We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists



186,000

200M



Our authors are among the

TOP 1% most cited scientists





WEB OF SCIENCE

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

## Interested in publishing with us? Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected. For more information visit www.intechopen.com



## Anesthesia for Thoracic Surgical Procedures

January Tsai, Teresa Moon, Shital Vachhani, Javier Lasala, Peter H Norman and Ronaldo Purugganan

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/56104

## 1. Introduction

As thoracic surgery evolved, anesthesia evolved in parallel, allowing even the most complicated surgical procedures to be performed relatively safely. This co-evolution mirrors the close association of the thoracic surgeon and anesthesiologist when caring for their patients. This unique association is predicated on the nature of thoracic procedures, where the surgeon and anesthesiologist share a "thoracic workspace" - the surgeon operating on vital thoracic structures and the anesthesiologist managing ventilation, oxygenation, and hemodynamics. Because of this close partnering, it is valuable for thoracic surgeons to be familiar with anesthetic considerations exclusive to their patients.

## 2. Considerations for One-Lung Ventilation (OLV)

Thoracic Surgery poses unique challenges to the anesthesiologist, including surgery in the lateral decubitus position, an open thorax, manipulation of thoracic organs, potential for major bleeding, and, unique among all potential surgery scenarios, the need for lung isolation.

#### 2.1. Physiologic effects of lung isolation

Successful lung isolation (one-lung ventilation, OLV) requires the management of oxygenation, ventilation, and pulmonary blood flow. Remarkably, OLV decreases total minute ventilation minimally. In fact, it has been shown that the non-isolated lung receives close to the same minute ventilation as ventilation to two lungs. The rate of  $CO_2$  elimination undergoes minimal changes because  $CO_2$  is readily diffusible and has no plateau in its dissociation curve.



When a patient is placed on OLV, inevitably a shunt is developed. The non-dependent lung is no longer being ventilated but is still perfused, resulting in a right to left shunt. When this occurs, the pulmonary system has physiological adaptations to decrease this shunt. Given that the patient is in the lateral decubitus position, one of the responses is a decrease in blood flow to the non-dependent lung due to gravitational forces. These effects are significant because the pulmonary system has a much lower blood pressure than the systemic circulation. Another adaptation is hypoxic pulmonary vasoconstriction of the vascular supply in the non-dependent lung. Hypoxic pulmonary vasoconstriction is a physiological phenomenon in which pulmonary arteries constrict in the presence of hypoxia (unlike the systemic circulation), redirecting blood flow to the dependent lung. Surgical compression of the non-dependent lung can also serve as a way of decreasing shunt as the pulmonary vasculature is compressed. One last factor contributing to a decrease in shunt fraction is appeic oxygenation—residual oxygen in the non-dependent isolated lung diffusing into the pulmonary circulation. All these factors combined allow for better oxygenation during OLV.

#### 2.2. Preoperative anesthetic evaluation of the thoracic surgery patient

Patients undergoing OLV should undergo a perioperative assessment of their respiratory function that includes testing of lung mechanical function, pulmonary parenchymal function, and cardiopulmonary reserve. The best assessment of respiratory function comes from a history of the patient's quality of life [1]. It is useful to think of respiratory function in three related but independent areas: respiratory mechanics, gas exchange, and cardio-respiratory interaction [2].

The most valid test for perioperative assessment of respiratory mechanics is the predicted postoperative forced expiratory volume in one second (ppoFEV1). This test is the best at predicting post thoracotomy respiratory complications [3].

Percentage of predicted postoperative (ppo) FEV1 after lobectomy is given by

 $ppoFEV1 = preoperative FEV1 \ x \ \frac{No. of segments remaining}{total \ No. of segments}$ 

Nakahara et al found that patients with a ppoFEV1 of more than 40% had no or only minor post resection respiratory complications [4]. Major respiratory complications were only seen in the sub group with ppoFEV1 < 40%; post-operative mechanical ventilator support was seen in those < 30%.

For the assessment of lung parenchymal function, the most useful test of the gas exchange capacity is the diffusing capacity for carbon monoxide (DLCO). This test correlates with the total functioning surface of the alveolar-capillary interface. The DLCO is used to calculate a post resection value using the same calculation as FEV1. A ppoDLCO less than 40% of predicted correlates with increased cardiac and respiratory complications and is relatively independent of the FEV1 [5].

Stair climbing is the most traditional test of respiratory function in the assessment of cardiopulmonary interaction. Ability to climb three flights or more is closely associated with a decrease in morbidity and mortality. The ability to climb fewer than two flights is associated with a very high risk [6]. The "gold standard" for assessment is formal laboratory exercise testing with maximal oxygen consumption. Climbing five flights of stairs approximates a  $VO_2$  max value of >20 ml/kg/min and less than one flight is associated with values <10 ml/kg/ min (S9). Ventilation-perfusion (V/Q) scintigraphy can also be used as a preoperative assessment when pulmonary resection is to be undertaken. This modality is particularly helpful for patients undergoing pneumonectomy or any patient with a ppoFEV1 less than 40% [2].

Slinger et al. proposed a "3-legged" stool of pre-thoracotomy respiratory assessment, which encompasses the prior mentioned pre-operative tests [7]. This model summarizes the results of those tests and reveals that patients have lower expected post-operative morbidity if they have a ppoFEV1 > 40%, cardio-pulmonary reserve with a VO<sub>2</sub> max >15 ml/kg/min, and lung parenchymal function with a ppoDLCO >40%. These three tests are the most valid for pre-operative assessment. Other tests that can be used are maximal volume ventilation (MVV), residual volume/total lung capacity (RV/TLC), and forced vital capacity (FVC), but these are less valid for respiratory mechanics. Stair climbing (two flights), a 6-minute walk, and measurement in the change in SpO<sub>2</sub> (<4%) during exercise are other tests that can be used to measure cardio-pulmonary reserve. Measurement of arterial blood gas values can also serve as a respiratory assessment; indicators of good prognosis are PaO<sub>2</sub> > 60 and a PaCO<sub>2</sub> < 45.

In regards to post-thoracotomy anesthetic management, Slinger et al. devised an algorithm derived from pre-operative assessment using ppoFEV1 [7]. If the patient's ppoFEV1 is > 40% and the patient is awake, alert, warm, and comfortable, immediate postoperative extubation is recommended. If the ppoFEV1 is between 30-40%, extubation should be considered based on exercise tolerance, DLCO, V/Q scan, and associated diseases. If the ppoFEV1 < 30%, staged weaning from mechanical ventilation is recommended. However, when the patient has a functioning thoracic epidural catheter providing adequate analgesia, extubation may be attempted even at ppoFEV1 values as low as 20% [7].

#### 2.3. Tracheo-bronchial anatomy for lung isolation

Knowledge of tracheo-bronchial anatomy is important for achieving and maintaining proper lung isolation. Other chapters in this text describe lung and bronchial anatomy in detail. Features of the anatomy that are relevant to anesthetic considerations are presented here.

A critical landmark when placing lung isolation devices is the primary carina, where the trachea splits into two main bronchi. The diversion angle differs between these main bronchi, with the right bronchi angled at 25 degrees and the left bronchus at 45 degrees. Because of the steeper angle of diversion of the right main bronchus, foreign bodies (including lung isolation devices) are more likely to travel into this bronchus. Left and right side double lumen tubes (DLTs) are designed with curvatures to accommodate left or right main bronchi diversion angles to make intubation into the specified main bronchi easier (Figure 1).

Because of the steeper angle of the right mainstem bronchus, it is not uncommon to inadvertently intubate the right mainstem when intending to intubate the left mainstem with a DLT (using blind or non fiberoptic guided placement techniques). Operators unfamiliar with distal bronchial anatomy sometimes confuse secondary carinas with the primary carina. For example, the right main bronchus divides at the secondary carina into the upper lobar



**Figure 1.** Left (top) and right (bottom) conformations of double lumen tubes. Note the right upper lobe ventilation lumen on the right conformation tube.

bronchus and bronchus intermedius; this secondary carina may be mistaken for the primary carina when viewed under bronchoscopy. Therefore, knowledge of distal bronchial anatomy is fundamental in confirming correct placement as well as in correcting misplacement.

Knowledge of distal bronchial anatomy is essential for additional reasons. First, the operator must recognize that a right DLT has an additional slot to allow for ventilation of the right upper lobe and must place it at the correct depth and rotational alignment to assure adequate ventilation of all three lobes. Secondly, anatomy is abnormal in a small percentage of patients. For example, in up to 2% of patients, the right bronchus originates directly from the supra carinal trachea (a so-called bronchus suis) [8]. Abnormal anatomy is also seen in patients who have had previous lung surgeries. The operator must be able to recognize and respond to abnormal anatomy by selecting the appropriate device to provide effect lung isolation in any scenario.

#### 2.4. Indications for lung isolation

Patient pathology and/or operative requirements determine the indication for OLV. Patients with lung pathology may need lung protection. For example, OLV may be used to protect the unaffected lung from contamination with pus or blood from the affected lung. Alternatively, OLV may be used to provide differential lung ventilation to minimize volutrauma and barotrauma to the affected lung while optimizing ventilation to the non-affected lung. Certain operative scenarios require OLV. Because it optimizes visualization of the operative site, OLV is absolutely indicated in closed procedures (for example, thoracoscopic surgery) but is also useful in open procedures to maximize exposure.

#### 2.5. Lung isolation devices

Three standard methods for lung isolation include DLT, bronchial blockers, and mainstem intubation.

#### 2.5.1. DLT

The standard device for providing lung isolation is the DLT. It provides reliable lung isolation, offers the ability to suction both lungs, allows for bilateral differential lung ventilation with minimal device manipulation, and allows for simple procedures such as bronchoalveolar lavage. DLTs range in size from 28 to 41 Fr. Posteroanterior (PA) chest x-ray is the standard method for sizing comparison between DLT, trachea, and bronchial diameter [9]. However, patient sex, age, and height are commonly used to choose DLT size. As discussed above, DLTs are made in right-side and left-side conformations to accommodate the differences in the anatomy of the right and left main bronchi (i.e., the right upper lobe branch).

#### 2.5.2. SLT with bronchial blocker

Bronchial blockers used with conventional single lumen tubes have advantages in difficult airways, in patients with indwelling endotracheal or tracheostomy tubes, in patients who are nasally intubated with SLTs, and in cases where sub-segmental blockade may be required [10]. Bronchial blockers have several disadvantages, however. They are easier to displace and provide limited suction and drainage to the isolated lung, which may lead to an accumulation of pus, blood or secretions [11]. They are deployed in the operative lung, which may interfere with the surgical procedure, and the device must be repositioned for contralateral lung isolation.

Despite their specific enhancements, bronchial blockers are essentially modeled after vascular embolization catheters (albeit with high compliance low pressure cuffs and a deflation port). They are manufactured as separate units or units integrated with an endotracheal tube. Separate units include the Cohen Flexi-tip BB (Cook Critical Care), Fuji Uni-blocker (Fuji Systems, Tokyo) (Figure 2A) and the Arndt wire-guided BB (Cook Critical Care, Bloomington, IN) (Figure 2B). An example of an integrated unit is the Univent tube (Fuji Systems, Tokyo).

#### 2.5.3. Mainstem intubation

Mainstem bronchial intubation with an SLT may be used for lung isolation in emergent scenarios or in pediatric cases. However, with this method, exhalation of the operative lung is limited, airway protection at the vocal cords is compromised, and the endotracheal tube tip is advanced into the operative lung; lastly, repositioning is required if contralateral isolation is needed. Furthermore, standard endotracheal tubes may be too short to effectively mainstem intubate either main bronchi; specialized longer tubes, such as Micro Laryngoscopy Tubes (MLTs), may be required.

#### 2.6. Difficult airway and lung isolation

*Campos* describes two categories of patients at risk for difficult intubation during OLV: those with complications related to the upper airway and those related to the lower airway [12]. The former include a 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, previous hemiglossectomy or hemimandibulectomy, and



Figure 2. Examples of bronchial blockers. (A) Fuji Uni-blocker (Fuji Systems, Tokyo); (B) Arndt wire-guided BB (Cook Critical Care, Bloomington, IN).

tumors of the upper airway. Lower airway risk factors include an existing tracheotomy, a distorted tracheobronchial anatomy, and compression at the entrance of the left mainstem bronchus. Patients with any of the above conditions might pose a difficulty for lung isolation with a conventional DLT and might be candidates for SLT placement with subsequent lung isolation with a bronchial blocker. However, if a DLT is indicated, fiberoptic intubation may be used to facilitate placement [13]. However, because of the long length of the DLT, it is difficult to maintain distal control of the fiberscope, especially with patients having longer oral to vocal cord distance. Additionally, the small diameter bronchoscope required (to assure fit for the DLT) results in an inferior view and restricts suction capabilities. Therefore, new generation indirect laryngoscopes may be preferable. Indirect laryngoscopes (e.g., CMAC [Storz, Tuttlingen, Germany], GlideScope [Verathon,Bothell, WA], Airtraq (Prodol Meditec S.A., Vizcaya, Spain)) improve airway grade and have been shown to improve the ease of intubation with DLTs in patients with difficult airways [14].

#### 2.7. Confirming proper lung isolation

Regardless of the device used for lung isolation, the anesthesiologist must confirm correct placement of the device. Chest auscultation has traditionally been used to confirm correct DLT placement. The process is straightforward in patients with normal pulmonary anatomy. First, inflate both tracheal and bronchial balloons and auscultate to confirm bilateral breath sounds (if bilateral breath sounds are absent, suspect malposition – the DLT may be too deep). Next,

sequentially clamp the tracheal and bronchial inflow limbs of the DLT and auscultate the chest. Absent breath sounds corresponding to the tracheal or bronchial lumen clamped, should be confirmed. Different malposition scenarios may be deduced depending on type of DLT (L v. R), intended mainstem to be intubated, DLT lumen occluded and the absence or presence of breath sounds. Although auscultation is an important tool in situations where fiberoptic bronchoscopy is unavailable, studies have shown a large margin of positioning error when it is not used [15-18]. Fiberoptic confirmation is required for proper positioning of bronchial blockers because they lack basic ergonomic design features that enable blind placement (like curvature or specialized ventilation port configurations of DLTs). Furthermore, because malpositioned lung isolation devices may be potentially be fatal, and auscultation is usually not an option intraoperatively, fiberoptic bronchoscopy has become the standard for proper placement and maintenance of lung isolation devices.

### 3. Intraoperative care for the thoracic surgical patient

#### 3.1. Ventilator strategies for one-lung ventilation

For thoracic surgery, the incidence of pulmonary complications now out-numbers that of cardiovascular complications [19], and pulmonary complications are the most common cause of postoperative death in esophageal cancer patients [20]. Injury from one-lung ventilation (OLV) can manifest as re-expansion pulmonary edema (REPE), acute lung injury (ALI), or acute respiratory distress syndrome (ARDS). While late causes of ALI (3-10 days after surgery) are secondary to bronchopneumonia or aspiration, early ALI is predicted by high intraoperative ventilation pressures, increased surgery duration, excessive intravenous volume replacement, pneumonectomy, and preoperative alcohol abuse [21]. Most likely, a combination of a patient's health status, intraoperative fluid management, the use of epidural analgesia, inflammatory responses due to surgical manipulation, alveolar recruitment, and reexpansion/ reperfusion lung injury [22, 23] underlie the development of ALI following OLV [24]. While chronic patient risk factors are difficult to modify, protective ventilatory strategies and judicious fluid use may decrease the incidence of ALI [21].

Prior ventilatory schemes focused on the detrimental effects of atelectasis, primarily increased pulmonary shunt via local alveolar hypoxia and hyperoxia. Tidal volumes of 10-12mL/kg were advocated, as it was previously held that tidal volumes <8mL/kg resulted in decreased functional residual capacity (FRC) and worsening atelectasis in the dependent lung. The lowest positive end-expiratory pressure (PEEP) for acceptable oxygenation and normal arterial CO<sub>2</sub> levels (35 to 38 mmHg) were suggested [24]. OLV was achieved with parameters similar to two-lung ventilation, with consequent stimulation of stretch-activated cation channels, oxygen-derived free radicals, activated neutrophils, and cytokine upregulation contributing to increased microvascular-alveolar permeability [25].

The current strategy to minimize OLV-associated lung injury utilizes so-called lung protective ventilation. Overdistension (volutrauma), excessive transpulmonary pressure resulting in barotrauma, repeated opening and closing of alveoli resulting in ateletotrauma, and biotrauma

caused by inflammatory mediators are considered contributing factors to ventilator-induced lung injury (VILI). These factors combined may induce inflammatory changes in pulmonary alveolar and vascular endothelium, predisposing them to pathological apoptosis and necrosis. In this way, VILI can both exacerbate existing lung injury and sensitize the lung to further injury via a two-hit model [26]. Reduction of tidal volumes during OLV to 5ml/kg was shown to reduce alveolar concentration of TNF- $\alpha$  and sICAM-1 [27] (will it be obvious to the reader what implications this has?). Moreover, with fixed tidal volumes of 9mL/kg, the addition of 5cm H<sub>2</sub>O PEEP was associated with better oxygenation and earlier extubation [28]. PEEP improves the (ventilation:perfusion) V:Q relationship via increased FRC at end expiration. However, excessive PEEP may redistribute blood flow away from the dependent ventilated lung. Thus, protective ventilation consists of:

- maintaining the fraction of inspired O<sub>2</sub> (FiO<sub>2</sub>) as low as possible to avoid absorption atelectasis and worsening shunt [29]
- PEEP above the lower inflection point on the static pressure-volume curve
- a tidal volume of 5-6 mL/kg, plateau pressures of less than 20 cm H<sub>2</sub>O above the PEEP value
- peak inspiratory pressures less than 35 cm H<sub>2</sub>O
- respiratory rate (RR) 10-18
- inspiratory:expiratory (I:E) ratio 1:2 to 1:3
- permissive hypercapnia
- preferential use of pressure-limited ventilatory modes [24].

Hypoxemia may require continuous positive airway pressure (CPAP) to the nondependent lung, allowing apneic oxygenation and increasing overall partial pressure of  $O_2$  (pa $O_2$ ). Permissive hypercapnia is generally tolerated with protective ventilator strategies during OLV. Not only does hypocapnia worsen parenchymal and ischemia-reperfusion injury [30], but hypercapnia itself may have beneficial effects on serum cytokine levels, apoptosis, and free radical injury [31]. The optimal level of pa $CO_2$  has not been determined.

Pressure controlled ventilation achieves lower airway pressure, and the homogeneous distribution of inspired gas allows recruitment of collapsed lung and improved oxygenation [32]. This method is thought to minimize end-inspiratory distension and collapse of lung units and has demonstrated a decreased inflammatory response, improved lung function, and earlier extubation [28]. As compared with conventional ventilation, this protective strategy was associated with improved survival at 28 days, a higher rate of weaning from mechanical ventilation, and a lower rate of barotrauma in patients with ARDS. However, protective ventilation was not associated with a higher rate of survival to hospital discharge [25]. Even with protective lung ventilatory strategies, it is possible that certain patchy segments of alveoli are intermittently and inconsistently recruited, resulting in impaired surfactant effectiveness and barotrauma.

Lung protective ventilation primarily refers to the dependent lung, which shows a more pronounced inflammatory response than the nonventilated lung [33, 34]. However, it is likely

that the overall postoperative clinical picture amounts to the combination of differing insults to the operative and nonoperative lung. Hypoxia-induced lung inflammation [30] and stress-induced mechanical injury affects the operative lung as well, as the atelectatic, nonventilated lung is periodically inflated to assess air leaks. Additionally, the operative lung is subject to pulmonary contusion due to surgical manipulation and mechanical trauma. After 30 minutes of OLV, the collapsed lung releases inflammatory mediators into the epithelial lining fluid, indicating tissue insult and possibly resulting in systemic physiological changes [35]. Finally, barotrauma may occur at the end of OLV as previously atelectatic alveolar units are recruited.

The contribution of the type of anesthetic to the inflammatory response and clinical outcomes is currently unknown. Studies comparing propofol to volatile anesthetics such as sevoflurane and desflurane have yielded conflicting results [36]. Overall, differences in surgical time, duration of OLV, and laboratory techniques in existing studies have complicated interpretation of the data[24]. Volatile agents are thought to have immune-modulating effects. While previous work showed anti-inflammatory effects of propofol, recent studies have demonstrated decreased inflammatory markers in both the operative and nonoperative lung with volatile anesthesia[36-38]. Sugasawa and colleagues found that sevoflurane use was significantly associated with a suppressed inflammatory response compared to propofol [38]. Thus, the choice of anesthetic agent and other drugs such as ropivacaine, ketamine, thiopental, and dexmedetomidine may have anti-inflammatory effects that may be protective during lung surgery with OLV. Further study is needed to elucidate the role of these agents [39].

In conclusion, lung protective ventilator strategies which minimize Fi0<sub>2</sub>, barotrauma, and volutrauma are currently being used during OLV. Optimal lung protection, however, is multifactorial and may also depend on fluid administration techniques and perioperative drug administration. Alternative lung protective strategies for experimental or rescue use, such as extracorporeal membrane oxygenation and high-frequency oscillatory ventilation are discussed elsewhere.

#### 3.2. Fluid therapy — Goal directed therapy for thoracic surgery

Intravenous fluids are administered perioperatively in order to optimize systemic oxygen delivery to meet metabolic demands. Cardiac preload, afterload, and contractility are frequently used as surrogate indicators of global tissue perfusion. Inadequate intravascular volume can predispose to ischemia and end-organ dysfunction. Excessive fluid administration, on the other hand, can lead to tissue edema and compromised perfusion. In the operative setting, surgical insults may theoretically cause an inflammatory response characterized by alterations in microvascular integrity, allowing abnormal transmicrovascular fluid flux. Due to this increase in microvascular permeability, interstitial edema may develop, which decreases es  $O_2$  diffusion, resulting in hypoxic cell injury. This injury propagates a vicious cycle involving further cell death and the subsequent release of inflammatory cytokines.

In esophagectomy patients, the goal of intraoperative fluid administration is to balance perfusion pressure and oxygen delivery to vital organs including the gut mucosa, while preventing excessive fluid accumulation that may delay recovery of gastrointestinal function, impair wound and anastomotic healing, coagulation, and cardiac and respiratory function. Restrictive fluid regimens were thought to result in better gastrointestinal recovery time, reduced overall morbidity[40], improved respiratory parameters, decreased incidence of postoperative pulmonary complications, and shorter recovery periods [41]. Conversely, fluid overload had a direct negative relationship to function and structure of the intestinal anastomoses [42].

The thoracic surgery population is particularly prone to pulmonary complications, which have significant implications for patient outcomes. In the setting of pulmonary resection, for example, postoperative pulmonary edema confers a high mortality risk. Three significant risk factors include right pneumonectomy, increased perioperative intravenous fluids, and increased postoperative urine output [43]. Patel (1992) found that fluid replacement of greater than 3L in the 24 hours surrounding surgery was correlated with increased mortality [44]. While pulmonary edema is associated with fluid overload, there is no clear causal relationship [45]. With histology compatible with ARDS, postpneumonectomy pulmonary edema occurs despite a normal PAOP, and the high protein content of edema fluid points toward low-pressure endothelial damage[46]. Nevertheless, appropriate fluid administration may mitigate the deleterious effects of pulmonary pathology.

Traditional static cardiac preload measures such as CVP may fail to provide reliable estimations of actual preload and cardiac responses to fluid therapy. Studies on supine patients have demonstrated improved intraoperative hemodynamic stability, reduced ICU admissions, lower incidence of complications, and reduced mortality after major surgery with the use of dynamic preload indicators and goal-directed fluid therapy (GDT) [47, 48]. Commonly used monitors include esophageal Doppler monitoring and measures of arterial pulse pressure variation with respiration, such as the Lithium Dilution Cardiac Output (LiDCOplus) system and FloTrac/Vigileo. Using an esophageal Doppler probe, Gan (2002) found that GDT in patients undergoing major elective general, urologic, or gynecologic surgery with an anticipated blood loss of greater than 500mL resulted in an earlier return of bowel function, lower incidence of postoperative nausea and vomiting, and decreased length of postoperative hospital stay [49].

GDT does not consistently result in either increased or decreased amounts of fluid administered. One study[50] showed that the GDT group received more volume. However, in a cohort of septic patients, GDT patients received significantly more fluid during the first six hours than those assigned to standard therapy; but in the overall period from baseline to 72 hours after the start of treatment there was no significant difference between the two groups in the total amount of fluid administered. Early GDT provided significant outcome benefits: of the patients who survived to hospital discharge, those assigned to standard therapy had significantly longer hospital stays than those with early GDT[51].

Slinger describes one rational approach to fluid administration [45]. The thorax is not assumed to be a third space. Total positive fluid balance in the first 24 hours postoperatively should not exceed 20ml/kg or approximately 3L of crystalloid. Unless the patient is at high risk of developing renal insufficiency, urine output of greater than 0.5mL/kg/hr is probably unnecessary. In the case of reduced tissue perfusion, as in the case of epidural-induced sympathec-

tomy, it is preferable to invasively monitor and use GDT. The use of inotropes may be preferable to aggressive fluid overload.

One limitation of GDT, however, involves the extrapolation of studies correlating cardiac output measurements via PACs with those obtained via dynamic indices during abdominal surgery to thoracotomy patients who are positioned laterally and subjected to varying intrathoracic conditions, such as exposure to atmospheric pressure and OLV. The value of dynamic preload indicators in the thoracic population has not been systematically examined. Possible problems with extending the use of this device to thoracic surgery patients include lung compliance and intrathoracic pressure variations during positioning changes or insufflation for RATS, laparoscopy and changing intraabdominal pressure, the open chest, pressure changes with VATS, and differing ventilatory settings (TV, PEEP, OLV, DLV). One study has shown that GDT is at least not deleterious or does not result in pulmonary fluid overload when used for thoracic surgery requiring lateral thoracotomy and OLV[52]. While changing from the supine to the reverse Trendelenburg or prone positions significantly alters SV and thus SVV, 30° left or right recumbent and supine positions do not appear to affect SV or SVV measurements [53]. Kobayashi concludes that SVV, as displayed on the Vigileo monitor, is considered an accurate predictor of intravascular hypovolemia and is a useful indicator for assessing the appropriateness and timing of applying fluid for improving circulatory stability, but only during the perioperative period after esophagectomy [54]. De Waal (2002) demonstrated that while PiCCO-derived dynamic preload indicators were able to predict fluid responsiveness under closed-chest conditions, both static and dynamic preload indicators failed to predict fluid responsiveness in open-chest conditions [55]. Stroke volume variation (SVV) and pulse pressure variation (PPV) seem to be critically dependent on the undisturbed transmission of these pressure changes to cardiovascular structures within the closed thorax [56]. For example, sternotomy alone decreases SVV [57]. Additionally, one study [58] found that SVV could predict fluid responsiveness in patients undergoing OLV with acceptable levels of sensitivity and specificity only when tidal volumes were at least 8mL/kg. They state that dynamic indices of preload are based on the concept that positive pressure ventilation induces variations in SV. By definition, this concept requires that the preload is significantly affected by cyclic changes in intrathoracic and transpulmonary pressures, and these changes may be too small when patients undergoing OLV are ventilated with low tidal volumes (i.e. 6mL/kg). In short, the ability of SVV to predict volume responsiveness in thoracotomy patients is currently unknown.

Finally, the optimal type of fluid is debatable. Some animal models have demonstrated greater interstitial edema with crystalloid administration and better preserved effective capillary cross-sectional area in the colloid group[59]. Other studies conclude that when given in similar volumes, colloids are more beneficial for anastomotic healing than crystalloid [24, 42]. Improved microcirculatory blood flow and tissue oxygen tension were observed after abdominal surgery in one animal model [60, 61]. However, no difference in anastomotic healing was found in another animal model of colloid use [62]. To date, no consensus has been reached as to the superiority of crystalloids versus colloids. Pulmonary edema due to excessive crystalloid may clear faster than that caused by colloids.

In summary, intelligent fluid administration is vital to maintaining tissue perfusion and minimizing edema in the perioperative period. New methods of GDT based on SVV may offer useful tools to guide clinicians during thoracic surgery cases. However, the applicability of this technology to the thoracic population has not been fully investigated. Most likely, avoiding fluid overload by tailoring GDT in an educated manner to the patient's specific deficit and type of fluid loss yields optimal results.

#### 3.3. Special intraoperative monitoring

Since thoracic surgery involves hemodynamic shifts with a goal of tight, goal-directed fluid therapy, knowledge of cardiac output (CO) and fluid responsiveness is important in the perioperative period. The historical gold standard for evaluation of left ventricular enddiastolic pressure (LVEDP), thermodilution (TD) uses a pulmonary artery catheter (PAC) to generate a measured time/temperature curve, from which CO can be calculated. These measurements are averaged over 2-9 minutes, so monitoring is not continuous. Recent studies show that fluid management based on TD may not improve patient outcomes and may, in fact, increase morbidity and mortality. PAC use itself may be complicated by arrhythmia, infection, pulmonary artery rupture, and damage to right heart structures [63]. PAC use may be unreliable due to the low pressure environment of the pulmonary vascular tree and the interference by hydrostatic pressure. With pre-existent pulmonary hypertension PAC use may become more reliable but conversely have more chance of a complication. The standard deviation (SD) for TD is about 1 L/minute or about 20% of the average CO [64]. Clearly, reliable and less-invasive methods of measuring CO are needed. Current options include lithium dilution, esophageal Doppler monitoring (EDM), pulse contour cardiac output systems, partial CO<sub>2</sub> rebreathing, and thoracic electrical bioimpedance.

Two methods of generating continuous CO measurements require a central venous catheter (CVC), which is arguably invasive, though less so than pulmonary artery catheterization. PiCCO (PULSION Medical Systems AG, Munich, Germany) generates CO via thermodilution from a CVC to a femoral or axillary arterial line. Using the Stewart-Hamilton principle, cold-saline thermodilution is used to provide calibration of the continuous CO analysis. Similarly, PulseCO (LiDCO Ltd, London, England) uses the Stewart-Hamilton equations as applied to lithium chloride (0.15 - 0.3 mmol for an average adult) dilution from a CVC or peripheral vein to an arterial line. The arterial lithium concentration-time curve can be subject to error in the presence of certain muscle relaxants. Recalibration is recommended after changes in patient position, therapy or condition. Clinical studies have demonstrated that over a wide range of cardiac outputs the LiDCO method is at least as accurate as thermodilution [65, 66].

Esophageal doppler monitoring uses a continuous wave sensor on the end of a probe which measures the velocity of blood flow within the descending thoracic aorta. Nomogram estimated aortic cross-sectional area based on the patient's weight, height, and age enables calculation of left ventricular (LV) stroke volume (SV) from the area of the velocity-time waveform. The total time that blood is traveling in a forward direction within the area is the systolic flow time, which is corrected for heart rate to give the corrected flow time, which is a good index of systemic vascular resistance and is sensitive to changes in LV preload. There is

positive correlation between measures of cardiac output made simultaneously with the esophageal doppler and a thermodilution PAC [67]. Limitations of this monitor include assumptions of the diameter of the aorta based on the weight and height of the patient, a learning curve requiring about 12 probe placements [68], the need for patient sedation, and inability to be used during esophagectomies. This method has good validation; however, it only measures aortic blood flow and not true CO, and this may be potentially influenced by disproportionate changes in blood flow between the upper and lower body, although this is only important at the extremes of CO.

Pulse pressure (PP) methods measure the pressure in an artery over time to derive a waveform and use this information to calculate cardiac performance. However, any measure from an artery includes the changes in pressure associated with changes in vascular characteristics such as compliance and impedance. Physiologic or therapeutic changes in vessel diameter seen in the arterial waveform are assumed to reflect changes in CO. The ambiguity of the combined results of CO and vascular tone limits the application of PP methods. The values obtained by the LiDCOplus can be calibrated daily based on CO values generated by the LiDCO using the CVC waveform. It can also be used independently, as with the FloTrac/Vigileo (Edwards Lifesciences LLC, U.S.A.), which is an uncalibrated pulse contour analysis-based hemodynamic monitor that estimates CO utilizing a standard arterial catheter. The device consists of a pressure transducer which derives left-sided CO from a sample of arterial pulsations using an algorithm which calculates the product of the standard deviation of the arterial pressure wave (AP) (over 20 seconds) and a vascular tone factor (Khi) to generate stroke volume. Khi is derived from computer analysis of the morphologic change of the arterial pressure waveforms on a bit by bit basis based on the principle that changes in compliance or resistance affect the shape of the arterial pressure waveform. The equation in simplified form is as follows: SV=std(AP) \* Khi or BP x k(constant). CO is then derived utilizing the equation CO=HR\*SV. Only perfused beats that generate an arterial waveform should be counted for HR. While these monitors do not require intracardiac catheterization with a pulmonary artery catheter, they do require an arterial line. The benefits of this technology include the short time required for set up and data acquisition.

Disadvantages include its inability to provide right-sided heart pressures or mixed venous oxygen saturation. In addition, arterial monitoring systems are unable to predict changes in vascular tone and can therefore only estimate changes in vascular compliance. Some consider the measurement of pressure in the artery to calculate flow in the heart physiologically oversimplified and of questionable accuracy and benefit [64, 69]. The sensor is only indicated for adult use and has not been validated in patients with ventricular assist devices or intra-aortic balloon pumps. Absolute values during aortic regurgitation may be affected although trending may be appropriate. This monitor is dependent upon a high fidelity pressure tracing, which is compromised by spontaneous ventilation, atrial fibrillation or ectopy, severe peripheral constriction with vasopressor use, hypothermia, or dynamic autonomic states such as sepsis. In those instances, femoral artery cannulation or insertion of a PAC may be considered. Finally, in a study comparing these devices, although the PAC, FloTrac, LiDCO and PiCCO display similar mean CO values, they trended differently in response to therapy and showed

different interdevice agreement. In the clinically relevant low CO range (< 5 L/min), agreement improved slightly. Thus, utility and validation studies using only one CO device may potentially not be extrapolated to equivalency of using another similar device [70].

The Fick principle allows multiple substitutions for O<sub>2</sub> consumption, including CO<sub>2</sub> clearance. Based on the ratio of the change in end-tidal  $CO_2$  (et $CO_2$ ) and  $CO_2$  elimination, the Noninvasive Cardiac Output (NICO) device (Novametrix Medical Systems, Inc., Wallingford, CT, USA) calculates CO using a disposable rebreathing loop which allows intermittent partial rebreathing in 3 minute cycles. This system contains a CO<sub>2</sub> sensor which uses infrared light absorption, a disposable airflow sensor or differential pressure pneumotachometer, a specific disposable rebreathing loop, and a pulse oximeter. The production of CO<sub>2</sub> (VCO<sub>2</sub>, mL/min) is calculated from minute ventilation and its instantaneous CO<sub>2</sub> content, where the CaCO<sub>2</sub> (mL/100 mL of blood) is estimated from etCO<sub>2</sub> (mmHg). The rebreathing cycle induces an increase in  $etCO_2$  and mimics a drop in  $CO_2$  production.  $CO_2$  production is calculated as the product of CO<sub>2</sub> concentration and air flow during a breathing cycle, and the arterial content of  $CO_2$  (CaCO<sub>2</sub>) is derived from the etCO<sub>2</sub> and the CO<sub>2</sub> dissociation curve. The obtained differences of these values are then used to calculate CO, such that  $CO=\Delta VCO_2/(S \times \Delta etCO_2)$ , where S is the slope of the CO2 dissociation curve. The NICO system provides rapid, reliable CO values for mechanically ventilated patients with minor lung abnormalities and stable ventilatory settings [71].

The NICO system is also limited. For example, intrapulmonary shunt can affect the estimation of CO. Also, in patients undergoing thoracic surgery with OLV, the device underestimated CO compared with thermodilution CO at all measurement times [72]. With worsening pulmonary injury or hemodynamic compromise contributing to increasing shunt and dead space, assumptions made for calculating CO are less likely to approximate actual values. This technique reliably measures CO in patients affected by diseases causing low levels of pulmonary shunt, but underestimates it in patients with shunt higher than 35% [73]. In summary, compared to TD methods, the partial  $CO_2$  rebreathing technique is non-invasive, can easily be automated, and can provide real-time and continuous cardiac output monitoring. Large outcome studies demonstrating use of this device are still lacking.

Impedance cardiography (ICG) or thoracic electrical bioimpedance (TEB) uses changes in thoracic impedance over the cardiac cycle to generate CO. A constant magnitude, high frequency, low amplitude current is applied longitudinally across a segment of thorax. Using Ohm's Law, the voltage difference within the current field is proportional to the electrical impedance (Z). Contraction of the heart produces a cyclical change in transthoracic impedance of about 0.5%. Upon ventricular ejection, a time-dependent cardiac-synchronous pulsatile impedance change is observed,  $\Delta Z(t)$ , which constitutes the time-variable total transthoracic impedance indicates greater intrathoracic fluid volume and blood flow. TEB has waveform characteristics representing points in the cardiac cycle. The first derivative (dz/dt) of the waveform is used to identify the maximum upslope point, which is used to calculate the Velocity Index (VI). The VI is indicative of aortic blood velocity, such that impaired contractility is reflected by a decreased VI. By synchronizing fluid volume changes with the cardiac cycle, the change in

impedance can be used to calculate SV, CO, and systemic vascular resistance [74]. TEB equipment consists of both noninvasive and invasive devices, of which the former has gained more acceptance. Examples include the Bio-Z Dx (Sonosite Inc®, Bothell, WA) and the niccomo® (medis GmbH, Ilmenau, Germany). Some studies comparing TEB-derived CO to TD have found significant correlation between the methods, but inaccuracies were observed with severe tachycardia, low CO, or frequent arrhythmias [75]. Questions with respect to the reliability and validity of this technique have led some to advocate its use only in research settings [76]. The clinical use of TEB has yet to be established.

Transesophageal echocardiography (TEE) is a method of ultrasound-based cardiac imaging which allows real-time visualization of anatomic structure and function. In the specific setting of thoracic surgery, TEE can be used to monitor ventricular function, valvular function, and wall motion changes reflective of ischemia during positioning changes, volume shifts, OLV, or surgical resection. Intrathoracic tumors may be visible in some exams, and compression or infiltration of structures such as the pulmonary artery or innominate vein may be visualized. Tumor invasion of the heart may be appreciated, as can other anatomic abnormalities resulting from the underlying disease process or iatrogenic causes. Intraoperative hemodynamic instability of unknown cause and the need for evaluation of affected cardiac and pulmonary structures will likely satisfy the Appropriate Use Criteria for Echocardiography [77]. Common contraindications to TEE use include some features present in the thoracic surgery population such as known esophageal strictures, perforation, lacerations or large diverticula. Relative contraindications also obviate TEE use in esophagectomies: dysphagia or odynophagia, recent upper GI bleeding, extensive radiation to the chest and mediastinum, and esophageal varices.

In terms of global cardiac function, the transgastric short-axis view provides a snapshot of left and right ventricular ejection fraction. Calculation of CO is also possible with two-dimensional (2D) Doppler measurements, such that CO = Aortic valve area (AVA) x heart rate (HR) x velocity time integral (TVI). AVA may be measured by planimetry of the AV via the midesophageal AV short axis view, with the imaging plane at approximately 30°. Another common method of calculating AVA is with the continuity equation, which states that the flow in one area must equal the flow in a second area if there are no shunts between the two areas. In practical terms, the flow from the left ventricular outflow tract (LVOT) is compared to the flow at the level of the aortic valve:

# Aortic Value Area $(cm^2) = \frac{LVOT \ diameter^2 x \ 0.78540 \ x \ LVOT \ TV \ 1}{Aortic \ Value \ TV \ 1}$

Where the CSA LVOT  $(cm^2) = 0.785 \times LVOT$  Diameter2

TVI is an integral of instantaneous blood flow velocities during one cardiac cycle. To measure the LVOT TVI, the pulsed-Doppler sample volume is positioned just proximal to the aortic valve so that the location of the velocity recording matches the LVOT diameter measurement. When the sample volume is optimally positioned, the recording shows a smooth velocity curve with a well-defined peak and narrow band of velocities throughout systole. The TVI is measured by tracing the dense modal velocity throughout systole. The same is done for the AV TVI. TEE assessment of cardiac and intrathoracic structures and function is a clinically established method that plays a critical role in the diagnosis and management of perioperative hemodynamic instability in many institutions [78]. However, its main disadvantage is that its use requires extensive training and a skilled operator [68]. Some measurements may be challenging to acquire and subject to methodical error or inability to obtain images adequately parallel to the ultrasound plane. Hemodynamic measurements obtained with TEE compared to TD with a PAC have resulted in agreements ranging from good [79] to possessing "accuracy limitations" [80]. A significant source of this inconsistency may result from interoperator variability. Further, in the instance of thoracic cases, proper contact with the stomach and esophagus in the lateral position can hinder the acquisition of adequate images. Other inconveniences include the expense of the equipment and the fact that an image cannot be easily fixed in order to provide continuous cardiac output readings without the presence of an expert user.

In summary, the physiologic and hemodynamic challenges inherent to thoracic surgery may require not only monitoring via an arterial wave pressure measurement, but possibly other modalities as well. PAC, lithium dilution, EDM, pulse contour cardiac output systems, partial  $CO_2$  rebreathing, TEB, and TEE constitute such alternatives. While validation of these methods may be forthcoming, reasonable application of these modalities may improve perioperative management and overall patient outcomes.

#### 3.4. Special operative scenarios and anesthetic considerations

#### 3.4.1. VATS versus open thoracotomy

The decision as to whether a particular surgery can be performed using a video-assisted thoracoscopic or an open thoracotomy approach is a decision usually made by the surgeon. In 2007, at the International Society of Minimally Invasive Cardiothoracic Surgery conference, evidence revealed that VATS can be recommended to reduce overall postoperative complications, can reduce pain and overall functionality over the short term, improve delivery of adjuvant chemotherapy delivery, and can be recommended for lobectomy in clinical stage I and II non-small cell lung cancer patients. The recommendations were based on data derived from single and multiple randomized studies, but with conflicting evidence and/or divergence of opinion about the usefulness or efficacy of the procedure [81]. No general consensus using multiple randomized clinical trials has been done as to the preference of surgical technique. The bottom line is that with the learning curve for the VATS procedure, individual surgeons choose their own preferred method of surgical intervention. The role of an anesthesiologist is to be prepared for any lung surgery, both of which usually encompass one-lung ventilation, either through a double-lumen tube or a bronchial blocker as a general anesthetic. A minor VATS procedure such as pleural biopsy or thoracentesis can actually be done with local anesthesia +/- intravenous sedation [82]. These procedures are rare in the operating room however, and most VATS procedures are in actuality done under general anesthesia. An endobronchial ultrasound is done at our institute in the pulmonary lab as a general anesthetic with a laryngeal mask airway. Although a single-lumen endotracheal tube can be used under general anesthesia for open thoracotomy, the operative lung field would also undergo positive pressure ventilation, making it technically more difficult for the surgeon. In small infants, a balloon tipped bronchial blocker can be placed to isolate the lungmer[83] or placing ETT into the mainstem of the nonoperative lung are also other options if a double lumen tube is too large to be placed.

It is estimated that double lung tube placement has resulted in iatrogenic injury in 0.5-2 per 1000 cases of DLT placement[84], so care must be made to decrease these complications. One advantage of a double lumen tube above a bronchial blocker is the ability to suction out the operable lung if and when necessary, and increased intraoperative stability with the tube itself. The bronchial blocker is often difficult to obtain lung isolation in the right lung due to the takeoff of the right upper lobe being so close to the carina, but this technique is necessary to understand in case a double lumen is unable to be placed (in patients with abnormal anatomy) [85], or if a patient is already intubated with a single lumen tube with a difficult airway and needs lung isolation. There have been a number of cases where both are used successfully however. The key is having the lung isolated, and understanding physiology to understand how to utilize hypoxic pulmonary vasoconstriction to each patient's advantage.

In a thoracoscopic procedure, the surgeon does not have the ability to push the operative lung out of his/her way like an open thoracotomy. Thus, the importance of the lung being deflated is made apparent. Sometimes, a suction catheter can be placed in the operable lung to facilitate deflation of the lung. It is important to know if the surgeon is to insufflate with carbon dioxide, so that complications of insufflation can also be recognized. A VATS procedure is, although for the patient sometimes easier to manage postoperatively, for the surgeon and anesthesiologist comes with various difficulties. One of these difficulties has to do with not having enough access or visualization in cases where the pulmonary artery or another major vessel is inadvertently traumatized and the patient is bleeding. Therefore, it is always important to have blood available for a possible blood transfusion in both open thoracotomies and VATS procedures. An arterial line is necessary to keep a close eye on hemodynamics during both types of procedures. The positioning for both usually entails a lateral decubitus position, and pressure points must be checked. The postoperative pain level for patients with a thoracoscopic procedure is usually less than the open thoracotomy patient though this has been questioned. Chronic pain rates may be similar with VATS and open thoracotomies. A status post VATS procedure patient can achieve pain control with IV medications, while an epidural is usually recommended for thoracotomy patients. These methods of pain control will be discussed in a later chapter.

#### 3.4.2. Airway disruptive surgeries

Airway disruptive surgeries require special communication between the surgeon and anesthesiologist as to what is going to be required intraoperatively. With surgical and anesthetic advances, now more than half the trachea can be safely excised in selected cases[86]. A tracheal resection is something done rarely, requiring the anesthesiologist and surgeon to share the airway. The type of anesthetic utilized depends on the skill of the anesthesiologist, and the experience within each independent institution as to the best way to carry out this surgical procedure. There have been many case reports depicting many different methods of maintaining oxygenation and ventilation for a patient while still undergoing a thoracic procedure that compromises the trachea or bronchus. The main anesthetic concern is always adequate ventilation and oxygenation when the airway is essentially open. It is also important to both the anesthesiologist and surgeon to protect the integrity of the new tracheal anastomosis postoperatively. Steroids are often given to help decrease airway edema. A high  $FiO_2$  is necessary to help maintain oxygenation during periods of ventilatory pauses, but a close eye should be kept on electrocautery use. If indeed it is being used, then the lowest  $FiO_2$  that the patient can tolerate should be kept to help prevent airway fire. An arterial line is a good monitor to check for innominate compression (such as in a medianstinoscopy) during surgical dissection.

A technique where a laryngeal mask airway is utilized with high-frequency jet ventilation for a patient with tracheal stenosis has also been reported. In this otherwise healthy patient with tracheal stenosis from prolonged intubation, an LMA was placed and the patient was put on positive pressure ventilation. A sterile 6-mm flexible tube was placed in the distal trachea and the patient adequately oxygenated/ventilated while the dissection and lesion was resected. Once the tracheal anastomosis started, a jet ventilator was placed in the distal trachea and the patient jet-ventilated for tracheal anastomosis. Once completed, the patient was once again placed on positive pressure ventilation through the LMA while the patient was awakened, found adequately spontaneously ventilating, and extubated successfully[87]. There are disadvantages to using high-frequency jet ventilation such as during exhalation there may be air trapping from the stenotic lesion, the catheter could become occluded by blood and displaced, and there might be distal aspiration of debris or blood[88].

More routinely, an endotracheal tube can be placed above the area of stenosis. Once surgical exposure is done, a separate tube can be placed distal to the stricture and the patient placed on the ventilator with sterility across the field. Once the trachea is resected, the primary endotracheal tube can be passed distal to the lesion and the anastomosis completed.

Another case has been reported in a patient with critical trachea stenosis. The patient underwent femoral-femoral extracorporeal bypass prior to induction. An endotracheal tube was placed after induction, and the patient was maintained on the endotracheal tube and positive pressure ventilation as he/she was weaned from the cardiopulmonary bypass machine[89].

A prospective study has been done in patients with upper tracheal stenosis that were managed with a cervical epidural anesthesia, local anesthesia and conscious sedation while maintaining spontaneous ventilation throughout the resection[90]. Although only twenty consecutive patients were enrolled, the outcome had a high level of patient satisfaction and immediate feedback from the patient throughout the procedure. This bypasses the need for jet ventilation or positive pressure ventilation, and enables communication with the patient throughout the surgical procedure.

Post resection, usually the patient is extubated with their neck in a flexed position to put less tension on the anastomosis. Not infrequently the patients chin is sutured to the manubrium sterni with a heavy stitch to maintain the flexion. A smooth extubation with minimal coughing/ bucking is preferred for the same reason. Extubation is important post operatively to reduce the positive pressure on the suture line as well. Pain control is often not an issue, a tracheal

resection is not a very painful procedure, and intravenous narcotics and local anesthesia should be adequate for control.

#### 3.4.3. Endotracheal tube exchange (Double to single lumen tube exchange)

These days, double lumen tubes are routinely used for surgeries requiring lung isolation. If extubation is unable to be accomplished at the conclusion of the surgery, the decision must be made to either keep the double lumen in place, or exchange it for a single lumen tube. Less than 1% of patients, however, require mechanical ventilation after surgery[91]. Exchanging the double lumen tube avoids the potential obstruction of the airway that can occur when secretions/blood get lodged in the bronchial tube. Also, the nursing staff that is to be taking care of the patient postoperatively might not understand how to troubleshoot a double lumen endobronchial tube, so misuse of the tube may occur including airway rupture.

Exchanging a double-lumen endobronchial tube to a single-lumen endotracheal tube has many considerations and should be approached with some trepidation. An airway that was initially easy to place the double lumen in might not be easyafter the surgery with volume shifts and edema. If it is thought the airway might be lost in the exchange, leaving the double lumen in overnight with the head of the bed elevated to help alleviate edema might be the safest option. It has been shown that the flow resistances of modern double lumen tubes are actually much lower than previously supposed, so the need to change them is not as important during spontaneous ventilation and weaning from the ventilator as previously thought[92]. The effective diameter of each lumen of an adult double lumen endobronchial tube is comparable to a 6.0-7.0 mm outside diameter ETT [93], so adequate oxygenation/ventilation is manageable without exchanging the tube. If an exchange is necessary, there are a few options described. The first option is using a tube exchanger to facilitate the exchange of the double lumen tube to a single lumen. First, adequate anesthesia and suctioning down both lumens of the double lumen should be done.  $FiO_2$  should be 1.0. A tube exchanger is placed after being lubricated through the tracheal lumen, both cuffs are deflated, and the double lumen is removed over the stylet. A single lumen is then placed, sometimes while performing a direct laryngoscopy to facilitate the exchange. There are other scenarios described using the Eschmann stylet as a tube exchanger in various alternative ways [94]. The easiest and quickest method to exchanging the tube is just by performing a direct laryngoscopy after the patient is adequately anesthetized. If visualization of the cords is easy while the double lumen is still in place, it can be withdrawn and a single lumen placed under direct visualization.

Whichever technique is chosen, the safety of the patient comes first. If it is unsafe to change the tube out, an alternative is to just pull out the double lumen so the bronchial cuff is in the trachea, thus operating as a single lumen tube. Understanding that the airway anatomy and ease of visualization might not be the same as it was preoperatively is very important. Certainly it will not improve.

#### 3.4.4. Post-operative need for bronchoscopy prior to emergence

Certain surgical scenarios may require fiberoptic bronchoscopic examination after completion of the surgical procedure, but prior to patient emergence (if extubation is planned). These

scenarios include the examination of the integrity of anastomotic sites, the examination of anatomic structures (e.g., the vocal cords) to ensure proper postoperative function, and the clearing of debris (tissue, secretions, and blood) from the proximal and distal airways. During fiberoptic bronchoscopic examination, the anesthesiologist must meticulously plan airway control techniques to ensure an optimal environment for bronchoscopy as well as adequate patient oxygenation and ventilation.

When a single-lumen endotracheal tube (SLT) is already in use, the procedure is usually straightforward. If a bronchial blocker is used in combination with an SLT for lung isolation, one simply removes the blocker from the SLT to facilitate fiberoptic bronchoscopy (bronchoscopy could also be performed with the blocker in place, if needed). However, one must keep in mind that the internal diameter of the indwelling SLT must be large enough to accommodate an appropriately sized bronchoscope, especially if adequate suction (provided by larger bronchoscopes) is required to clear debris.

When a double-lumen endotracheal tube (DLT) is used for lung isolation, the procedure is more complicated. Fiberoptic bronchoscopy with a DLT in place is difficult because of the specialized tube's design and required positioning. First, the internal diameters of the dual lumens of the DLT are small. This limits the size of bronchoscopes that may be used (3.6 - 4.9mm outer diameter)—smaller bronchoscopes do not provide the view or possess the suctioning capabilities of larger bronchoscopes. Second, DLTs are considerably longer and more invasive than conventional SLTs. DLTs are positioned (post intubation) so that the distal opening of the tracheal lumen closely abuts the primary carina with the distal bronchial end placed in the appropriate mainstem bronchi (for which the DLT was designed). Therefore, a properly placed DLT restricts direct bronchoscopic examination of a majority of the trachea and mainstem bronchi. Comprehensive bronchoscopic examination in this scenario requires removal of the DLT and subsequent replacement with an SLT or supraglottic airway device (e.g. Laryngeal Mask Airway<sup>TM</sup> - LMA North America, San Diego, CA, U.S.A.) in an anesthetized patient.

Supraglottic airway devices do not require endotracheal intubation and are preferred over reintubation with an SLT because they [1] reduce the possibility of trauma to fresh surgical anastomosis sites within the airways, [2] improve the visualization of proximal airway structures – vocal cords, proximal trachea – that would be otherwise obstructed by SLTs, [3] accommodate larger bronchoscopes for improved visualization and suctioning, and [4] are less complicated to place than SLTs and do not require neuromuscular blockade for easy placement. In patients with non-difficult airways, supraglottic airway devices may be immediately placed after deep extubation (in a blind fashion). In patients with difficult airways, supraglottic airway devices may be pre-positioned posterior to the DLT prior to extubation. This allows for fiberoptic visual confirmation of the device's proper positioning (by continuous visualization of the glottic opening) prior to, during, and after extubation. Once positioning of the supraglottic airway device and adequate ventilation are confirmed, fiberoptic examination of the airways may proceed. Upon completion of the bronchoscopic exam, the patient may be emerged from anesthesia with the device in place without the need for reintubation.

#### 3.4.5. Pulmonary procedures in out-of-O.R. settings

A trend is growing toward performing pulmonary procedures in specialized non-O.R. pulmonary procedure suites, rather than the traditional operating room. These procedures may be performed for diagnostic or therapeutic purposes and include flexible/rigid bronchoscopy, pleuroscopy, tracheo-bronchial stent placement or dilation, and endobronchial ultrasound-guided lymph node sampling [95]. In these settings, special anesthetic considerations must be made regarding choice of agents, airway devices, and ventilatory modes.

#### a. Agents

A total intravenous anesthetic (TIVA) approach is the most practical mode of anesthetic delivery in these settings. A TIVA-based approach avoids volatile anesthetic agents that could be lost from airways in procedures that involve a breach of the airway (and/or the airway device). Loss of agent through a breach could result in inadequate anesthetic levels, exposure of personnel to volatile agents, combustion and airway fire (N2O), or production of toxic products after pyrolysis. Furthermore, special ventilatory modes (such as jet-ventilation) necessary for certain pulmonary procedures preclude the use of volatile anesthetics [96].

Two anesthetic challenges during pulmonary procedures are [1] providing adequate anesthesia during alternating periods of high and low stimulation (in which anesthetic requirements also fluctuate rapidly), and [2] rapid recovery post-procedure [96]. The intravenous agents propofol, remifentanil, and lidocaine have specific advantages in these situations, primarily as a result of their pharmacokinetic/pharmacodynamic profiles. The standard sedativehypnotic for TIVA administration is propofol, and, in fact, propofol is the only sedativehypnotic that is used on a standard basis for continuous infusion. Only propofol has the combination of quick onset, short half-life, rapid redistribution, amnesia, effective airway reflex depression, wide anesthetic depth range, and antiemetic properties. It does not, however, provide analgesia; therefore, narcotics are usually added to a TIVA regimen. Narcotics provide analgesia, reduce the propofol dosage needed, and also suppress the cough reflex. Remifentanil is an ultra-short acting narcotic (context sensitive half-life: 3-5 minutes) that is metabolized by nonspecific tissue and plasma esterases; therefore, it is ideal intraooperatively to manage moments of high stimulation while avoiding over-accumulation of narcotic when stimulation subsides [97]. In patients for whom post-procedure pain control or cough suppression is needed, a longer-acting narcotic may be coadministered with remifentanil. Lastly, intravenous lidocaine is a useful adjunct to propofol and remifentanil in TIVA. Lidocaine is an amide-type local anesthetic that reduces the need for both propofol and narcotics; it also suppresses airway reflexes and is an effective post-procedure anti-tussive [98].

#### **b.** Airway devices

Airway management for pulmonary procedures must address the need for adequate patient oxygenation/ventilation, permit complete examination of areas of interest of the airway, and accommodate the necessary diagnostic and/or interventional instruments needed for the procedure. In most cases, supraglottic airways (e.g., Laryngeal Mask Airway<sup>TM</sup>) meet these requirements and are the airway devices of choice. They are easy to place without the need for specialized equipment, are an integral part of the standard difficult airway algorithm, may be

used in spontaneously or mechanically ventilated patients, and provide limited airway protection from regurgitation. Furthermore, supraglottic airways may be easily used as a bridge in a case where definitive airway control will be managed via rigid bronchoscopy/jetventilation. In such a case, the supraglottic airway is placed as a temporary airway conduit during induction, is removed once the rigid bronchoscopy begins, and is replaced at the end of the procedure to serve as the airway conduit until emergence from anesthesia.

**c.** Ventilatory modes

Patient ventilation/oxygenation during pulmonary procedures may be spontaneous or mechanical, depending on the requirements of the procedure. Adequacy of oxygenation and ventilation is measured by pulse oximetry and end-tidal CO2 measurement. It is important to note that while end-tidal CO2 detection is vital in confirming adequate ventilation, it is often inconsistent due to airway breach and suctioning inherent during pulmonary procedures. Of the various mechanical ventilation modes, jet-ventilation deserves particular attention. Jet-ventilation is typically associated with rigid bronchoscopy. In this situation, total airway control will be in the hands of the interventionalist/surgeon, with the anesthesiologist controlling the jet-ventilator. Control of jet ventilation may be by automated jet delivery systems or manually by the anesthesiologist. Automated systems have several benefits over manual delivery, including greater control of delivered FiO2 and respiratory frequency, duration, and flow. Additionally, automation gives anesthesia personnel greater freedom to attend to other aspects of the anesthetic care.

#### 3.4.6. Post anesthesia recovery considerations for patients undergoing thoracic procedures

The immediate post-operative care of the thoracic surgical patient is focused on ensuring conditions that optimize oxygenation/ventilation and recognizing possible post-operative complications inherent to thoracic surgery.

a. Extubation

If feasible, immediate post-operative extubation is favored to avoid unnecessary hemodynamic stress, the disruption of fresh surgical sites from continued intubation, positive-pressure ventilation, and/or coughing, and the development of ventilator-associated pneumonia [99]. However, the tentative respiratory condition of the typical thoracic surgery patient warrants careful consideration when making the decision to extubate (see preoperative anesthetic evaluation above). The physician must not only optimize routine respiratory criteria for extubation – pH  $\geq$  7.30, FiO2  $\leq$  0.4-0.5, PaO2/FiO2 > 150-200, PEEP  $\leq$  5-8 cmH2O, RR  $\leq$  30 bpm, SpO2  $\geq$  90%, PaO2  $\geq$  60, PaCO2  $\leq$  50, Vt > 5 ml/kg, VC >15 ml/kg, NIF > -20 cm H2O – but must also recognize the variable nature of emergence from anesthesia and consider the state of other important clinical variables [100]. These variables include the ability to follow commands, the return of airway protective reflexes, adequate reversal of neuromuscular blockade (with good motor strength), adequate pain control, normothermia, hemodynamic stability, and normal electrolyte values. Additionally, the rapid shallow breathing index (RSBI - the ratio of respiratory frequency to tidal volume (f/VT)) combines superior sensitivity (97%) and negative predictive value (95%) when predicting weaning success [101, 102]. Once extubation is achieved, the focus is on optimizing pulmonary physiology; three fundamental measures are essential. First, supplemental oxygen should be administered and adequate ventilation confirmed, because hypoxia and hypercarbia are well known to increase pulmonary vascular resistance [103]. Second, the patient should be positioned supine with the head of the bed elevated (semi-Fowler's position) to lessen the risk of aspiration and decrease the work of breathing. Third, pain control must be evaluated; pain increases sympathetic tone, elevating pulmonary artery pressures and pulmonary vascular resistance, and elicits respiratory splinting that limits ventilation and results in hypercapnea.

In some cases, continued intubation and mechanical ventilation is required postoperatively. Under these circumstances, it is important to achieve the transition from positive pressure to spontaneous ventilation as quickly as possible. In addition, extubation criteria should be assessed frequently so that extubation may be acheived as soon as possible.

**b.** Post-operative Complications

Operations involving vital thoracic structures place patients at higher risk of life-threatening post-operative complications. An in-depth discussion of these complications can be found in chapters detailing the post-operative course of these patients. This section focuses on select complications that may occur in the immediate post-operative recovery period: injuries in the conducting airways, pneumothorax, and cardiac herniation.

i. Injuries in the conducting airways

Advanced anesthetic airway management and surgical manipulation predispose the thoracic surgery patient to a variety of post-operative airway complications. Injuries range from erythema/edema (most commonly) to vocal cord injuries and tracheo-bronchial rupture (TBR) (rarely). Supportive therapy with supplemental humidified oxygen is adequate for mild symptoms of airway edema; however, constant monitoring for worsening respiratory obstruction is paramount. Iatrogenic vocal cord injuries resulting from intubation and/or damage to the recurrent laryngeal nerve may lead to airway compromise and increase risk of aspiration, if the damage is bilateral. Dyspnea, stridor, and inability to phonate are symptoms commonly associated with bilateral vocal cord injury/paralysis. If respiratory distress is present, the airway should be definitely controlled via intubation or tracheostomy. TBR caused by DLT intubation is extremely rare, with a reported incidence of less than 0.5 % [84]. Hemoptysis and subcutaneous crepitus (in the neck and upper chest area) are the most common presenting symptoms with respiratory distress and/or collapse occurring in advanced cases [104]. If TBR is suspected and surgical intervention planned, general anesthesia should be induced while preferably maintaining spontaneous ventilation to avoid worsening of the injury by barotrauma. Initial airway control with a supraglottic airway is preferred, when possible, to avoid further injury that can occur with endotracheal intubation. Further, a supraglottic airway allows for complete fiber-optic examination of the trachea, bronchi, and distal airways. Fiberoptic examination of the tracheobronchial tree is important to confirm the diagnosis of TBR and to locate the lesion. Once the location and extent of the injury is determined, the type and application of airway control may be chosen and surgical repair undertaken. In extreme situations, cardio-pulmonary bypass may be required to assure oxygenation and ventilation.

#### ii. Pneumothorax

Pneumothorax is a potentially grave immediate postoperative complication that may necessitate prompt intervention. The creation of a pneumothorax is inherent in any procedure involving the breach of the thoracic cavity. The severity of pneumothorax is determined by its magnitude and whether it is in communication externally with atmospheric pressure. A pneumothorax of small volume is usually well tolerated; however, with increased magnitude, it exerts considerable effects to the heart and vasculature in the confined space of the thoracic cavity. These may lead to hemodynamic collapse and respiratory compromise - a tension pneumothorax. Chest drainage tubes are used to decrease the magnitude of a pneumothorax by providing an avenue of escape for trapped air (and/or blood, secretions, etc.) from the thoracic cavity. Specialized "balanced" drainage systems have been developed for certain operations, such as pneumonectomy. Balanced systems provide a buffer to prevent excessive negative or positive intrathoracic pressures from developing, lowering the chance for both tension pneumothorax and cardiac herniation (see below) [105]. In circumstances where chest tubes are not placed or where the drainage system malfunctions, tension pneumothorax may develop. In this scenario, intrathoracic pressures must be relieved immediately via needle decompression and/or emergent chest tube insertion. One must recognize that contralateral pneumothorax is also a possibility from anesthetic (contralateral central venous catheters, epidural (paramedian) placement, barotrauma) as well as surgical (breach of the contralateral pleura) insult [106]. Care must be taken to avoid clamping chest tubes after thoracotomy to avoid formation of a pneumothorax.

#### iii. Cardiac herniation

Cardiac herniation, although rare, is a potentially fatal postoperative complication most commonly associated with disruption of the pericardium – most commonly during the course of or after a pneumonectomy. The usual presenting symptoms are generalized hypotension and tachycardia; however, right versus left sided cardiac herniation may present with additional distinct signs and symptoms inherent to the physiologic disruption unique to the direction of herniation [107, 108]. Leftward herniation places the heart at risk for myocardial ischemia and arrhythmias, because of the potential constriction of the ventricles by pericardial tissue during the course of the herniation [107, 108]. Rightward herniation predisposes the patient to superior vena cava (SVC) syndrome - head, neck and upper-extremity cyanosis, edema, etc. - secondary to torsion and obstruction of the SVC and inadequate cardiac preload because of impaired venous drainage [107, 108]. After assessing signs and symptoms, cardiac herniation may be confirmed via imaging - chest x-ray and/or echocardiography. Immediate surgical intervention to reduce the herniation and correct the pericardial defect is paramount to prevent further hemodynamic collapse [107, 108]. The gravity of cardiac herniation warrants recovery measures to help minimize its occurrence. Avoid patient positioning with the operative side dependent, to reduce gravitational effects favoring herniation. As discussed above, early extubation is favored to alleviate the effects of positive pressure ventilation and its tendency to instigate and worsen herniation. Lastly, avoid negative pressure via chest drainage tubes (preferably using balanced chest drainage systems in pneumonectomies) to minimize a vacuum effect that may predispose to herniation [107, 108].

## 4. Pain management for the thoracic surgical patient

#### 4.1. Post-thoracotomy pain syndrome

Thoracotomies continue to cause substantial pain because of the degree of surgical injury. Insult to the intercostal nerves, soft tissue damage and inflammation, bone and joint disturbance, and visceral manipulation all contribute to the severity of pain[88]. The estimated incidence of chronic pain following thoracotomy is between 30-40%, with approximately 10% with severe disabling pain [109, 110]. Pain control is crucial after thoracic surgery not only for immediate pain relief, but also to prevent pulmonary complications.

"Pain that recurs or persists along a thoracotomy scar at least two months following the surgical procedure" [111] is the definition of post-thoracotomy pain syndrome (PTPS). Poor pain management after thoracotomy may contribute to PTPS [112]. The pain is largely described as aching, with tenderness and numbness at or around the surgical incision/scar [113]. In contrast to acute pain, which mostly affects respiratory function, PTPS may be responsible for inability to perform daily activities. Although PTPS likely plays a negative role in daily life, its impact is unclear because these subjective phenomena have not been reliably assessed [113, 114].

Although video assisted thoracic surgery (VATS) was anticipated to reduce pain when compared to traditional posterolateral thoracotomy, its smaller port sites do not necessarily avoid intercostal nerve injury owing to aggressive manipulation of the scopes and instruments. The pain associated with VATS is not significantly different to that of thoracotomy[115] and there are conflicting differences in the incidence of PTPS [113, 114]. It is unclear if patients with preventative analgesia by way of thoracic epidural analgesia have fewer propensities to develop PTPS [114]. Other regional techniques have not yet been studied in this capacity [114]. There is also conflicting evidence of the causality of acute pain on PTPS [114].

There are many modalities of postoperative pain control that will be briefly explained here.

#### 4.2. Systemic analgesics

Opioids have a long-standing history of providing effective pain relief. It is the unwanted sideeffects that discourage their use including: nausea, vomiting, respiratory depression, ileus, biliary spasms, urinary retention, sedation, and pruritis. Opioids can be given by many routes – oral, intravenous, intramuscular, transdermal, transmucosal. Intravenous patient controlled analgesia (PCA) allows for increased safety, less opioid use, ability to titrate to individual needs, and some increase in patient satisfaction [116]. Using opioids alone may lead to intolerable side effects, which has led to the concomitant use of other drug classes for their synergistic effects.

Ketamine is an *N*-methyl-D-aspartate (NMDA) antagonist that has direct spinal effects as well as depresses the thalamus and activates the limbic system. It acts at the phencyclidine binding site and has been used as an induction agent. At lower doses, it provides effective analgesia.

The use of low dose intraoperative ketamine offers decreased postoperative pain and morphine consumption [117, 118].

Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit conversion of arachidonic acid to prostaglandin E2 in inflamed areas via cyclooxygenase (COX). It is suggested that the maximum daily dose of NSAIDs should be given/ordered because small doses of NSAIDs are not useful in acute pain relief [118]. When given in conjunction with opioids, NSAIDs reduced the postoperative opioid utilization and decreased unwanted opioid side effects [118]. NSAIDs should be used cautiously in those susceptible to its side effects including risk of renal injury, bleeding and peptic ulcers, asthma and bronchospasm. COX-2 selective inhibitors were developed to avoid the unwanted side effects of NSAIDs and may play a role as an adjunct in postoperative pain control.

#### 4.3. Thoracic epidural

Thoracic epidural refers to analgesic technique of injecting medication into the epidural space, the potential space that surrounds the spinal cord. A segmental block results with coverage both above and below the injection site. A single injection into the epidural space may be performed, or a catheter may be inserted for prolonged infusion. For post-thoracotomy pain relief, commonly a catheter is inserted via midline or paramedian technique in order to provide intermittent boluses as well as a continuous infusion for pain control. Infusions usually consist of a local anesthetic, an opioid, or a mixture of the two in order to optimize their synergistic effects [119] while reducing the individual doses and side effects [119, 120]. As the nerve roots leave the foramen and become peripheral nerves, they cross through the epidural space where they are bathed in the epidural solution.

The mechanism of action differs between local anesthetics and opioids. Local anesthetics block sodium channels ultimately leading to blocked nerve conduction. The density of local anesthetic blockade is primarily dependent on the concentration of local anesthetic present, and dermatomal spread of blockade is dependent on the volume infused. Also remember that the level of somatic block may be smaller than the sympathetic block because the somatic fibers are less sensitive [121]. Opioids bind to presynaptic and postsynaptic opioid receptors in the substantia gelatinosa, which inhibits the presynaptic release and postsynaptic response to neurotransmitters [121]. In a systemic review of randomized trials, Joshi et al. found that patients with thoracic epidural analgesia had a significantly lower pain scores and needed less supplemental analgesia compared to systemic opioid analgesia [122].

Adverse effects may be from various aspects of epidural placement. Those associated with needle and catheter placement include back pain, inadvertent dural puncture, post dural puncture headache, trauma to spinal cord or nerves, and neuropathy (usually transient). Dural puncture may lead to post dural puncture headache. The headache is usually characterized by severe fronto-occipital pain with head elevation that subsides, sometimes completely, upon return to the supine position [88]. The loss of CSF through the small puncture site may be enough to cause traction on the brain causing pain. Most patients' symptoms completely resolve after a few days to a week. Those that are not able or not willing to wait for spontaneous resolution may opt to undergo an epidural blood patch. Neurologic injury may be the most

feared complication of epidural analgesia. Nerve injury is usually transient and may occur from direct trauma to the nerves or spinal cord during needle insertion. A more devastating nerve injury can result from an epidural hematoma or abscess. Spinal hematoma occurs very rarely, approximately less than 1 in 150,000 [88]. Although rare, if it is not detected and treated promptly, it leads to irreversible paraplegia. The occurrence of hematoma has been on the rise, whether it is from increased coexistence of anticoagulation and regional anesthesia technique or from increased reporting [123]. Infection can occur from ineffective sterile preparation, contaminated drugs, an underlying infection, or bacteremia. Any of these sources can cause an infection at the insertion site or lead to spread of infection from the skin along the indwelling catheter into the epidural space causing meningitis (if the dura was punctured) or abscess which could ultimately result in cord compression [123].

Effects related to epidural injection of local anesthetic are usually dose related and include hypotension, motor block, systemic toxicity, and urinary retention. Epidural opioid administration may result in adverse effects that are similar to their parenteral administration. These include pruritis, nausea, urinary retention, decreased arousability, ileus, and respiratory depression. Respiratory depression is the most concerning of the adverse effects and thus necessitates a monitored setting. After epidural injection, in the following 2-4 hours, early respiratory depression can occur which is likely due to the systemic absorption of the opioid [124]. Some opioids are more hydrophilic than others and have a tendency to remain in the CSF causing possible spread and delayed respiratory depression (usually occurs after 4 hours).

Relative contraindications to epidural include sepsis or bacteremia, infection at the insertion site, hypovolemia or shock, coagulopathy or thrombocytopenia, increased intracranial pressure (for risk of brain herniation if accidental dural puncture). One should use caution with patients who have underlying neurological diseases as not to confuse effects of the epidural versus pre-existing neurological deficits. The only absolute contraindication to epidural placement is patient refusal [88].

#### 4.4. Thoracic paravertebral nerve block

TPVB involves injecting local anesthetic into the space adjacent to the thoracic vertebrae, which contains the spinal intercostal nerves. The boundaries of the space include the parietal pleura anterolaterally, the superior costotransverse ligament posteriorly, and medially by a portion of the vertebral body, intervertebral disc and intervertebral foramen [125]. The paravertebral space is continuous with the epidural space, intercostal space, and contralateral paravertebral space (by way of the prevertebral and epidural spaces). The caudal boundary of the space is at the origin of the psoas, while the cranial boundary is unknown. Cranially, radiographic dye has been noted after a thoracic paravertebral injection in the cervical area [126]. The intercostal nerves, dorsal rami, sympathetic chain and associated vessels lie within the fat of the paravertebral space [126]. A percutaneous technique is classically described whereby a needle is inserted into the space until a subtle loss of resistance is met followed by aspiration to ensure that the lung or pleura has not been breached before injecting small amounts of local anesthetic or insertion of a catheter [125]. The injection of local anesthetic can also be performed under direct visualization by the surgeon prior to the closure of the chest wall.

Injection of local anesthetic into the paravertebral space can give varying degrees of analgesia. The injection may remain localized to the area of injection producing a single level ipisilateral block, or it can spread to the above and below adjacent levels, as well as to the epidural space and contralateral paravertebral space. For example, Eason found that a single injection of 15ml of 0.375% bupivacaine spread over 4 spaces [125]. Similarly, 15ml of 0.5% bupivacaine injection led to a unilateral 5 level dermatome somatic block and 8 level sympathetic block [127].

Advantages of TPVB are many. TPVB is easy to learn and has a high success rate [126]. Successful placement of TPVB also can eliminate some unwanted effects of epidural analgesia such as spinal cord injury, spinal hematoma, excessive hypotension (owing to only a unilateral sympathetic blockade), and urinary retention [128]. Also, the nursing care required after TPVB is no different than normal post-surgical care [129]. A meta-analysis identified TPVB as having equivalent pain relief after thoracic surgery with less major side effects and decreased pulmonary complications to that of epidural analgesia [130].

Adverse effects of TPVB include accidental pleural puncture, which could lead to a pneumothorax. The incidence of puncture and pneumothorax are 0.8% and 0.5% respectively, which is similar to other anesthetic procedures with pneumothorax risk [128]. Other adverse effects include relative hypotension, failed block, and vascular puncture.

Contraindications to TPVB are similar to those of epidural placement including infection at the insertion site, bacteremia, epyema. Another relative contraindication would be if the patient has had a previous thoracotomy because the ipsilateral paravertebral space may have been altered or obliterated as a result of surgery [124]. With respect to anticoagulation, the paravertebral space is less vascular than the epidural space, and paravertebral vessel puncture is less common [128, 129].

#### 4.5. Intercostal nerve block

The intercostal nerve provides sensory and motor innervation to chest wall and is found in the costal groove of each rib. Intercostal nerve blockade provides unilateral sensory and motor anesthesia to these areas. Local anesthetic is commonly injected 5 to 7 cm from the midline over several sections owing to the great deal of overlap between the intercostal nerves. There are different approaches to intercostal nerve blocks for thoracic procedures. The simplest is to inject local anesthetic around several intercostal nerves during thoracotomy when the chest wall is open. Cryotherapy, continuous infusion or successive boluses of local anesthetic are also options [131].

Direct intercostal nerve block is most easily done by direct visualization during thoracotomy, but can also be done percutaneously. Local is injected over multiple segments inferior to the rib with caution to avoid intravascular injection. Usually a small amount (2-5ml) of local is injected two to three spaces above and below the incision [131]. Cryoanalgesia interrupts nerve conduction for 1 to 3 months as a result of the freezing and subsequent damage of the myelin sheath [131] and is associated with long term intercostal neuralgia [132]. Extrapleural and interpleural infusion of local anesthetic are also techniques to block the intercostal nerves. Peeling back the pleura from the chest wall can create an extrapleural pocket, and a catheter can be introduced percutaneously into the space. After closure of the thoracotomy, an infusion of local anesthetic will fill the extrapleural space which leads to an intercostal block. Interpleural catheters can be inserted percutaneously to attain an intercostal nerve block, but one must keep in mind that a large volume of the anesthetic may be lost to the chest tubes. Interpleural anesthesia requires diffusion across the pleura and sub pleural space in order to attain an intercostal nerve blockade. Single shot direct intercostal nerve block appears to have the same or superior pain control compared to epidural on the day of surgery, but after the effects of the local anesthesia have been exhausted, epidural anesthesia is superior to intercostal nerve block [131-133] Detterbeck states that extrapleural infusion of local anesthetic is more effective than systemic narcotics, and at least as good as thoracic epidural. Extrapleural intercostal nerve block provides a unilateral blockade, so the amount of urinary retention and hypotension are decreased, and there is not a need for special monitoring because the risk of respiratory depression is minimal [131]. Pain relief from interpleural infusion is inconsistent [131].

Systemic absorption of local anesthetic is notoriously high for intercostal nerve block due to the vascularity of the area of injection. There are no specific absolute contraindications to intercostal nerve blocks. They should be avoided in patients in whom high systemic levels of local anesthetics will not be well tolerated such as those with seizure disorders.

#### 4.6. Elastomeric pumps

Wound infiltration with local anesthetic targets the peripheral level of pain, and has been used widely in minor surgical procedures [134, 135]. The relatively short-term duration of the local infiltration limits the usefulness of one-time wound infiltration for more major thoracic surgery. An elastomeric pump connected to a multi orifice catheter allows for continuous local anesthetic incisional infusion. Implementation of this technique is quite simple, with a minimal technical failure incidence [116]. A catheter is threaded in or near the insult and connected to a reservoir pump of local anesthetic by way of a flow-limiting valve. The surrounding tissues are then continuously bathed in the local anesthetic at 4ml/hr. By providing anesthesia at the site of insult there may be less need for systemic narcotics, and avoid many systemic narcotic effects including postoperative nausea and vomiting. It is also believed that local anesthetic at the wound site can decrease the local inflammatory response which may in turn decrease pain and hyperalgesia [116]. Wheatley et al found that using an elastomeric pump is a safe and effective adjunct for post-thoracotomy pain relief. Also, patients had lower pain scores and decreased narcotic need when compared to thoracic epidural analgesia alone [136]. Although local anesthetic toxicity is always a concern with infusions, the incidence of systemic toxicity is low [116]. Wound infiltration is safe and not associated with increased acute wound-related complications or long-term effects on wound healing [137].

#### 4.7. Anticoagulation

Hemorrhagic complications from neuraxial blockade are of great concern. Epidural analgesia is usually not initiated in patients who have a preexisting coagulopathy. The following are

some consensus guidelines assembled by the American Society of Regional Anesthesia and Pain Medicine [138]:

- **1.** Thrombolytic therapy
- Avoid thrombolytic for 10 days after neuraxial puncture,
- It is not clear how long to wait after thrombolytic therapy for safe performance of neuraxial anesthesia,
- If neuraxial block is at or near time of thrombolytic therapy neurologic checks should be none no less than every 2 hours,
- There is no recommendation for removal of neuraxial catheters in unexpected thrombolytic therapy
- 2. Subcutaneous unfractionated heparin
- Review of other medications that may affect clotting is advised
- There is little risk of spinal hematoma
- Placement of the block prior to therapy may be desirable although increased risk is not demonstrated in the presence of subcutaneous heparin
- In twice-daily doses epidurals may be placed before the next scheduled dose, the catheter can coexist with regimen, and preferably the catheter can be removed one hour prior to next dose
- Thrice daily doses or more than 10,000units unfractionated heparin there is no data published, but it is advised not to maintain an epidural catheter with this regimen
- If the patient has received more than four days of heparin, a platelet count should be obtained prior to block or removal of catheter in the instace of heparin induced thrombocytopenia
- After needle placement, wait one hour to administer heparin
- Wait 2-4 hours after heparin to remove cathers, resume therapy one hours after removal of catheter
- Bloody placement may increase risk of hematoma, but the case does not necessarily need to be cancelled.
- 3. Low-Molecular Weight Heparin
- A bloody placement does not mandate cancellation of the case, however LMWH should be delayed for 24 hours
- Epidural placement should happen 10-12 hours after last does
- If the patient is on higher dose LMWH, one should wait 24 hours to place epidural
- Do not place epidural at 2 hours after dose peak anticoagulation activity

- Twice daily doses should not be initiated with an indwelling catheter, and must be removed before the first dose
- Once-daily dosing may start 6-8 hours postoperatively, the catheter can be maintained, removal after 10-12 hours of last dose
- 4. Oral Anticoagulants Warfarin
- INR should be normalized prior to neuraxial technique
- If initial does of warfarin is given more than 24 hours prior to surgery, INR should be checked prior to neuraxial block
- If low-dose warfarin therapy is ongoing during epidural anesthesia, neurological evaluations and daily INR checks are advised
- Catheters should be removed when INR is less than 1.5, and neurological assessment should be continued for 24 hours
- If 1.5 < INR < 3, catheters should be cautiously removed
- If the INR is more than 3, the dose of warfarin should be held/reduced
- 5. Antiplatelet Medications
- NSAIDs have no specific concerns or added risk with epidural with or without catheter placement, unless concurrent medications affecting clotting
- The risk of bleeding with clopidogrel, ticlopidine, and GP IIB/IIIA inhibitors is not known.
- 7 and 14 days should elapse between discontinuation of ticlopidine and clopidogre, respectively, and placement of neuraxial block
- Platelet function normalization must occur before placement of neuraxial block if discontinued for only 5-7 days
- Epidural catheters should not be maintained while on GP IIB/IIIA inhibitor therapy
- 6. Herbals
- They do not create risk that impedes with neuraxial block
- Garlic inhibits platelet aggregation, increases fibrinolysis
- Ginko inhibits platelet-activating factor
- Ginseng has the potential to inhibit coagulation
- 7. Thrombin inhibitors
- Monitored by aPTTT
- Anticoagulation effect present for 1-3 hours
- There are no pharmacologic reversals



- Neuraxial techniques are best avoided
- 8. Fondaparinux
- Factor Xa inhibitor
- Unknown risk of spinal hematoma

## 5. Conclusion

The challenges of thoracic anesthesia are unique among all anesthetic subspecialties. Its practitioners must be well-versed in a wide range of anesthetic management principles, from advanced airway techniques to ventilations strategies and pain management. The two subspecialties of thoracic surgery and thoracic anesthesia continue to co-evolve to improve patient safety and surgical outcomes.

#### Author details

January Tsai, Teresa Moon, Shital Vachhani, Javier Lasala, Peter H Norman and Ronaldo Purugganan<sup>\*</sup>

\*Address all correspondence to: rpurugga@mdanderson.org

Department of Anesthesia and Perioperative Medicine, Division of Anesthesia and Critical Care, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

### References

- [1] BTS guidelines: guidelines on the selection of patients with lung cancer for surgery-Thorax. [Guideline Practice Guideline]. (2001). Feb;, 56(2), 89-108.
- [2] Slinger, P. Update on anesthetic management for pneumonectomy. Curr Opin Anaesthesiol. [Review]. (2009). Feb;, 22(1), 31-7.
- [3] Brunelli, A, & Rocco, G. Spirometry: predicting risk and outcome. Thorac Surg Clin. [Review]. (2008). Feb;, 18(1), 1-8.
- [4] Nakahara, K, Ohno, K, Hashimoto, J, Miyoshi, S, Maeda, H, Matsumura, A, et al. Prediction of postoperative respiratory failure in patients undergoing lung resection for lung cancer. Ann Thorac Surg. (1988). Nov;, 46(5), 549-52.

- [5] Beckles, M. A, Spiro, S. G, Colice, G. L, & Rudd, R. M. The physiologic evaluation of patients with lung cancer being considered for resectional surgery. Chest. [Guideline Practice Guideline]. (2003). Jan;123(1 Suppl):105S-14S.
- [6] Olsen, G. N, Bolton, J. W, Weiman, D. S, & Hornung, C. A. Stair climbing as an exercise test to predict the postoperative complications of lung resection. Two years' experience. Chest. (1991). Mar;, 99(3), 587-90.
- [7] Slinger, P, & Johnston, M. Preoperative assessment for lung cancer surgery. In: Slinger P, editor. Progress in thoracic anesthesia: a society of cardiovascular anesthesiologists monograph. 1st ed. Baltimore: Lippincott, Williams, and Wilkins; (2004)., 1-27.
- [8] Ghaye, B, Szapiro, D, Fanchamps, J. M, & Dondelinger, R. F. Congenital bronchial abnormalities revisited. Radiographics. [Review]. (2001). Jan-Feb;, 21(1), 105-19.
- [9] Slinger, P. Choosing the appropriate double-lumen tube: a glimmer of science comes to a dark art. J Cardiothorac Vasc Anesth. [Comment Editorial]. (1995). Apr;, 9(2), 117-8.
- [10] Lohser, J. Managing hypoxemia during minimally invasive thoracic surgery. Anesthesiol Clin. (2012). Dec;, 30(4), 683-97.
- [11] Narayanaswamy, M, Mcrae, K, Slinger, P, Dugas, G, Kanellakos, G. W, 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. [Comparative Study Randomized Controlled Trial]. (2009). Apr;, 108(4), 1097-101.
- [12] Campos, J. H. Lung isolation techniques for patients with difficult airway. Curr Opin Anaesthesiol. [Review]. (2010). Feb;, 23(1), 12-7.
- [13] Brodsky, J. B. Lung separation and the difficult airway. Br J Anaesth. [Review]. (2009). Dec;103 Suppl 1:i, 66-75.
- [14] Purugganan, R. V, Jackson, T. A, Heir, J. S, Wang, H, & Cata, J. P. Video laryngoscopy versus direct laryngoscopy for double-lumen endotracheal tube intubation: a retrospective analysis. J Cardiothorac Vasc Anesth. (2012). Oct;, 26(5), 845-8.
- [15] Benumof, J. L. The position of a double-lumen tube should be routinely determined by fiberoptic bronchoscopy. J Cardiothorac Vasc Anesth. [Editorial]. (1993). Oct;, 7(5), 513-4.
- [16] Read, R. C, Friday, C. D, & Eason, C. N. Prospective study of the Robertshaw endobronchial catheter in thoracic surgery. Ann Thorac Surg. (1977). Aug;, 24(2), 156-61.
- [17] Burton, N. A, Watson, D. C, Brodsky, J. B, & Mark, J. B. Advantages of a new polyvinyl chloride double-lumen tube in thoracic surgery. Ann Thorac Surg. (1983). Jul;, 36(1), 78-84.

- [18] Alliaume, B, Coddens, J, & Deloof, T. Reliability of auscultation in positioning of double-lumen endobronchial tubes. Can J Anaesth. [Comparative Study]. (1992). Sep;, 39(7), 687-90.
- [19] Fleischmann, K. E, Goldman, L, Young, B, & Lee, T. H. Association between cardiac and noncardiac complications in patients undergoing noncardiac surgery: outcomes and effects on length of stay. Am J Med. [Research Support, U.S. Gov't, P.H.S.]. (2003). Nov;, 115(7), 515-20.
- [20] Law, S, Wong, K. H, Kwok, K. F, Chu, K. M, & Wong, J. Predictive factors for postoperative pulmonary complications and mortality after esophagectomy for cancer. Ann Surg. (2004). Nov;, 240(5), 791-800.
- [21] Licker, M, De Perrot, M, Spiliopoulos, A, Robert, J, Diaper, J, Chevalley, C, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. Anesth Analg. [Research Support, Non-U.S. Gov't]. (2003). Dec;, 97(6), 1558-65.
- [22] Kooguchi, K, Kobayashi, A, Kitamura, Y, Ueno, H, Urata, Y, Onodera, H, et al. Elevated expression of inducible nitric oxide synthase and inflammatory cytokines in the alveolar macrophages after esophagectomy. Crit Care Med. [Research Support, Non-U.S. Gov't]. (2002). Jan;, 30(1), 71-6.
- [23] Misthos, P, Katsaragakis, S, Milingos, N, Kakaris, S, Sepsas, E, Athanassiadi, K, et al. Postresectional pulmonary oxidative stress in lung cancer patients. The role of onelung ventilation. Eur J Cardiothorac Surg. (2005). Mar;discussion 82-3., 27(3), 379-82.
- [24] Ng, J. M. Update on anesthetic management for esophagectomy. Curr Opin Anaesthesiol. [Review]. (2011). Feb;, 24(1), 37-43.
- [25] Amato, M. B, Barbas, C. S, Medeiros, D. M, Magaldi, R. B, Schettino, G. P, Lorenzifilho, G, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med. [Clinical Trial Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (1998). Feb 5;, 338(6), 347-54.
- [26] Lionetti, V, Recchia, F. A, & Ranieri, V. M. Overview of ventilator-induced lung injury mechanisms. Curr Opin Crit Care. [Research Support, Non-U.S. Gov't Review]. (2005). Feb;, 11(1), 82-6.
- [27] Schilling, T, Kozian, A, Huth, C, Buhling, F, Kretzschmar, M, Welte, T, et al. The pulmonary immune effects of mechanical ventilation in patients undergoing thoracic surgery. Anesth Analg. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2005). Oct;table of contents., 101(4), 957-65.
- [28] Michelet, P, Journo, D, Roch, X. B, Doddoli, A, Marin, C, & Papazian, V. L, et al. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. Anesthesiology. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2006). Nov;, 105(5), 911-9.

- [29] Mols, G, Priebe, H. J, & Guttmann, J. Alveolar recruitment in acute lung injury. Br J Anaesth. [Review]. (2006). Feb;, 96(2), 156-66.
- [30] Kilpatrick, B, & Slinger, P. Lung protective strategies in anaesthesia. Br J Anaesth. [Review]. (2010). Dec;105 Suppl 1:i, 108-16.
- [31] Curley, G, Laffey, J. G, & Kavanagh, B. P. Bench-to-bedside review: carbon dioxide. Crit Care. [Research Support, Non-U.S. Gov't Review]. (2010).
- [32] Tugrul, M, Camci, E, Karadeniz, H, Senturk, M, Pembeci, K, & Akpir, K. Comparison of volume controlled with pressure controlled ventilation during one-lung anaesthesia. Br J Anaesth. [Clinical Trial Comparative Study Randomized Controlled Trial]. (1997). Sep;, 79(3), 306-10.
- [33] Sugasawa, Y, Yamaguchi, K, Kumakura, S, Murakami, T, Kugimiya, T, Suzuki, K, et al. The effect of one-lung ventilation upon pulmonary inflammatory responses during lung resection. J Anesth. (2011). Apr;, 25(2), 170-7.
- [34] Zingg, U, Forberger, J, Frey, D. M, Esterman, A. J, Oertli, D, Beck-schimmer, B, et al. Inflammatory response in ventilated left and collapsed right lungs, serum and pleural fluid, in transthoracic esophagectomy for cancer. Eur Cytokine Netw. [Research Support, Non-U.S. Gov't]. (2010). Mar;, 21(1), 50-7.
- [35] Komatsu, Y, Yamamoto, H, Tsushima, K, Furuya, S, Yoshikawa, S, Yasuo, M, et al. Increased Interleukin-8 in Epithelial Lining Fluid of Collapsed Lungs During One-Lung Ventilation for Thoracotomy. Inflammation. (2012). Jul 21.
- [36] De Conno, E, Steurer, M. P, Wittlinger, M, Zalunardo, M. P, Weder, W, Schneiter, D, et al. Anesthetic-induced improvement of the inflammatory response to one-lung ventilation. Anesthesiology. [Randomized Controlled TrialResearch Support, Non-U.S. Gov't]. (2009). Jun;, 110(6), 1316-26.
- [37] Schilling, T, Kozian, A, Kretzschmar, M, Huth, C, Welte, T, Buhling, F, et al. Effects of propofol and desflurane anaesthesia on the alveolar inflammatory response to onelung ventilation. Br J Anaesth. [Randomized Controlled Trial]. (2007). Sep;, 99(3), 368-75.
- [38] Sugasawa, Y, Yamaguchi, K, Kumakura, S, Murakami, T, Suzuki, K, Nagaoka, I, et al. Effects of sevoflurane and propofol on pulmonary inflammatory responses during lung resection. J Anesth. [Randomized Controlled Trial]. (2012). Feb;, 26(1), 62-9.
- [39] Blumenthal, S, Borgeat, A, Pasch, T, Reyes, L, Booy, C, Lambert, M, et al. Ropivacaine decreases inflammation in experimental endotoxin-induced lung injury. Anesthesiology. [In Vitro Research Support, Non-U.S. Gov't]. (2006). May;, 104(5), 961-9.
- [40] Nisanevich, V, Felsenstein, I, Almogy, G, Weissman, C, Einav, S, & Matot, I. Effect of intraoperative fluid management on outcome after intraabdominal surgery. Anesthesiology. [Clinical Trial Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2005). Jul;, 103(1), 25-32.

- [41] Kita, T, Mammoto, T, & Kishi, Y. Fluid management and postoperative respiratory disturbances in patients with transthoracic esophagectomy for carcinoma. J Clin Anesth. (2002). Jun;, 14(4), 252-6.
- [42] Marjanovic, G, Villain, C, & Timme, S. zur Hausen A, Hoeppner J, Makowiec F, et al. Colloid vs. crystalloid infusions in gastrointestinal surgery and their different impact on the healing of intestinal anastomoses. Int J Colorectal Dis. (2010). Apr;, 25(4), 491-8.
- [43] Zeldin, R. A, Normandin, D, Landtwing, D, & Peters, R. M. Postpneumonectomy pulmonary edema. J Thorac Cardiovasc Surg. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.]. (1984). Mar;, 87(3), 359-65.
- [44] Patel, R. L, Townsend, E. R, & Fountain, S. W. Elective pneumonectomy: factors associated with morbidity and operative mortality. Ann Thorac Surg. (1992). Jul;, 54(1), 84-8.
- [45] Slinger, P. D. Perioperative fluid management for thoracic surgery: the puzzle of postpneumonectomy pulmonary edema. J Cardiothorac Vasc Anesth. [Review]. (1995). Aug;, 9(4), 442-51.
- [46] Zarins, C. K, Rice, C. L, Peters, R. M, & Virgilio, R. W. Lymph and pulmonary response to isobaric reduction in plasma oncotic pressure in baboons. Circ Res. [Research Support, U.S. Gov't, P.H.S.]. (1978). Dec;, 43(6), 925-30.
- [47] Mayer, J, Boldt, J, Mengistu, A. M, Rohm, K. D, & Suttner, S. Goal-directed intraoperative therapy based on autocalibrated arterial pressure waveform analysis reduces hospital stay in high-risk surgical patients: a randomized, controlled trial. Crit Care. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2010). R18.
- [48] Benes, J, Chytra, I, Altmann, P, Hluchy, M, Kasal, E, Svitak, R, et al. Intraoperative fluid optimization using stroke volume variation in high risk surgical patients: results of prospective randomized study. Crit Care. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2010). R118.
- [49] Gan, T. J, Soppitt, A, Maroof, M, Moalem, H, Robertson, K. M, Moretti, E, et al. Goaldirected intraoperative fluid administration reduces length of hospital stay after major surgery. Anesthesiology. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2002). Oct;, 97(4), 820-6.
- [50] Bundgaard-nielsen, M, Holte, K, Secher, N. H, & Kehlet, H. Monitoring of peri-operative fluid administration by individualized goal-directed therapy. Acta Anaesthesiol Scand. [Review]. (2007). Mar;, 51(3), 331-40.
- [51] Rivers, E, Nguyen, B, Havstad, S, Ressler, J, Muzzin, A, Knoblich, B, et al. Early goaldirected therapy in the treatment of severe sepsis and septic shock. N Engl J Med. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2001). Nov 8;, 345(19), 1368-77.

- [52] Haas, S, Eichhorn, V, Hasbach, T, Trepte, C, Kutup, A, Goetz, A. E, et al. Goal-directed fluid therapy using stroke volume variation does not result in pulmonary fluid overload in thoracic surgery requiring one-lung ventilation. Crit Care Res Pract. (2012).
- [53] Daihua, Y, Wei, C, Xude, S, Linong, Y, Changjun, G, & Hui, Z. The effect of body position changes on stroke volume variation in 66 mechanically ventilated patients with sepsis. J Crit Care. (2012). Aug;27(4):416 e, 7-12.
- [54] Kobayashi, M, Koh, M, Irinoda, T, Meguro, E, Hayakawa, Y, & Takagane, A. Stroke volume variation as a predictor of intravascular volume depression and possible hypotension during the early postoperative period after esophagectomy. Ann Surg Oncol. [Comparative Study Research Support, Non-U.S. Gov't]. (2009). May;, 16(5), 1371-7.
- [55] De Waal, E. E, Rex, S, Kruitwagen, C. L, Kalkman, C. J, & Buhre, W. F. Dynamic preload indicators fail to predict fluid responsiveness in open-chest conditions. Crit Care Med. [Research Support, Non-U.S. Gov't]. (2009). Feb;, 37(2), 510-5.
- [56] Denault, A. Y, Gasior, T. A, & Gorcsan, J. rd, Mandarino WA, Deneault LG, Pinsky MR. Determinants of aortic pressure variation during positive-pressure ventilation in man. Chest. [Research Support, U.S. Gov't, Non-P.H.S.]. (1999). Jul;, 116(1), 176-86.
- [57] De Blasi, R. A, Palmisani, S, Cigognetti, L, Iasenzaniro, M, Arcioni, R, Mercieri, M, et al. Effects of sternotomy on heart-lung interaction in patients undergoing cardiac surgery receiving pressure-controlled mechanical ventilation. Acta Anaesthesiol Scand. (2007). Apr;, 51(4), 441-6.
- [58] Suehiro, K, & Okutani, R. Influence of tidal volume for stroke volume variation to predict fluid responsiveness in patients undergoing one-lung ventilation. J Anesth. (2011). Oct;, 25(5), 777-80.
- [59] Morisaki, H, Bloos, F, Keys, J, Martin, C, Neal, A, & Sibbald, W. J. Compared with crystalloid, colloid therapy slows progression of extrapulmonary tissue injury in septic sheep. J Appl Physiol. [Comparative Study Research Support, Non-U.S. Gov't]. (1994). Sep;, 77(3), 1507-18.
- [60] Hiltebrand, L. B, Kimberger, O, Arnberger, M, Brandt, S, Kurz, A, & Sigurdsson, G. H. Crystalloids versus colloids for goal-directed fluid therapy in major surgery. Crit Care. [Research Support, Non-U.S. Gov't]. (2009). R40.
- [61] Kimberger, O, Arnberger, M, Brandt, S, Plock, J, Sigurdsson, G. H, Kurz, A, et al. Goal-directed colloid administration improves the microcirculation of healthy and perianastomotic colon. Anesthesiology. [Comparative Study Research Support, Non-U.S. Gov't]. (2009). Mar;, 110(3), 496-504.
- [62] Hotz, B, Hotz, H. G, Arndt, M, Holmer, C, Buhr, H. J, & Ritz, J. P. Fluid resuscitation with human albumin or hydroxyethyl starch--are there differences in the healing of

experimental intestinal anastomoses? Scand J Gastroenterol. [Comparative Study Research Support, Non-U.S. Gov't]. (2010). , 45(1), 106-14.

- [63] Connors, A. F. Jr., Speroff T, Dawson NV, Thomas C, Harrell FE, Jr., Wagner D, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. Jama. [Multicenter Study Research Support, Non-U.S. Gov't]. (1996). Sep 18;, 276(11), 889-97.
- [64] Su, N. Y, Huang, C. J, Tsai, P, Hsu, Y. W, Hung, Y. C, & Cheng, C. R. Cardiac output measurement during cardiac surgery: esophageal Doppler versus pulmonary artery catheter. Acta Anaesthesiol Sin. [Clinical Trial Randomized Controlled Trial]. (2002). Sep;, 40(3), 127-33.
- [65] Linton, R, Band, D, Brien, O, Jonas, T, & Leach, M. R. Lithium dilution cardiac output measurement: a comparison with thermodilution. Crit Care Med. [Clinical Trial Comparative Study Research Support, Non-U.S. Gov't]. (1997). Nov;, 25(11), 1796-800.
- [66] Linton, R. A, Jonas, M. M, Tibby, S. M, Murdoch, I. A, Brien, O, & Linton, T. K. NW, et al. Cardiac output measured by lithium dilution and transpulmonary thermodilution in patients in a paediatric intensive care unit. Intensive Care Med. [Comparative Study Research Support, Non-U.S. Gov't Validation Studies]. (2000). Oct;, 26(10), 1507-11.
- [67] Schober, P, Loer, S. A, & Schwarte, L. A. Perioperative hemodynamic monitoring with transesophageal Doppler technology. Anesth Analg. [Review]. (2009). Aug;, 109(2), 340-53.
- [68] Lefrant, J. Y, Bruelle, P, Aya, A. G, Saissi, G, Dauzat, M, De La Coussaye, J. E, et al. Training is required to improve the reliability of esophageal Doppler to measure cardiac output in critically ill patients. Intensive Care Med. [Comparative Study]. (1998). Apr;, 24(4), 347-52.
- [69] Takala, J, Ruokonen, E, Tenhunen, J. J, Parviainen, I, & Jakob, S. M. Early non-invasive cardiac output monitoring in hemodynamically unstable intensive care patients: a multi-center randomized controlled trial. Crit Care. [Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2011). R148.
- [70] Hadian, M, Kim, H. K, Severyn, D. A, & Pinsky, M. R. Cross-comparison of cardiac output trending accuracy of LiDCO, PiCCO, FloTrac and pulmonary artery catheters. Crit Care. [Comparative Study Research Support, N.I.H., Extramural]. (2010). R212.
- [71] Chaney, J. C, & Derdak, S. Minimally invasive hemodynamic monitoring for the intensivist: current and emerging technology. Crit Care Med. [Review]. (2002). Oct;, 30(10), 2338-45.
- [72] Ng, J. M, Chow, M. Y, Ip-yam, P. C, Goh, M. H, & Agasthian, T. Evaluation of partial carbon dioxide rebreathing cardiac output measurement during thoracic surgery. J

Cardiothorac Vasc Anesth. [Comparative Study Evaluation Studies Research Support, Non-U.S. Gov't]. (2007). Oct;, 21(5), 655-8.

- [73] Rocco, M, Spadetta, G, & Morelli, A. Dell'Utri D, Porzi P, Conti G, et al. A comparative evaluation of thermodilution and partial CO2 rebreathing techniques for cardiac output assessment in critically ill patients during assisted ventilation. Intensive Care Med. [Comparative Study Research Support, Non-U.S. Gov't Validation Studies]. (2004). Jan;, 30(1), 82-7.
- [74] Bernstein, D. Impedance cardiography: Pulsatile blood flow and the biophysical and electrodynamic basis for the stroke volume equations. Journal of electrical bioimpedance. (2010). , 1(1), 2-17.
- [75] Spinale, F. G. (1988). Comparison of bioimpedance and thermodilution methods for determining cardiac output: experimental and clinical studies. Updated in 1995. Ann Thorac Surg. [Comparative Study]. 1995 Aug;, 60(2), 483-4.
- [76] Wang, D. J, & Gottlieb, S. S. Impedance cardiography: more questions than answers. Curr Heart Fail Rep. [Review]. (2006). Sep;, 3(3), 107-13.
- [77] Douglas, P. S, Garcia, M. J, Haines, D. E, Lai, W. W, Manning, W. J, Patel, A. R, et al. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 Appropriate Use Criteria for Echocardiography. A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance American College of Chest Physicians. J Am Soc Echocardiogr. [Practice Guideline]. (2011). Mar;, 24(3), 229-67.
- [78] Shillcutt, S. K, Markin, N. W, Montzingo, C. R, & Brakke, T. R. Use of rapid "rescue" perioperative echocardiography to improve outcomes after hemodynamic instability in noncardiac surgical patients. J Cardiothorac Vasc Anesth. [Evaluation Studies]. (2012). Jun;, 26(3), 362-70.
- [79] Perrino, A. C. Jr., Harris SN, Luther MA. Intraoperative determination of cardiac output using multiplane transesophageal echocardiography: a comparison to thermodilution. Anesthesiology. [Clinical Trial]. (1998). Aug;, 89(2), 350-7.
- [80] Brennan, J. M, Blair, J. E, Hampole, C, Goonewardena, S, Vasaiwala, S, Shah, D, et al. Radial artery pulse pressure variation correlates with brachial artery peak velocity variation in ventilated subjects when measured by internal medicine residents using hand-carried ultrasound devices. Chest. [Clinical Trial]. (2007). May;, 131(5), 1301-7.
- [81] Downey, R. J, Cheng, D, Kernstine, K, Stanbridge, R, Shennib, H, Wolf, R, et al. Video-Assisted Thoracic Surgery for Lung Cancer Resection: A Consensus Statement of

the International Society of Minimally Invasive Cardiothoracic Surgery (ISMICS) 2007. Innovations (Phila). (2007). Nov;, 2(6), 293-302.

- [82] Brodsky, J. B, & Cohen, E. Video-assisted thoracoscopic surgery. Curr Opin Anaesthesiol. (2000). Feb;, 13(1), 41-5.
- [83] Hammer, G. B, Fitzmaurice, B. G, & Brodsky, J. B. Methods for single-lung ventilation in pediatric patients. Anesth Analg. [Review]. (1999). Dec;, 89(6), 1426-9.
- [84] Massard, G, Rouge, C, Dabbagh, A, Kessler, R, Hentz, J. G, Roeslin, N, et al. Tracheobronchial lacerations after intubation and tracheostomy. Ann Thorac Surg. (1996). May;, 61(5), 1483-7.
- [85] Slinger, P. Lung isolation in thoracic anesthesia, state of the art. Can J Anesth. (2001). RR5., 13.
- [86] Pinsonneault, C, Fortier, J, & Donati, F. Tracheal resection and reconstruction. Can J Anaesth. [Review]. (1999). May;46(5 Pt 1):439-55.
- [87] Adelsmayr, E, Keller, C, Erd, G, & Brimacombe, J. The laryngeal mask and high-frequency jet ventilation for resection of high tracheal stenosis. Anesth Analg. [Case Reports]. (1998). Apr;, 86(4), 907-8.
- [88] Barash, P. G, Cullen, B. F, & Stoelting, R. K. Clinical anesthesia. Philadelphia: Lippincott; (1989).
- [89] Zhou, Y. F, Zhu, S. J, Zhu, S. M, & An, X. X. Anesthetic management of emergent critical tracheal stenosis. J Zhejiang Univ Sci B. [Case Reports]. (2007). Jul;, 8(7), 522-5.
- [90] Macchiarini, P, Rovira, I, & Ferrarello, S. Awake upper airway surgery. Ann Thorac Surg. (2010). Feb;discussion 90-1., 89(2), 387-90.
- [91] Brodsky, J. B, & Lemmens, H. J. Left double-lumen tubes: clinical experience with 1,170 patients. J Cardiothorac Vasc Anesth. [Review]. (2003). Jun;, 17(3), 289-98.
- [92] Slinger, P. D, & Lesiuk, L. Flow resistances of disposable double-lumen, single-lumen, and Univent tubes. J Cardiothorac Vasc Anesth. [Comparative Study]. (1998). Apr;, 12(2), 142-4.
- [93] Hannallah, M. S, Miller, S. C, Kurzer, S. I, & Tefft, M. C. The effective diameter and airflow resistance of the individual lumens of left polyvinyl chloride double-lumen endobronchial tubes. Anesth Analg. (1996). Apr;, 82(4), 867-9.
- [94] Rusch, V. W, Freund, P. R, & Bowdle, T. A. Exchanging double-lumen for single-lumen endotracheal tubes after thoracotomy. Ann Thorac Surg. (1991). Feb;, 51(2), 323-4.
- [95] Ross, A. F, & Ferguson, J. S. Advances in interventional pulmonology. Curr Opin Anaesthesiol. [Review]. (2009). Feb;, 22(1), 11-7.

- [96] Purugganan, R. V. Intravenous anesthesia for thoracic procedures. Curr Opin Anaesthesiol. [Review]. (2008). Feb;, 21(1), 1-7.
- [97] Kapila, A, Glass, P. S, Jacobs, J. R, Muir, K. T, Hermann, D. J, Shiraishi, M, et al. Measured context-sensitive half-times of remifentanil and alfentanil. Anesthesiology.
   [Clinical Trial Comparative Study Randomized Controlled TrialResearch Support, Non-U.S. Gov't]. (1995). Nov;, 83(5), 968-75.
- [98] Altermatt, F. R, Bugedo, D. A, Delfino, A. E, Solari, S, Guerra, I, Munoz, H. R, et al. Evaluation of the effect of intravenous lidocaine on propofol requirements during total intravenous anaesthesia as measured by bispectral index. Br J Anaesth. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2012). Jun;, 108(6), 979-83.
- [99] Higgins, T. L. Postthoractomy Complications. In: Kaplan JA, Slinger P, editors. Thoracic Anesthesia. Third ed. Philadelphia: Elsevier; (2003).
- [100] MacIntyre NRCook DJ, Ely EW, Jr., Epstein SK, Fink JB, Heffner JE, et al. Evidencebased guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. Chest. [Consensus Development Conference Guideline Practice Guideline Review]. (2001). Dec;120(6 Suppl):375S-95S.
- [101] Meade, M, Guyatt, G, Cook, D, Griffith, L, Sinuff, T, Kergl, C, et al. Predicting success in weaning from mechanical ventilation. Chest. [Meta-Analysis Research Support, U.S. Gov't, P.H.S.]. (2001). Dec;120(6 Suppl):400S-24S.
- [102] Epstein, S. K, & Ciubotaru, R. L. Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. Am J Respir Crit Care Med. (1998). Aug;, 158(2), 489-93.
- [103] Viitanen, A, Salmenpera, M, & Heinonen, J. Right ventricular response to hypercarbia after cardiac surgery. Anesthesiology. [Research Support, Non-U.S. Gov't].
  (1990). Sep;, 73(3), 393-400.
- [104] Hofmann, H. S, Rettig, G, Radke, J, Neef, H, & Silber, R. E. Iatrogenic ruptures of the tracheobronchial tree. Eur J Cardiothorac Surg. [Evaluation Studies]. (2002). Apr;, 21(4), 649-52.
- [105] Deslauriers, J, & Gregoire, J. Techniques of pneumonectomy. Drainage after pneumonectomy. Chest Surg Clin N Am. [Historical Article Review]. (1999). May;xii., 9(2), 437-48.
- [106] Venuta, F, Boehler, A, Rendina, E. A, De Giacomo, T, Speich, R, Schmid, R, et al. Complications in the native lung after single lung transplantation. Eur J Cardiothorac Surg. (1999). Jul;, 16(1), 54-8.

- [107] Zellos, L, Jaklitsch, M. T, Al-mourgi, M. A, & Sugarbaker, D. J. Complications of extrapleural pneumonectomy. Semin Thorac Cardiovasc Surg. (2007). Winter, 19(4), 355-9.
- [108] Chambers, N, Walton, S, & Pearce, A. Cardiac herniation following pneumonectomy--an old complication revisited. Anaesth Intensive Care. [Case Reports Review].
  (2005). Jun;, 33(3), 403-9.
- [109] Gotoda, Y, Kambara, N, Sakai, T, Kishi, Y, Kodama, K, & Koyama, T. The morbidity, time course and predictive factors for persistent post-thoracotomy pain. Eur J Pain. (2001)., 5(1), 89-96.
- [110] Kehlet, H, Jensen, T. S, & Woolf, C. J. Persistent postsurgical pain: risk factors and prevention. Lancet. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't Review]. (2006). May 13;, 367(9522), 1618-25.
- [111] Merskey, H, & Bogduk, N. Classification of chronic pain : descriptions of chronic pain syndromes and definitions of pain terms. 2nd ed. ed. Seattle: IASP Press; (1994).
- [112] Katz, J, Jackson, M, Kavanagh, B. P, & Sandler, A. N. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. Clin J Pain. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (1996). Mar;, 12(1), 50-5.
- [113] Wildgaard, K, Ravn, J, & Kehlet, H. Chronic post-thoracotomy pain: a critical review of pathogenic mechanisms and strategies for prevention. Eur J Cardiothorac Surg. [Research Support, Non-U.S. Gov't Review]. (2009). Jul;, 36(1), 170-80.
- [114] Wildgaard, K, & Kehlet, H. Chronic post-thoracotomy pain,ÄîWhat is new in pathogenic mechanisms and strategies for prevention? Techniques in Regional Anesthesia & Pain Management. (2011). , 15(3), 83-9.
- [115] Landreneau, R. J, Mack, M. J, Hazelrigg, S. R, Naunheim, K, Dowling, R. D, Ritter, P, et al. Prevalence of chronic pain after pulmonary resection by thoracotomy or video-assisted thoracic surgery. J Thorac Cardiovasc Surg. [Comparative Study]. (1994). Apr;discussion 85-6., 107(4), 1079-85.
- [116] Liu, S. S, Richman, J. M, Thirlby, R. C, & Wu, C. L. Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: a quantitative and qualitative systematic review of randomized controlled trials. J Am Coll Surg. [Meta-Analysis Review]. (2006). Dec;, 203(6), 914-32.
- [117] Roytblat, L, Korotkoruchko, A, Katz, J, Glazer, M, Greemberg, L, & Fisher, A. Postoperative pain: the effect of low-dose ketamine in addition to general anesthesia. Anesth Analg. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (1993). Dec;, 77(6), 1161-5.
- [118] Camu, F, & Vanlersberghe, C. Pharmacology of systemic analgesics. Best Pract Res Clin Anaesthesiol. [Review]. (2002). Dec;, 16(4), 475-88.

- [119] Kaneko, M, Saito, Y, Kirihara, Y, Collins, J. G, & Kosaka, Y. Synergistic antinociceptive interaction after epidural coadministration of morphine and lidocaine in rats. Anesthesiology. (1994). Jan;, 80(1), 137-50.
- [120] Scott, D. A, Blake, D, Buckland, M, Etches, R, Halliwell, R, Marsland, C, et al. A comparison of epidural ropivacaine infusion alone and in combination with 1, 2, and 4 microg/mL fentanyl for seventy-two hours of postoperative analgesia after major abdominal surgery. Anesth Analg. [Clinical Trial Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (1999). Apr;, 88(4), 857-64.
- [121] Morgan, G. E, Mikhail, M. S, & Murray, M. J. Clinical anesthesiology. 4th ed. ed. New York: Lange Medical Books/McGraw Hill ; London : McGraw-Hill [distributor]; (2006).
- [122] Joshi, G. P, Bonnet, F, Shah, R, Wilkinson, R. C, Camu, F, Fischer, B, et al. A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. Anesth Analg. [Research Support, Non-U.S. Gov't Review]. (2008). Sep;, 107(3), 1026-40.
- [123] Wheatley, R. G, Schug, S. A, & Watson, D. Safety and efficacy of postoperative epidural analgesia. Br J Anaesth. [Review]. (2001). Jul;, 87(1), 47-61.
- [124] Norman, P. H, & Kowalski, M. D. A. Postoperative analgesia for thoracotomy patients: A current review. In: Franco KL, Putnam JB, editors. Advanced therapy in thoracic surgery. 2nd ed. ed. Hamilton, Ont.; London: B.C. Decker; (2005)., 1-31.
- [125] Eason, M. J, & Wyatt, R. Paravertebral thoracic block-a reappraisal. Anaesthesia. [Case Reports]. (1979). Jul-Aug;, 34(7), 638-42.
- [126] Karmakar, M. K. Thoracic paravertebral block. Anesthesiology. [Review]. (2001). Sep;, 95(3), 771-80.
- [127] Cheema, S. P, Ilsley, D, Richardson, J, & Sabanathan, S. A thermographic study of paravertebral analgesia. Anaesthesia. [Research Support, Non-U.S. Gov't]. (1995). Feb;, 50(2), 118-21.
- [128] Naja, Z, & Lonnqvist, P. A. Somatic paravertebral nerve blockade. Incidence of failed block and complications. Anaesthesia. [Clinical Trial]. (2001). Dec;, 56(12), 1184-8.
- [129] Richardson, J, & Sabanathan, S. Thoracic paravertebral analgesia. Acta Anaesthesiol Scand. [Review]. (1995). Nov;, 39(8), 1005-15.
- [130] Davies, R. G, Myles, P. S, & Graham, J. M. 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. [Comparative Study Meta-AnalysisResearch Support, Non-U.S. Gov't Review]. (2006). Apr;, 96(4), 418-26.

- [131] Detterbeck, F. C. Efficacy of methods of intercostal nerve blockade for pain relief after thoracotomy. Ann Thorac Surg. [Research Support, Non-U.S. Gov't Review]. (2005). Oct;, 80(4), 1550-9.
- [132] Wurnig, P. N, Lackner, H, Teiner, C, Hollaus, P. H, Pospisil, M, Fohsl-grande, B, et al. Is intercostal block for pain management in thoracic surgery more successful than epidural anaesthesia? Eur J Cardiothorac Surg. [Clinical Trial Comparative Study-Randomized Controlled Trial]. (2002). Jun;, 21(6), 1115-9.
- [133] Meierhenrich, R, Hock, D, Kuhn, S, Baltes, E, Muehling, B, Muche, R, et al. Analgesia and pulmonary function after lung surgery: is a single intercostal nerve block plus patient-controlled intravenous morphine as effective as patient-controlled epidural anaesthesia? A randomized non-inferiority clinical trial. Br J Anaesth. [Comparative Study Randomized Controlled Trial]. (2011). Apr;, 106(4), 580-9.
- [134] Dahl, J. B, Moiniche, S, & Kehlet, H. Wound infiltration with local anaesthetics for postoperative pain relief. Acta Anaesthesiol Scand. [Research Support, Non-U.S. Gov't Review]. (1994). Jan;, 38(1), 7-14.
- [135] Kehlet, H, & Dahl, J. B. Anaesthesia, surgery, and challenges in postoperative recovery. Lancet. [Review]. (2003). Dec 6;, 362(9399), 1921-8.
- [136] Wheatley, G. H. rd, Rosenbaum DH, Paul MC, Dine AP, Wait MA, Meyer DM, et al. Improved pain management outcomes with continuous infusion of a local anesthetic after thoracotomy. J Thorac Cardiovasc Surg. [Comparative Study Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.]. (2005). Aug;, 130(2), 464-8.
- [137] Baig, M. K, Zmora, O, Derdemezi, J, Weiss, E. G, Nogueras, J. J, & Wexner, S. D. Use of the ON-Q pain management system is associated with decreased postoperative analgesic requirement: double blind randomized placebo pilot study. J Am Coll Surg. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. (2006). Feb;, 202(2), 297-305.
- [138] Horlocker, T. T, Wedel, D. J, Rowlingson, J. C, Enneking, F. K, Kopp, S. L, Benzon, H. T, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). Reg Anesth Pain Med. [Practice Guideline]. (2010). Jan-Feb;, 35(1), 64-101.