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Special Article

The Year in Thoracic Anesthesia: Selected Highlights From 2021

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THIS SPECIAL ARTICLE is the fifth in an annual series for the *Journal of Cardiothoracic and Vascular Anesthesia*. The authors would like to thank the editor-in-chief, Dr. Kaplan; the associate editor-in-chief, Dr. Augoustides; and the editorial board for the opportunity to expand this series, the research highlights of the year that specifically pertain to the specialty of thoracic anesthesia. The highlights of this year include new developments in the preoperative assessment and prehabilitation of thoracic surgery patients, updates on the use of devices for one-lung ventilation (OLV) in adults and children, updates on the anesthetic management of these patients, including protective ventilation, regional anesthesia, and outcomes when enhanced recovery after thoracic surgery protocols are followed, as well as the use of expanding indications for extracorporeal membrane oxygenation (ECMO) and nonintubated video-assisted thoracic surgery (NIVATS).

Preoperative Evaluation and Prehabilitation

This year, the literature has focused on the use of radiologic imaging, ventilatory efficiency, and physical measures to determine outcomes in patients undergoing thoracic surgery, as well as comparing different prehabilitation strategies on outcomes following lung resections and coronary bypass procedures.

Mayanagi et al[1] examined psoas muscle cross-sectional area using computed tomography (CT) in 187 patients who underwent esophageal resection for cancer. Of the patients, 71% met the criteria for sarcopenia preoperatively. Unlike lung transplant patients, sarcopenia was not associated with postoperative complications except for a higher incidence of

This article reviews thoracic anesthesia highlights of the year 2021, including new developments in the preoperative assessment and prehabilitation of thoracic surgical patients, updates on the use of devices for one-lung ventilation in adults and children, updates on the anesthetic management of these patients, including the use of protective ventilation, regional anesthesia, and outcomes when enhanced recovery after thoracic surgery protocols are followed, as well as the use of expanding indications for extracorporeal membrane oxygenation and non-intubated video-assisted thoracic surgery.

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postoperative dysphagia.[1] In an observational study of 313 esophagectomy patients,[2] an elevated ventilatory efficiency (VE/VCO_2) was the only cardiopulmonary exercise testing (CPET) variable that independently predicted long-term survival. An elevated ventilatory inefficiency also has been shown to predict mortality in other patient populations, including heart failure and patients undergoing lung resection for cancer.[3]

In an observational study of 78 patients undergoing lung cancer surgery, Bille et al[4] preoperatively measured patient physical activity using pedometers for 15 consecutive days. They found that patients in the lowest 2 quartiles of physical activity experienced increased rates of cardiac and respiratory complications without statistically significant differences in length of stay or readmissions. The 6-minute walk test was investigated in 2 studies as a less resource-intensive alternative to CPET. In a cohort of 108 esophagectomy patients, Kondo et al[5] reported that a 6-minute walk distance (6MWD) of >480 meters independently predicted postoperative survival. Marjanski et al.[6] examined a cohort of 125 pneumonectomy patients, finding similarly that a 6MWD >500 m was associated with improved survival.

The next series of articles describe the benefits of respiratory and multimodal prehabilitation on outcomes after cardiothoracic surgery. Bibo et al[7] compiled a 'best evidence' review of respiratory prehabilitation in patients undergoing pulmonary resection. They concluded that preoperative physiotherapy improves exercise capacity and reduces complications and hospital length of stay. This was confirmed in a meta-analysis by Pu et al[8] that identified 10 studies of respiratory prehabilitation for lung cancer resection. The pooled mean difference in length of stay associated with preoperative respiratory training was -3.4 days. Respiratory training reduced pulmonary complications with an odds ratio (OR) of 0.37 (95% CI 0.18-0.7). Amin et al[9] randomized 72 patients undergoing coronary artery bypass surgery to one of 3 different preoperative respiratory physiotherapy regimens 1 day prior to surgery (volume-oriented incentive spirometry, flow-oriented incentive spirometry, or diaphragmatic breathing exercise). Patients in the volume-oriented group had significantly better pulmonary function tests and 6-minute walk distances, as well as superior patient-reported functional recovery.

In the multimodal prehabilitation literature, Tenconi et al[10] reported results from a single center, randomizing 140 lung cancer patients to 14 sessions of preoperative and postoperative multimodal prehabilitation versus standard care.[10] The multimodal prehabilitation regimen consisted of education, pulmonary rehabilitation, and aerobic and strength training. The mean improvement in 6MWD was 48.9 m in the prehabilitation group, whereas patients in the standard care group experienced a worsening 6MWD of -7.5 m. In a cohort of 139 patients undergoing prehabilitation prior to major abdominal and thoracic surgery, Malot et al[11] compared the 6MWD in young and elderly (age >65) patients undergoing multimodal prehabilitation prior to surgery, and found that elderly patients benefitted to a similar extent compared to nonelderly patients, suggesting that prehabilitation can be successfully employed in elderly frail patients.[11] Gravier et al[12] randomized 36 lung cancer surgery patients to a prehabilitation program composed of 15 sessions of aerobic, inspiratory muscle, and resistance exercise training over a time period of either 3 or 5 weeks.[12] They found that the condensed 3-week regimen produced similar or better CPET results without worsening adherence, suggesting that a benefit to prehabilitation can be achieved with shorter time intervals typical for oncologic surgical patients. Ferreira et al[13] reported findings from a randomized single-center trial comparing 4 weeks of multimodal prehabilitation to 8 weeks of postoperative rehabilitation in 95 patients undergoing lung cancer surgery.[13] Their intervention included home-based exercise training, nutrition optimization, and anti-anxiety techniques. They found no differences in functional capacity as measured by 6MWD or patient-reported functional recovery between groups. The authors concluded that "home-based multimodal prehabilitation …. was as effective as the same intervention initiated after surgery." In a small study of 18 patients undergoing lung cancer surgery, Finley et al[14] showed that a surgeon-delivered exercise prescription, combined with an activity tracker, were sufficient to increase patients' physical activity levels in nearly half of patients.[14] They suggested augmenting such a program with more practitioner contact would be necessary to maximize benefits from this low-resource approach.

Devices for One-Lung Ventilation: Adult

Double-lumen endobronchial tubes (DLT) and bronchial blockers (BB) are important tools to establish OLV. Differences in outcomes between these devices continue to be an area of interest. In addition, there is ongoing research regarding the proper use of these devices, including the determination of the optimal DLT size for each patient.

Moreault et al examined bronchial pressures and the absorption of ambient air into the operative lung during OLV.[15] In this trial, patients undergoing VATS were randomized into 4 groups based on the device type and parameter being measured. The airway pressure was measured in 19 patients (n = 9 for BB, n = 10 for DLT), and the air absorption was measured in 20 patients (n = 10 for BB, n = 10 for DLT). Measurements were obtained before and after pleural opening. The ambient air was calculated using a setup involving a bag, syringe, and pneumotachometer. For the patients in whom bronchial pressure was being measured, the pressure was transduced using a catheter that was connected to either the BB or DLT. Measurements in both groups were taken for 60 minutes during OLV. Interestingly, the mean (standard error) amount of absorption of ambient air was similar between the BB and DLT groups, 630 (86) mL *v* 504 (85) mL, for a mean difference of 126 mL (95% CI -128 to 380, p = 0.31), respectively. The majority of this air absorption occurred prior to the incision of the pleura. The bronchial pressure prior to pleural incision was also similar between the BB and DLT groups, -31 (10) cmH_2O *v* -20 (5) cmH_2O, for a mean difference of -11 cmH_2O (95% CI -33 to 12, p = 0.44), respectively. After the pleural incision,

bronchial pressures resembled atmospheric pressure for both groups. Overall, the authors concluded that the period between initiation of OLV and opening of the pleura is characterized by air entry into the non-ventilated lung when the airway device is open to ambient air, and this may be avoided by occluding the device lumen.[15] Another question is the minimal cuff volume required to maintain OLV while minimizing tracheobronchial injuries. Yamada et al performed a randomized trial to compare a capnogram-based technique in 27 patients to pressure-based cuff inflation in 29 patients.[16] In both groups, a 12-French (Fr) suction catheter was inserted into the nonventilated lumen of the DLT in a sealed manner. Using this model, a flat line on the capnogram was believed to represent sampling only from the nonventilating lung and undiluted by air proximal to the cuff. For the capnogram-based group, the bronchial was cuff inflated to a pressure of 20 cmH_2O, and air was removed or added at 0.1-mL increments to find the minimum volume that would provide a flat capnogram. For the cuff inflation group, air was used to inflate the cuff to a pressure of 20 cmH_2O, and the volume was measured. A leak was determined based on the capnogram waveform. These methods were performed before and after chest opening. The primary outcome was the cuff sealing volume, for which the mean (SD) was 1.00 (0.65) mL *v* 1.44 (0.59) mL for the capnogram and pressure-based cuff inflation groups, respectively (mean difference -0.44, 97.5% CI -0.78 to -0.11; p = 0.010). Interestingly, after chest opening, the volumes dropped to 0.65 (0.66) *v* 1.22 (0.45) mL, respectively (mean difference -0.58, 97.5% CI -0.88 to -0.27, $p < 0.001$). This suggested that the bronchial cuff may need less volume than anticipated than 20 cmH_2O, and it also indicates that volume may be removed after chest opening.[16]

A controversy that seems to recur is whether video laryngoscopy (VL) is superior to direct laryngoscopy (DL) with a Macintosh blade when placing a DLT. Karczewska et al performed a systematic review and meta-analysis of 25 randomized controlled trials.[17] Notably, there were several types of VL systems that were used across these studies. Data regarding successful first-time intubation were available from 23 studies. There was no significant difference between the success rates for the VL and DL groups, 87.9% *v* 84.5%, respectively (OR 1.64, 95% CI 0.95-2.86, p = 0.08, $I^2 = 61\%$). When the authors examined a subset of the VL group that specifically used a videoscope or tube, there was an advantage favoring VL (91.5%) over DL (84.9%) (OR 1.86, 95% CI 1.16-2.99, p = 0.01, $I^2 = 0\%$). Interestingly, the speed of intubation was faster in the VL versus DL group, 43.4 ± 30.4 seconds *v* 54.0 ± 56.3 seconds (mean difference -11.87, 95% CI -17.06 to -6.68, $p < 0.001$, $I^2 = 99\%$).[17] Notably, the high degree of heterogeneity confers uncertainty in this finding. Adverse events in both groups were similar.

Another controversy is selecting a DLT size. A larger tube may risk airway trauma, while a smaller tube is also thought to risk airway injury due to cuff overinflation, as well as increasing the resistance to airflow. Often, a DLT size is selected using the sex and height of the patient, but this strategy may result in inaccuracies.[18] In a 2-part trial, Zhang et al investigated the role of CT and ultrasound (US) in left DLT size selection.[18] In part 1, 120 patients had DLT size determined based on sex and height. The transverse diameter of the cricoid cartilage was measured using US and CT using multiplanar reconstruction. Judgment about whether the DLT was appropriately sized was based on parameters such as ease of insertion and quality of lung isolation. Difficulty inserting the DLT guided by bronchoscopy or cuff inflation with small volumes of air suggested an oversized tube. The DLT was considered undersized primarily based on whether excessive cuff inflation was needed to achieve lung isolation. For part 1, the DLT size was determined to be undersized in 28 out of 120 (23.3%) patients, appropriate in 70 out of 120 (58.3%) patients, and oversized in 22 out of 120 (18.3%) patients. The appropriately-sized group had better outcomes in terms of intubation times, number of intubation attempts, quality of lung isolation, and incidence of dysphagia. The authors used the cricoid measurement data from the appropriately-sized group to determine the proper sizing for 32-Fr (US: <15.88 mm, CT: <15.74 mm), 35 Fr (US: 15.88-16.80 mm, CT: 15.74-16.65 mm), 37 Fr (US: 16.75-17.81 mm, CT: 16.56-17.68 mm), and 39-Fr (US: 17.80-18.88 mm, CT: 17.65-18.52 mm) DLTs.[18] Notably, the ranges sometimes have a small overlap. In part 2 of the study, patients were randomized to have the left DLT size selected based on US (n = 51) or CT (n = 51) measurements using the range determined in part 1. The sizing was judged to be appropriate in 46 out of 51 patients in the US group, and in 48 out of 51 patients in the CT group, resulting in 90.2% and 94.1% accuracy, respectively (p = 0.097). Overall, more patients received appropriately-sized DLTs when either US or CT was used compared to conventional sizing based on sex and height (92.2% *v* 58.3%).

Instead of sizing the DLT, Nguyen et al sought to determine the effect of using a 35-Fr DLT for all patients, regardless of sex, height, or airway measurements.[19] In this investigation, patients were randomized to be intubated with a 35-Fr DLT (n = 25) or a DLT based on height (n = 25). In the group for whom sizing was based on height, 7 patients were intubated with a 35-Fr DLT, whereas the other 18 patients received larger DLTs. Eight patients were partially excluded from analysis for various reasons, such as intubation with VL (6 patients) or because of reintubation with a single-lumen tube (2 patients). One patient in the 35-Fr group required use of a 32-Fr DLT. Overall, there were no significant differences in the number of intubation attempts, the incidence of repositioning, the grade of view obtained by laryngoscopy, or the incidence of dysphagia. Oxygenation, when measured before induction and at 5 and 10 minutes after OLV, was also similar between the 2 groups. Limitations of this trial included the small sample size and exclusion of data in 8 patients.

While the use of a DLT versus BB is commonly debated regarding intraoperative management, Yu et al sought to determine the effect on postoperative outcomes.[20] Records from 2000 to 2012 were retrospectively reviewed, and patients in whom a BB was used were matched with 3 random DLT patients based on age range, sex, and year of surgery. This

resulted in a sample of 1,898 BB patients and 5,694 DLT patients. They reported that the primary outcome of respiratory infection, respiratory failure, occurred more frequently in the BB than DLT group for both 1-year readmissions for respiratory infection (12.4% *v* 9.0%, adjusted OR 1.46, 95% CI 1.22-1.74, p < 0.0001) and respiratory failure (5.7% *v* 4.3%, adjusted OR 1.38, 95% CI 1.09-1.76, p = 0.0088). Secondary outcomes included in-hospital mortality, which was also higher in the BB group (3.0% *v* 1.6%, adjusted OR 2.03, 95% CI 1.40-2.94, p = 0.0002). Limitations of this trial included its retrospective nature.[2] It is also interesting to note that prior to matching, the entire sample had 92,697 patients after exclusions, and 90,703 of these received a DLT. The authors mentioned that Taiwan had a "restricted claim rule" for a BB, which may explain its limited use, although the details of this rule are not provided.[2] Given the clear preference for a DLT, it would be helpful to know the circumstances explaining why a BB was chosen for these specific cases. For example, since a BB may be advantageous in cases in which the patient is already intubated, one should consider whether any of these patients in the BB group were already intubated and whether their pulmonary disease could have been more severe prior to surgery.

Devices for One-Lung Ventilation OLV: Pediatric

A big area of interest this year is pediatric OLV. OLV in children can be a demanding anesthetic. Children present unique physiologic considerations for OLV. Ventilation-perfusion (V-Q) mismatch occurs easily because a less rigid cartilaginous rib cage leads to greater compression of the dependent lung, which reduces lung compliance.[21] Additional physiologic characteristics that can lead to hypoxemia and affect OLV include weak respiratory support, alveolar hypoplasia, and increased metabolic demand.[22] Furthermore, functional residual capacity in infants is closer to residual volume, making airway closure more likely in the dependent lung even during tidal ventilation.[21] A retrospective cohort study by Templeton et al reported that the prevalence of hypoxemia (oxygen saturation [SpO_2] <90% for 3 minutes) and severe hypoxemia (SpO_2 <90% for >5 minutes) during pediatric OLV were 26% and 18%, respectively, and that the use of a BB was associated with a lower risk of hypoxemia.[23] Zhang et al also studied the effects of gas exchange in infants with OLV via BB. Significantly worse P_aO_2:F_IO_2 ratio, pulmonary dynamic compliance, and $P_{A\text{-}a}O_2$ gradient during OLV were observed when compared to two-lung ventilation (TLV).[22] This is because of anatomic differences; specifically, the left side mainstem bronchus is smaller than the right side, often requiring an endotracheal tube (ETT) 1 half-size smaller.[21] This size difference makes lung isolation difficult in children in the 0-to-3-month range, in whom a 3.0 cuffed ETT might be too large for the left mainstem bronchus.[24] Furthermore, the distance from the carina to takeoff of the left upper lobe can be 3x the distance of the carina to the right upper lobe, allowing for some margin of error in placing a BB on the left. In children younger than 8, the takeoff of the right upper lobe is fewer than 1 cm from the carina, making lung isolation challenging with a right BB.[21]

In children younger than 2, endobronchial intubation with an ETT 1 half-size smaller than normal is the easiest method for OLV. Physical disadvantages to endobronchial intubation include inadequate seal, inadequate collapse of the operative lung, and the inability to suction or to provide continuous positive-pressure ventilation (CPAP) to the operative lung.[21] The use of an extraluminal BB is a viable alternative for OLV in these patients. Extraluminal techniques involve placing the BB first, then intubating the trachea.[24] Guiding an extraluminal BB into the left mainstem bronchus can be problematic. Kapoor et al described a case study with 2 patients in whom manual rightward subcricoid tracheal pressure on the left side of the trachea improved tracheal bronchial alignment, allowing the passage of an extraluminal BB into the left mainstem bronchus.[22] Yonezawa et al described a case report of 2 patients in whom the ETT slip tip end was removed, the Fogarty catheter placed, and the slip tip end was replaced.[24] This process allowed quicker placement and allowed the BB to be secured. The use of specialized blockers may also aid in placement. The Arndt (Cook Medical, Bloomington, IN) blocker and Fuji blocker (Ambu, Columbia, MD) are available in pediatric sizes.

When determining the appropriate size for a BB in a child, note that for intraluminal placement, a 4.5-mm internal diameter ETT is the smallest tube that will accommodate both a 2.2-mm flexible fiberoptic bronchoscope and 5-Fr blocker, limiting the use of an intraluminal blocker to children >3-to-4 years old.[21] Balloon inflation should occur under direct visualization to avoid mucosal and bronchial trauma that can lead to major complications.[25] Care should be taken when using the Fogarty and pediatric Arndt blockers because these are low-volume, high-pressure cuffs. Researchers noted that while the Arndt has a linear relationship between cuff size and inflation pressure, the Fogarty demonstrates a late acute rise in diameter, which prevents step-wise inflation in the blocker balloon. The inflation pressure that was recorded, 160-to-250 cmH_2O for Arndt and >1,000 cmH_2O for the Fogarty, is concerning.[25] The smallest DLT is 26-Fr and should not be used in children younger than 8.[26] In female adolescents, the cutoff point is 160 cm. The recommendation for those <160 cm is a 35-Fr DLT, and a 37-Fr is recommended for those >160 cm. For adolescent male patients <170 cm, a 39-Fr is recommended, and for male patients >170 cm, a 41-Fr is recommended.[21]

With regard to intraoperative conditions, Huang et al compared artificial pneumothorax via CO_2 insufflation to bronchial occlusion in 72 infants aged 2-to-8 months. They reported that bronchial occlusion provided superior surgical exposure, resulting in shorter surgical duration, lower central venous pressures, higher mean arterial pressures, lower $PaCO_2$, and higher partial pressure of oxygen (PaO_2) levels.[27] This was confirmed by an additional study comparing BBs versus artificial pneumothorax that was conducted in 33 infants aged 2-to-12 months.[28] They measured the degree of lung collapse on a scale of 0 (no lung deflation) to 10 (complete lung deflation). The degree of lung inflation was significantly less in the

extraluminal BB group (9/10 for extraluminal *v* 8/10 for CO_2 pneumothorax). The mean arterial pressure was lower in the pneumothorax group at 10 minutes (43 mmHg) and 30 minutes (42 mmHg) after initiation of OLV compared to the BB group (57 mmHg and 53 mmHg, respectively). Intraoperative $PaCO_2$ was higher in the pneumothorax group, but both groups normalized once returning to TLV.[28]

Patients undergoing middle and lower lobar lung surgeries can be candidates for selective lobar BB.[29] After placement of a BB and intubation in children approximately 5 months old, they used fiberoptic bronchoscopy to guide the blocker into the left lower or right middle and/or lower lobe. When compared to the use of a standard mainstem BB, selective BB did not result in a difference in the degree of lung collapse or hemodynamics, but did improve the oxygenation index at 10 minutes after starting and 10 minutes after ending OLV.[29] In patients in whom a selective blockade is feasible, it may improve oxygenation during surgery when OLV is required.

One-Lung Ventilation (OLV) Anesthetic Management

The currently selected literature in the anesthetic management of OLV includes a range of updates, including those in regard to pulmonary drug delivery, anesthetic choice and lung injury, cerebral oxygenation, and monitoring modalities.

This year, there was renewed interest in the use of inhaled medications. Pengyi et al published a randomized controlled trial (RCT) comparing the effect of inhaled prostaglandin E1 (PGE_1) administration on oxygenation during OLV with a lower fraction of inspired oxygen (F_IO_2) in 90 patients undergoing thoracotomy for esophagectomy.[30] They were divided into the following 3 groups: group A received 60% $F_IO_2$with 0.1 ug/kg PGE_1, group B received 40% F_IO_2 and 0.1 ug/kg PGE_1, and group C received 40% $F_IO_2$and 0.2 ug/kg PGE_1, with the primary outcomes of oxygenation and pulmonary shunt during OLV and a secondary outcome of oxidative stress. They reported that the addition of PGE_1 provided adequate oxygenation with 40% F_IO_2 and that the higher dose of PGE_1 reduced the incidence of oxidative stress, suggesting a role for PGE_1 in reducing the complications of hyperoxia during OLV.

Selective lobe ventilation as a novel pulmonary drug delivery platform was highlighted by Maracaja et al.[31] Citing lobar mechanical heterogeneity in acute respiratory distress syndrome (ARDS) and V-Q regional changes, including in coronavirus disease 2019, they developed a device that allows selective lobar ventilation. Two selective lobar novel customizable modes include differential positive end-expiratory pressure (PEEP) and asynchronous ventilation. The “shuttle” ETT includes a tracheal lumen, as well as 2 individual cuffed distal components for advancement into selected lobes and is currently in the development phase.

Another focus of the literature this year was the effect of anesthetic choice on pulmonary complications. A meta-analysis of 8 RCTs reviewed the effects of sevoflurane versus propofol on the inflammatory response in lung resection.[32] Noting the sometimes-fatal cytokine release in lung resection, they compared systemic inflammatory cytokines as the primary outcome. The secondary outcome was the level of inflammatory cytokines in bronchoalveolar lavage of both the dependent and nondependent lungs. The authors reported that there was no difference in the systemic response but a minor reduction of interleukin-6 (IL-6) in the bronchoalveolar lavage in the sevoflurane group. Li et al, in an RCT, compared propofol, sevoflurane, and desflurane effects on postoperative pulmonary complications (PPCs) after lung resection in 555 patients.[33] No difference was found. Citing no consensus for volatile anesthetics versus total intravenous anesthesia, Lee et al also tackled this same question in pulmonary resection in a retrospective study of 579 patients in Korea.[34] Again, no difference was seen in postoperative pulmonary complications, although the total intravenous anesthesia patients had shorter intensive care unit (ICU) and hospital lengths of stay, reduced air leak, and a shorter time to thoracotomy tube removal.

The role of dexmedetomidine (DEX) in thoracic surgery was examined in 2 studies. A double-blind RCT by Ran et al compared intraoperative DEX infusion to saline in 102 patients.[35] The DEX group received a loading dose of 0.5 ug/kg upon entering the operating room, followed an infusion of 0.5 ug/kg that was discontinued at the end of OLV. Both the saline and DEX groups received hydromorphone patient-controlled analgesia (PCA), with the DEX group receiving an additional 200 ug of DEX. The endpoint was the incidence of cognitive decline compared with the saline group. They reported that there was no difference in cognitive dysfunction in either group, and that approximately one-third of the patients experienced cognitive decline. The DEX group experienced less postoperative pain and reduced hospital expenses, including a shorter period of hospitalization. A meta-analysis from Bai et al examined 20 clinical trials, with 870 patients undergoing OLV with DEX, and concluded that DEX significantly attenuates OLV-associated lung injury via decreased inflammatory responses.[36] Intraoperative DEX resulted in decreased IL-6, tumor necrosis factor-alpha, and other inflammatory cytokines and ameliorated oxygenation issues, though various component studies displayed heterogeneity in their results. Another study compared DEX to opioids in an RCT, comparing opioid and nonopioid techniques in 100 patients undergoing VATS.[37] Both groups received thoracic paravertebral nerve blocks with either DEX or remifentanil, with attention paid to the postoperative pain index. Unsurprisingly, given the comparative half-lives of the 2 arms, pain scores were similar, but blood glucose values were significantly higher in the opioid-free anesthetic group. Sato et al, in an RCT, examined the effect of desflurane-remifentanil compared to propofol-remifentanil on regional cerebral oxygenation changes in 50 patients, and reported that the effects of desflurane and propofol were equivalent.[38] A prospective cohort study by Cui et al sought an association between cerebral desaturation and postoperative delirium in patients undergoing thoracotomy with OLV, by measuring cerebral oxygen saturation with near-infrared spectroscopy.[39] Delirium was assessed through postoperative day 5, in relation to minimum cerebral saturation during the case, with secondary analysis

examining the area under the curve of hypoxemic events. They reported that delirium occurred in 20% of 175 patients, and that cerebral desaturation <90% of the baseline for the left and <85% for the right, but not the nadir value itself, may be associated with increased risk for delirium. The accuracy of noninvasive continuous arterial pressure monitoring in OLV, using a proprietary finger cuff algorithm currently in clinical practice, was evaluated in a South Korean study.[40] Arterial cannulation was compared to ipsilateral ClearSight (Edwards Lifesciences) readings in 26 patients, essentially showing acceptable agreement with invasive monitoring.

Protective One-Lung Ventilation (OLV)

In thoracic patients, PPCs can have high morbidity. Protective ventilation has been demonstrated to decrease the rate of those complications. Nevertheless, there is no precise definition of protective ventilation. Neto et al attempted to develop a scale using patient characteristics and intraoperative factors called the "Local Assessment of Ventilatory Management During General Anesthesia for Surgery" scale that would predict the incidence of PPCs.[41] This was a prospective, international, 1-week observational study to identify the incidence of patients at increased risk of PPCs. Nijbroek et al performed a post hoc analysis of this study to further investigate whether there is a sex difference in the use of low-tidal-volume ventilation.[42] Results showed that women were twice as likely not to receive low-tidal-volume ventilation (relative risk ratio 2.1 [95% CI 1.9-2.1], $p < 0.001$) because of the use of actual body weight instead of predicted body weight to determine tidal volumes. This discrepancy was more pronounced in women who were at the lowest quintile of height since height is necessary for the calculation of predicted body weight.

Colquhoun et al[43] performed a multicenter observational cohort study, including a total of 3,232 thoracic surgical patients who underwent OLV for various surgical procedures, to determine the effect of OLV on the incidence of PPCs. Their results demonstrated that protective ventilation during OLV was not found to be associated with a reduction in the risk of pulmonary complications (adjusted OR, 0.86; 95% CI 0.56 to 1.32; $p = 0.480$), major morbidity (adjusted OR, 0.81; 95% CI 0.55-1.19, $p = 0.283$), or mortality (adjusted OR, 0.81; 95% CI 0.55-1.19, $p = 0.281$). More specifically, tidal volumes ≤5 mL/kg or lower, PEEP >5 cmH_2O, or modified driving pressure or P_{MAX} did not reduce the incidence of 30-day PPCs.

Previous studies suggested that because of differences in individual characteristics, a fixed PEEP is not appropriate for every patient. Li et al performed a systematic review and meta-analysis of 8 studies comparing the rate of PPCs between an individual versus a fixed PEEP group during OLV.[44] The individualized PEEP group had a lower number of PPCs, with a risk ratio of 0.52 (95% CI 0.37-0.73; $p = 0.0001$). In addition, the measured partial pressure of oxygen (PaO_2) and oxygenation index during OLV were higher in the individualized group (mean difference of PaO_2 was 34.20 mmHg, with 95% CI 8.92-59.48; $p = 0.0004$; the mean difference of the oxygenation index was 49.07 mmHg, with 95% CI 27.21-70.92; $p < 0.0001$), suggesting that an individualized approach to PEEP is beneficial. In another study comparing PEEP, Zhang et al performed a prospective RCT with 58 patients who underwent elective thoracoscopic lobectomy.[45] In this study, there were 2 groups, one with individualized PEEP and one with a set PEEP at 5 cmH_2O. In the individualized group, the optimal PEEP was found to be 8.8 ± 2.4 cmH_2O by titrating PEEP according to pulmonary compliance. They also reported a correlation between optimal PEEP and body mass index ($r = 0.756$, $p < 0.01$), and forced vital capacity ($r = 0.406$, $p < 0.05$). There were no significant differences between the 2 groups in hemodynamics, respiratory mechanics, the partial pressure of carbon dioxide ($PaCO_2$), pH, and postoperative complications. Nevertheless, the oxygenation in the individualized PEEP group was significantly higher at the end of OLV. In combination with increased lung compliance and decreased driving pressure, individualized PEEP is recommended by the authors.

Summarizing the pros and cons of PEEP in thoracic anesthesia, Battaglini et al[46] published an expert's opinion article. PEEP minimizes atelectrauma, promotes more homogeneous ventilation, and by keeping the alveoli open, it improves the V-Q ratio and arterial oxygenation. On the other hand, PEEP can cause barotrauma, volutrauma, and compression of small interalveolar vessels that can lead to a worsening of the V-Q ratio. In addition, PEEP can decrease preload, leading to hemodynamic impairment and increasing the amounts of fluids and vasoactive medications required. In conclusion, the authors suggested that PEEP for every patient should be individualized according to their best lung compliance using their ideal driving pressure.[46]

Sawasdiwipachai et al assessed the efficacy of high-flow humidified oxygen (HFHO) as an alternative to CPAP in the nonventilated lung during OLV with paralysis.[47] A prospective randomized crossover trial with 28 patients undergoing elective thoracotomy was performed. Both CPAP and HFHO improved oxygenation (PaO2), with no difference between the 2 modalities (95% CI 12.84-21.87, $p = 0.597$). Nevertheless, even though HFHO was superior in surgical conditions (lung deflation) ($p < 0.001$), it is less cost-effective but generates more noise.

Previous reports in animal studies showed that hypoxic stimuli could reduce intrapulmonary shunt and hypoxemia due to hypoxic pulmonary vasoconstriction. Yoon et al completed a prospective, single-center, parallel-group, double-blind RCT with 136 patients to test whether repeated intermittent hypoxic stimuli to the operative lung can reduce hypoxemia during OLV.[48] In the intermittent hypoxia group, before OLV, the nondependent lung was not ventilated for 2 minutes and then ventilated for 2 minutes before the initiation of OLV. This was repeated 5 times. Compared to the continuous normoxia group, hypoxemia was less frequent, and oxygenation was improved in the intermittent hypoxia group during OLV (risk ratio [95% CI] 0.35 [0.15-0.84], $p = 0.012$).

In an attempt to reduce complications during OLV, Jain et al used lung US-guided titration of inspiratory pressure in a

pressure-controlled ventilation (PCV) mode during OLV.[49] They performed a prospective, randomized, parallel-group, double-blinded trial with 40 patients; group A received a volume-targeted PCV tidal volume of 9 mL/kg for TLV and 5 mL/kg for OLV, while group B received US-guided PCV (inspiratory pressure with 2 cmH_2O increments every 15 seconds, according to US-guided alveolar aeration at the base of the dependent lung). Compared to group A, the PaO_2 was significantly higher in group B, while acid–base status remained preserved. The airway pressures and tidal volume were marginally higher in group B than group A during OLV, without any clinical sequelae.

Fluid management during lung surgery is also of great importance. Dynamic preload parameters such as pulse-pressure variation (PPV) and stroke-volume variation (SVV) as predictors of fluid responsiveness are widely used on mechanically ventilated patients. These parameters are not as effective during OLV because of the decrease of intrathoracic pressure cyclic variation. Jun et al performed a prospective observational study using a PEEP challenge maneuver from 0-to-10 cmH_2O of PEEP with 40 patients, and demonstrated that the ΔPPV and ΔSVV were accurate predictors of fluid responsiveness.[50] On the other hand, Choi et al[51] performed a similar prospective study with 40 patients, investigating the predictive ability of PPV and SVV for fluid-responsiveness during OLV with CO_2 gas inflation (8 mmHg), while maintaining a closed chest. The area under the receiver operating characteristic curve was used for estimation of this predictive ability. The area under the receiver operating characteristic curve of PPV was 0.65 (95% CI 0.47-0.83, p = 0.113) and of SVV 0.64 (95% CI 0.45-0.82, p = 0.147). Those results showed that SVV and PPV could not predict fluid responsiveness regardless of the direction of the lateral decubitus position.[51] Similarly, Kimura et al assessed the reliability of recruitment maneuver-induced hemodynamic changes in predicting fluid responsiveness in 30 patients undergoing OLV under closed-chest conditions.[52] Hemodynamic variables were recorded during OLV before and after recruitment maneuvers. After applying recruitment maneuvers, volume expansion was performed. The study found that recruitment maneuver-induced decreases in stroke volume and blood pressure can predict fluid responsiveness, but both SVV and PPV showed poor ability to predict fluid-responsiveness during OLV. These studies suggested that more research is needed to determine how to measure fluid-responsiveness during OLV.

When isolating the operative lung, the common practice is to leave the bronchoscopy port of that side open to ambient air. In order to test deflation times and quality, Somma et al performed a prospective single-blinded RCT on 30 patients requiring OLV during VATS.[53] The control group had the operative lung lumen of the DLT left open to air, while the intervention group had the operative lumen clamped until after pleural opening. The median time to lung deflation was faster in the intervention group (95% CI, $p < 0.001$). Slower deflation for the control group was attributed to ambient air entrainment, resulting in renitrogenation, leading to increased residual gas in the lung at the time of pleural opening.

NIVATS is widely performed for different types of thoracic procedures. Benefits include lower risk of intrapulmonary shunt and shorter surgical time and hospital stay. However, the risk factors for hypoxia during NIVATS are not clear. Lan et al performed a large single-center retrospective cohort study with 2,742 patients to determine those risks.[54] Age (older age, p = 0.011), higher body mass index and revised cardiac risk index level (p = 0.033 and p = 0.031), anesthesia method (epidural anesthesia, p = 0.005), the technical level of surgeons (fewer than 10 years of VATS training, p = 0.009), stair-climbing ability (lower composition of stair-climbing 322 m, $p < 0.001$), and type of thoracic procedure (more anatomic lung surgery and mediastinal mass resection, p = 0.033) were associated with intraoperative hypoxia ($p < 0.05$). Patients with hypoxia were associated with intraoperative hypercapnia and longer stay in the ICU, but overall did not affect complications and postoperative hospital stay.

Newer technologies are constantly incorporated in the operating room. Oxygen reserve index (ORI) is an oxygenation monitoring parameter that provides additional information for oxygenation status through a novel noninvasive pulse oximeter device. Other parameters that this device can measure are the SpO_2, perfusion index (PI), and perfusion pleth variability. A prospective observational cohort study of 120 patients showed that ORI is sensitive and specific in predicting hypoxemia (SpO_2 <95%), with an $FIO_2 > 50\%$, from 5 minutes after intubation in the supine position up to 30 minutes after the start of OLV.[55] In addition, ORI can predict hypoxemia 5-to-6 minutes earlier than pulse oximetry value. Another prospective, randomized, cross-sectional study of 50 patients showed that with the guidance of ORI, hyperoxemia could be prevented during OLV, and that the use of an F_IO_2 higher than 80% was correlated with a higher duration of hospital stay.[56]

Extracorporeal Membrane Oxygenation (ECMO)

Advances in thoracic surgery and anesthesia are allowing patients with more advanced disease and limited physiologic reserve to obtain immediate life-saving and life-sustaining surgery. In the 21st century, perhaps the greatest technologic advancement that has increased surgical candidacy for patients with thoracic disease is ECMO. Venoarterial (VA) ECMO has been used extensively and is now arguably the standard of care for lung transplant recipients who require mechanical circulatory support[57]; however, the application of ECMO to support thoracic surgery is now commonplace for surgical procedures involving the upper and lower airways, large mediastinal tumors, complicated lung resections, and in trauma patients with airway disruption or massive thoracic bleeding.[58] The thoracic anesthesiologist is also encountering, with increasing frequency, critically ill patients on venovenous (VV) ECMO support who require intrathoracic and airway procedures or who require support for postoperative ARDS. In this year's thoracic year in review, the developments in the use of ECMO to support the care of thoracic surgical patients are highlighted.

There were no fewer than 29 articles published in 2021 on the use of ECMO in thoracic surgery. While most of these were case reports, there were several retrospective single-center case series. Huang et al evaluated the outcomes of 22 patients from 2012 to 2020 who received perioperative ECMO during thoracic surgery.[59] Of the 5 patients who received ECMO support for complex thoracic surgery (3 VV, 1 VA), all survived to hospital discharge with no major complications reported. All but 1 patient was decannulated in the operating room. Three patients received ECMO support for severe chest trauma. Two of 3 patients survived, with the third dying of a severe infection. The remainder of the cohort received ECMO support for postoperative ARDS or for lung transplantation. Zhang et al discussed 15 cases of ECMO-assisted thoracic surgery, including 3 airway traumas, 2 airway tumors, and 5 thoracic masses requiring vena cava resection.[60] All but 2 patients were weaned from ECMO in the operating room, and all patients survived to hospital discharge. Kim et al completed a multivariate analysis of risk factors for mortality after ECMO-supported thoracic surgery in 63 patients over a 7-year time frame.[61] The overall 30-day survival for this cohort was 73%, and independent risk factors for mortality were advanced age and intraoperative cardiac arrest. In the 30-day mortality group, the indication for ECMO was almost exclusively for ECMO-facilitated cardiopulmonary resuscitation following a cardiac arrest during surgery. Only 2 of 11 patients given intraoperative ECMO-facilitated cardiopulmonary resuscitation survived, and, in both cases, ECMO was started quickly because of favorable patient positioning and for an arrest that occurred before surgical incision. These 3 case series are the latest data that demonstrate a high level of safety and acceptable mortality for patients supported with ECMO for high-risk thoracic surgery. All 3 cohorts included patients requiring ECMO support for high-grade airway tumors, preoperative pulmonary insufficiency with the need for thoracic surgery, and for cardiopulmonary support because of mediastinal compression, massive bleeding, or trauma demonstrating the wide applicability of intraoperative ECMO.

ECMO provides temporary airway and hemodynamic support in patients with mediastinal masses that cause high-grade tracheobronchial or great vessel compression. Ramanathan et al presented their data and local protocols on VA ECMO for patients presenting with mediastinal masses.[62] Of the 74 patients presenting with mediastinal masses over a 5-year time period requiring a Chamberlain procedure for tissue diagnosis, 26 were deemed high risk. All high-risk patients received femoral vessel access with the ECMO team on standby in the operating room. Five patients required emergent cannulation and VA ECMO support for hemodynamic instability during anesthesia. Although all patients were stable throughout the procedure, 2 patients died in the hospital from postoperative infection and septic shock while on ECMO.

In major airway surgery, the benefits of ECMO arguably outweigh the risks of conventional ventilation with endotracheal intubation or jet ventilation. During airway surgery, ECMO avoids the need for instrumenting the airway in patients with life-threatening tracheal and carinal stenosis, prevents hypercapnia during interrupted ventilation or during high-frequency jet ventilation, provides a clear and unobstructed surgical field, and arguably improves the dissection and reconstruction of the airways. Extracorporeal life support (ECLS) has been used to support patients during major airway surgery for more than 30 years. A systematic review of 78 cases over 31 years comparing the use of cardiopulmonary bypass, VV ECMO, or VA ECMO to support ventilation during major airway surgery was conducted by O'Malley et al.[63] The clinical presentations included cancer of the central airways in 57% of patients, followed by central airway stenosis or central airway injury. In a majority of cases, ECLS was used to reduce the risk of airway obstruction, and cannulation was initiated at the time of induction. Cannulation was most often in a peripheral configuration, and only rarely was it required postoperatively. Of interest, 30-day mortality in nonemergent cases was 0%, and only 5.3% in emergency cases, demonstrating the safety and feasibility of ECLS in major airway surgery. In fact, several recent case series have shown no major complications for airway procedures performed with ECMO assistance.[64-68]

The data published in the past year continue to support the use of ECMO in patients undergoing thoracic surgery. Heparin-bonded circuits, lower heparin dosing, and increasing technical expertise are a few explanations for the widespread adoption of ECMO. When used in a controlled elective fashion, the data suggest the rates of complications and in-hospital mortality are low, and likely have increased the candidacy for surgery for critically ill patients and in patients who would otherwise be unable to tolerate the cardiorespiratory trespass associated with the surgical procedure. While ECMO appears to be widely adopted for patients undergoing airway surgery and with mediastinal masses, the outcomes are less favorable in trauma when massive bleeding is anticipated or when used in ECMO. These findings should be taken with a degree of caution as they are likely affected by selection bias, and no controlled trials have been conducted in this population. The larger case series come from large-volume centers where the use of ECMO during thoracic surgery is well-established, and it remains to be seen whether similar outcomes can be seen in smaller centers with more limited experience. In summary, data from the past year demonstrated that ECMO is safe and feasible as a means of supporting cardiorespiratory function during thoracic surgery.

Regional Anesthesia for Thoracic Surgery

2021 has been a very prolific year in terms of publications on regional anesthesia for thoracic surgery, studying both neuraxial and fascial plane techniques and outcomes using these techniques.

Neuraxial Techniques

Okuda et al evaluated the effect of epidural anesthesia on the inflammatory response in patients undergoing lung cancer surgery, and randomized 60 patients to receive either thoracic

epidural analgesia (TEA) or a remifentanil infusion for intraoperative analgesia.[69] They measured concentrations of tumor necrosis factor-alpha, interleukin (IL)-6, and IL-10 in the lung epithelial lining fluid and blood prior to OLV, at OLV initiation (T1), and 30 minutes after the end of OLV (T2). They reported that although the levels of all inflammatory markers were increased at T2, the TEA group had a lower level of IL-6 than the remifentanil group, suggesting that TEA could attenuate the local inflammatory response during lung cancer surgery. No postsurgical patient outcomes were reported. In a prospective, randomized study by Xu et al, the addition of epidural analgesia to general anesthesia (compared to general anesthesia alone) was not associated with recurrence-free, overall, or cancer-specific survival (even though recurrence-free survival was higher in the epidural group), but was associated with better short-term outcomes such as improved analgesia, less opioid consumption, fewer ICU admissions, and even shorter hospital stays.[70] This study, however, was powered for the reduction of cancer recurrence by about one-third, but the CI for recurrence-free survival ranged from a 40% reduction in the hazard to a 35% increase. Therefore, it is still possible that regional anesthesia and analgesia decrease cancer recurrence by amounts that might still be considered clinically significant.

The thought that robot-assisted thoracic surgery and its minimally invasive nature might result in less need for aggressive perioperative pain control was tested by Kawagoe et al., who performed a retrospective review of 107 patients who underwent robot-assisted thoracic surgery at a single institution, and received either TEA or intercostal nerve blocks + PCA for perioperative pain control.[71] TEA proved superior in terms of pain scores and rescue analgesic requirements, with a similar side effect profile compared to PCA. Soltan et al[72] published a case series of 100 patients undergoing laparoscopic sleeve gastrectomy under combined thoracic spinal-epidural anesthetic in whom this technique was successfully used in 99% of the patients, with only 1 case of conversion to general anesthesia because of severe pain and anxiety. While this was only a single-center case series, the review authors here anticipate seeing more and more reports of this "unorthodox" technique, as it has been defined by some authors.[72]

The thoracic paravertebral space is a highly vascular space, and, therefore, the risk of local anesthetic toxicity can occur with thoracic paravertebral blocks (PVBs). An RCT by Yamazaki at al investigated the effect of the addition of 5 μg/mL of epinephrine to a single-shot PVB with 1 mg/kg of 0.25% levobupivacaine, and found that it significantly decreased both peak plasma concentration and the time to achieve this level, in agreement with the literature available for other types of regional anesthetic techniques. Therefore, the authors concluded that this intervention is a useful strategy to reduce the occurrence of local anesthetic toxicity.[73] A recent meta-analysis performed by Xiong et al compared the efficacy of PVB versus erector spinal plane (ESP) block, with the primary outcome being postoperative pain scores and secondary outcomes being opioid consumption, additional analgesic requirement, and postoperative nausea and vomiting (PONV) 24 hours postsurgery, and found that for thoracic surgery, PVB was superior to ESP block in terms of pain and opioid consumption, while they found no differences in PONV at 24 hours.[74]

Fascial Plane Blocks

2021 saw the updated procedure-specific postoperative pain management guidelines for VATS by the European group, consisting of anesthesiologists and surgeons that for almost 2 decades has been producing "*evidence-based practical pain management recommendations for specific procedures.*" The consensus group reviewed publications and developed guidelines based on 1,070 studies, with 69 being RCTs.[75] Their recommendations included the use of the PVB as the first-line block for thoracic surgery (preferred over TEA because of a reduction in hypotension), with ESP blocks being the next choice if PVBs are contraindicated and the serratus anterior plane (SAP) block being used as a second choice to the ESP block. The use of ESP over SAP was decided using 3 studies, with 2 of the studies favoring the ESP block. The other guidelines recommended the use of acetaminophen and nonsteroidal anti-inflammatory drugs for analgesia, dexmedetomidine intraoperatively when opioids could not be administered, and the use of opioids when other analgesic modes fail. They did not recommend the use of intravenous lidocaine infusions, gabapentinoids, corticosteroids, magnesium, wound infiltration, intrapleural analgesia, and intercostal nerve block because of the paucity of literature on these therapies.

The fascial blocks that have been studied this year include the ESP, SAP, pectoral nerve block (PEC), rhomboid intercostal block, and intercostal blocks. Huang et al performed a recent trial sequential analysis (TSA) on ESP blocks by presenting a recent TSA of a meta-analysis published in 2020, which found comparable analgesic efficacy between patients receiving ESP and PVB blocks.[76,77] This more recent TSA contradicted the results of the meta-analysis by showing the failure of the cumulative Z-curve to cross the futility boundary when comparing these 2 blocks, and indicating that there is insufficient and inconclusive evidence for analgesic efficacy, indicating that more trials (and meta-analyses) are required to better assess ESP and PVB blocks.[76]

A recent prospective RCT by Elsabeeny et al compared TEA, ESP, and SAP block in 51 patients undergoing posterolateral thoracotomy for lung cancer, and reported that pain scores were significantly lower in the TEA group compared with the SAP group, but similar to the ESP group.[78] Moreover, no patient in the TEA group required intraoperative or postoperative narcotics, as opposed to 88% and 47% of patients in the SAP and ESP group, respectively, even though total opioid consumption was only different between SAP and the other techniques and not between TEA and ESP. The authors concluded that "Erector spinae plane block can be used as an effective and safe alternative to TEA and shows superior analgesic profile to serratus anterior plane block."

A prospective RCT on the use of continuous ESP block for postoperative analgesia in VATS was recently published by Piskin et al and showed that, compared to placebo, the use of

continuous ESP blocks resulted in a lower total opioid consumption 48 hours after surgery and fewer opioid rescue doses.[79] A study by Bliss et al compared the ESP block to TEA that assessed postoperative recovery in 30 consecutive patients with severe pectus excavatum undergoing Nuss repair.[80] The patients received a continuous ESP block placement that was compared to a historical cohort of patients in whom TEA was used for postoperative pain management. The authors found that while pain scores and opioid consumption were significantly higher in the ESP group, these patients ended up having a shorter hospital stay because they were discharged home with the catheter still in place, despite their worse pain, as opposed to the TEA cohort who had to stay until the epidural catheter was discontinued.

Qui et al performed a prospective, randomized trial on thoracoscopic lobectomy patients, comparing general anesthesia with no block to general anesthesia with either a deep or superficial serratus plane block.[81] They evaluated pain scores for up to 24 hours after surgery, and found that while both superficial and deep serratus blocks were superior to general anesthesia alone, patients in the superficial serratus plane block group experienced progressively lower pain scores over time (0.12/h) versus patients in the deep serratus plane group for up to 24 hours when they were significantly different. Therefore, the authors concluded that superficial is more effective than deep serratus plane block after thoracic surgery. A retrospective, observational, single-center study by Semyonov et al. examined the results of a survey aimed at determining the presence of postthoracotomy pain syndrome in patients who underwent elective VATS during a 14-month period and who received either an SAP block or systemic analgesia.[82] Despite not reaching statistical significance, a trend toward less overall pain and pain in the upper and lower posterior thorax occurred in the SAP block group was shown. A similar study by Zhao et al assessed the effect of a single-shot preoperative SAP versus intercostal block on the development of persistent postsurgical pain at 3 months after surgery, and found no difference between the 2 groups in the incidence of persistent postsurgical pain.[83] An RCT by Dikici et al evaluated the effect of SAP versus infiltration analgesia in 60 patients undergoing elective VATS, and found that a single-shot SAP was associated with less pain and opioid consumption and a shorter time-to-mobilization when compared to simple infiltration.[84]

A prospective, randomized, placebo-controlled study performed by Luo et al. compared the effectiveness of US-guided PECS II block (performed with 0.5% ropivacaine, 25 mL) in 40 patients undergoing VATS lobectomy in terms of intraoperative and postoperative narcotic consumption at 24 hours, pain scores, and hemodynamics.[85] The authors found that patients in the PECS II group experienced better hemodynamic stability and had less narcotic requirement intraoperatively and postoperatively (and fewer rescue doses in the postanesthesia care unit), but pain scores were the same after 24 hours, underlining the need for more prolonged analgesia in thoracic surgery.[85] Rhomboid intercostal block (RIB) is a relatively new block that has not received much attention yet was described in 2018 with or without a subserratus plane block (RISS).[86,87] Deng et al published a prospective, randomized, controlled study on the efficacy of these blocks in 90 patients for elective unilateral VATS. Patients were randomized into 3 groups—no block, RIB (0.375% ropivacaine, 20 mL), and RISS (0.375% ropivacaine, 40 mL)—and then evaluated for pain and opioid consumption within the first 24 hours after surgery.[88] The authors found that both RIB and RISS were superior to no block, but RISS was superior to RIB in terms of pain scores and opioid consumption.

Despite their widespread use, intercostal nerve blocks (ICNBs) are generally considered inferior to all of the other fascial blocks in terms of perioperative pain control. A recent systematic review and meta-analysis of 66 studies and more than 5,000 patients showed that TEA and PVB were associated with a much higher opioid-sparing effect compared to single-injection ICNBs, but the ICNBs were associated with a reduction in opioid usage for the first 24 hours, suggesting that the ICNB may be most beneficial for patients in whom TEA and PVB are not indicated.[89]

Enhanced Recovery After Thoracic Surgery (ERATS)

Evidence-based support for ERATS has continued to strengthen with larger studies and more robust data. In 2021, 2 large meta-analyses were published that assessed the effect of ERATS. The first meta-analysis by Li et al[90] analyzed 21 studies, with a total of 6,480 patients undergoing lung resection surgery. The authors concluded that the patients enrolled in ERATS had a lower risk of complications (relative risk 0.64) and a shorter length of stay. A subgroup analysis suggested that patients on an ERATS pathway had lower incidences of urinary, pulmonary, cardiac, and surgical complications without any effect on mortality or readmission rate.[90] Similarly, a second meta-analysis by Khoury et al[91] reviewed 15 studies with a total of 7,098 participants. They found a strong benefit for ERATS with regard to length of stay (reduction of approximately 3 days) and a modest reduction in the readmission rate.[90]

Other studies released in 2021 also demonstrated a positive effect of ERATS.[91-95] One such retrospective cohort study analyzed 1,749 patients undergoing oncologic lung resection, 691 of whom were enrolled in ERAS. The ERAS group experienced a shorter length of stay (4.0 *v* 6.0, $p < 0.001$), lower in-hospital costs ($p < 0.001$), and a lower rate of PPCs (15.2% *v* 19.5%, $p = 0.022$).[96] Interestingly, ERAS enrollment was the sole independent predictive factor for pulmonary complications (OR 0.601, 95% CI 0.434-0.824, $p = 0.002$). Several centers have described early discharge (postoperative day 1) or even same-day surgery utilizing an ERATS pathway.[97-100] Similarly, ERAS for esophagectomy has been associated with reduced length of stay, pain scores, and total hospital costs.[101] In a study of nearly 500 patients undergoing esophagectomy, the ERAS cohort experienced a reduction in complications, particularly pulmonary complications such as pneumonia (39% *v* 14%, $p < 0.001$) and respiratory failure (17% *v* 12%, $p < 0.001$).[102]

Although traditional outcome metrics have been used as surrogates for the success of an ERAS program (ie, length of stay, hospital costs), there has been an interest in different outcome metrics that focus instead on *quality* of recovery and functional recovery metrics. Specifically, Thompson et al[103] looked at "process-of-care" outcomes as markers of recovery. These included time to "out-of-bed," independent ambulation, enteral fluid intake, as well as chest tube and urinary catheter removal. In their retrospective review, ERATS patients outperformed non-ERAS thoracic patients in these measures, as well as in length of stay, 6-minute walk test, and incidence of 30-day emergency department visit.[103]

Multimodal analgesia continues to be an area of focus within the ERATS literature.[104] Razi et al[105] performed a retrospective analysis of 372 patients undergoing RVATS and open thoracotomy (310 and 62 patients, respectively). RVATS patients who received a multimodal analgesic approach (opioid-sparing analgesics and the use of liposomal bupivacaine into intercostal space and surgical sites) saw a reduction in pain scores. The thoracotomy group experienced a slight increase in postoperative pain scores, which was presumed to be due to the elimination of TEA in this ERATS pathway. Both groups had a dramatic reduction in the amount of post-discharge opioid prescribed (480.0-150.0 for VATS [$p < .001$] and 887.5-150.0 for thoracotomy [$p < .001$]).[105] Kodia et al[106] sought to analyze whether the infiltration of intercostal spaces and surgical wounds with liposomal bupivacaine afforded benefit over infiltration with bupivacaine with epinephrine. Two hundred and fifty-two patients were included, and those who received liposomal bupivacaine experienced better subjective pain control and decreased opioid requirements postoperatively, without an increase in hospital costs.[106] A retrospective, propensity-matched study of 1,630 patients undergoing lung cancer resection studied whether ketamine and dexmedetomidine infusions decreased opioid use or pain scores in the postanesthesia recovery unit. While the initial analysis suggested a reduction in opioid consumption and pain score, these effects were not significant once adjusted for multiplicity.[107]

Overall, several papers released in 2021 support the efficacy and improvement in outcomes related to ERATS. The quality of this research continues to improve as the implementation of ERATS has become more widespread.

Non-intubated Thoracic Surgery (NTS)

Over the past decade, there has been growing interest in performing thoracic surgical procedures in non-intubated, spontaneously ventilating patients without the use of general anesthesia. In these cases, lung isolation is achieved by an iatrogenic pneumothorax, obviating the need for double-lumen endotracheal tubes or BBs. While controversial, reported advantages of NTS include more rapid postoperative recovery and reductions in ICU and hospital length of stay, postoperative cardiopulmonary complications, laryngeal or tracheal injuries associated with airway instrumentation, and complications associated with general anesthesia, such as PONV.[108-110]

While the growing body of NTS-related literature suggests expanding the use of this technique, there is limited data to describe how widespread adoption has been. In fact, a recent survey by the European Society of Anaesthesiology published in 2021, which provided an overview of airway and regional anesthesia practice patterns for 474 thoracic surgical centers in Europe, did not even address the topic of NTS.[111]

In 2019, a survey was conducted in Italy by the multidisciplinary Italian Network for Investigation of Non-intubated Thoracic surgery group to review the use, techniques, and outcomes of NTS for parenchymal disease in 55 Italian centers that performed more than 100 thoracic operations per year. Seventy-eight percent of responding centers reported performing NTS, most commonly for pleural effusions (86% of responding centers) and pleural pathologies (81%), and less commonly for parenchymal pathologies (38%). NTS was primarily performed in patients with severe comorbidities or preexisting respiratory impairment (67%) and less frequently in patients without comorbidities (38%). Reported contraindications to NTS for parenchymal pathologies included obesity (60%), preoperative need for noninvasive ventilation (42%), major lung resections (49%), and anticipated difficult airway (70%), with fewer contraindications noted by more experienced centers.[5]

Preoperative management and intraoperative sedation strategies were similar at most institutions performing NTS for parenchymal pathology, but a range of regional anesthetic techniques was utilized. The vast majority of these centers (90%) reported performing preoperative counseling for patients prior to NTS, with most using a multidisciplinary team. A variety of intraoperative management strategies were utilized, including aerosolized lidocaine (52%), vagal block (14%), and pleural nebulized lidocaine (14%). Intraoperative sedation was largely provided by anesthesiologists and included propofol and opioids. Regional techniques were commonly used at experienced centers and included paravertebral blocks (37%), SAP blocks (32%), epidural catheters (32%), and intercostal nerve blocks (32%). Thirty-one percent of centers reported converting to general anesthesia at least once, and 79% reported transitioning to general anesthesia when a minimally invasive procedure required conversion to an open technique.[5]

Advantages of NTS reported by experienced centers were consistent with those described in previously published studies and included more rapid postoperative recovery (80%), reduction in complications from anesthesia or mechanical ventilation (57% and 61%, respectively), and reduction in ICU admission (52%). There does appear to be a learning curve associated with NTS, as the authors note that more experienced centers reported greater benefits than risks. The most frequently reported challenges with this technique included coughing and movement during the procedure (76%), airway management (74%), and challenges with addressing intraoperative complications with a non-intubated patient (68%). However, reported advantages appear to bolster ongoing interest in pursuing NTS, with 72% of centers reporting a belief that case volume will continue to grow.[5]

The results of this survey indicate that NTS is currently being performed for parenchymal disease at a limited number of experienced thoracic surgical centers in Italy, and the use of this technique is likely to grow.[111] However, generalizability of these survey findings may be limited as other published studies demonstrate different practice patterns and primary indications for NTS in other countries, such as China and Taiwan.[112] Additional multicenter investigation is required better define the scope, appropriate patient population, advantages, and limitations of this technique.

In summary, research continues to focus on improving the perioperative management of thoracic surgical patients. These include preoperative strides in prehabilitation and ERATS, improvements in intraoperative management of OLV, including the placement of OLV devices in adults and children, protective ventilation, anesthetic management, and regional techniques, expanding the indications for ECMO for challenging procedures, and the role of NTS in this patient population in an effort to improve patient outcomes.

Conflict of Interest

None.

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