initial ventilation was done.

23.6.2 Median Tracheal Stenosis

The ventilation steps are the same as in upper stenoses. In mid-tracheal stenosis, the approach is the partial cervico-sternotomy. At this level, the most common ones are post-tracheostomy stenoses, those with the tracheostomy tube in place, double stenosis and those caused by the invasion of thyroid tumors.

Comments. In case of tracheal compressions and invasions by thyroid tumors, the tracheal lumen is narrow and deformed (Fig. 23.3). Initially, the ETT must be positioned using the bronchoscope or the ventilation can be performed through the laryngeal mask [41]. Preserving at least one recurrent nerve is important for post-anesthesia extubation (Fig. 23.4). In case of double stenosis (Fig. 23.1), that

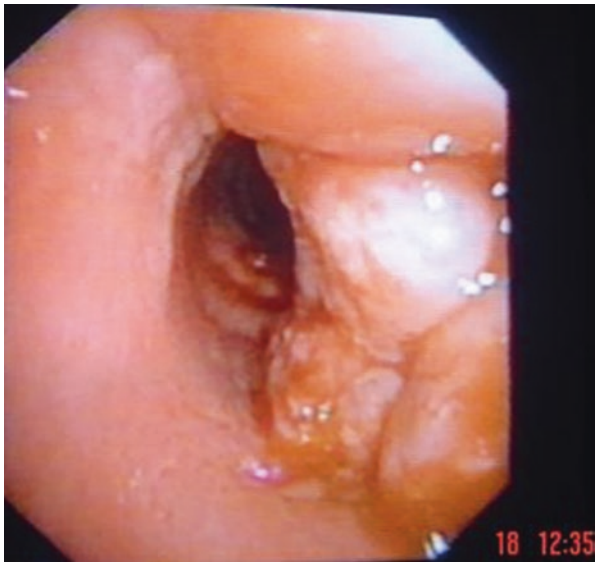

Fig. 23.3 Thyroid tumor invading mid-trachea

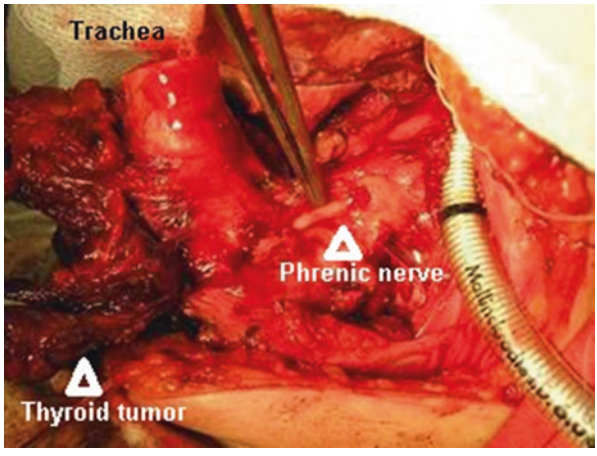

Fig. 23.4 Thyroidectomy with tracheal resection. Detecting the recurrent nerve

can be excised en bloc (less than 6.5 cm long), the dilation by rigid bronchoscopy is recommended to facilitate the ventilation from induction to distal tracheal sectioning.

23.6.3 The Distal Trachea (Minus the Carina) is Resected Following the Same Ventilation and Surgical Rules Like in the Case of the Other Tracheo-tracheal Anastomosis

Most often, the lesions are benign, but they can be malignant, too (metastasis, cystic adenoid carcinoma). The surgical approach is either by sternotomy or, more rarely, by right thoracotomy [42]. After the distal resection of the trachea, one-lung ventilation may be applied either by using a no. 6 or less ETT for "cross field" ventilation of the left lung, preferably, or HFJV by a catheter placed by the surgeon, preferably on the right or alternatively left-right. In the end, ventilation is provided by the ETT, initially placed above the anastomosis.

Comments. Cross-field ETT in the main bronchus is suppressed, after passing the suture threads of the anterior part of the anastomosis. Until it closes, there is an apneic period and the patient is pre-oxygenated with 100% oxygen.

23.6.4 Carinal Resections with or Without Lung Resection

Carinal resections are the biggest challenge for the anesthetic-surgical team. The surgical approach is important for the succession of the ventilation steps. This is usually performed by right thoracotomy for the resection of the carina, with or without right sleeve pneumonectomy, or median sternotomy for the isolated carinal resection. In case of left sleeve pneumonectomy, much more uncommon, the surgical approach is controversial, with different solutions described here: a clamshell incision or a median sternotomy, with or without anterior left thoracotomy [43], or by simple left posterior-lateral thoracotomy, or a 2-step approach consisting of left thoracotomy for left pneumonectomy followed by right thoracotomy for carinal resection and anastomosis between the trachea and the right main bronchus or a right thoracotomy for carinal resection and reconstruction followed by video-assisted left pneumonectomy [44].

During the *isolated carinal resection*, usually for rare tumoral diseases (adenoid cystic carcinoma, mucoepidermoid carcinoma, metastasis), the reconstruction is done either by creating a neo-carina of the two main bronchi and anastomosis in the trachea (Figs. 23.5a, b and 23.6) or by other anastomotic arrangements between one of the main bronchi and the trachea and the lateral implantation of the other bronchus. Initially, the ventilation can be achieved by a regular ETT positioned in the trachea above the tumor lesion. The HFJV catheter is inserted through the ETT to the right and the left bronchus is severed, then to the left for the right bronchus. The HFJV is kept as long as the neo-carina is built, as well as the anastomosis between the carina and the trachea is achieved (Fig. 23.5a, b). Until the end of the intervention ventilation is ensured by the initial ETT.

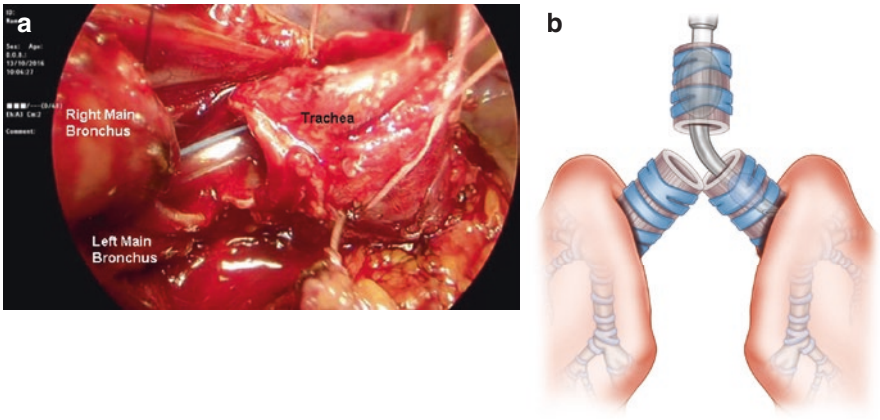

Fig. 23.5 (**a**, **b**) HFJV during carinal resection and anastomosis between the neo-carina and the trachea

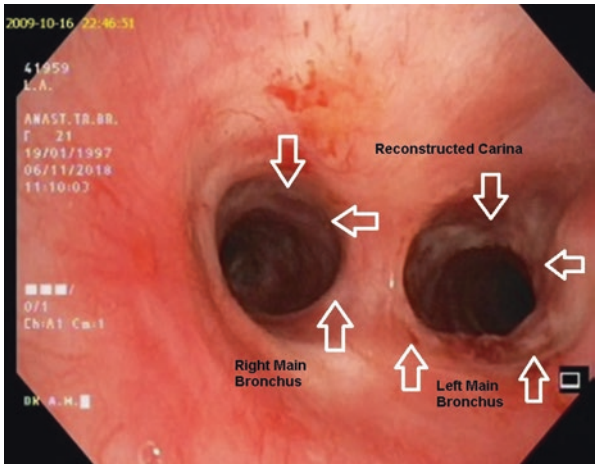

Fig. 23.6 Carinal resection with reconstruction—2-years later

During the *right tracheal sleeve pneumonectomy*, the succession of the ventilation steps is initially on the left double–lumen tube (DLT), until isolating the right lung. Then the DLT is retracted in the trachea and the HFJV is inserted on its bronchial branch to the left bronchus [45] (Fig. 23.7). After performing the left tracheobronchial anastomosis, the ventilation is maintained traditionally on the tracheal DLT.

During the *left tracheal sleeve resection*, the procedure can be the same or the DLT intubation in the right main bronchus may be applied.

Comments. Depending on the type of tracheobronchial reconstruction, "cross-field" ventilation with ETT may be applied in a main bronchus, alternating with HFJV, after DLT retraction in the trachea. An example is left tracheobronchial anastomosis with lateral implantation of the other main bronchus after carinal resection. However, the HFJV catheter is preferred for being thin and enabling the passage of

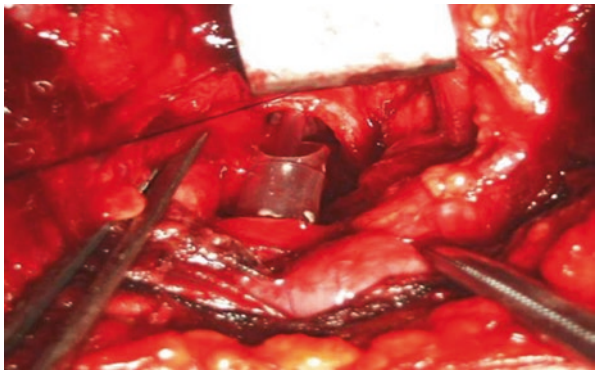

Fig. 23.7 Left DLT retracted in the trachea. HFJV catheter for left bronchus ventilation

the threads in a more convenient space. The oxygenation must be well monitored as there can be moments of apnea. The carinal resection on a single lung can be done with the succession of oro-tracheal ETT, HFJV alternating with apneic periods until the completion of the tracheobronchial anastomosis.

An extracorporeal support technique (ECMO or cardio-pulmonary by-pass) is rarely used in adults in this type of surgical interventions, but may be a temporary option in certain situations [46]. The benefits of the method in elective surgery would concern a better surgical exposure in the delicate moments when an adequate control of ventilation is required. Lang et al. reported in 2015 a series of 10 cases of complex tracheobronchial resections using ECMO in oncologic patients [47]. The authors recommend for the technique to be used only in carefully selected cases, as there are many unknown impediments and complications. Experimented centers managing complex cases must be equipped with ECMO and a team trained to apply this method [46].

23.6.5 Esotracheal and Esobronchial Fistulas

Tracheal resections performed while repairing esotracheal fistulas occurring after prolonged intubation may pose significant problems during anesthesia. Usually, the patients have a tracheostomy and come after a long stay in hospital, with recurrent pulmonary infections and risk of gastric aspiration. The tracheal and esophageal defect can be repaired by a single surgical intervention [48], the resected tracheal part being sometimes long, including the fistula segment. The ventilation steps are similar to those used in tracheal resections with preexisting tracheostomy: ventilation on the tracheostomy tube, then "cross-field" ventilation on distal trachea and, in the end, ventilation on oro-tracheal ETT introduced after closing the esophagus and the posterior part of the tracheo-tracheal anastomosis [49].

Comments. The intervention is recommended to patients with spontaneous breathing [49], but there are reports of cases when the tracheo-esophageal defect had to be repaired in mechanically ventilated patients [50]. Sometimes, because of the long length of the resected tracheal part or of the precarious state of the patient,

the tracheostomy tube may remain in place postoperatively [51, 52] or the sutures are protected by a Montgomery or Hebeler Safe-T-Tube for mechanically ventilated patients [50].

23.6.6 Stenosis of the Large Bronchi: Bronchial Sleeve Resection

The main bronchi are resected in case of benign stenosis, frequently post-tuberculosis or sleeve-resection or in case of lung tumors of the upper pulmonary lobes with bronchial involvement. Tracheal intubation is done with DLT or with ETT with bronchial blocker to separate pulmonary ventilation until the broncho-tracheal anastomosis is achieved.

23.7 Recovery from Anesthesia

Recovery from anesthesia, preferably in the operating room, is the objective recommended in most patients that were subject to tracheal and/or main bronchi resections [10]. The pharmacological technique must be adapted to this purpose, whether it is a TIVA technique or another type of combined anesthesia. The opioid medication and the muscle relaxants must be gradually reduced or antagonized towards the end of the surgical intervention. Nausea and vomiting may endanger the suture and cause gastric aspiration. Cervical incisions and even sternotomies do not necessarily require postoperative opioid analgesia and the administration of central antiemetics is indicated. The association with epidural analgesia in case of thoracotomies is also recommended. In case of upper and median tracheal resections and of the widespread ones, the anterior flexion of the neck is recommended to be maintained for 4–8 days by "guardian stitches" between the submental and presternal skin [53] or by special orthesis, in particular for non-cooperative patients [54].

Comments. Maintaining a nasotracheal tube in the first day after surgery, to protect the anastomosis or rather in case of edema of glottis or damage of the laryngeal nerves is the preferred extubation method for certain authors [55], but it is very rarely needed in reality. Another method, again highly uncommon, in patients with early postoperative respiratory difficulties, is maintaining a temporal tracheostomy, two rings below the anastomosis [56]. More than 90% of tracheal resection patients can be extubated in the operating room [56].

Early complications are rare in case of tracheal resections and the fatal ones occur exceptionally, usually related to anastomosis (anastomosis dehiscence, vascular fistulas) [56]. They are more common in carinal ones, directly proportionate with the experience of the center where they are performed [57]. Thus, mortality due to tracheal resections may go down to 1% [9] and due to carinal ones, to 3–12% [58]. The most frequent complications unrelated to anastomosis are dysphonia, dysphagia and wound infection. The pediatric population, large laryngotracheal resections, diabetes mellitus, preoperative tracheostomy and re-intervention are the main risk factors [10].

23.8 High Frequency Jet Ventilation (HFJV)

HFJV is the most commonly used method of high frequency ventilation in the surgery of the trachea and the large airways. V_T administered intermittently, with a high instantaneous gas flow is much smaller that the anatomically dead space of the airways. The respiratory rate is high (usually >60 breaths/min) and the expiration is passive [59]. The gas exchanges are complex and incompletely clarified. The mechanisms of convection, of augmented diffusion (Taylor dispersion), spike formation generated in the center of the airway while the gas exits the lung at the periphery of the airway by a helical pattern (coaxial flow), cardiogenic mixing of gas lost to the pericardium or pendelluft are most commonly responsible. During the surgical interventions on the large airways, HFJV is delivered in an open system because the inspiratory V_T (1–3 ml/kg body weight) and expiratory V_T cannot be currently measured [60] and practically there is no risk of barotrauma. Gas exchanges are monitored by pulse oximetry which is usually supplemented with the intermittent gas analysis on the radial arterial catheter, especially for $PaCO_2$ assessment during longer interventions. There are special catheters with dedicated lumen for capnography or it can be recorded on a channel of the rigid bronchoscope if the frequency is temporarily down to less than 10 breaths per min [61, 62]. There are several models of High Jet Frequency Ventilators, Mansoon III Acutronic/Switzerland or TwinStream Carl Reiner GmbH/Austria being commonly used in Europe. The gas injection catheters have multiple side holes to increase turbulence or have a basket tip, both reducing the catheter whip lesions.

The regular settings of HFJV in the surgery of the trachea and large bronchi are a FiO_2 that usually ranks between 0.6 and 1, respiratory rate (F), between 60 and 180/min injection pressure or driving pressure (ΔP), between 0.3 and 3 bar, and an inspiration time around 40% [61]. During this type of ventilation, there is a positive end-expiratory pressure (PEEP), which is why the settings of the alarms must include a Power Pressure alarm (PP) that we usually set at 10 cm H_2O because in case of tight tracheal stenosis, auto-PEEP may increase fast [63]. The alarm for the peak inspiratory pressure (PIP) is usually set at 20 cm H_2O and is also important on the one hand as an element of protection for barotraumas, but also in practical terms, detecting the obstruction of the catheter with blood secretions or tumoral tissue or impossibility of expiration, which causes the non-initiation of the next inspiration. The humidifier system that can be attached is useful in long-term interventional bronchoscopy and less used during tracheobronchial interventions when the large airways are open. Attention should also be given to a follow-up of certain observational and clinical elements, such as the regular movement of the thorax, auscultation and the noise produced by releasing the air jet.

The benefits of HFJV in the surgery of the trachea and large bronchi are obvious and exceed the likely complications that are rare and generally easy to prevent by a regular team using this equipment (Table 23.5).

Table 23.5 Main benefits and complication of HFJV during tracheobronchial surgery

Benefits	Complications
– Indicated in tracheo-pulmonary surgery – Ventilation by tracheoscope for preoperative tracheal dilation – Well-placed catheter for ventilating a selected zone of the lung (placed under fiber optic vision) – Ventilation on catheter by laryngeal mask or ETT – With DLT or rigid bronchoscope connected to the Jet-converter and conventional ventilation – Protective ventilation (Low airway pressure) – Surgical convenience – Optimal oxygenation and efficient CO_2 removal	– Barotrauma (pneumothorax, subcutaneous emphysema, pneumomediastinum) during rigid bronchoscopy – Hypercapnia and less frequently hypoxemia, especially in patients with preexisting severe respiratory condition – Hemodynamic instability (poor ASA physical status) – Contamination of the surgical field with blood, secretions and tissue

23.9 Conclusions

Resections with reconstruction of the large airways require specially trained staff, specific technical equipment, in particular for the HFJV, and access to a form of extracorporeal circulatory support.

Anesthesia during this type of interventions implies a succession of ventilation methods, depending on the surgery steps and site of the resected segment (upper, median or distal trachea, carina or main bronchus, with or without lung tissue).

Hermes Grillo has probably best summarized the need to promote centers that specialize in this type of interventions: “In dealing with apparently simple, yet complex problems that are not frequently encountered, such as tracheal reconstruction, the best results for our patients will be obtained if the work is concentrated in special units where a continuing commitment has been made to this type of work” [2].

References

1. Grillo HC, Dignan EF, Miura T. Extensive resection and reconstruction of mediastinal trachea without prosthesis or grafts: an anatomical study in man. J Thorac Cardiovasc Surg. 1964;48:741–9.
2. Grillo HC. Notes on the windpipe. Ann Thorac Surg. 1989;47(1):9–26.
3. Gelbard A, Francis DO, Sandulache VC, Simmons JC, Donovan DT, Ongkasuwan J. Causes and consequences of adult laryngotracheal stenosis. Laryngoscope. 2015;125:1137–43.
4. Wain JC. Postintubation tracheal stenosis. Semin Thorac Cardiovasc Surg. 2009;21:284–9.
5. Sarper A, Ayten A, Eser I, Ozbudak O, Demircan A. Tracheal stenosis after tracheostomy or intubation: review with special regard to cause and management. Tex Heart Inst J. 2005;32(2):154–8.

6. Kim SS, Khalpey Z, Hsu C, Little AG. Changes in tracheostomy and intubation related tracheal stenosis: implications for surgery. Ann Thorac Surg. 2017;104:964–70.
7. Walz MK, Peitgen K, Thürauf N, Trost HA, Wolfhard U, Sander A, et al. Percutaneous dilatational tracheostomy—early results and long-term outcome of 326 critically ill patients. Intensive Care Med. 1998;24:685–90.
8. Grillo HC, Mark EJ, Mathisen DJ, Wain JC. Idiopathic laryngotracheal stenosis and its management. Ann Thorac Surg. 1993;56:80–7.
9. Nouraei SM, Middleton SE, Nouraei SA, Virk JS, George PJ, Hayward M, et al. Management and prognosis of primary tracheal cancer: a national analysis. Laryngoscope. 2014;124:145–50.
10. Wright CD, Grillo HC, Wain JC, Wong DR, Donahue DM, Gaissert HA, et al. Anastomotic complications after tracheal resection: prognostic factors and management. J Thorac Cardiovasc Surg. 2004;128:731–9.
11. Tschernko EM, Aigner C. Lung surgery and extracorporeal oxygenation. In: Şenturk M, Sungur MO, editors. Postoperative care in thoracic surgery. Cham: Springer International Publishing; 2017. p. 199–206.
12. Sandberg W. Anesthesia and airway management for tracheal resection and reconstruction. Thorac Anesth. 2000;38:55–75.
13. Rispoli M, Nespoli MR, De Simone MG, Mattiacci DM, Buono S, Corcione A, et al. EZ-blocker in tracheal surgery. J Cardiothorac Vasc Anesth. 2015;29:89–90.
14. Siciliani A, Rendina EA, Ibrahim M. State of the art in tracheal surgery:a brief literature review. Multidiscip Resp Med. 2018;13:34–40.
15. Hatipoglu Z, Turktan M, Avci A. The anesthesia of trachea and bronchus surgery. J Thorac Dis. 2016;8:3442–51.
16. Mehta Y, Arora D, Vats M. Epidural analgesia in high risk cardiac surgical patients. HSR Proc Intens Care Cardiovasc Anesth. 2012;4:11–4.
17. Hobai IA, Chhangani SV, Alfille PH. Anesthesia for tracheal resection and reconstruction. Anesthesiol Clin. 2012;30:709–30.
18. Purugganan RV. Intravenous anesthesia for thoracic procedures. Curr Opin Anaesthesiol. 2008;21:1–7.
19. Brull SJ, Aaron F, Kopman AF. Current status of neuromuscular reversal and monitoring: challenges and opportunities. Anesthesiology. 2017;126:173–90. https://doi.org/10.1097/ALN.0000000000001409.
20. Liu J, Li S, Shen J, Dong Q, Liang L, Pan H, et al. Non-intubated resection and reconstruction of trachea for the treatment of a mass in the upper trachea. J Thorac Dis. 2016;8:594–9. https://doi.org/10.21037/jtd.2016.01.56.
21. Loizzi D, Sollitto F, De Palma A, Pagliarulo V, Di Giglio I, Loizzi M. Tracheal resection with patient under local anesthesia and conscious sedation. Ann Thorac Surg. 2013;95:e63–5.
22. Macchiarini P, Rovira I, Ferrarello S. Awake upper airway surgery. Ann Thorac Surg. 2010;89:387–91.
23. Dodge-Khatami A, Tsang V, Roebuck D, Elliott M. Management of congenital tracheal stenosis: a multidisciplinary approach. Images Paediatr Cardiol. 2000;2:29–39.
24. Butler CR, Speggiorin S, Rijnberg FM, Roebuck DJ, Muthialu N, Hewitt RJ, et al. Outcomes of slide tracheoplasty in 101 children: a 17-year single-center experience. J Thorac Cardiovasc Surg. 2014;147(6):1783–9. https://doi.org/10.1016/j.jtcvs.2014.02.069.
25. Rinieri P, Peillon C, Bessou J-P. National review of use of extracorporeal membrane oxygenation as respiratory support in thoracic surgery excluding lung transplantation. Eur J Cardio-Thoracic Surg. 2015;21:517–22.
26. Lei J, Su K, Li XF, Zhou YA, Han Y, J Huang LJ, et al. Ecmo-assisted carinal resection and reconstruction after left pneumonectomy. J Cardiothorac Surg. 2010;5:89–91.
27. Keeyapaj W, Alfirevic A. Carinal resection using an airway exchange catheter-assisted venovenous ECMO technique. Can J Anaesth. 2012;59:1075–6.
28. Schieren M, Böhmer A, Dusse F, Koryllos A, Wappler F, Defosse J. New approaches to airway management in tracheal resections-a systematic review and meta-analysis. J Cardiothorac Vasc Anesth. 2017;31:1351–8.

29. Lui SY, Khalid K, Yew JJ, Zaliza I, Abidina Z. Emergency airway management in a patient with acquired subglottic stenosis. Indi J Med Spec. 2018;9:94–6.
30. Chao YK, Liu YH, Hsieh MJ, Wu YC, Liu HP, Wang CJ, et al. Controlling difficult airway by rigid bronchoscope – an old but effective method. Interact Cardiovasc Thorac Surg. 2005;4:175–9. https://doi.org/10.1510/icvts.2004.098038.
31. Acres JA, Kryger MH. Clinical significance of pulmonary function tests: upper airway obstruction. Chest. 1981;80:207–11.
32. Polverosi R, Vigo M, Baron S, Rossi G. Valutazione delle lesioni tracheobronchiali con TC spirale. Confronto traendoscopia virtuale e broncoscopia. Radiol Med. 2001;102:313–9.
33. Puchalski J, Musani AI. Tracheobronchial stenosis: causes and advances in management. Clin Chest Med. 2013;34:557–67. https://doi.org/10.1016/j.ccm.2013.05.002.
34. Hoppe H, Walder B, Sonnenschein M, Vock P, Dinkel HP. Multidetector CT virtual bronchoscopy to grade tracheobronchial stenosis. AJR Am J Roentgenol. 2002;178:1195–200.
35. Morshed K, Trojanowska A, Szymanski M, Trojanowski P, Szymanska A, Smolen A, et al. Evaluation of tracheal stenosis: comparison between computed tomography virtual tracheobronchoscopy with multiplanar reformatting, flexible tracheofiberoscopy and intra-operative findings. Eur Arch Otorhinolaryngol. 2011;268:591–7.
36. Macchiarini P, Verhoye JP, Chapelier A, Fadel E, Dartevelle P. Evaluation and outcome of different surgical techniques for postintubation tracheoesophageal fistulas. J Thorac Cardiovasc Surg. 2000;119:268–76.
37. Friedel G, Kyriss T, Leitenberger A, Toomes H. Long-term results after 110 tracheal resections. Ger Med Sci. 2003;1:10.
38. Zardo P, Kreft T, Hachenberg T. Airway management via laryngeal mask in laryngotracheal resection. Thorac Cardiovasc Surg Rep. 2016;5:1–3.
39. D'Andrilli A, Ciccone AM, Venuta F, Ibrahim M, Andreetti C, Massullo D, et al. Long-term results of laryngotracheal resection for benign stenosis. Eur J Cardiothorac Surg. 2008;33:440–3.
40. Adelsmayr E, Keller C, Erd G, Brimacombe J. The laryngeal mask and high-frequency jet ventilation for resection of high tracheal stenosis. Anesth Analg. 1998;86:907–8.
41. Schieren M, Egyed E, Hartmann B, Aleksanyan A, Stoelben E, Wappler F, et al. Airway Management by laryngeal mask airways for cervical tracheal resection and reconstruction: a single-center retrospective analysis. Anesth Analg. 2018;126:1257–61.
42. Mitchell JD, Mathisen DJ, Wright CD, Wain JC, Donahue DM, Allan JS, et al. Resection for bronchogenic carcinoma involving the carina: long-term results and effect of nodal status on outcome. J Thorac Cardiovasc Surg. 2001;121:465–71.
43. Gilbert A, Deslauriers J, McClish A, Piraux M. Tracheal sleeve pneumonectomy for carcinomas of the proximal left main bronchus. Can J Surg. 1984;27:583–5.
44. Tse DG, Vadehra N, Iancu L. Left tracheal sleeve pneumonectomy: a combined approach. J Thorac Cardiovasc Surg. 2005;129:454–5.
45. Cordos I, Bolca C, Paleru C, Posea R, Stoica R. Sixty tracheal resections--single center experience. Interact Cardiovasc Thorac Surg. 2009;8:62–5.
46. Hoetzenecker K, Klepetko K, Keshavjee S, Cypel M. Extracorporeal support in airway surgery. J Thorac Dis. 2017;9:2108–17.
47. Lang G, Ghanim B, Hötzenecker K, Klikovits T, Matilla JR, Aigner C, Taghavi S, Klepetko W. Extracorporeal membrane oxygenation support for complex tracheo-bronchial procedures. Eur J Cardiothorac Surg. 2015;47:250–5.
48. Oliaro A, Rena O, Papalia E, Filosso PL, Ruffini E, Pischedda F, et al. Surgical management of acquired non-malignant tracheo-esophageal fistulas. J Cardiovasc Surg (Torino). 2001;42:257–60.
49. Stoica R, Cordoş I. Surgical and anesthetic coordination during tracheal and carinal resections and reconstruction. Chirurgia (Bucur). 2007;102:681–6.
50. Fiala P, Cernohorsky C, Cermak J, Patek J, Krepela E, Mouckova M. Tracheal stenosis complicated with tracheoesophageal fistula. Eur J Cardiothorac Surg. 2004;25:127–30.

51. Daddi N, Tassi V, Belloni GP, Mattioli S. The surgical repair of benign tracheo-oesophageal/pharyngeal fistula in patients on mechanical ventilation for severe neurological injuries. Eur J Cardiothorac Surg. 2016;49:1279–81.
52. Dartevelle P, Macchiarini P. Management of acquired tracheoesophageal fistula. Chest Surg Clin N Am. 1996;6:819–36.
53. D'Andrilli A, Maurizi G, Andreetti C, Ciccone AM, Ibrahim M, Poggi C, et al. Long-term results of laryngotracheal resection for benign stenosis from a series of 109 consecutive patients. Eur J Cardiothorac Surg. 2016;50:105–9.
54. Mueller DK, Becker J, Schell SK, Karamchandani KM, Munns JR, Jaquet B. An alternative method of neck flexion after tracheal resection. Ann Thorac Surg. 2004;78:720–1.
55. Marulli G, Rizzardi G, Bortolotti L, Loy M, Breda C, Hamad A-M, et al. Single-staged laryngotracheal resection and reconstruction for benign strictures in adults. Interact Cardiovasc Thorac Surg. 2008;7:227–30.
56. Ashiku SK, Kuzucu A, Grillo HC, Wright CD, Wain JC, Lo B, et al. Idiopathic laryngotracheal stenosis: effective definitive treatment with laryngotracheal resection. J Thorac Cardiovasc Surg. 2004;127:99–107.
57. Bibas BJ, Terra RM, Oliveira AL Jr, Tamagno MFL, Minamoto H, Cardoso PFG, et al. Predictors for Postoperative Complications AfterTracheal Resection. Ann Thorac Surg. 2014;98:277–82.
58. Tapias LF, Ott HC, Mathisen DJ. Complications following carinal resections and sleeve resections. Thorac Surg Clin. 2015;25:435–47.
59. Chitilian HV, Kaczka DW, Melo V. Respiratory monitoring. In: Miller's anesthesia. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015. p. 1541–79.
60. Buczkowski PW, Fombon FN, Lin ES, Russell WC, Thompson JP. Air entrainment during high-frequency jet ventilation in a model of upper tracheal stenosis. Br J Anaesth. 2007;99:891–7.
61. Frietsch T, Krafft P, Becker HD, Buelzebruck H, Wiedemann K. Intermittent capnography during high-frequency jet ventilation for prolonged rigid bronchoscopy. Acta Anaesthesiol Scand. 2000;44:391–7.
62. Klein U, Karzai W, Gottschall R, Gugel M, Bartel M. Respiratory gas monitoring ruring high-frequency jet ventilation for tracheal resection using a double-lumen jet catheter. Anesth Anal. 1999;88:224–6.
63. Pawlowski J. Anesthetic considerations for interventional pulmonary procedures. Curr Opin Anaesthesiol. 2013;26:6–12.

Pediatric Thoracic Anesthesia

24

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24.1 Introduction

Pediatric patients undergoing thoracic surgery can present unique challenges to the anesthesiologist. Firstly, their unique anatomical and physiological characteristics render them at higher risk for hypoxemia during and after the procedure. Their size does not allow for the use of standard equipment often times requiring the anesthesiologist to get creative with the tools at hand. Their behavior will likely not allow them to cooperate despite the best laid anesthetic plan. And lastly, the large variety in pathology, some of which can be rare, adds more difficulty to the whole procedure. In this chapter we will discuss the above in more detail as well as go over the techniques that have been used successfully to take care of this patient population during thoracic surgery.

24.2 Pediatric Anatomy and Physiology

Pediatric patients have several key differences in anatomy and physiology compared to the adult which the anesthesiologists must be aware to successfully take care of these patients during thoracic surgery. The most prominent airway characteristics are listed below [1]:

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- Large head, short neck and a prominent occiput.
- Tongue is relatively large.
- Larynx is high and anterior, at the level of C3–C4.
- Epiglottis is long, stiff and U-shaped.
- Preferential nasal breathing
- Airway is funnel shaped and narrowest at the level of the cricoid cartilage.
- Airway is small and prone to develop edema resulting in airway obstruction.

In terms of respiratory physiology, the pediatric patients have a baseline limited respiratory reserve during normal two lung ventilation due to several reasons listed below [2]:

- Horizontal ribs prevent the 'bucket handle' action seen in adult breathing and limit an increase in tidal volume. Ventilation is primarily diaphragmatic.
- The chest wall is significantly more compliant than that of an adult. Subsequently, the Functional Residual Capacity (FRC) is relatively low. FRC decreases with apnea and anesthesia causing lung collapse.
- Minute ventilation is rate dependent as there is little means to increase tidal volume.
- The closing volume is larger than the FRC until 6–8 years of age. This causes an increased tendency for airway closure at end expiration. Thus, neonates and infants generally need intermittent positive pressure ventilation during anesthesia and would benefit from a higher respiratory rate and the use of positive and expiratory pressure (PEEP).
- Muscles of ventilation are easily subject to fatigue due to low percentage of Type I muscle fibers in the diaphragm. This number increases to the adult level over the first year of life.
- The alveoli are thick walled at birth. There is only 10% of the total number of alveoli found in adults. The alveoli clusters develop over the first 8 years of life.
- Apneas are common post operatively in premature infants.
- High O_2 consumption compared to adult.

24.2.1 Effects of the Lateral Decubitus Position and One Lung Ventilation (OLV) in Children

In children up to age 8 years, the chest wall compliance is high, the lungs are easily compressed by external pressures, the functional residual capacity is low and the oxygen consumption is high. All of these measures render children more vulnerable to the unwanted effects of the lateral decubitus position together with OLV, when compared to adults. The dependent lung is under pressure. Inhalational anesthetics inhibit hypoxic pulmonary vasoconstriction and blood flow to the operative lung cannot be reduced. Ventilation/perfusion is easily mismatched, atelectasis formation and hypoxemia are almost inevitable [10].

Unlike adults, oxygenation is higher in the nondependent lung rather than the dependent one (healthy lung), especially in neonates and infants. The reason for this is that children have easily compressible chest wall. FRC becomes equal to the residual volume in the dependent lung and small airways begin to close even in tidal volume values. Hydrostatic pressure between dependent and nondependent lungs is minimal because of the small size of the children. Therefore, the advantage of better oxygenation in the nondependent lung is heralded. As a result, compared to adults, children are at greater risk for developing hypoxemia or airway complications during thoracoscopic surgery or thoracotomy, even though one lung ventilation is not used [2].

24.3 Preoperative Evaluation

Preoperative evaluation and patient preparation are mandatory in order to reduce perioperative complications in thoracic surgery in children. The required fasting time and premedication recommendations are similar to other surgical patients. In summary, 2 h nil per os (NPO) for clear fluids, 4 h for breast milk, and at least 6 h for milk formula or light meal, is recommended per the American Society of Anesthesiology guidelines [3]. The most important task is the diagnosis and evaluation of the acute and chronic pulmonary and cardiac pathologies. Dyspnea and decreased tolerance to exercise are signs indicating decreased pulmonary reserve [2].

Lung auscultation must be performed in either supine or sitting position. Pathologic sounds such as rhonchus or wheezing should be evaluated. Blood gas analysis is not mandatory in children. It is usually sufficient to evaluate peripheral oxygen saturation and venous bicarbonate concentrations which is always elevated in children with chronic carbon dioxide (CO_2) retention [2]. Although respiratory function tests are not recommended in asymptomatic patients, they may be useful to determine the progression of disease [4, 5]. Radiologic appearance of the pathologies must be examined by the anesthesiologist. This examination may help the anesthesiologist to be ready for possible problems such as difficult intubation or blood loss.

Pediatric and adult thoracic surgeries differ in terms of indication. In adults, the indication is usually limited to infections, tumors, and lobe resections. Usual indications in younger children are congenital diseases, such as pulmonary sequestration, congenital diaphragmatic hernia, trachea-esophageal fistulas, congenital lobar emphysema, vascular rings and tracheal stenosis. Usual indications in older children and adolescents are infections, mediastinal masses and musculoskeletal deformities.

24.4 Anesthetic Techniques

24.4.1 Flexible Bronchoscopy

Flexible bronchoscopy is an endoscopic technique which enables to visualize and evaluate the trachea and bronchi mainly for diagnostic procedures. In pediatric anesthesia is it performed often times to evaluate the patency of the airway. In order to asses for dynamic obstructions spontaneous ventilation is necessary. Thus,

sedation supplemented with topical anesthesia is usually satisfactory for this procedure. Optionally a laryngeal mask airway can be utilized while providing general anesthesia. If the flexible bronchoscopy is being done for other purposes, such as takin biopsy samples, general endotracheal anesthesia with or without paralysis is adequate.

24.4.2 Rigid Bronchoscopy (RB)

Rigid Bronchoscopy (RB) is mainly therapeutic in nature. It is used in the diagnosis and treatment of intraluminal obstructions or extra luminal mass effects. Due to the stimulating effects it is performed under general anesthesia. The indications of RB in pediatric patients are the same with the adult patients; but the most frequent indication is the tracheobronchial foreign body (FB) aspiration [6]. Broncho alveolar lavage, endobronchial biopsy, dilatation of the subglottic stenosis, tracheal stent application, laser surgery, cryotherapy and diagnostic procedures may also be performed under RB.

24.4.3 Thoracic Surgery

The goal of anesthesia during RB is to ensure adequate depth of anesthesia, provide effective analgesia, decrease airway secretions, restore hemodynamic stability, preserve airway patency at the end of the procedure. All stages of anesthesia including induction, maintenance, ventilation and emergence are critical and will be discussed next.

24.4.3.1 Preoperative Period

FB removal offers some differences with other bronchoscopic procedures. First, it is always performed under emergent conditions; second, the patient is usually totally healthy before FB aspiration. For this reason, pre-anesthetic evaluation of the routine laboratory tests is not beneficial and is time consuming. It is essential to inform parents about the perioperative risks of the procedure and to obtain a written consent. The fasting time should be in the recommended limits. If not (as in emergent cases), measures to reduce the aspiration risk should be taken. The decrease in the production of saliva and anxiety are the beneficial effects of premedication. Albuterol sulfate and budesonide inhalations are reported to be advantageous in reducing perioperative pulmonary complications [20]. The knowledge of the type, place and aspiration time of the FB is important. If it is above the carina, there is a total obstruction risk and face mask ventilation or ventilation after endotracheal intubation may be impossible. Penetrating objects may cause pneumomediastinum or subcutaneous emphysema. Organic materials may swell progressively and result in total obstruction. The anesthesiologist must know the aspiration time in order to predict the airway edema or granulation tissue formation [7].

24.4.3.2 Intraoperative Period

Performing general anesthesia in pediatric patients is always a challenging task, but the situation becomes more complicated in RB procedures, even in previously healthy children. RB indications usually include airway obstruction or respiratory system pathologies and children have limited pulmonary oxygen reserve and high oxygen consumption rate. Furthermore; the surgeon, the anesthesiologist and the nurse share the same space creating a risk of chaos [8].

The shaving chin position (with head extension by keeping a shoulder roll, chin pointing upwards) is given. This is the ideal position to restore airway continuity. Monitoring should include electrocardiography, oxygen saturation via pulse oximetry, noninvasive blood pressure and body temperature [9]. Monitoring of the end tidal CO_2 values is not possible. Transcutaneous CO_2 analysis may provide a continuous estimation of the arterial CO_2 values. Total intravenous anesthesia (TIVA) is commonly used during RB, therefore bispectral index monitor is recommended in order to assess the depth of anesthesia.

24.4.3.3 Ventilation Techniques

There are four ventilation techniques during RB [2]. The choice of the ventilation technique depends on the patient's condition and the anesthesiologist's preference.

1. Apneic oxygenation: After preoxygenation, the patient is not ventilated until the periphery oxygen saturation begins to fall. This allows the surgeon a brief period of time to perform an intervention. At the end of this period, the patient is ventilated. This cycle is repeated during the procedure. The technique is not preferred in pediatric patients because of their limited oxygen reserves.
2. Spontaneous assisted ventilation: In this technique, the patient is ventilated with a bag and flexible tubing attached to the ventilation port of the RB, with high flow oxygen. Ventilation is spontaneously maintained by the patient and assisted by the anesthesiologist, when required. Generally, total intravenous anesthesia is administered, but despite the disadvantage of the environment air pollution, some centers use volatile anesthetics through the ventilation port of the bronchoscope. The advantages of this technique are the preservation of the patient's spontaneous ventilation during the procedure, decreased risk of migration of the FB to another site because of the absence of positive pressure. Nevertheless, spontaneous ventilation may be disrupted as a result of the increased airway resistance caused by the instruments inside the RB. Laryngospasm is another risk [10–12].
3. Positive pressure ventilation: This is the most commonly used technique. In this technique, anesthesia circuit is connected to the ventilation port of the RB. Positive pressure is created manually by the reservoir bag or by the anesthesia machine. Muscle relaxation is required. The advantages are the decrease of atelectasis risk, improvement in oxygenation and decrease in airway resistance. As the air leak through the outer part of the RB is inevitable, adequate tidal volume may not be delivered; this is the most frequent disadvantage of this ventila-

tion technique. Maintaining effective ventilation may only be possible by increasing flows and prolonging inspiratory times, bringing the risk of air trapping in airways distal to the stenotic areas. Another disadvantage is the dislocation of the FB by the effect of positive pressure. During positive pressure ventilation, the viewing port must be occluded in order to deliver an effective breath through the ventilation port of the RB [13]. It is advised to use spontaneous ventilation for the removal of proximally located FBs and positive pressure ventilation for the removal of distally located FBs [14].

4. Low-frequency jet ventilation (LFJV): This technique is preferred in order to prevent hypoventilation resulting from the air leak through the outside the RB. It can be applied via Sanders or Manujet III injector (VBM, Germany). High oxygen pressure created by the hospital medical gas system (wall piped oxygen) is applied to the ventilation port of the RB. This pressure is regulated and reduced by an adjustable valve, manually. It runs through the RB with a high flow, leading to a negative pressure within the airways. This creates an air corridor outside the RB and air is entrained to alveoli (Venturi effect). This technique allows the delivery of tidal volumes between 1 and 3 ml/kg. Ventilatory parameters used during LFJV vary with age group (Table 24.1). The resulting alveolar ventilation is the total of the volume delivered by the injector and the entrained air. Low-frequency jet ventilation offers the advantages of allowing bronchoscopic interventions to be performed without cessations. Complications include barotrauma, inability to predict FiO_2 and monitor $ETCO_2$, FB dislocation and blowing of blood and debris materials to distal airways resulting in inadequate gas exchange. LFJV should not be used in patients with tracheobronchial mucosa injury or low respiratory compliance [15]. In addition to standard monitoring, monitoring of chest wall rise, depth of anesthesia, SpO_2 and transcutaneous pressure of CO_2 (if available) is essential during LFJV.

   Whatever the ventilation technique is, the key of an uncomplicated procedure is the cooperation of the surgeon and the anesthesiologist.

   The choice of anesthesia method depends on the experience of the surgeon and the anesthesiologist. The major concern during anesthesia induction is to minimize airway reactivity. Concerning FB removal, face mask ventilation may cause a FB to move, resulting in complete obstruction. Inhalational or intravenous agents or both may be administered. During maintenance, short acting agents such as propofol, dexmedetomidine, remifentanil and short acting muscle relaxants are administered as the procedure is generally quite short. Nitrous oxide is not recommended, because many patients undergoing RB have air trapping to some extent.

Table 24.1 LFJV parameters according to age groups

Patient age group	Frequency/minute	Injection (driving) pressure
Neonate	40	0.5 bar
Infant	40	1 bar
Children	20–30	2 bar

Preservation of the spontaneous breathing during the procedure decreases the risk of FB dislocation, but unwanted motion, cough, retching, bronchospasm and laryngospasm are found to be more common compared to controlled ventilation. Nevertheless, there is still no consensus regarding the most effective ventilation method (spontaneous or controlled). In cases of spontaneous ventilation, anesthesia should be induced with sevoflurane, maintained with sevoflurane together with propofol infusion, together with topical lidocaine 1% (to diminish airway reflexes and anesthetic agent's doses) [25].

Severe complications can occur during RB [16]. These are closely related to the patient's condition, the severity of the pathology, the experience of the surgeon and the anesthesiologist.

Hypoxia-induced cardiac arrest is a major cause of death. Mortality is closely related to the general state of the children, at admission, the quality of anesthesia induction and the insertion success of the bronchoscopy.

The complications are as follows:

(a) Death (0.42%)
(b) Severe laryngeal edema
(c) Bronchospasm (Necessitating tracheostomy or endotracheal intubation)
(d) Pneumothorax and pneumomediastinum
(e) Hypoxic arrest during induction, maintenance or recovery period
(f) Hypoxic brain injury
(g) Tracheal or bronchial laceration
(h) FB dislocation
(i) Failure to perform RB (Necessitating thoracotomy or tracheostomy, depending of the pathology)

5. Ventilation during the postoperative period:

The choice of the ventilation technique after the procedure depends on the severity of the pathology, the patient's medical condition, the effectivity of the ventilation and the degree of edema in airways. In uncomplicated cases, spontaneous ventilation is assisted via a face mask; but endotracheal intubation should be preferred in patients having severe pathologies together with impotent airways and ineffective ventilation. After the recovery, hospital stay is strictly recommended [17]. If the patient has no previous respiratory failure and has completed the procedure without complication, he may be referred to the ward. Otherwise, follow up in intensive care is mandatory.

24.4.3.4 Sternotomy

In children, sternotomy is generally performed for the biopsy or removal of the mediastinal tumors. A detailed history and physical examination are extremely important. Anesthesiologists should focus on the respiratory system symptoms such as difficulty in breathing, cyanosis or stridor aggravated by motion, cough or straining. Wheezing unresponsive to the bronchodilators, recurrent pneumonia, persistent atelectasis, pericardial invasion, arrhythmias, pulsus paradoxus or signs of the superior vena cava syndrome are the warning pathologies for a complicated perioperative period. Echocardiographic examination is mandatory in children with

mediastinal tumors in order to determine a possible mass effect. The riskiest period is the induction of anesthesia especially in previously symptomatic children. Decrease in the sympathetic tonus, loss of the spontaneous ventilation and physiologic changes related to patient position diminish compensatory mechanisms. Children with mediastinal mass are in increased risk of severe airway obstruction and hemodynamic instability. The pediatric surgeon must be ready to perform emergent rigid bronchoscopy (RB) during the anesthesia induction of children with a mediastinal mass, in cases of total obstruction as a result of a mass effect. During induction of anesthesia, preservation of the spontaneous ventilation to secure the airway continuity is recommended. In cases of superior vena cava obstruction symptoms, induction must be performed in the sitting position and intravenous lines must be inserted into the lower limb veins. If possible, biopsy must be taken under local anesthesia. Chemotherapy or radiotherapy must be done to shrink tumors before surgery. A cardiopulmonary bypass circuit on standby should be considered for extremely high-risk cases.

24.4.3.5 Two Lung Ventilation with Manual Retraction

Several thoracic procedures, for example patent ductus arteriosus ligation, vascular ring resection and tracheo-esophageal fistula repair, can be performed with a single lumen tube positioned in the trachea providing ventilation to both lungs with the surgeon retracting the lungs as necessary. This is typically for short procedures in small infants where the surgeon is operating in the chest cavity but not directly on the lungs. This technique is especially helpful in the management of emergencies such as acute hemorrhagic conditions or tension pneumothorax. Lung injury is a concern and thus retraction should be kept to the minimum necessary. It is also possible for the surgeon to insufflate carbon dioxide (CO_2) into the pleural space to displace the lung if a thoracoscopy is being performed.

24.4.3.6 Lung Isolation and OLV

OLV is a ventilation strategy which facilitates surgical exposure in thoracoscopy or thoracotomy [18]. Unlike adult patients, OLV is not easy in children, especially in neonates and infants, because of the equipment limitations. Nevertheless, technology is advancing daily and equipment available to help anesthesiologists in performing OLV has been developed. OLV has other advantages other than surgical exposure, they include:

- Decreasing the over distention of the pathologic lobe, in congenital lobar emphysema.
- Differentiating the normal lung tissue from the pathologic one.
- Decreasing the potential trauma to the lung tissue, caused by the retractors.
- Decreasing the risk of contamination of the healthy lung by secretions, blood or infected materials originating from the diseased lung.

We will discuss next different ways to achieve OLV in pediatric patients.

Selective Bronchial Intubation

Selective bronchial intubation with a regular single lumen tube can be achieved readily and is the simplest to achieve one lung ventilation. The endotracheal tube (ETT) is advanced while auscultating breath sounds until the sound is lost on the desired side. Confirmation can be obtained by noting an acute drop in end tidal CO_2 as the tube enters a mainstem bronchus. Being that the left bronchus has a more acute angle of separation from the trachea than the right bronchus (45° versus 25°) it is much more common for the tube to be advance into the right mainstem bronchus. Rotating the patient's head to the right side helps to decrease angle the left bronchus improving the chance of a left mainstem bronchus intubation. Also rotating the ETT 180° so the bevel is pointing to the left helps direct the tube to the left bronchus. Alternatively, and with higher first pass success rate, the tube can be guided with a fiber-optic bronchoscope. It should be noted that the bronchi have a smaller diameter than the trachea and thus a tube that is too big could cause trauma to the bronchus. If an uncuffed tube is being used there is chance of a leak which might not allow for full lung collapse. Cuffed tubes should not be placed too far into the bronchus since the cuff can occlude the upper lobe of the selected bronchus, especially when intubating the right mainstem bronchus [19]. It is recommended the cuff to partially remain in the trachea. A major downside to selective bronchial intubation is that it is not possible to ventilate, apply suction, or continuous airway pressure (CPAP) to the nondependent lung. Several variations of this technique have been described. Marraro described an endobronchial bilumen tube consisting of two uncuffed tube joined together with the bronchial tube being longer than the tracheal one. It is developed for children under 3 years old [20]. Tsujimoto et al., described a micro laryngeal ETT that can be advanced into the desired bronchus, through the intubating laryngeal mask airway, with the aid of flexible fiber-optic bronchoscopy (FOB) [21]. High frequency jet ventilation (HFJV) and high frequency oscillatory ventilation (HFOV) is another option and can be indicated in short procedures. They provide optimal surgical field while allowing blood gas exchange. There is inability to monitor end tidal CO_2 ($EtCO_2$) which might be overcome by transcutaneous CO_2 ($PtcCO_2$) monitoring (Table 24.2).

Table 24.2 Approach to one lung ventilation by age

Age	ETT	Feasible one lung ventilation technique	Fiber-optic size
Newborn–2 years	3.0–4.5 mm	Endobronchial intubation/5F Parallel BB	<2.2 mm
2–8 years	4.5–6.0 mm	5F BB Coaxial/Endobronchial Intubation	2.2–2.8 mm
8–10 years	6.0–7.0 mm	5F BB coaxial/4.0 Univent Tube	2.8–4 mm
>10 years	7.0 mm plus	7F BB Coaxial/26 or higher Double Lumen Tube/4.0 or higher Univent Tube	2.8–4 mm

Bronchial Blocker

Another option for lung separation is the placement of a bronchial blocker (BB) in the operative side. A major advantage of this technique is the BB balloon can be deflated allowing quick ventilation to the operative lung if necessary. The smallest bronchial blockers in the market are the 5 French (F) Arndt blocker (Cook Medical, Indiana, USA) and the Uniblocker (Fuji System Corporation, Tokyo, Japan). They are both smaller versions of the 9F blockers from each company and are intended to be used in the same way, inside (also called coaxial) the ETT (Fig. 24.1) with the major difference to all the other blockers being that the 5F Uniblocker does not have a suction port. It should be noted that the 5F BB has a higher-pressure balloon than the 9F BB balloon used in adults and caution is warranted when inflating it [22]. Being that a fiber-optic bronchoscope is necessary for the placement of all bronchial blockers, placing them becomes a challenge when the ETT inner diameter is small. The most common pediatric fiber-optic bronchoscope size available is 2.2 mm in outer diameter. Since both the FOB (2.2 mm) and the 5F BB (1.67 mm) must fit inside the ETT plus some room for maneuvering them, the minimum recommended ETT inner diameter is 4.5 mm. Since there are many different models and sizes of fiber-optic bronchoscopes in the market it is best if the anesthesiologist checks that both the FOB being used and the BB fit inside the intended tube ex vivo. In small patients where the BB and the FOB do not fit inside the tube, i.e. ETT 4 mm or smaller, lung separation can still be achieved with a BB, however it must be placed outside (also referred as parallel) the ETT (Figs. 24.2a, b and 24.3). Our routine practice when doing this is, after assuring the patent is fully anesthetized and paralyzed, to perform a laryngoscopy with the adequate size blade, passing the 5F blocker through the glottis and advancing it gently until soft resistance is met, followed by intubation of the trachea with the desired ETT tube. Typically, we use cuffed ETT to minimize having to reintubate for leaks. After verifying the trachea has been properly intubated and end tidal CO_2 ($EtCO_2$) is confirmed, an FOB is placed inside the tube to visualize the carina and position the BB into the proper bronchus. The adapter included with BB can be used to ventilate while the FOB is being used. Most of the time the BB is in the right mainstem bronchus and needs to be pulled back. If collapse of the right lung is desired the balloon of the BB is placed

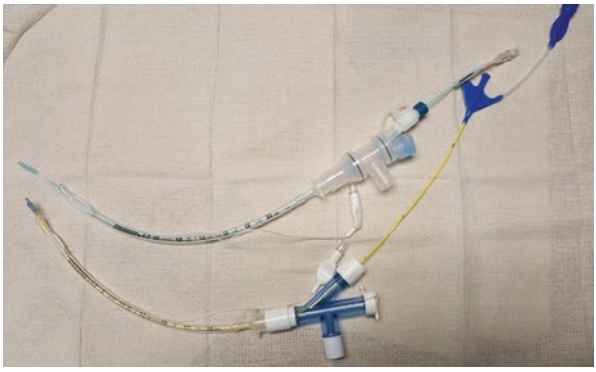

Fig. 24.1 5F Uniblocker and 5F Arndt blocker with its own ventilator adapter when used inside the tube (coaxially)

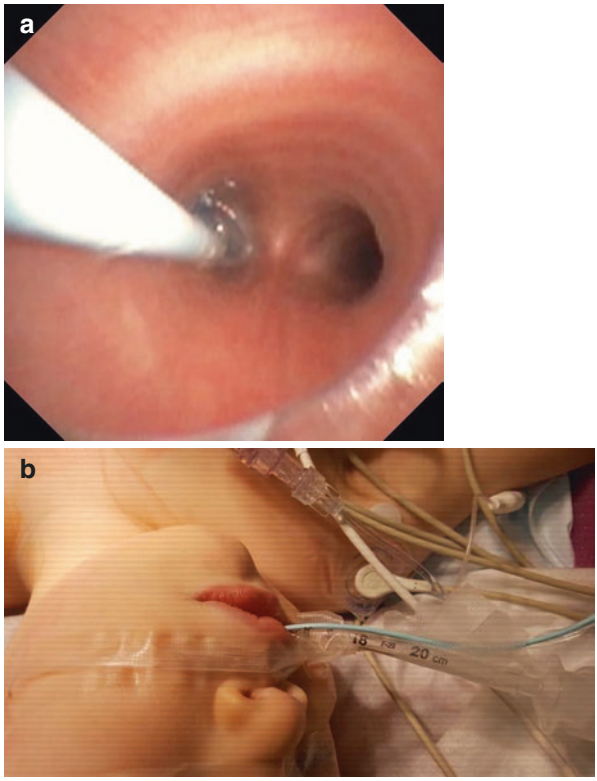

Fig. 24.2 (**a**) Uniblocker placed in left mainstem bronchus outside a 4.0 ETT visualized through a 2.2 fiber-optic scope. (**b**) Uniblocker placed outside a 4.0 mm ETT

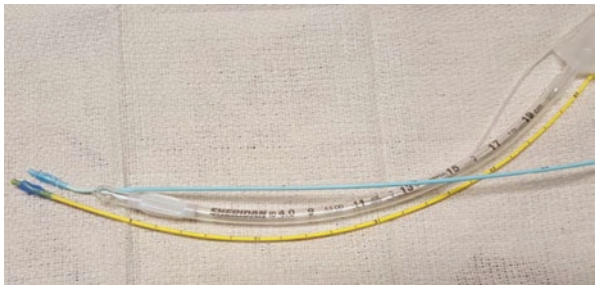

Fig. 24.3 5 French (F) Uniblocker and 5F Arndt blocker when used outside the tube (parallel)

very shallow in the right mainstem bronchus to avoid blocking the right upper lobe. Visualization of the cuff as it is being inflated is mandatory to avoid injuring the bronchus or herniation of the cuff into the trachea. If it is desired to block the left mainstem bronchus then the BB must be pulled above the carina and, taking advantage of the hockey stick design of the Uniblocker (or alternatively manually shaping the distal end of the Arndt blocker into a hockey stick, since we do not use the lasso with this technique), rotating it so that the hockey stick shape directs the BB into the left bronchus. As mentioned previously, rotating the head of the patient to the right side can help bring the left bronchus into a more direct angle. It must be recognized

that when placing a BB outside the tube it can be much more difficult to manipulate the BB into the left bronchus compared to when placed inside the ETT, especially if it migrates out of the bronchus mid procedure. Care must be taken to ensure the ETT and BB are properly secured in place and not to allow any motion such as neck flexion or any undue pulling on the circuit that can displace the BB. Our preference is to advance the BB far into the desired bronchus while the patient is supine and, after the patient has been fully positioned, to pull the BB out into the correct distance into the bronchus after we are certain the patient will remain immobile. Alternatively, Fogarty catheters or Miller atrial septostomy balloons have been described when small BB have not been available but being that they have a high-pressure low volume balloons caution is recommended to avoid injuring the bronchus [2].

Univent Tube

The Univent tube (Fuji System Corporation, Tokyo, Japan) is a single lumen tube with a bronchial blocker balloon already integrated in the wall of the tube [13]. The blocker balloon has a hockey stick shape at the end and is advanced and rotated into position. Albeit narrow, the lumen of the second tube may be served to deliver oxygen, inhalational agents or suction the operated lung; but this property is only present in Univent tubes with an ID of 6 mm or greater. The Univent tube's blocker balloon has low-volume, high-pressure properties, so over distention or long-term use may cause damage of the tracheal mucosa [23]. Dislodgement of the balloon during surgery is quite difficult, because it is strictly connected to the main endotracheal tube [2]. Due to the simplicity of its design It would seem ideal for lung isolation in small pediatric patients. However, the outer diameter is much larger than a regular single lumen tube with the same inner diameter. For example, the smallest Univent tube in the market has a 3.5 mm inner diameter but an outer diameter of at least 7.5–8 mm per the manufacturer, which would compare to a regular 5.5 mm tube. Thus, it is useful for children older than 6 years of age, in which case it is likely preferable to use a regular single lumen tube with a BB inside, which provides a larger area to ventilate and less resistance to flow. In the scenario of a patient needing to remain intubated post procedure, the BB can be simply pulled out instead of requiring the Univent tube to be replaced a regular single lumen tube.

Double Lumen Tube

Double lumen tubes are the preferred method for lung separation in older children. Just as with adults, it provides true lung isolation, it allows for suction, and application of CPAP. The smallest in the market is 26F Rusch (Teleflex, North Carolina, USA). Both right and left sided tubes are available. Its outer diameter is 8.67 mm which is close to the outer diameter of a 6.5 mm regular single tube (8.9 mm). Other pediatric sizes available in the market are 28F and 32F, both made by Rusch and Mallinckrodt (United Kingdom). Thus, they are recommended for children older than 8 years of age [24]. A small pediatric FOB is required to be able to enter each lumen. In adults, the correct length of the tube is directly proportionate to the height

of the patient, but there is not a clear proportion in children. The use of right DLTs is not preferred in small children because of the high risk of occluding the right upper lobe. This is an anatomical disadvantage of the children and the tube manipulation does not overcome it. A similar disadvantage is present in left-sided DLTs such as occluding the left upper lobe bronchus by the advanced bronchial tip. The technique for placement is the same as in adults and will not be described here.

Hypoxemia Management During OLV

Hypoxemia during OLV is almost inevitable, especially in small children. As in adults, CPAP use or intermittent ventilation of the nondependent lung, PEEP application to the dependent lung may improve oxygenation [10].

24.4.3.7 Monitoring

Standard monitoring including electrocardiogram, pulse oximeter, blood pressure measurement, end tidal CO_2 monitoring ($EtCO_2$), and temperature are the minimum requirement for any thoracic procedure involving general anesthesia. Invasive arterial blood pressure monitoring is usually not required unless there is expectation of a long or complicated procedure, poor cardiopulmonary status, or possibility of large blood loss. If in doubt it is probably best to err on the side of caution and obtain arterial access. In terms of venous access most cases can be done with two large bore, for age, peripheral intravenous catheter. Central venous access is rarely required, but if there is poor peripheral venous access or any comorbidity that might require the patient to need any vasoactive infusions, it is reasonable to obtain. Transcutaneous CO_2 ($PtcCO_2$) is recommended when the operative procedure does not allow for end tidal CO_2 monitoring.

24.4.3.8 Pain Management

Pain management after thoracic surgery in pediatric patients presents unique challenges. In young patients that may not be able communicate properly the identification and assessment of pain presents a challenge in itself. Even when pain has been properly identified and assessed, providing adequate analgesia without risking over sedation and respiratory depression can be difficult. Pain is a very complex experience involving a multitude of factors, the most obvious being the tissue trauma, but also just as important, the anxiety and coping mechanisms of the child along with the parents [25]. Left untreated, pain can have physical consequences such as hyperglycemia, protein catabolism, increased oxygen consumption, increased blood pressure, diaphragmatic splinting, decreased cough, decreased tidal volume, decreased Functional Residual capacity (FRC), and decreased bowel motility [26].

Chronic pain after thoracotomy, also referred to as post thoracotomy pain syndrome, is defined by the International Association for the Study of Pain as pain along the thoracotomy incision that persist after 2 months following the surgical procedure [27]. Its incidence is estimated around 50% in adults but appears to be lower in 20% children [28, 29]. Preemptive analgesia, particularly regional anesthesia, may help to reduce its incidence [30, 31].

Regional Modalities

The most basic form of regional anesthesia is surgical wound infiltration with local anesthetic. It has low risk and can be easily performed by the surgeon. Care must be taken not to exceed the toxic amount of local anesthetic. Doses of bupivacaine of up to 3 mg/kg, and lidocaine up to 5 mg/kg have been found to be below the toxic range [32, 33]. It should be noted that clearance and protein binding for local anesthetic agents are reduced in infants below 6 months of age thus the dose is recommended to be halved in these patients. Preemptive local anesthetic infiltration prior to incision for thoracotomy did not reduce postoperative pain in a study by Cerfolio et al. [34].

Thoracic epidural catheters are the most common modality for pain management in adult thoracic anesthesia [35]. It seems obvious that local anesthetic delivered at the corresponding thoracic level will provide superior pain control. The administration of local anesthetics at the thoracic level is easily titratable, and provides the additional advantage of sympathetic blockade and superior blunting of stress response otherwise not achieved by other techniques. In pediatric patients, epidural catheter placement is performed in the same manner and following the same safety guidelines as for adults with the major difference being that both, the American Society of Regional Anesthesia and the and the European Society of Regional Anesthesia, recommend that all regional anesthesia in children should be performed during general anesthesia or deep sedation [36, 37]. Also, in infants less than 1 year it is common practice to thread the epidural catheter from the caudal space to the desired thoracic location [38]. Ultrasound imaging has been found to be helpful in guiding the catheter to the proper location [39]. Maximum infusion rates for lidocaine of 1 mg/kg per h, and for bupivacaine of 0.2–0.3 mg/kg per h have been recommended for young infants [33, 40]. Again, the dose should be halved for infants younger than 6 months. The concomitant use of opioids allows the use of lower concentrations of local anesthetics and decreases the risk of local anesthetic toxicity.

Paravertebral catheters have emerged as an alternative to the epidural catheter route for management of post thoracotomy pain. When performed unilaterally they have been found to provide comparable pain control with fewer side-effects such as nausea, vomiting, and hypotension, when compared to an epidural catheter technique [41].

Single shot epidural techniques are typically administered in younger children at the caudal epidural space. Since administering a local anesthetic at the caudal or even lumbar epidural level will not reach adequate thoracic levels, single shot caudal techniques are mostly limited to the use of hydrophilic opioids and in particular preservative free morphine. Morphine, easily administered via the caudal space in younger children (typically but not limited to children <5 years of age) will provide a long-lasting analgesic effect. Its peak analgesic effect is 4–7 h [42], and its duration of action has been reported up to 24 h [43]. Even though neuraxial opioids don't offer the potential advantages of a sympathetic thoracic epidural block achieved with local anesthetic agents, epidurally administered opioids have been shown to provide excellent analgesia, pulmonary function, and early ambulation [44]. Side

effects related to neuraxial opioids include nausea and vomiting, pruritus, somnolence, respiratory depression, and urinary retention. Close post-operative monitoring for 24 h is mandatory when neuraxial opioids are utilized. Alternative drugs such as the alpha 2 receptor agonist clonidine, ketamine, and magnesium have been used in the epidural space to minimize undesirable side effects of opioids such as respiratory depression, and to prolong analgesic effects [45–47].

Insertion of an epidural catheter can lead to several complications such as misplacement, knotting, and migration, especially if advanced too far, rupture, infection, leakage, epidural hematoma, and neurologic injury. The true incidence of neuraxial anesthesia complications is not known. Severe complications of epidural catheters, defined as infection, local anesthetic toxicity, cardiac arrest, drug error causing harm, or neurologic injury, in pediatric patients have been estimated around 1 in 2000 patients in one study, with permanent neurologic injury at 1 in 10,000 patients [48]. Whereas another reported zero neurologic complications in 150,000 single shot caudal anesthetics [49]. At the moment it does not appear children are at higher from neuraxial techniques risk than adults [50].

Intravenous Modalities

Intravenous opioids although highly effective for pain management, have the downside of having periods of heavy sedation early after being administered, transitioning into periods of low analgesic effect when wearing off. In addition, nausea, pruritus, urinary retention, and constipation are common side effects. Long acting opioids such as morphine, hydromorphone, and even methadone provide a steadier pain control than short acting opioids such as fentanyl.

Acetaminophen is a non-opioid, centrally acting analgesic. Acetaminophen used in combination with opioids leads to improved analgesia and a decrease in opioid dosing and their side effects [51]. Non-Steroidal Anti-inflammatory Drugs (NSAIDS), particularly ketorolac, have been shown to reduce postoperative opioid requirements in pediatric surgical patients, including neonates and premature babies [52].

Dexmedetomidine is a sedative agent that confers sedation by selectively binding to central alpha 2 adrenoceptors. Although at this point it is only approved by the FDA for use in adults for up to 24 h, it has been widely used in children even for prolonged periods of time [53]. It has become popular in pediatric anesthesia since it is associated with a lower incidence of emergence delirium after inhalational anesthesia in children [54, 55]. Preemptive use of intravenous dexmedetomidine was reported to reduce the incidence of post thoracotomy pain syndrome in adults undergoing coronary artery bypass grafting [56]. However, in another study, when administered via a paravertebral catheter even though it was associated with lower post-operative pain and opioid consumption, it had no effect in the incidence of post thoracotomy pain syndrome. It must be noted that pre-operative teaching also plays a role in anxiety reduction [57].

Ketamine, an N-methyl D-aspartic acid (NMDA) receptor antagonist, is a dissociative hypnotic with analgesic properties when used in low doses. It has been shown to reduce in lower pain scores in the postoperative period in adults [58].

Taking it all together, a complete multimodal approach to pain management covers different factors involved in the experience of pain. Local anesthetic to block the transition of the nociceptive signal, and anti-inflammatory to reduce tissue trauma, an NMDA receptor antagonist to prevent central sensitization to pain, opioids to enhance inhibitory pathways, and a preoperative teaching and/or a sedative for anxiolysis.

24.5 Conclusion

Anesthesia for pediatric thoracic surgery is quite challenging. It is essential to perform a detailed preoperative evaluation, have a knowledge of characteristics of different age groups and applicable two-lung or OLV strategies, and also have a full anesthetic plan that includes pain management strategies. Furthermore, it must be stressed that communication between the surgeon and the anesthesiologist, such as sharing the surgical plan, any acute changes in ventilation parameters, heart rate or blood pressure, and the post-operative plan, is extremely important in order to reduce complications.

References

1. Sunder RA, Haile DT, Farrell PT, Sharma A. Pediatric airway management: current practices and future directions. Pediatr Anesth. 2012;22(10):1008–15.
2. Madden K, Khemani RG, Newth CJ. Paediatric applied respiratory physiology–the essentials. Paediatr Child Health. 2009;19(6):249–56.
3. American Society of Anesthesiologists Committee. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology. 2011;114(3):495.
4. Yuan N, Skaggs DL, Davidson Ward SL, Platzker AC, Keens TG. Preoperative polysomnograms and infant pulmonary function tests do not predict prolonged post-operative mechanical ventilation in children following scoliosis repair. Pediatr Pulmonol. 2004;38:256–60.
5. Stocks J. Infant respiratory function testing: is it worth all the effort? Paediatr Anaesth. 2004;13:537–40.
6. Akcora B, Celikkaya ME, Ozer C. Bronchoscopy for foreign body aspiration and effects of nebulized albuterol and budesonide combination. Pak J Med Sci. 2017;33(1):81–5.
7. Fidkowski CW, Zheng H, Firth PG. The anesthetic considerations of tracheobronchial foreign bodies in children: a literature review of 12,979 cases. Anesth Analg. 2010;111:1016–25.
8. Sinha V, Talagauara Umesh S, Jha SG. Rigid bronchoscopy in pediatric patients. Ind J Otolaryngol Head Neck Surg. 2017;69(4):449–52.
9. Ciftci AO, Bingöl-Koloğlu M, Senocak ME, Tanyel FC, Buyukpamukçu N. Bronchoscopy for evaluation of foreign body aspiration in children. J Pediatr Surg. 2003;38(8):1170–6.
10. Cai Y, Li W, Chen K. Efficacy and safety of spontaneous ventilation technique using dexmedetomidine for rigid bronchoscopic airway foreign body removal in children. Paediatr Anaesth. 2013;23:1048–53.
11. Chai J, Wu XY, Han N, Wang LY, Chen WM. A retrospective study of anesthesia during rigid bronchoscopy for airway foreign body removal in children: propofol and sevoflurane with spontaneous ventilation. Paediatr Anaesth. 2014;24:1031–6.

12. Chen KZ, Ye M, Hu CB, Shen X. Dexmedetomidine vs remifentanil intravenous anaesthesia and spontaneous ventilation for airway foreign body removal in children. Br J Anaesth. 2014;112:892–7.
13. Annigeri RV, Patil RS. A retrospective analysis on anesthetic management during rigid bronchoscopy in children with foreign body aspiration: propofol and sevoflurane with controlled ventilation. Anesth Essays Res. 2017;11(4):871.
14. Liu Y, Chen L, Li S. Controlled ventilation or spontaneous respiration in anesthesia for tracheobronchial foreign body removal: a meta-analysis. Pediatr Anesth. 2014;24(10):1023–30.
15. Evans E, Biro P, Bedforth N. Jet ventilation. Contin Educ Anaesth Crit Care Pain. 2007;7(1):2–5.
16. Roberts S, Thornington RE. Paediatric bronchoscopy. Contin Educ Anaesth Crit Care Pain. 2005;5(2):41–4.
17. Andreoli SM, Kofmehl E, Sobol SE. Is inpatient admission necessary following removal of airway foreign bodies? Int J Pediatr Otorhinolaryngol. 2015;79(9):1436–8.
18. Fabila TS, Menghraj SJ. One lung ventilation strategies for infants and children undergoing video assisted thoracoscopic surgery. Ind J Anaesth. 2013;57:339–44.
19. Lammers CR, Hammer GB, Brodsky JB, Cannon WB. Failure to isolate the lungs with an endotracheal tube positioned in the bronchus. Anesth Analg. 1997;85:944.
20. Pawar DK, Marraro GA. One lung ventilation in infants and children: experience with Marraro double lumen tube. Paediatr Anaesth. 2005;15:204–8.
21. Tsujimoto S, Fujiwara S, Tashiro C. How to perform differential lung ventilation in pediatric cases? Anesthesiology. 1999;91:327.
22. Golianu B, Hammer GB. Pediatric thoracic anesthesia. Curr Opin Anesthesiol. 2005;18(1):5–11.
23. Hammer GB, Brodsky JB, Redpath JH, Cannon WB. The Univent tube for single-lung ventilation in paediatric patients. Paediatr Anaesth. 1998;8:55–7.
24. Semmelmann A, Kaltofen H, Loop T. Anesthesia of thoracic surgery in children. Paediatr Anaesth. 2018;28(4):326–31.
25. Rabbitts JA, Groenewald CB, Tai GG, Palermo TM. Presurgical psychosocial predictors of acute postsurgical pain and quality of life in children undergoing major surgery. J Pain. 2015;16(3):226–34.
26. Kehlet H. Manipulation of the metabolic response in clinical practice. World J Surg. 2000;24(6):690–5.
27. Gerner P. Postthoracotomy pain management problems. Anesthesiol Clin. 2008;26(2):355–67.
28. Karmakar MK, Ho AM. Postthoracotomy pain syndrome. Thorac Surg Clin. 2004;14:345–52.
29. Kristensen AD, Pedersen TA, Hjortdal VE, Jensen TS, Nikolajsen L. Chronic pain in adults after thoracotomy in childhood or youth. Br J Anaesth. 2009;104(1):75–9.
30. Gottschalk A, Cohen SP, Yang S, Ochroch EA. Preventing and treating pain after thoracic surgery. Anesthesiology. 2006;104(3):594–600.
31. Andreae MH, Andreae DA. Regional anaesthesia to prevent chronic pain after surgery: a Cochrane systematic review and meta-analysis. Br J Anaesth. 2013;111(5):711–20.
32. Berde CB. Toxicity of local anesthetics in infants and children. J Pediatr. 1993;122(5):S14–20.
33. Morton NS. Local and regional anaesthesia in infants. Contin Educ Anaesth Crit Care Pain. 2004;4(5):148–51.
34. Cerfolio RJ, Bryant AS, Bass CS, Bartolucci AA. A prospective, double-blinded, randomized trial evaluating the use of preemptive analgesia of the skin before thoracotomy. Ann Thorac Surg. 2003;76:1055–8.
35. Goto T. What is the best pain control after thoracic surgery? J Thorac Dis. 2018;10(3):1335.
36. Ivani G, Suresh S, Ecoffey C, Bosenberg A, Lonnqvist PA, Krane E, Veyckemans F, Polaner DM, Van de Velde M, Neal JM. The European Society of Regional Anaesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine joint committee practice advisory on controversial topics in pediatric regional anesthesia. Reg Anesth Pain Med. 2015;40(5):526–32.
37. Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society

of Regional Anesthesia and Pain Medicine evidence-based guidelines. Reg Anesth Pain Med. 2018;43(3):263–309.
38. Gunter JB, Eng C. Thoracic epidural anesthesia via the caudal approach in children. Anesthesiology. 1992;76:935–8.
39. Ponde VC, Bedekar VV, Desai AP, Puranik KA. Does ultrasound guidance add accuracy to continuous caudal-epidural catheter placements in neonates and infants? Pediatr Anesth. 2017;27(10):1010–4.
40. Biebuyck JF, Yaster M, Maxwell LG. Pediatric regional anesthesia. Anesthesiology. 1989;70(2):324–38.
41. Davies R, Myles P, Graham J. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy—a systematic review and meta-analysis of randomized trials. Br J Anaesth. 2006;96:418–26.
42. Bailey BL, Rhondeau S, Schafer PG, et al. Dose-response pharmacology of intrathecal morphine in human volunteers. Anesthesiology. 1993;79:49–59.
43. Stoelting RK. Intrathecal morphine – an under used combination for postoperative pain management. Anaesth Analg. 1989;68:707–9.
44. Glenski JA, Warner MA, Dawson B, Kaufman B. Postoperative use of epidurally administered morphine in children and adolescents. Mayo Clin Proc. 1984;59(8):530–3.
45. De Negri P, Ivani G, Visconti C, et al. The dose-response relationship for clonidine added to a postoperative continuous epidural infusion of ropivacaine in children. Anesth Analg. 2001;93:71–6.
46. Cook B, Grubb DJ, Aldridge LA, Doyle E. Comparison of the effects of adrenaline, clonidine and ketamine on the duration of caudal analgesia produced by bupivacaine in children. Br J Anaesth. 1995;75:698–701.
47. Bilir A, Gulec S, Erkan A, Ozcelik A. Epidural magnesium reduces postoperative analgesic requirement. Br J Anaesth. 2007;98:519–23.
48. Llewellyn N, Moriarty A. The national pediatric epidural audit. Pediatr Anesth. 2007;17(6):520–33.
49. Giaufre E, Dalens B, Gombert A. Epidemiology and morbidity of regional anesthesia in children: a one-year prospective survey of the French-Language Society of Pediatric Anesthesiologists. Anesth Analg. 1996;83(5):904–12.
50. De Tommaso O, Caporuscio A, Tagariello V. Neurological complications following central neuraxial blocks: are there predictive factors? Eur J Anaesthesiol. 2002;19(10):705–16.
51. Walker SM. Pain after surgery in children: clinical recommendations. Curr Opin Anaesthesiol. 2015;28(5):570.
52. Papacci P, De Francisci G, Iacobucci T, et al. Use of intravenous ketorolac in the neonate and premature babies. Paediatr Anaesth. 2004;14:487–92.
53. Hammer GB, Philip BM, Schroeder AR, et al. Prolonged infusion of dexmedetomidine for sedation following tracheal resection. Pediatr Anesth. 2005;15:616–20.
54. Isik B, Arslan M, Tunga AD, Kurtipek O. Dexmedetomidine decreases emergence agitation in pediatric patients after sevoflurane anesthesia without surgery. Paediatr Anaesth. 2006;16:748–53.
55. Ibacache ME, Munoz HR, Brandes V, Morales AL. Single-dose dexmedetomidine reduces agitation after sevoflurane anesthesia in children. Anesth Analg. 2004;98:60–3.
56. Moghaddam MJ, Barkhori A, Mirkheshti A, Hashemian M, Mohajerani SA. The effect of preemptive dexmedetomidine on the incidence of post-thoracotomy pain syndrome in patients undergoing coronary artery bypass grafting. Anesth Pain Med. 2016;6(3):e36344.
57. Guo P. Preoperative education interventions to reduce anxiety and improve recovery among cardiac surgery patients: a review of randomised controlled trials. J Clin Nurs. 2015;24(1-2):34–46.
58. Gorlin AW, Rosenfeld DM, Ramakrishna H. Intravenous sub-anesthetic ketamine for perioperative analgesia. J Anaesthesiol Clin Pharmacol. 2016;32(2):160.

Robot-Assisted Thoracic Surgery and Anesthesia

25

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25.1 Introduction

From the time of ancient civilizations there have been many accounts of automated devices or automats representing humans in appearance. Through the industrial age, there appeared more practical applications, by replacing humans in performing repetitive or dangerous tasks, which humans prefer or are unable to do because of size limitations, or which take place in dangerous environments.

The term robot, which means forced labor in Czech language, was first used in the begin of the last century by Karel Capek in his play entitled Rossum's Universal Robots and presented in 1921, introducing the term robot into English and other languages.

Actually, a robot means a machine capable of carrying out a complex series of actions automatically. Robots have either their control embedded within, or are guided by external, human control.

Robots have become incorporated into daily life over the last half-century: what was once only science fiction has now become a reality. Robots are used widely in all kinds and types of activities and domains: from house holding, to grass movers, to leisure, to industry, and most recently medicine, enhancing the development of certain types of surgical interventions. Today, everyone living in the developed world benefits from the advances in robotics in everyday life. While robots are commonly employed in the healthcare laboratory setting, they have been more slowly

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integrated into clinical medicine. Over the last two decades, research in surgical robotics has been continually increasing with a geometric rise in the number of manuscripts published each year. Surgical robotics is an evolving field aiming to take advantage of the features of robotics that have made them so valuable in other industries nishiharadierk.

In 1985, the first surgical application of industrial robotic technology was described when an industrial robotic arm was modified to perform a stereotactic brain biopsy with 0.05 mm accuracy. This served as the prototype for Neuromate (Integrated Surgical Systems, Sacramento, CA, USA) which received Food and Drug Administration (FDA) approval in 1999 [1]. In 1992, the Robodoc (Integrated Surgical Systems, Sacramento, CA, USA) was introduced for use in hip replacement surgery. Whereas the Robodoc has been used in thousands of patients in Europe, it has not yet received FDA approval in the United States because of concerns regarding complication rates [2–4]. Similar devices have been designed for use in knee replacement and temporal bone surgery, but neither device has yet completed clinical testing nor received FDA approval [5, 6].

The potential for widespread clinical application of the newly developed telerobotic devices was commercially recognized and in 1997, Intuitive Surgical's daVinci surgical system was used to perform a laparoscopic cholecystectomy in Belgium [7]. In 1999, Computer Motion Inc. introduced the Zeus surgical system, which differed from daVinci primarily in the configuration of the surgeon's workstation.

Robotic assisted thoracic surgery (RATS) started in a few centers in the mid-late 1990s. The first report was made at the beginning of the year 2000 [8].

Despite the fact that thoracic surgery is one of the fastest growing techniques, the results of RATS are reported very rarely. Yet we may not recognize any major advantage in the outcome when compared to video assisted thoracic surgery (VATS), but certainly, the superior capabilities of the robotic surgery could be beneficial. More experience in RATS may provide superior results in oncological, physiological and life quality measurements [9].

25.2 Surgical Point of View for Thoracic Robotic Surgery

25.2.1 Advantages, Disadvantages, Learning Curves

In the beginning, RATS was mainly compared with the VATS. This technique gained recognition in thoracic surgery from the 1990s and some articles even reported significant improvements in comparison with open surgery. Advantages of video assisted thoracic surgery were less trauma and pain [10], shorter chest drainage duration, decreased hospital stay [11–13], preservation of short-term pulmonary function [14], reduced pain, fewer complications. The robotic surgery is of course also a minimally invasive technique, and therefore, it will be difficult to show differences in the future with VATS.

Like the VATS did years ago, RATS is a surgical technique that is getting more and more integrated in the spectrum of thoracic surgery. The spread of initial

minimally invasive techniques was slow considering limitations (limited maneuverability and unstable camera platform) [8] and poor ergonomics. Often, one specific technique, either VATS or RATS, is chosen by one particular surgeon. Availability of the robotic platform is the mean reason. A minority of thoracic surgeons is trained in both minimal invasive techniques and so it will be difficult to obtain large comparative studies with those equipoise experts. Also, worldwide, there are areas where robotic platform has integrated very well and other areas where RATS-programs are just starting up.

Of course, the costs for the use of a robotic system are an important factor here. Since VATS does not have such an expensive price tag, its penetration is much greater. Unfortunately, there is no real standardization of the VATS, which seems to be more the case with RATS. Furthermore, the learning curve for VATS is greater than for RATS (50 cases versus 25 cases) [15]. Obviously, the original way of training of the surgery must be taken into account. Previously everyone was trained for open surgery through the thoracotomy or sternotomy, later on, the video assisted thoracic surgery was started up. In the group of people who have not switched to video assisted thoracic surgery, there are a number of surgeons that immediately switched to RATS bypassing VATS. Those who switched from VATS to RATS, of course, already had a minimal invasive thoracic surgery learning curve, which might be the explanation for the need of a smaller number of cases before getting to expertise.

Advantages of RATS are of course the 3D vision, the use of the robot-controlled and hinged instruments, and the ergonomic aspect for the surgeon. Movements are more precise, filtered and scaled. Therefore, improved surgical precision and accuracy is possible.

The robotic system is not perfect: loss of tactile feedback, increased operation time, distance between the surgeon and the patient. Training and learning to work with this system can overcome these issues. The big disadvantage remains the high cost price of the system and the parts that are needs for an operation. Instruments can only be used in a limited way (10–20 uses), which leads to considerable costs. Some articles indicate a shorter hospital stay, which means that part of the higher cost price for the material could be recovered.

Another aspect is of course the specific training that is required. If this can be done on a dual console system, there is of course a better guidance of the start-up. The ‘student’-surgeon and the experienced surgeon (proctor) have the same picture and switching the instruments between the two consoles is easy. Also, in case of bleeding, there is often more and better control possible because the robots’ arms remain standing in the same position and therefore are not dependent on a human factor (movements, distraction, …). An emergency thoracotomy can always be performed while the bleeding remains under stable control, much better than with a video assisted thoracic procedure. Training with a single console is possible but more difficult.

The big advantage is actually a personal one, for the surgeon. Ergonomics for the surgeon on the robotic console cannot be compared with the situation during a video assisted thoracic operation. Sitting down on a comfortable chair at the console is

completely different from standing with two surgeons sideways from a patient and looking at a screen. The torsion of the body leads to stresses in the back and legs.

In the meantime, the technique has been considered safe, reproducible and there is an association with a reduced duration of stay, low morbidity and mortality [12]. Recent articles on RATS mention equally good oncological results in the medium term. Larger series show that the visualization and dissection of lymph nodes in the mediastinum goes more smoothly so that more nodal stations are procured. This gives a better staging of the disease and consequently a more adapted therapy [11]. The robot was primarily intended for cardiac surgery, but the current machine is intended for different surgical disciplines. This has also ensured that the RATS has developed well in recent years and the number of procedures continues to increase.

25.2.2 The Robot Assisted Lobectomy

The lobectomy is the most commonly performed oncologic procedure in which a precise anatomical dissection of the lung is performed. Each center has now developed a technique, usually in function of the type of the robotic system. Where there used to be more three-armed systems, there is now a rise of operating techniques where the four arms can be used. This led to more standardization (3- or 4-arms) of the technique and it can also be used for resection of all lobes. The older system is more dependent of correct positioning above the patient due to the lesser mobility of the central attachment of the robotic arms. This created situations where accessibility for the anesthesiologist to the patient was impaired, and that may be crucial in critical situations. This issue was cleared with the use of a last, improved model of the robotic system.

The mortality is comparable to the other techniques, open and video assisted surgery. Long-tern oncologic results are consistent with other large series using VATS or thoracotomy [15]. The morbidity is also the same and there are no specific complications due to the robotic system described in the literature (in case of thoracic surgery). Blood loss is not significantly different in comparative ranges between VATS and RATS [16].

25.2.3 The Robot Assisted Segmentectomy

The number and proportion of early-stage lung cancers is likely to increase due to the growth and aging the population and the low-dose chest CT screening programs of high-risk populations.

Due to the extra movement possibilities of the robotic arms and new preoperative visualization techniques of vascular structures with indocyanine green and creation of anatomic 3D-models for preoperative planning, segmentectomy (sublobar anatomical resection in a lobe) has become an intervention that can also be performed by more surgeons in a mini-invasive way. Video assisted thoracic surgery experts perform this technically demanding operation in difficult circumstances. The use of

the robot has made the operation more accessible. The meticulous dissection of hilar, bronchial, and vascular lymph nodes is possible and very important for the correct staging of early lung cancer.

Metastases in the lungs can thus be removed and wider resection margins are obtained. Resections of small early lung cancers in high-risk individuals are also possible with the aid of the robot system. To give the oncological validation for sublobar anatomical resections in small lung cancer, two studies are in progress, namely CATGB 140503 (USA) and JCOG 0802 (Japan). The future will show whether this attitude can be applied to all patients with clinical stage 1A disease without having to make oncological compromises. Segmentectomy has been proven safer than lobectomies [17]. It gives even less complications when performed thoracoscopically compared to open surgery. This is why some surgeons advocate that a sublobar anatomical resection has to be closed surgery, giving new challenges. The robotic platform will probably be more useful in this type of operations.

Our surgical technique is a four-arm set up. The anesthetized, ventilated patient is positioned on a vacuum mattress in lateral decubitus. The chest is elevated with an inflatable balloon placed under the patient so that the thorax is the highest point, horizontalized. The robot is positioned in the back of the patient. Four ports are used and one assistants-port.

The camera is located on the intersection of the eighth or ninth intercostal space and posterior axillary line. From here the second port is placed 8 cm to the anterior side, the third port 8 cm to the posterior side, the fourth 8 cm in 45° up and posteriorly, respecting 6 cm from the midline of the spine. A 12-mm laparoscopic port is place supradiaphragmatically, under visualization with a 30° camera, and after insufflation of CO_2, at a pressure of 5 mmHg. This port is used for suctioning, stapling and retraction. It's also this ports' entry point that will be enlarged to approximately 4 cm at the end of the operation for retraction of the specimen. Instruments that are used are the spatula in the right hand, the bipolar forceps in the right and the tip-up forceps also in the right hand. The spatula is changed with the Cadière-forceps for passing behind structures. The assistant port is used for the stapling devices. After the removal of the specimen, one drain is placed in the anterior robotic port. Patient is awake and extubated in the operating room.

25.2.4 The Robot Assisted Thymectomy

Minimal invasive thymectomy is indicated for a majority of patients with myasthenia gravis and early-stage thymoma [18]. The robotic approach offers a better mediastinal dissection, may improve cosmetic results and reduce postoperative pain [19]. This results in accelerated recovery. Size is generally accepted as a factor for the choice of operative approach, although there are no guidelines. Masses smaller than 4 cm on imaging techniques resected by robotic assisted thoracic surgery give better results for quality of life postoperatively [20].

Our technique is a three-arm technique, but if the size of the patient's thorax allows it, we use a four-arm technique. The patient is in dorsal decubitus on a

vacuum mattress, slightly tilted (30–45°) to the opposite site of the access site. The camera port is placed at the intersection of the fourth intercostal space and mid-axillary line. The second port almost in the axilla, under the anterior axillary fold, the third 8 cm distally of the camera port. The assistant's port is placed supradiaphragmatic in the eighth or ninth intercostal space, posterior axillary line. Insufflation of CO_2, at a pressure of 5 mmHg permits a good visualization of the mediastinum. Dissection is started caudally, until the upper pole of the thymus is released. The specimen is always removed in a bag and one chest drain is placed.

25.2.5 Summary of Surgical Point of View

Over the past decade robotic assisted thoracic surgery has grown and for sure, it will take an important place in the treatment of complex thoracic pathologies. The enhanced dexterity and 3D-visualization makes it possible to do this in the small space of the thoracic cavity. The need for adapted instrumentation is still actual.

25.3 Anesthetic Management of RATS

25.3.1 Are There Any Differences?

Given the relative recent introduction of RATS technique for thoracic surgery, there are no or very few studies describing the right anesthesia technique and the right analgesia to be used in this situation. Nevertheless, there is evidence for some differences as compared to classical VATS and some specific points, some of them commons for all types of robotic surgery that should be taken into consideration.

25.3.2 Understanding the Surgical Technique and Equipment and Patient Selection

First of all there is the bulkiness and particularity of the robot operating technology, which can be a disturbing factor in an operating room. The thoracic robot is different from other robot-assisted surgeries, because there is carbon dioxide insufflation, artificial pneumothorax, prolonged one-lung ventilation (OLV) and other factors that may influence significantly the respiratory and circulatory functions. Therefore, anesthesia for thoracic robotic surgery is more demanding as compared to anesthesia for general robotic surgical procedures.

A full understanding of not only the surgical technique, but of the related equipment, theirs impacts on he patient and the corresponding pathophysiological changes is necessary to ensure both success of the surgery and the safety of the patient.

Because of the different technique used as compared to other thoracic surgical procedures, including small incisions, artificial tension pneumothorax and prolonged OLV, the patients' selection is strict.

The patient's condition including a height above 130 cm and a weight more than 30 kg is necessary. The included patients should present for lobectomy, and lymph node dissection, esophageal surgery and resection of mediastinal neoplasm less than 5 cm. Lung function, arterial blood gases, chest X-ray and airway viable for endotracheal intubation and tolerating long OLV periods is necessary. No patients with acute coronary syndrome, heart failure, serious arrhythmia or valvular disease should be operated by RATS. Laboratory tests should be negative for coagulation, kidney and liver disorders. Finally, one of the most important points is that the patients should meet the requirements for conventional thoracotomy or thoracoscopic surgery.

The duration of surgery is longer than a classical VATS by 2–3 times, which consequently prolongs the period of OLV, thus may have a negative effect on outcome. There are no clear numbers of necessary cases for surgeons to reduce the duration; nevertheless, as stated before, with learning curves the duration exceeds minimally that of a VATS procedure.

25.3.3 Access to the Patient

Another major problem is that there is a longer OLV, but there is no or very small place to access to the head of the patient for control the position of the lung separating device by fiber-optic bronchoscopy, and the difficulty of fiber-optic bronchoscopy to the operated side.

25.3.4 Positioning of the Patient

Given the long duration of surgery and the lateral position of the patient, care should be taken for the correct positioning. With the taping of the head, instead of using protecting foam devices, cases of ear injury or facial numbness were already described.

Protecting the eyes with constructed, improvised devices as "classically" done, from two eye pads and tape is not efficient for protecting against pressure, costs a lot and needs time. Several companies are commercializing disposable, not too expensive eye protectors made from foam and having a transparent shell to protect and to can watch the eyes. These are available in different sizes.

With the positioning of the patient, care should be taken with the bending of the arms—in the standard lateral decubitus position; arms are restricted to less than 90° of angle. There should be enough place to allow the arms of the robot, without touching the patient.

There are robot assisted esophagectomies performed with the patient in prone position, but no major anesthetic complications were reported in these cases, despite

a rise in central venous pressure and mean pulmonary artery pressure, no hemodynamic instabilities were mentioned [21].

25.3.5 Intraoperative Monitoring, CO_2 Insufflation, Fluids

As compared to standard surgical techniques, no extra intraoperative monitoring is needed. However, it should be mentioned that given the difficulty of access to the patient and the difficulty of visualization of the "real" surgical field, intraoperative diagnosis could be altered.

An acute decrease in the arterial blood pressure can be caused by trocar insertion. However, other possible causes of intraoperative hypotension, as for example the position of the patient with the dependent leg bended and hanging should be evaluated also. Insufflation of carbon dioxide increases intrathoracic pressure, and secondary decreases preload, or even may cause pneumothorax and subcutaneous emphysema. The insufflation pressure of CO_2 should be start at not more than 5 cm H_2O, limited to maximum 10 cm H_2O or even less in compromised patients, under low flow (less than 2 l/min) which is described to be relative safe [22]. The potential remedies for enhance preload should be considered, like diminishing the insufflation pressure, inotropes, volume load and/or repositioning the patient.

Concerning the fluids, we know nowadays that they are not the trigger for post-pneumectomy pulmonary edema, but that contribute to its worsening. Restrictive versus goal-oriented fluid approach is still subject to debate. Thorough monitoring of fluid losses is difficult, given the "closed", hidden character of the operating field.

With the long duration of surgery, the urinary output and temperature should be monitored mandatorily.

Unfortunately, in case of RATS, and given the fact that the access to the head of the patient is limited, it's hard to imagine realizing transesophageal echocardiography during the surgery. Otherwise, very invasive monitoring devices of pulmonary pressures, cardiac output have been replaced by modern monitoring devices (Nicco, Picco, FloTrac, …).

During the procedure, as compared to open or even to VATS procedures, rapid diagnosis of occurring intraoperative surgical problems and complications like bleeding or pushing with the retractor on the left atrium are difficult, despite the on-screen visualization of one or two of the operating robotic arms, but not the other arms.

One of the major reasons is the bulkiness of the robot surgical device limiting the access to and round the patient, and raising the difficulty of evaluating of blood losses.

25.3.6 Communication

The space occupied by the robot, its arms, the console of the surgeon and the different screens not only limits the access of anesthesiologist to the patient and to the surgical field (despite its visualization on screens), but makes visual and verbal

communication with the surgeon difficult. The surgeon, sitting at his console and speaking through a microphone while the others have to shout back, makes verbal communication difficult and sometimes reaction times to the misunderstanding are prolonged. While it sounds easy to just communicate, the logistics aren't always enough adapted to this.

The control console can be in the direct opposite corner of the room with numerous obstacles to cross (hanging cables, portable monitors, scrub tables, etc.)

An arrangement of the operating room with the surgeon sitting at his console next to the anesthesiologist could be helpful for this [23]. Clear commands, synergistic actions and a good team working are necessary for the positive outcome of the operation.

25.3.7 Lung Separation Techniques

Lung separation and isolation is described in another chapter. However, we have to mention, the difficult access to the head of the patients, installed in a lateral decubitus position under the drapes, while the robot's arms are working above the patient, the possibility of displacement of the lung separation device is still present. The best lung separation method is the method that the anesthesiologist best knows. Double-lumen tubes may be used, either left or right sided, keeping in mind that in case of a right—sided double—lumen tube, the margin of safety for positioning is less than in case of a left—sided one. An alternative for double-lumen tubes, which can diminish the incidence of sore throat after anesthesia, is the use of single-lumen tubes with bronchial blockers, however the user should be trained with these devices. There is always the recommendation for every anesthesiologist to have an alternative for double-lumen tubes [24]. A helpful method might be the recently introduced left-sided double lumen tube with embedded camera in the tracheal limb (VivaSight, Ambu), connected to a screen, which permits a continuous visualization of the position of the DLT [25, 26].

25.3.8 Pain Management

Studies on postoperative pain after RATS are lacking, nevertheless it seems that RATS is associated with less postoperative pain. Indeed, patients notice more small painful regions, like pain from bladder catheters, more sore throat, pain from chest tubes and of course pain due to positioning, sometimes from cervico-facial numbness to shoulder pain. In order to reduce these painful regions, a bronchial blocker with a single-lumen tube instead of a double-lumen tube could be used, the need for very restrictive positioning should be evaluated, the need for postoperative bladder catheter evaluated, infiltration of chest tube insertion places with local anaesthetics done. Pain management after thoracic surgery is discussed in another chapter, but in most cases of RATS, thoracic epidural analgesia is not mandatory, a paravertebral block or intercostal infiltration might be enough associated with systemic analgesics.

25.3.9 Responsibility and Ethical Considerations

Even if described by Capek, the one who is credited with the popularization of robotics in a collection of short stories published between 1938 and 1942 is the Russian writer Isaac Asimov. Asimov is best known for his three laws governing robot behaviour. Asimov conceived his laws of robotics to impose order on the free will of his fictional robots (Astounding Science-Fiction, March 1942, ed. John W Campbell Jr, Street & Smith Publications Inc., 1942.03.00). Either they are embedded with a control, or controlled from outside, there are some robotic laws that should be respected: they should not injure a human being, must obey orders given by a human being ad must protect its own existence as far as it does not conflict with higher law. The laws of robotics presume that the terms "human beings" and "robots" are understood and well defined.

The human factors play an essential role in the safe delivery of patient care. They are the major contributors to adverse outcomes. The robots used in medicine and surgery, as well as for thoracic surgery are tele-operated robots, which raises the question of responsibility in case of their use.

There are no cases yet described in RATS for robot dysfunction, nevertheless, there are several in other types of robot surgery.

Robotic thoracic surgery may open new perspectives in the practice of thoracic surgery. Special training and experience along with high quality assessment are required in order to provide state-of-the-art treatment. While the legal basis for professional liability remains exactly the same, litigation with the use of robotic surgery may be complex. In case of an undesirable outcome, in addition to physician and hospital, the manufacturer of the robotic system may be sued. In respect to ethical issues in robotic surgery, equipment safety and reliability, provision of adequate information, and maintenance of confidentiality are all of paramount importance. Also, the cost of robotic surgery and the lack of such systems in most of the public hospitals may restrict the majority from the benefits offered by the new technology. Some even raised the question if RATS was not just a simple marketing strategy without any beneficial effect as compared to standard VATS.

While surgical robotics will have a significant impact on surgical practice, it presents challenges so much in the realm of law and ethics as of medicine and health care.

Joint Commission International Accreditation Standards for Hospitals, 6th Edition, provides the basis for accreditation of hospitals throughout the world. Joint Commission International Standards define the performance expectations, structures, and functions that must be in place for a hospital to be accredited by JCI. A study done by JCI shows that accreditation for anesthesia and surgical care needs 304 standards and 1218 measurable elements (JCI Accreditation Standards for Hospitals, 6th Edition May 2018). Another study carried out by researchers at the University of Illinois at Urbana-Champaign, the Massachusetts Institute of Technology and Chicago's Rush University Medical Casimoventer [27] says that 144 deaths, 1391 injuries and 8061 device malfunctions were recorded out of a total of more than 1.7 million robotic procedures carried out between January 2000 and

December 2013 in the United States. This was based on reports submitted by hospitals, patients, device manufacturers and others to the US Food and Drug Administration, and the study notes that the true number could be higher. The researchers did not, however, compare accident rates with similar operations in which robots were not used and the study has not been peer reviewed, so these data should be considered carefully.

All the complications are from other types of robotic surgery and no serious device malfunctions were yet reported in RATS. More studies are needed to provide information about the safety and effectiveness of RATS compared with standard techniques and to delineate the nuances of RATS relative to VATS.

25.4 Conclusions

The management of the robotic thoracic surgical patient requires the knowledge of minimally invasive surgery techniques involving the chest. Familiarity with the robotic surgical system by the anaesthesiologists is mandatory. Management of one-lung ventilation techniques with a left-sided double-lumen endotracheal tube or an independent bronchial blocker is required, along with flexible fiber-optic bronchoscopy techniques. Patient positioning and prevention of complications such as nerve or crashing injuries while the robotic system is used. Recognition of the hemodynamic effects of carbon dioxide (CO_2) during insufflation in the chest is required. The possibility for conversion to open thoracotomy should be also kept in mind.

References

1. Varma TR, Eldridge PR, Forster A, Fox S, Fletcher N, Steiger M, et al. Use of the NeuroMate stereotactic robot in a frameless mode for movement disorder surgery. Stereotact Funct Neurosurg. 2003;80(1-4):132–5.
2. Nishihara S, Sugano N, Nishii T, Tanaka H, Nakamura N, Yoshikawa H, et al. Clinical accuracy evaluation of femoral canal preparation using the ROBODOC system. J Orthop Sci. 2004;9(5):452–61.
3. Honl M, Dierk O, Gauck C, Carrero V, Lampe F, Dries S, et al. Comparison of robotic-assisted and manual implantation of a primary total hip replacement. A prospective study. J Bone Joint Surg Am. 2003;85-A(8):1470–8.
4. Zipper SG, Puschmann H. [Nerve injuries after computer-assisted hip replacement: case series with 29 patients]. Z Orthop Ihre Grenzgeb 2005;143(4):399–402.
5. Cobb J, Henckel J, Gomes P, Harris S, Jakopec M, Rodriguez F, et al. Hands-on robotic unicompartmental knee replacement: a prospective, randomised controlled study of the acrobot system. J Bone Joint Surg Br. 2006;88(2):188–97.
6. Federspil PA, Geisthoff UW, Henrich D, Plinkert PK. Development of the first force-controlled robot for otoneurosurgery. Laryngoscope. 2003;113(3):465–71.
7. Ballantyne GH. Robotic surgery, telerobotic surgery, telepresence, and telementoring. Review of early clinical results. Surg Endosc. 2002;16(10):1389–402.
8. Melfi FM, Menconi GF, Mariani AM, Angeletti CA. Early experience with robotic technology for thoracoscopic surgery. Eur J Cardiothorac Surg. 2002;21(5):864–8.

9. Toker A. Robotic thoracic surgery: from the perspectives of European chest surgeons. J Thorac Dis. 2014;6(Suppl 2):S211–6.
10. Demmy TL, Curtis JJ. Minimally invasive lobectomy directed toward frail and high-risk patients: a case-control study. Ann Thorac Surg. 1999;68(1):194–200.
11. Daniels LJ, Balderson SS, Onaitis MW, D'Amico TA. Thoracoscopic lobectomy: a safe and effective strategy for patients with stage I lung cancer. Ann Thorac Surg. 2002;74(3):860–4.
12. McKenna RJ Jr, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. Ann Thorac Surg. 2006;81(2):421–5; discussion 5–6.
13. Dylewski MR, Ohaeto AC, Pereira JF. Pulmonary resection using a total endoscopic robotic video-assisted approach. Semin Thorac Cardiovasc Surg. 2011;23(1):36–42.
14. Nagahiro I, Andou A, Aoe M, Sano Y, Date H, Shimizu N. Pulmonary function, postoperative pain, and serum cytokine level after lobectomy: a comparison of VATS and conventional procedure. Ann Thorac Surg. 2001;72(2):362–5.
15. Veronesi G. Robotic thoracic surgery: technical considerations and learning curve for pulmonary resection. Thorac Surg Clin. 2014;24(2):135–41.
16. Park BJ. Robotic lobectomy for non-small cell lung cancer: long-term oncologic results. Thorac Surg Clin. 2014;24(2):157–62, vi.
17. Ghaly G, Kamel M, Nasar A, Paul S, Lee PC, Port JL, et al. Video-assisted thoracoscopic surgery is a safe and effective alternative to thoracotomy for anatomical segmentectomy in patients with clinical stage I non-small cell lung cancer. Ann Thorac Surg. 2016;101(2):465–72; discussion 72.
18. Schwartz GS, Yang SC. Robotic thymectomy for thymic neoplasms. Thorac Surg Clin. 2014;24(2):197–201, vii.
19. Ismail M, Swierzy M, Ruckert RI, Ruckert JC. Robotic thymectomy for myasthenia gravis. Thorac Surg Clin. 2014;24(2):189–95, vi–vii.
20. Balduyck B, Hendriks JM, Lauwers P, Mercelis R, Ten Broecke P, Van Schil P. Quality of life after anterior mediastinal mass resection: a prospective study comparing open with robotic-assisted thoracoscopic resection. Eur J Cardiothorac Surg. 2011;39(4):543–8.
21. Kim DJ, Hyung WJ, Lee CY, Lee JG, Haam SJ, Park IK, et al. Thoracoscopic esophagectomy for esophageal cancer: feasibility and safety of robotic assistance in the prone position. J Thorac Cardiovasc Surg. 2010;139(1):53–9 e1.
22. Wolfer RS, Krasna MJ, Hasnain JU, McLaughlin JS. Hemodynamic effects of carbon dioxide insufflation during thoracoscopy. Ann Thorac Surg. 1994;58(2):404–7; discussion 7–8.
23. Campos JH. An update on robotic thoracic surgery and anesthesia. Curr Opin Anaesthesiol. 2010;23(1):1–6.
24. Campos J, Ueda K. Update on anesthetic complications of robotic thoracic surgery. Minerva Anestesiol. 2014;80(1):83–8.
25. Koopman EM, Barak M, Weber E, Valk MJ, de Schepper RT, Bouwman RA, et al. Evaluation of a new double-lumen endobronchial tube with an integrated camera (VivaSight-DL()): a prospective multicentre observational study. Anaesthesia. 2015;70(8):962–8.
26. Szarpak L, Kurowski A, Zasko P, Karczewska K, Czyzewski L, Bogdanski L, et al. Double-lumen tube tracheal intubation in a manikin model using the VivaSight Double Lumen: a randomized controlled comparison with the Macintosh laryngoscope. Am J Emerg Med. 2016;34(1):103–4.
27. Alemzadeh H, Raman J, Leveson N, Kalbarczyk Z, Iyer RK. Adverse events in robotic surgery: a retrospective study of 14 years of FDA data. PLoS One. 2016;11(4):e0151470.

Interventional Bronchology

26

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26.1 Introduction

Bronchoscopy, or direct examination of the tracheobronchial tree, is considered one of the most significant advances in the diagnosis of respiratory illnesses, creating an important sub-discipline in many reference hospitals [1].

Flexible bronchoscopy is considered the diagnostic procedure and basic therapeutic approach to pneumology. This allows for the obtaining of mediastinum and pulmonary parenchyma samples, as well as from the respiratory tract. From this perspective, the numerous therapeutic techniques permitted through flexible bronchoscopy are increasing with more techniques readily available including the use of cryotherapy and cryobiopsy with flexible probes, argon plasma coagulation and electrocautery, or in other cases the implantation of prostheses and devices that can be used in airway leakage and pulmonary emphysema treatments.

Additionally, flexible bronchoscopy is an endoscopic technique with low morbidity and mortality rates, supported by a relatively short invasive period for bronchial biopsies and the aspiration of secretions. An objective there of is to find the least irritable means of inspecting the airway, considering the irritations to the oropharynx produced by the bronchoscope such as coughing and chocking sensations. Additionally, frequent observations include patient anxiety in cases where chronic pulmonary

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pathologies may result in the diagnosis of lung cancer. Considering this, common practice by pneumologists recommend bronchoscopic procedures under sedation or general anaesthetic. The type of which depends on the difficulty and length of the procedure, as well as the patients current comorbidities or objections [2–4].

Such procedures present numerous advantages for the patient including a reduction in procedural duration and an increase in benefits [5, 6]. Additionally, the patient's recollection of the procedure may result uncomfortable or unpleasant. On account of this, recently little objection has been made to patient sedation before an endoscopic respiratory examination. From this perspective, anaesthetics are used in more complex procedures, including flexible bronchoscopy, due to the technical complexity or characteristics of the patient undergoing the procedure. This is especially relevant in the case of rigid bronchoscopy.

Bronchoscopy originates from the end of the nineteenth century. Up to this point, direct exploration of the lower respiratory tract was considered an overly dangerous procedure, considering the belief that contact with tracheal mucosa could produce haemoptysis, putting the patient's life in danger. In 1897, however, Doctor Gustav Killian, an otorhinolaryngologist from the University of Freiburg (Germany), performed the first direct laryngoscopy on a patient with dyspnoea, cough, haemoptysis and foreign body aspiration. Using a Kirstein laryngoscope, Killian was able to visually inspect the right primary bronchi and observe the presence of a solid abnormality. Through esophagoscopy and under a local anaesthetic using cocaine, Killian was able to extract the foreign object. Today, Killian is considered the father of modern bronchoscopy.

Some years later, Doctor Chevalier Jackson, a North American doctor offered an alternative without the need for a laryngoscope; autonomous rigid bronchoscopy. This self-illuminated bronchoscope possessed a small bulb in its distal extremity, providing the advantage of endobronchial lesion visualisation. This presented arguably one of the most significant advances in bronchoscopy, with greater ability for visual diagnosis as well as providing an improvement for possible treatment procedures.

In 1966, the Japanese Doctor Shigeto Ikeda introduced the first flexible bronchoscope, providing a revolution in endoscopic bronchial procedures. From this moment onwards, the use of rigid bronchoscopy fell significantly. However, towards the end of the twentieth century, it is once again important as a resaul of the rise in different therapeutic techniques included the use of laser procedures, the implant and handling of endobronchial prostheses among other procedures that have come to be known as interventional bronchoscopy.

26.2 Rigid Bronchoscopy

26.2.1 Introduction

The most commonly used rigid bronchoscope today is the Dumon-Harrell. This equipment consists in a stainless steel, straight and hollow metallic tube with a circular light. The diameter for adults varies between 6.5 and 14 mm, with a total longitude that oscillates around 29 cm for tracheal processors (tracheoscopes) and

40 cm for endoscopic bronchial procedures (bronchoscope). The distal extremity is bevelled, allowing easier manoeuvrability around the vocal chords and stenotic areas. The proximal end (handle) consists of at least three orifices, two lateral and one frontal, where the optic instruments are inserted. This may include a flexible bronchoscope and diverse instruments such as fibre optics, tweezers, puncture needles and probes, to name a few. Considering the use of anaesthetics, the third orifice connects to a ventilation system (Fig. 26.1).

The latest models of bronchoscopes are able to monitor exhaled gases as well as the pressure in the respiratory tract, usefully providing a *jet* type ventilation system. Monitoring oxygen concentrations is especially useful for laser based approaches and electrotherapy; procedures that require a <40% concentration of oxygen to avoid igniting the respiratory tract.

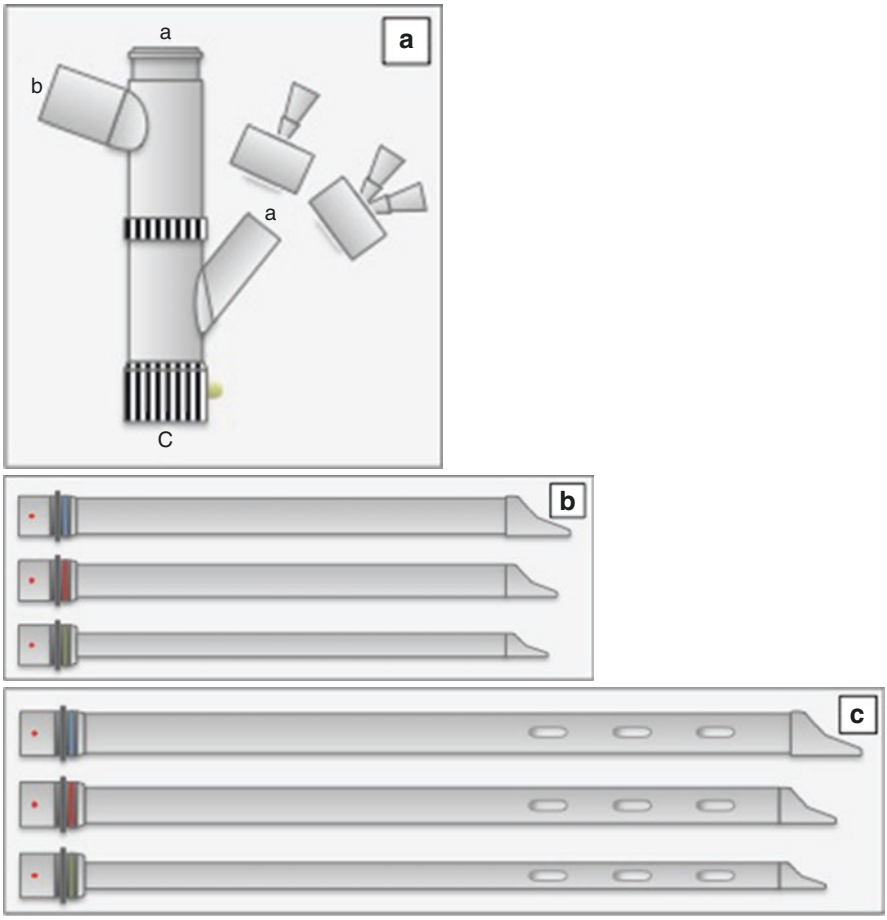

Fig. 26.1 Rigid bronchoscope parts including the (**a**) handle, (a) frontal and lateral inputs with two pieces for the introduction of fibres for laser and catheter aspiration, (b) connections for ventilation, (c) connections for tracheobronchoscopes and rigid bronchoscopes. (**b**) Tracheobronchoscopes of different diameters. (**c**) Rigid Bronchoscope of different diameters

26.2.2 Indications

Rigid bronchoscopy is utilised for a multitude of different diagnostic and therapeutic procedures. While flexible bronchoscopy is more common for diagnostic methods, rigid bronchoscopy continues to be ideal for complex cases, allowing a greater control of the respiratory tract, breathing, blood, secretions and obtaining large samples.

For therapeutic procedures rigid bronchoscopy continues to be the ideal solution, especially in the exeresis of benign and malignant endobronchial lesions. Preferable use of this technique provides a fast and safe method for dilating the airway in the case of stenosis. As in the case of endobronchial lesions and the mechanical resection or "debulking" and placement of endobronchial prostheses (Table 26.1). Nevertheless, mixed procedures of both rigid and flexible bronchoscopy are considered more efficient in cases where both modalities are required.

26.2.3 Contraindications

Contraindications specific to this procedure are relative and directly related with the clinical state of the patient.

Table 26.1 Indication of rigid bronchoscopy

Therapeutic rigid bronchoscopy	• Dilation of the tracheobronchial stenosis.
	• Procedural instruments: – Positioning of the bronchial prosthesis. – Endobronchial laser – Cryosurgery – Electrotherapy – Photodynamic therapy
	• Extraction of foreign bodies.
	• Post-transplant pulmonary tracheobronchial stenosis treatment
	• Control of the threatening haemoptysis
Diagnostic rigid bronchoscopy	• Tracheobronchial stenosis
	• Tracheoesophageal fistula
	• Diagnostic tracheobronchial obstruction
	• Malignant tumours
	• Benign tumours
	• Extrinsic compressions
	• Tracheobronchomalacia
	• Hemoptysis

26.3 Endoscopic Pneumological Techniques Using Anesthesia

26.3.1 Introduction

Asides from rigid bronchoscopy, there are other techniques in flexible bronchoscopy that require anaesthesia. These include, and are not limited to, Endobronchial Ultrasound-guided Transbronchial Needle Aspiration (EBUS-TBNA), bronchial laser and electrocautery treatments, endobronchial coagulation with argon plasma, cryotherapy, cryobiopsy, balloon dilation, volume reduction techniques and handling of endobronchial fistula, and finally, treatment techniques of the alveolar and pleural respiratory tracts.

26.3.2 EBUS

EBUS is a technique that allows the combined use of conventional bronchoscopy and ultrasonography in the same flexible bronchoscope. This allows the examination and evaluation of nearby lesions to the respiratory tract, as well as endobronchial ultrasound-guided transbronchial needle aspiration via an ultrasound probe located on the end of the bronchoscope (EBUS-TBNA) (Fig. 26.2).

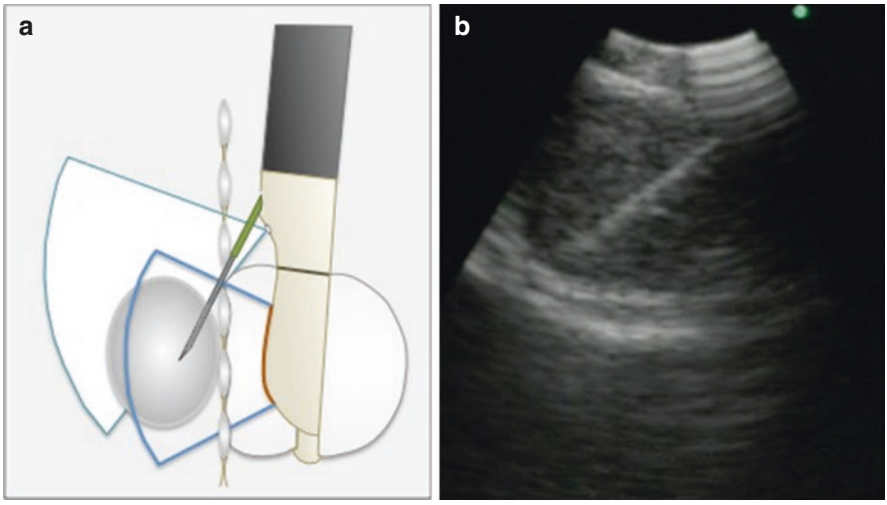

Fig. 26.2 Figure presenting a (**a**) diagram of the ecobronchoscope's extremities and (**b**) ultrasonographic image of the puncture of a mediastinal adenopathy

Table 26.2 Indications for endobronchial ultrasonography

• Diagnosis and staging of lung cancer
• Restaging of non-small lung cancer after induction treatment.
• Diagnosis of intrapulmonary masses
• Diagnosis of extrathoracic neoplasms including lymphoma
• Diagnosis of infections (tuberculosis, fungi and bacteria)
• Diagnosis of inflammatory granulomatous illnesses including sarcoidosis

The echobronchoscope is inserted orally and passed along until it reaches the trachea and bronchi. When the ultrasound transducer comes into contact with the wall of the respiratory tract, it obtains a high quality ultrasound image of the observed structures and lesions. The needle is then guided through the echobronchoscope's working canal with real time vision. Adenopathic cells, masses or mediastinal and perihilary cyst cells can then be obtained through aspiration.

Multiple studies recommend EBUS-TBNA as the primary tool for lung cancer diagnosis and staging, according to international guidelines such as the American College of Chest Physicians (ACCP) and the European Society for Medical Oncology (ESMO) [7, 8].

This consists in a minimally invasive, ambulatory procedure, however, much like other bronchoscopic interventions, requires a general anaesthetic and deep sedation. This procedure presents an important advantage of avoiding more invasive and costly surgical procedures such as mediastinoscopy that in turn require the patient to be hospitalised for a number of days.

Indications are shown in Table 26.2.

26.3.3 Endobronchial Laser Surgery

Endobronchial Laser Surgery uses laser energy projected via a fibre optic probe. The most frequently used is the Neodymium Yttrium Aluminium Garnet (Nd-YAG). The thermic effect of the laser transforms absorbed energy by the tissue into heat. Depending on the amount of applied energy, the laser can produce coagulation, cuts or vaporisation.

The main use of this technique is the recanalisation of the primary respiratory tract, obstructed by anomalous tissue that restricts ventilation. In neoplastics, the laser is initially used for photocoagulation, facilitating the resection without drawing blood. This technique is also employed in the treatment of benign stenosis in airways of multiple causes. Primarily, this techniques contraindication is found in cases where airways are extrinsically compressed or the distal bronchial bed is non-functional. Patients presenting untreated coagulopathies or marked hypoxemias are also contraindicative of this technique.

Laser treatment can be administered in either a flexible or rigid bronchoscope, however, rigid approaches are preferred. The rigid bronchoscope allows for greater control of possible bleeding and aspiration of continuous material. Additionally, this technique is useful for mechanic dilations of the airway and the implantation of endoprostheses.

Throughout its use, this procedure requires constant smoke extraction and control of oxygen concentrations (<40%), thus avoiding the likelihood of igniting flammable substances.

The most frequent complications include haemorrhaging, the perforation of tracheobronchial or vascular tracts and burns produced by ignition. In addition, there is a possibility of ocular damage produced by reflected energy throughout its use, obligating both the patient and medical attendees to wear protection at all times.

26.3.4 Endobronchial Electrosurgery: Coagulation Using Argon Plasma

Endobronchial electrosurgery applies the use of electrically produced heat via a high frequency current through a probe, electroscalpel or diathermy electrodes. This equipment is guided using either a flexible or rigid bronchoscope. Use of this technique intends to coagulate, vaporize and cut anomalous tissue (Fig. 26.3).

Coagulation with argon plasma is a non-contact procedure using argon gas as a conductor for the electrical current. Depending on the type of probe, equipment, electrical current and applied energy, this technique can act differently on the effected tissue. Throughout the procedure, constant suction is required to extract the removed tissue, blood and the vapour produced. Similar to laser treatment, the concentration of oxygen should remain low (<40%) [9, 10].

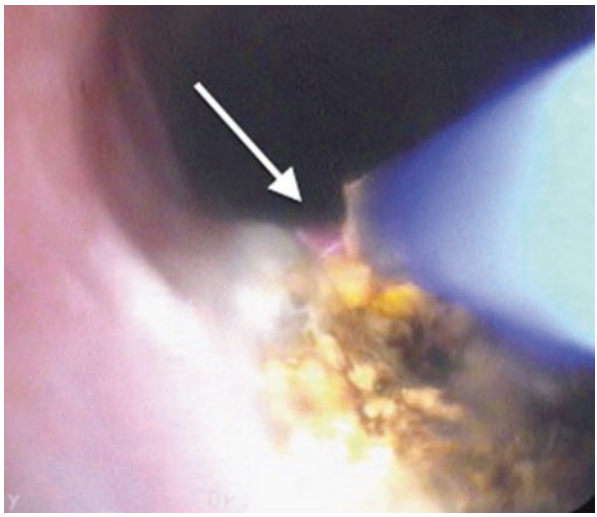

Fig. 26.3 Electrocoagulation with argon plasma of a bronchial mucosa lesion. The coagulated tissue presents an irregular surface texture. Note the electrical sparks directed towards the area of interest

Indications for this procedure are similar to those of laser surgery. The most important indication being the removal of obstructions such as malignant tumoural lesions, as well as benign intraluminal growths in the trachea and bronchi. Contraindications include the presence of pacemakers susceptible to electronic interference as well as when used close to metallic objects including prostheses and sutures. Generally, this procedure is relatively safe and well received when carried out by an experienced professional and following the correct guidelines. Complications may include bleeding and puncturing of the airway. Combustion is also possible when carried out in highly concentrated rich conditions.

26.3.5 Cryotherapy

Cryotherapy is the use of extremely low temperatures for the destruction of tissue whereby the area is rapidly frozen and thawed in multiple cycles. The application of this technique was initially based on the Joule-Thompson physical principal: temperature of a gas decreases if it is submitted under a decrease in pressure. This decrease in pressure is obtainable through passing gas through a narrow opening. If the compressed gas is in liquid form, lowering the pressure produces an expansion that rapidly turns the liquid to gas. This effect is consequently accompanied by a clear drop in temperature.

Cryotherapy is employed through the use of cryoprobes that are manoeuvred through a flexible or rigid bronchoscope. The most commonly used gas is nitrous oxide or liquid nitrogen.

Tissue damage is produced in the area of contact with the extremity of the cryoprobe, whereby the process of freezing the tissue produces a direct effect in the formation of intra and extracellular ice crystals. The efficiency of this technique is directly proportional with the quantity of intracellular water present in the tissue and vascularisation. Grease, cartilage, connected and fibrotic tissues are cryoresistant. Tumours, nerve, granulomas and vascularisation are cryosensitive. Macroscopic effects are not immediate, unlike the case of laser therapy and electrosurgery, while cryotherapy is not sensitive to oxygen levels either. Complications are infrequent, and are normally in the form of bleeding, hyperaemia and an increase in secondary tissue volume.

Additionally, cryoadhesion is produced in the process of freezing the gas, creating the possibility of cryoextraction of foreign bodies, cryoresection of endobronchial tumours and the performing of cryobiopsies [11, 12].

26.3.6 Cryobiopsy

Cryobiopsy is an increasingly popular technique (Fig. 26.4a). Its use includes the sampling of bronchial or pulmonary masses, however more recently has also been used for the study of diffuse interstitial pulmonary diseases. The diagnostic success of this technique has been important in conventional transbronchial biopsies,

providing larger samples with greater preservation of pulmonary architecture. The primary complications produced include haemorrhaging and pneumothorax, occurring when the probe is placed in proximity with the visceral pleura. Preventing possible haemorrhaging is performed positioning a balloon dilator close to the area under study and, once the sample has been taken, inflating the balloon to control the haemorrhaging when and if produced (Fig. 26.4b).

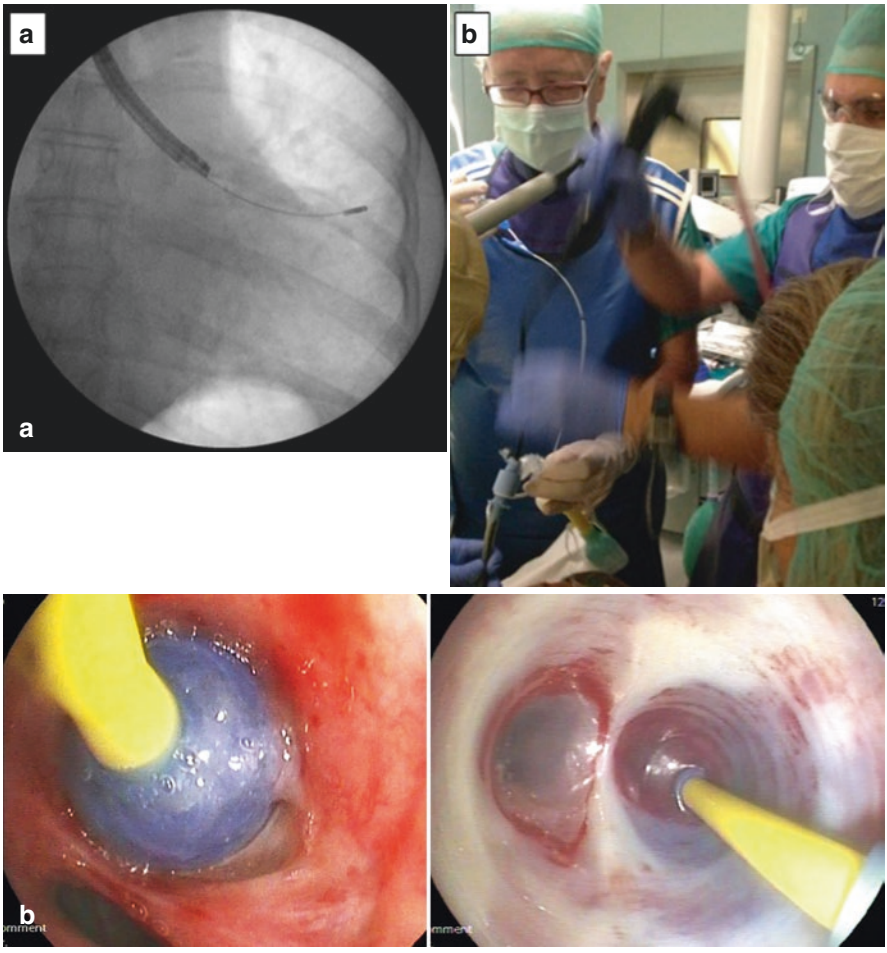

Fig. 26.4 (**a**) The position of a cryoprobe in the pulmonary parenchyma, (b) the moment in which the cryoprobe is retracted after 3 s of actively freezing the pulmonary parenchyma. Note the catheter balloon that is expanding immediately after the biopsy to control any possible bleeding. (**b**) Placement of the hemostatic balloon at the entrance of the segmental bronchus (a) where the cryobiopsy will be performed. Vision of the segmental bronchus (b), through the balloon with the bronchoscope, once the cryobiopsy is done and the balloon is inflated

26.3.7 Placement of Endobronchial Prostheses

Airway endoprosthetics (or *stents*) are placed in the tracheobronchial tree for maintaining airway patency and diameter. The indications and effects of this procedure are varied. This can be used to overcome possible stenosis, achieving the "vault effect", or preventing the growth of endoluminal tumours, achieving the "barrier effect". Two types of prosthesis are currently used, the first made from silicone and the second of mixed composition. Silicone prostheses were developed by Jean-François Dumon in the 1990s in Marseille. These consist in cylindrical prostheses whose external surface are covered in peak-like features that facilitate the fastening of the stent on the tracheal or bronchial wall. These prostheses come in various shapes and sizes. Some are even designed in a tracheobronchial or *diabolo* shape (a Y shape) to adapt to the place of the airway where they are needed.

Mixed prosthetics or metallic prostheses covered in silicone exist in various shapes and sizes (straight, conic, in Y or in J).

The different prostheses are normally positioned using a rigid bronchoscope. Some specific implant devices exist for silicone prostheses, allowing for their combined use with rigid bronchoscopes. Mixed prostheses can be placed using radiological control and laryngeal mask airways. However, these are not recommendable, considering the complications produced if the prosthesis is incorrectly positioned, resulting in repositioning or removal for precise insertion using a rigid bronchoscope. Rigid bronchoscopes provide the additional advantage of being able to use tweezers for higher precision.

26.3.8 Volume Reduction Techniques and the Treatment of Air Leaks

Emphysema is characterised by the irreversible progressive destruction of alveoli and a loss of surface area available for gas exchange, premature collapse of the airways with a consequent trapping of gas as well as hyperinsufflation. Techniques in endoscopic pulmonary volume reduction are used in advanced cases of emphysema and reduce hyperinsuflation to improve respiratory mechanics, lowering dyspnoea in patients. Candidates for this type of treatment include patients with severe emphysema (FEV_1: 20–50%; DLCO: 20–50%), significant hyperinsuflation (VR: >175–200%; TLC: >100%), symptomatics, do not present frequent exacerbations and are free of significant comorbidities.

Three endoscopic volume reduction techniques exist, including endobronchial valves, mechanic retraction and inflammatory pulmonary parenchyma.

Endobronchial valves are the most clinically advantageous in cases of complete lobar exclusion (absence of collateral interlobar ventilation). This is well studied through computerised tomography or by endoscopic means using the Chartis®

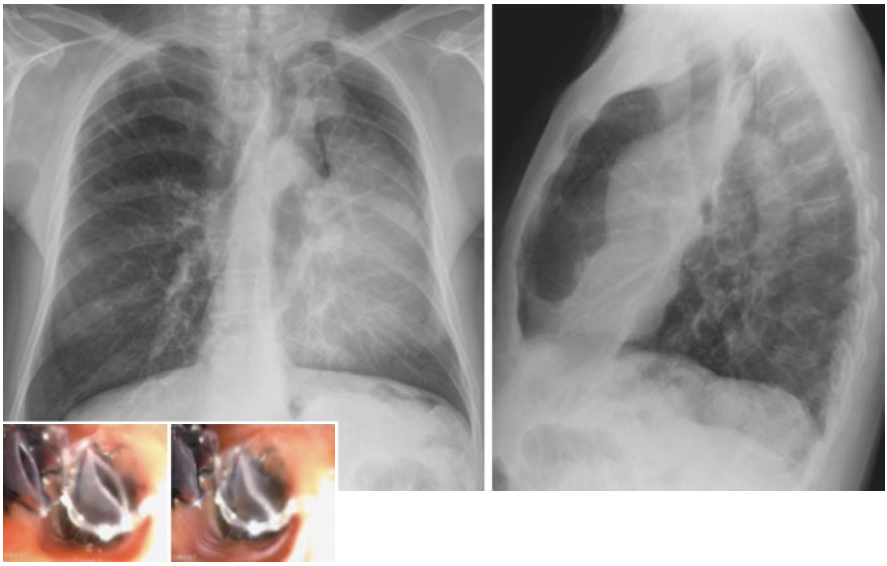

Fig. 26.5 Complete atelectasis of the upper left lobe produced by the positioning of various endobronchial valves. The valves are of the Zephyr type. Note how they open and close during exhalation and inhalation

catheter (Pulmonx Corp., Redwood City, CA, USA). These unidirectional valves produce a loss in pulmonary volume until reaching atelectasis of the respected lobe (Fig. 26.5). Two types are currently on the market: ZEPHYR® (EBV; Pulmonx Inc. Redwood City, CA, USA) and SPIRATION® (IBV Olympus Respiratory America, Redmond, WA, USA). Both are implanted using a flexible bronchoscope with the patient under sedation or anesthesia.

Endobronchial valves are also used for the treatment of air leaks when all other methods have failed or the patient is unable to have surgery.

Ablation using water vapour (Uptake Medical Corporation, Seattle, Washington, USA) uses a catheter and balloon that blocks the section under treatment. Through the catheter vapour is expelled at high temperatures between 3 and 10 s. This system generates an important inflammation of the pulmonary parenchyma consequently retracting parenchyma for scarring.

Coils (RePneu®, BTG Inc, Mountain View, CA, USA) are devices in a spiral shape made from a nickel-titanium alloy called nitinol. These are introduced through a catheter and, upon arrival at the pulmonary parenchyma retain their spiral shape, thus retracting the pulmonary parenchyma. Three sizes are available; 100, 125 and 150 mm. Treatment is bipulmonary, with a separation of 4–6 weeks between each procedure. Ten to 12 coils are used for upper while 12–14 are used for lower lobes. The procedure is carried out using a flexible bronchoscope and the patient is put under anaesthesia (Fig. 26.6).

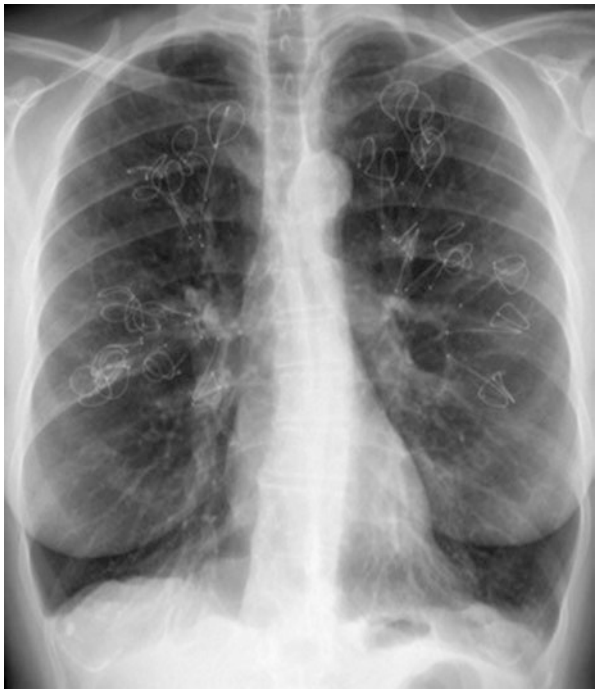

Fig. 26.6 Patient with coils in both upper lobes for the endoscopic treatment of emphysema

26.3.9 Endoscopic Treatment of Asthma: Bronchial Thermoplasty

Bronchial thermoplasty consists in the applied use of heat generated through radiofrequencies in the airways via a catheter introduced with a flexible bronchoscope. This technique requires the patient under anaesthetics in order to reduce the amount of bronchial smooth muscle contraction. This is used on patients with severe asthma that have a failed response to standard medical treatment. The aim of this technique is to reduce the frequency and severity of symptoms, reduce exacerbation and improve the patient's quality of life.

Treatment is carried out in three separate sessions with 3–4 week intervals. The first treatment is applied to the lower right lobe, the second to the lower left and finally both upper lobes are treated. For this, a Sistema Alair® generator (Asthmatx, Inc., Sunnyvale, CA, USA) is connected to the catheter where heat is transmitted using radio waves. The flexible probe is introduced using a bronchoscope, transmitting thermic energy to the wall of the airway through four expansible electrodes in contact with the bronchial mucosa. During a 10 s period the endobronchial temperate can reach up to 65 °C. Afterwards the electrodes are folded and pulled 5 mm away to treat the bronchial areas in proximity. This is carried out systematically to all of the pulmonary segments (bronchi of 3–10 mm) from the distal to proximal areas.

26.4 Bronchoscopy and Anesthesia

26.4.1 Monitoring Anaesthesia in Interventional Bronchology

Bronchoscopy used for advanced diagnostics and endobronchial or transbronchial treatments are considered a surgical procedure that is performed under surgical conditions.

To achieve the best results team work is essential between the surgeon, pneumologist, anaesthetist and any other medical staff. Before beginning any procedure, the respiratory state of the patient is defined, alongside the anaesthetic technique to be employed, the means of ventilation and the adequate extubation required.

Generally, simple procedures of a short duration only require local anaesthesia and sedation. For prolonged or more complex procedures, general anaesthetics and/or deep sedation is indicated. Respiratory depression, rejection of treatment by the patient's body, or complex procedures with unapparent complications are harder to handle when the patient is breathing spontaneously.

Intravenous anaesthesia is preferred over inhalation, especially in cases where airways are incompletely sealed and could lead to anaesthetic gas leaks.

The induction and maintaining of anaesthetics are generally induced using non-barbiturate means (normally propofol) and short-acting or ultra short-acting opioids such as remifentanil, alfentanil and fentanyl. Diverse adjuvants are additionally used to complement the stability and safety of the patient.

26.4.2 Preoperative Evaluation

A complete preoperative evaluation is fundamental. In this assessment, the patient is informed about the procedure that he/she will be put under, the possible associated risks as well as the nature of the sedation (deep sedation or general anaesthetics). For pathological idiosyncrasy some patients may present risk of ASA III and in some cases ASA IV. Preoperative studies should include haemograms, biochemical analysis, haemostasis, thorax radiography, electrocardiogram and occasionally spirometry. It is also necessary to include other complementary tests in function with the patient's medical history.

26.4.3 Monitoring Anaesthesia in Bronchology

Once in the operating theatre, the basic standard monitoring equipment is set up, essentially requiring SaO_2, continuous ECG, non-invasive arterial pressure monitoring and the patient in deep sleep.

Throughout bronchoscopy a series of physiological side effects should be monitored and considered when ventilating the patient including:

- An increase in airway resistance produced by a decrease in tracheal lumen. Such resistance is greater if the bronchoscope is introduced through an endotracheal tube.
- An increase in positive pressure at the end of exhalation.
- Decrease in ventilation for continuous suction of air, also produced by the presence of blood and serum.

These can affect the compliance and tidal volume in various degrees of hypoxemia and hypercapnia.

26.5 Approaches to Anaesthesia with a Rigid Bronchoscope

The induction of the patient under topical anaesthesia is recommended before the introduction of the rigid bronschoscope. The most used anaesthetic is lidocaine at 2% concentration. In our case, this is normally administered through a cricothyroid of 2–3 cm^3 with lidocaine at 4% concentration.

Preoxygenation for at least 5 min is a mandatory procedure, administering premedication of 1–1.5 μg/kg of fentanyl IV and 0.5 mg of atropine to minimize secretions. After anaesthetic induction and the administration of aforementioned opioids, and before the introduction of the bronchoscope, the patient is relaxed.

Cisatracurium and rocuronium are neuromuscular relaxants frequently employed in these cases. Rocuronium, nowadays, is mostly used because it allows for quick and complete recovery from its effects due to the presence of a specific antidote (Sugammadex). This provides an advantage when observing and analysing any complications that may have arisen during the procedure. Among these advantages is complete reversal of the anaesthetic effects after the procedure, a useful feature in patients that present limited respiration, a common situation with respiratory pathologies.

26.6 Ventilation Using Rigid Bronchoscopy

High frequency ventilation or *jet* ventilation is the most recommended in the field of diagnostic and therapeutic bronchoscopy. This type of ventilation allows for insufflation of the airway with a release of high pressure gas (0.3–3 bar) via a short and narrow catheter (12–16 G) linked to the side of the bronchoscope. For this, respiratory cycles between 60 and 600 rpm are employed, depending on the use of either jet or high frequency ventilation, followed by passive aspiration. Alongside this, other parameters need to be controlled including inspiratory time, driving pressure (0.3–3 bar) and the concentration of oxygen inspired.

This type of ventilation is useful in rigid bronchoscopy, especially in bronchopleural fistula reparation procedures. This is seen in how lowering gas leakage through the fistula is obtainable by a reduction in interthoracic pressure via

controlled mechanical ventilation [13]. On the other hand, this facilitates the distribution of gases and regulation of V/Q in oxygenation to areas of lower compliancy.

The main complication of *jet* ventilation is the appearance of barotrauma, pneumothorax, pneumomediastinum, subcutaneous emphysema and alterations to gas exchange (hypoxemia, hypercapnia), especially in patients with restrictive pulmonary pathologies [14].

Jet ventilation is not commonly used in our case, considering the long-lasting positive results obtained with conventional ventilation techniques.

Positive pressure ventilation is also a possibility, with periods of apnea in specific moments throughout the procedure and controlled either through mechanical or manual ventilation via the bronchoscope. Throughout this procedure, mechanical ventilation is controlled with an anaesthesia machine usually rich in O_2 and 100% punctual. This is not affected by intermittent episodes of manual ventilation nor by sporadic interruptions instilled by the pneumologist when stabilisation of the patient is needed.

Caution is advised in cases where the procedure relies on laser techniques, requiring the use of intermittent manual ventilation with periods of prolonged apnea, desaturation and, in the case of reaching higher than 40% O_2 concentration levels, an auxiliary oxygen source at 100%. Measuring oxygen levels is a fundamental procedure in order to avoid the risk of flares or igniting flammable substances when restarting the procedure.

Patients frequently present mild to moderate cases of hypercapnia towards the end of the procedure and during the removal of the bronchoscope. This is product of an open circuit ventilation system and is relatively hard to monitor. In such cases, it is recommended that the patient be connected to a mechanical ventilation system until CO_2 levels return to normal. In our case, the method of choice consists in the use of laryngeal masks, a more comfortable alternative to endobronchial tubes when the patient recovers consciousness (Fig. 26.7).

Fig. 26.7 Second generation laryngeal mask with open access to the glottis

Throughout the procedure, gastric protectors such as omeprazole or dexamethasone are employed to reduce pulmonary oedema, while methylprednisolone is used in the case of irritation. Benzodiazepines are generally avoided considering the likelihood that patients react poorly to respiratory depression when recovering from spontaneous ventilation. Many patients respond well to corticoids and nebulised bronchodilators.

26.7 Approaches to Anaesthesia with a Flexible Bronchoscope

The number of innovative invasive pneumological techniques are on the rise, providing their own anaesthetic implications including shared airways and the ability to perform the procedure outside of the operating theatre. Additionally, techniques attempt to confront the high number of preoperative respiratory problems, such as haemoptysis, intrinsic and extrinsic obstructions or chronic respiratory pathologies among others.

These procedures require the near complete immobilisation of the patient in order for effective performance. This is equally important when taking samples, considering the relevance of these results when making future procedural decisions (in the case of e.g. endobronchial volume reductions). Additionally, such decisions require the cooperation of both the pneumologist and anaesthesiologist. Firstly to decide on the means of intervening and secondly to ensure the permeability of the airway. Patients with a significant perioperative risk are those that present higher association with respiratory illnesses and risk of complications in the airways. Respiratory illnesses may include cancers, respiratory pathologies and smoking, while complications could include haemoptysis or mechanical obstructions to the airway.

The method of choice in orotracheal procedures generally begins under general anaesthetic. Modern practice, however, describes the use of multiple different supraglottic airway devices in assisted and controlled ventilation maintenance. In this case, we use new second generation laryngeal masks modified to provide sufficient illumination for ventilation as well as approaching the glottis and trachea. This also facilitates the gastroesophageal drainage in the case of possible reflux (Fig. 26.8).

These devices are ideal for carrying out EBUS, considering they provide all glottal light without restriction. Additionally, these facilitate probe access to the upper and lower paratracheal lymph nodes (ganglial regions 2 and 4), as opposed to endotracheal tubes that do not provide sufficient ultrasound beam alienation, impeding the observation of upper and lower paratracheal regions [15] (Fig. 26.8).

Upon using general anaesthetic, an intravenous technique is employed much like in the case of rigid bronchoscopy. Instillation of topical anaesthesia in the periglottic area is recommended, achieved through the aforementioned cricothyroid membrane.

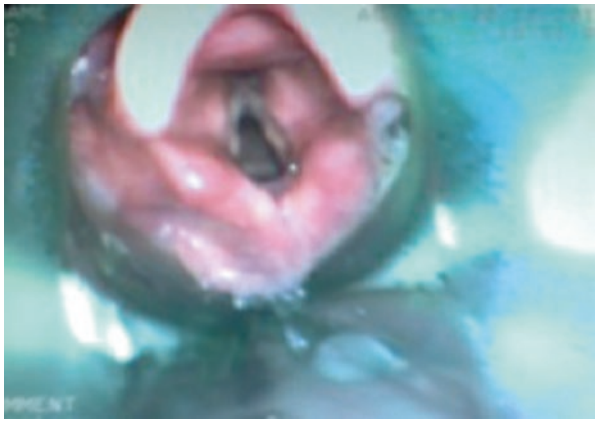

Fig. 26.8 Endoscopic vision of the supraglottic device

Preoxygenation of at least 5 min is initially carried out, followed by a premedication of 1–1.5 μg/kg of fentanyl IV and 0.5 mg of atropine to minimize secretions. After inducing the patient under anaesthetic and administering the opioids, a specific connection using a *Mainz* membrane is established before introducing the videobronchoscope. This prevents possible air leaks. In order to relax the patient, rocuronium is usually used. This allows a fast recovery and complete unblocking of the muscles, thanks to a specific antidote (Sugammadex). This provides the distinct advantage of identifying possible complications that may have occurred during the procedure. Nevertheless, the use of supraglottic airway devices provide the distinct advantage of allowing smaller doses of neuromuscular relaxants if promptly introducing 5 cm^3 of lidocaine at 2% endobronchial through the videobrochoscope's work canal. This reduces the coughing reflex and improves patient tolerance [16].

In recent years, multiple studies have achieved exceptional results when using dexmedetomidine, providing less secondary effects, however, this pharmaceutical product has been inadequately tested. Additionally, this product's prolonged half-life is still to be studied in detail in subsidiary cases of the major surgical ambulatory CMA as well as in EBUS and cryobiopsies [17].

The use of inhaled anaesthetics is not recommendable, thus avoiding air contamination, a frequent product in frequent flexible bronchoscopic suctions. On the other hand, this also restricts the determination of the fraction of inhaled halogenated anaesthetics [18]. Additionally, multiple publications have suggested that halogenates provoke local bleeding, product of local vasodilatation of the bronchial and pulmonary vessels.

Similar to the patients in the previous section, the administration of a gastric protector such as omeprazole is recommended. Similarly dexamethasone is used to reduce pulmonary oedema, while methylprednisolone is used in the case of irritation. As previously stated, benzodiazepines are not normally administered for similar reasons to those of rigid bronchoscopy. Patients can also benefit from corticoids and nebulised bronchodilators.

In the case of transbronchial needle aspiration through EBUS, many authors have discussed the performance benefits of patient sedation, comparable with tests using general anaesthesia [19–23]. Most conclude that the use of sedation in EBUS improves diagnosis and provides a safety profile comparable with that of deep sedation.

Considering this, the method of sedation for EBUS should be chosen individually according to the experience of the pneumologist and anaesthesiologist, whether additional procedures other than EBUS are needed, and the pre-calculated estimated duration of the procedure. Additionally the basal state of the patient should be confirmed. More often than not, a severe pathology is associated with this factor and needs to be checked.

After the conclusion of any interventional bronchological procedure overlooked by an anaesthesiologist, the patient is passed into the operating recovery room. There the patient is closely monitored to detect any possible complications, including laryngeal stridor, dyspnoea, haemoptysis bronchospasms or pneumothorax, to name a few.

After a few hours, those patients that benefit from the ambulatory circuit (CMA) are discharged with a sheet of recommendations and provided with a suitable analgesic treatment. Otherwise, the patient is moved to the pneumology ward for observation.

References

1. Ernst A, Herth FJF. Principles and practice of interventional pulmonology. New York, NY: Springer; 2013. 978-1-4614-4291-2.
2. Diette GB, White P Jr, Terry P, Jenckes M, Wise RA, Rubin HR. Quality assessment through patient self-report of symptoms prefiberoptic and postfiberoptic bronchoscopy. Chest. 1998;114(5):1446–53.
3. Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, et al. on behalf of the British Thoracic Society Bronchoscopy Guideline Group. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. Thorax. 2013;68:i1–44.
4. Disdier C, García Martínez E, Pérez Negrin LM. Premedicación y sedación en broncoscopia. Neumosur. 2004;16(3):197–207.
5. Cases Viedma E, Pérez Pallarés J, Martínez García MA, López Reyes R, Sanchís Moret F, Sanchís Aldás JL. Eficacia del midazolam para la sedación en la broncoscopia flexible. Un estudio aleatorizado. Arch Bronconeumol. 2010;46(6):302–9.
6. Cases E. Sedación en la broncoscopia flexible en el adulto. Controvers Med Resp. 2010;3(1):7–13.
7. Silvestri GA, et al. Chest. 2013;143(5 Suppl):e211S–50S.
8. Vansteenkiste J, et al. Ann Oncol. 2013;24(Suppl 6):vi89–98.
9. Herth FJF, Shah PL, Gompelmann D, editors. Interventional pulmonology (ERS monograph). Sheffield: European Respiratory Society; 2017.
10. Horinouchi H, Miyazawa T, Takada K, et al. Safety study of endobronchial electrosurgery for tracheobronchial lesions. J Bronchol. 2008;15(4):228.
11. DiBardino DM, Lanfranco AR, Haas AR. Bronchoscopic cryotherapy. Clinical applications of the cryoprobe, cryospray, and cryoadhesion. Ann Am Thorac Soc. 2016;13(8):1405–15.
12. Bolliger CT, Mathur PN, Beamis JF, et al. ERS/ATS statement on interventional pulmonology. Eur Respir J. 2002;19:356–73.

13. Lois M, Noppen M. Bronchopleural fistulas: an overview of the problema with special focus on endoscopic management. Chest. 2005;128:3955–65.
14. Fernandez-Bustamante A, Ibañez V, Alfaro JJ, De Miguel E, German MJ, Mayo A, et al. High-frequency jet ventilation in interventional bronchoscopy: factors with predictive value on high-frequency jet ventilation complications. J Clin Anesth. 2006;18:349–56.
15. Sarkiss M, Kennedy M, Riedel B, et al. Anesthesia technique for endobronquial ultrasound-guided fine needle aspiration of mediastinal lymph node. J Cardiothorac Vasc Anesth. 2007;21:892–86.
16. Lee HJ, Haas AR, Sterman DH, Solly R, Vachani A, Gillespie CT. Pilot randomized study comparing two techniques of airway anesthesia during curvilinear probe endobronchial ultrasound bronchoscopy (CP-EBUS). Respirology. 2011;16(1):102–6.
17. St-Pierre P, Tanoubi I, Verdonck O, et al. Dexmedetomidine versus remifentanil for monitored anesthesia care during endobronchial ultrasound-guided transbronchial needle aspiration: a randomized controlled trial. Anesth Analg. 2019;128(1):98–106.
18. Douadi Y, Bentayeb H, Malinowski S, et al. Anesthésie en échoendoscopie bronchique. Expérience du masque larynge. Rev Mal Respir. 2010;27:37–41.
19. Ando K, Ohkuni Y, Fukazawa M, et al. Sedation with meperidine for endobronchial ultrasound-guided transbronchial needle aspiration. J Bronchol Interv Pulmonol. 2010;17:329–33.
20. Yarmus LB, Akulian JA, Gilbert C, et al. Comparison of moderate versus deep sedation for endobronchial ultrasound transbronchial needle aspiration. Ann Am Thorac Soc. 2013;10:121–6.
21. Casal RF, Lazarus DR, Kuhl K, et al. Randomized trial of endobronchial ultrasound-guided transbronchial needle aspiration under general anesthesia versus moderate sedation. Am J Respir Crit Care Med. 2015;191:796–803.
22. Öztas S, Aktürk ÜA, Alpay LA, et al. A comparison of propofol-midazolam and midazolam alone for sedation in endobronchial ultrasound-guided transbronchial needle aspiration: a retrospective cohort study. Clin Respir J. 2017;11(6):935–41.
23. Aswanetmanee P, Limsuwat C, Kheir F, et al. The role of sedation in endobronchial ultrasound-guided transbronchial needle aspiration: systematic review. Endosc Ultras. 2016;5(5):300–6.

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The chapter was published with a mistake in references 25 (Rinieria P, Peillona C, Bessoub J-P. National review of use of extracorporeal membrane oxygenation as respiratory support in thoracic surgery excluding lung transplantation)

The same has been updated as:

25. Rinieri P, Peillon C, Bessou J-P. National review of use of extracorporeal membrane oxygenation as respiratory support in thoracic surgery excluding lung transplantation. Eur J Cardio-Thoracic Surg. 2015;21:517–22.

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