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Special Article

The Year in Thoracic Anesthesia: Selected Highlights from 2022

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This article reviews research highlights in the field of thoracic anesthesia. The highlights of this year included new developments in the preoperative assessment and prehabilitation of patients requiring thoracic surgery, updates on the use of devices for one-lung ventilation (OLV) in adults and children, updates on the anesthetic and postoperative management of these patients, including protective OLV ventilation, the use of opioid-sparing techniques and regional anesthesia, and outcomes using enhanced recovery after surgery, as well as the use of expanding indications for extracorporeal membrane oxygenation, specialized anesthetic techniques for airway surgery, and nonintubated video-assisted thoracic surgery.

THIS SPECIAL ARTICLE is the sixth 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 pertained to the specialty of thoracic anesthesia. The highlights of this year included new developments in the preoperative assessment and prehabilitation of patients requiring thoracic surgery, updates on the use of devices for one-lung ventilation (OLV) in adults and children, updates on the anesthetic and postoperative management of these patients, including protective ventilation, opioid-sparing techniques, regional anesthesia, and outcomes

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using enhanced recovery after surgery, as well as the use of expanding indications for extracorporeal membrane oxygenation (ECMO), specialized anesthetic techniques for airway surgery, and nonintubated video-assisted thoracic surgery (VATS).

Prehabilitation

The literature this year focused on preoperative risk stratification and optimization. Preoperative risk stratification included the use of cardiopulmonary exercise testing (CPET), the Geriatric Nutritional Index (GNRI), the neutrophil-to-lymphocyte ratio (NLR), and the effect of anemia on perioperative outcomes. Risk stratification using preoperative CPET-derived peak oxygen consumption (VO_{2max}) identifies high-risk patients and is recommended in international guidelines, with VO_{2max} >20 indicating low risk and VO_{2max} <10 indicating high risk.[1] Nieves-Alonzo compared the subjective assessment of estimated metabolic equivalents by questionnaire to objective measurement by CPET in 104 patients who underwent pulmonary resection, finding true functional capacity was overestimated significantly by subjective assessment, and reinforcing the need for objective measurement.[2] Ozova et al. reported the results of a prospective cohort study of 200 patients with gastroesophageal cancer undergoing CPET before resection. They reported that an anaerobic threshold level <11 mL/kg/min was highly predictive for any cardiovascular complication (p = 0.02, odds ratio [OR] 6.33; 95% CI 1.78-22.47), and an anaerobic threshold level <9.5 had the best predictive accuracy for major perioperative cardiac complications (sensitivity 93%, specificity 68%, positive predictive value 75%, negative predictive value 98.8%).[3] Another emerging CPET parameter, ventilatory efficiency, may add incremental value in the assessment of these patients. Ventilatory efficiency is the slope of the increase in minute ventilation in relation to carbon dioxide excretion (VE/VCO_2-slope). Mazur et al. compared VE/VCO_2-slope to VO_{2max} in predicting cardiovascular complications in a retrospective cohort of 346 lung resections, and reported that ventilatory efficiency was superior in predicting postoperative cardiac complications.[4] Kristensen et al. examined whether a VE/VCO_2-slope >35, determined to be an independent predictor of postoperative complications (POCs), improved preoperative risk assessment in a single-center cohort of 146 patients undergoing lobectomy for cancer.[5] In patients with a peak oxygen uptake between 10-20 mL/kg/min, a VE/VCO_2-slope ≥35 was associated with a 29% risk of major pulmonary complications or death within 30 days, compared to a risk of 13% for those with a VE/VCO_2-slope <35.

Although CPET is the gold standard, less resource-intensive forms of exercise testing, such as the 6-minute walk distance (6MWD), have shown prognostic value in lung and patients undergoing esophageal cancer surgery.[6] Kondo et al. reported on 5-year survival in a cohort of 108 patients who underwent esophagectomy, and observed that a 6MWD of <480 meters was a significant independent risk factor for overall survival (OS) (hazard ratio 3.33; 95% CI 1.37-8.11, p = 0.008) and recurrence-free survival (RFS) (hazard ratio 2.30; 95% CI 1.08-4.88, p = 0.030).[7] Boujibar et al. administered a 6-minute stepper test and sit-to-stand test in a cohort of 90 patients who required preoperative lung resection. For the 6-minute stepper test, they found a receiver operating characteristic (ROC) curve area of 0.82 (95% CI 0.75-0.90) for an optimum cut-off of 140 steps, and 0.85 (95% CI 0.77-0.93) for the number of lifts during the sit-to-stand test, with an optimum cut-off of 20 lifts.[8] A stair climbing test was used by Xiao et al. in a sample of 727 patients who required lung resection. Height achieved in floors climbed was an independent risk factor for postoperative cardiopulmonary complications (p < 0.001).[9] Tamagawa et al. examined the use of risk factors for coronary artery stenosis, including smoking, diabetes, hypertension, dyslipidemia, and ischemic heart disease, to determine the appropriate patient selection for the use of preoperative stress electrocardiography in the evaluation of 240 patients undergoing lung cancer resection, and found that patients with coronary risk factor scores of ≥3 were significantly more likely to have abnormal stress electrocardiography results and would benefit from more invasive cardiology studies.[10]

In a single-center study of 373 patients with esophageal cancer who underwent neoadjuvant therapy, Fang et al. evaluated the use of the GNRI, calculated as 1.489 × albumin (g/dL) + 41.7 × current weight/ideal weight, as a tool to predict POCs.[11] They reported that a low GNRI significantly correlated with POCs. Patients with lower GNRI had a higher POC rate compared with the high GNRI group (OR 2.023; 95% CI 1.208-3.389; p = 0.007). The NLR, previously linked to poor prognosis in other cancer and surgical populations, was shown to predict complications after esophagectomy.[12] An NLR cut-off of 2.30 was identified as having the greatest ability to predict complications, with a sensitivity of 76% and specificity of 65% in this patient population. Preoperative anemia, defined as hemoglobin <13 mg/dL in men and <12 mg/dL in women, was examined in a cohort of 5,029 patients undergoing lung resection for cancer.[13] The 90-day mortality for anemic and nonanemic patients was 5.6% and 3.1%, respectively (p < 0.001). After multivariate adjustment, preoperative anemia was not associated with increased 90-day mortality. However, a log-rank analysis demonstrated reduced OS for anemic patients (p < 0.001). After multivariate adjustment, preoperative anemia was found to be independently associated with reduced OS (HR 1.287, 95% CI 1.141-1.451, p < 0.001).

Preoperative Optimization

The literature for preoperative optimization of patients who require thoracic surgery focused on preoperative respiratory and muscle training with and without the use of aids. Fraile et al. developed a perioperative patient education and respiratory training application using a smartphone-based program that was found to be highly (90%) adopted in a study of 104 patients who required thoracic surgery. Patients ranged across all education levels, and included a number of older people (55.7% were >61 years of age), proving the broad applicability of the concept of smartphone apps as an enhanced recovery intervention.[14]

Ichikawa et al. performed a single-center study with 41 patients who required lobectomy, evaluating the effect of respiratory physiotherapy administered from 1 week preoperatively to 3 months postoperatively by serial measurements of pulmonary function and 6MWD test.[15] At hospital discharge, pulmonary function and functional capacity were decreased compared to preoperative values, but function recovered at 1 and 3 months postoperatively. Interestingly, reductions were similar between video-assisted thoracoscopy and open thoracotomy groups, suggesting that postoperative rehabilitation may be an area of interest.

An updated systematic review and meta-analysis on exercise training and POCs after surgery for non-small cell lung cancer (NSCLC) was published by Gravier et al.[16] This systematic search yielded 14 studies that included 791 patients. They reported that exercise training reduced overall POCs (10 studies, 617 participants, relative risk [RR] 0.58, 95% CI 0.45-0.75) and clinically relevant POCs (4 studies, 302 participants, Clavien−Dindo score ≥2 RR 0.42, 95% CI 0.25-0.69). The estimate of the effect of exercise training on mortality was very imprecise (6 studies, 456 participants, RR 0.66, 95% CI 0.20-2.22). The main risks of bias were a lack of participant blinding and selective reporting. Exercise training appeared to improve exercise capacity, pulmonary function, quality of life, and depression, although the clinical usefulness of the changes was unclear. Another meta-analysis examined prethoracic surgery respiratory muscle training and aerobic exercise training, including 25 studies and 2,070 patients undergoing both thoracic and cardiac surgeries.[17] Pooled estimates of the effect of respiratory muscle and aerobic exercise training on postoperative pulmonary complications (PPCs) were similar (OR 0.35 [$p = 0.006$] and 0.33 [$p < 0.00001$]), respectively. The length of stay (LOS) was reduced by 1.69 days ($p < 0.00001$) for respiratory muscle training and 1.79 days ($p = 0.0008$) for aerobic exercise training. Neither respiratory muscle training nor aerobic exercise training was associated with a significant difference in all-cause mortality compared with usual care, suggesting that the benefit of prehabilitation remains unclear.

Devices for OLV

One-lung ventilation is essential in most thoracic surgery, and double-lumen endobronchial tubes (DLT) and bronchial blockers (BBs) represent established devices to achieve lung isolation.[18] The debate regarding which devices are superior continues, with anesthesiologists valuing factors such as decreased time-to-device placement, reduced rates of device malposition, and reduced incidence of airway injury.[19] This section focuses on several studies published in the last year that provided insight into these topics.

In a prospective, randomized study, Morris et al. compared the positional stability of the EZ-blocker to the DLT in 163 patients who underwent thoracic surgery, defined as the number of repositionings per hour of surgery requiring OLV. Secondary outcomes included the degree of isolation and dysphagia on postoperative days (PODs) 1 and 2. The rate of repositioning per hour during OLV and surgical manipulation in left-sided cases was similar between the 2 devices—0.08 ± 0.15 versus 0.11 ± 0.3 ($p = 0.72$). In right-sided cases, the rate of repositioning was higher in the EZ-Blocker group compared with DLT—0.38 ± 0.65 versus 0.09 ± 0.21 ($p = 0.03$). Overall, the mean isolation scores for the EZ-Blocker versus the DLT were 2.76 versus 2.92 ($p = 0.04$) in left-sided cases and 2.70 versus 2.83 ($p = 0.22$) in right-sided cases. Median sore throat scores for left-sided cases were 0 *v* 5 ($p = 0.13$) POD 1 and 0 versus 5 ($p = 0.006$) POD 2 for the EZ-Blocker and left-sided DLT, respectively. This suggested that for left-sided surgery, the EZ-blocker provided comparable lung isolation with less dysphagia than the DLT, but for right-sided surgery, the DLT was superior for lung isolation.[18]

To compare the use of a DLT versus BB for VATS, Xiang et al. performed a meta-analysis of 5 randomized controlled trials (RCTs).[20] The primary outcome included the quality of lung isolation and the incidence of device malposition. Although the incidence of dysphagia was higher in the DLT group (OR 5.25; 95% CI 2.55-10.75), there were no statistically significant differences in the quality of lung isolation (OR 1.00; 95% CI 0.63-1.58) or incidence of malposition (OR 0.88; 95% CI 0.37-2.06). Notably, only 4 of the 5 trials reported on the quality of lung isolation and the incidence of malposition, and only 3 of the 5 trials reported on dysphagia.[20]

Despite common use, a DLT can be challenging to place compared to a single-lumen tube due to factors such as its large size and firmness.[21] Also, DLT placement may be more difficult in patients with obesity due to their potential for having a difficult airway. To investigate this, Mehta et al. retrospectively studied 1,459 patients who were difficult to intubate, defined as requiring more than 1 attempt. Of these patients, 1,040 had a body mass index (BMI) <30 kg/m^2, whereas 419 had a BMI ≥ 30 kg/m^2. After adjusting for other variables, every increase in BMI of 5 kg/m^2 was associated with a more difficult intubation (OR 1.06; 95% CI 1.002-1.11).[21] Although this difference was statistically significant, it was likely not clinically significant.

Another question is whether the composition of the DLT can affect the difficulty in placement. In a randomized trial, Kang et al. compared the ease of "railroading" with a silicone ($n = 23$) versus a polyvinyl chloride ($n = 23$) DLT.[22] The DLT was placed using a fiberoptic bronchoscope. The ease of railroading was determined based on the ease of advancing the DLT and the degree of maneuvering involved for proper placement. Overall, the DLT was easier to place in the silicone group. The railroading times were also shorter in the silicone group, with a mean difference of 7 seconds (95% CI 4-9, $p < 0.001$). Finally, there was a lower incidence of blood staining of the DLT in the silicone group compared to the polyvinyl chloride group during intubation (9.5% *v* 69.6%, $p < 0.001$) and extubation (13.0% *v* 47.8%, $p < 0.023$).[22] Notably, the trial was not blinded, and it is not clear whether these results are generalizable to practitioners who place the DLT using direct laryngoscopy.

Whereas a separate fiberoptic bronchoscope is often used to guide the DLT, the VivaSight 2 DLT (Ambu, Ballerup, Denmark) has an integrated video camera near the tip of the tube

to facilitate placement.[23] In a randomized trial, Palaczynski et al. compared the VivaSight DLT to the Robertshaw DLT (Dublin, Ireland), with the primary outcome being time for intubation. They reported that the time to intubation for the VivaSight was shorter (44 [33-66] *v* 125 seconds [110-172], $p < 0.001$). The VivaSight was also more likely to have a subjective assessment of placement difficulty graded as easy (71.9% *v* 43.6%, $p < 0.05$).[23] There were no significant differences in lung isolation or traumatic airway injury between the groups.

Besides airway trauma, some groups have investigated potential POCs due to lung isolation. Liu et al. retrospectively studied the incidence of PPCs, with the primary outcome defined as infection, aspiration pneumonitis, respiratory failure, pneumothorax, or atelectasis before hospital discharge in patients undergoing thoracic surgery for lung cancer.[24] A total of 1,721 patients were studied, with 868 receiving a DLT (Teleflex) and 853 receiving a BB (Hangzhou Tappa Medical Technology CO, Ltd). The primary outcome occurred in 31.6% of all patients, with pulmonary infection and pleural effusion being the most common complications. Interestingly, PPCs occurred in 25.1% of the BB group compared to 37.9% of the DLT group. Multivariate analysis confirmed the association of BBs with fewer PPCs (OR 0.582; 95% CI 0.461-0.735, $p < 0.001$). Other factors associated with PPCs included a smoking index of $\geq$400, a higher American Society of Anesthesiologists (ASA) physical status score, longer surgery, and in those receiving preoperative chemotherapy.[24] It is challenging to determine whether other factors, such as fluid administration or the extent of surgery, could have played a role in these results.

The correct placement of a DLT is determined typically by fiberoptic bronchoscopy. Kanavitoon et al. sought to compare fiberoptic bronchoscopy (n = 98) with lung ultrasound (n = 97) in determining proper DLT placement.[25] In a double-blinded, noninferiority RCT, patients who were intubated with a DLT had confirmation or adjustment of the DLT position based on the bronchoscopy or lung ultrasound findings (evaluation of lung sliding). The surgeon graded the quality of lung isolation using a scale of 1 to 4, with 1 being the best score. There were no significant differences in the number of patients achieving lung collapse sufficient for surgery (defined as grade 1 or 2) between the lung ultrasound group versus the bronchoscopy group (91.8% *v* 84.7%, respectively). Notably, the time needed to confirm DLT position, a secondary outcome, was shorter in the ultrasound group (3 [IQR 2-5] *v* 6 minutes [IQR 4-10], $p < 0.001$).[25] Although these results are encouraging regarding the use of lung ultrasound, patients who required fiberoptic bronchoscopy due to difficult intubation (n = 5) were excluded from the analysis. Furthermore, the authors did not state how many patients required adjustment of the DLT position; this information would be helpful to distinguish the accuracy of lung ultrasound to confirm the proper position of the DLT versus the ability of ultrasound to guide repositioning of the DLT.

Despite the ongoing use of conventional DLTs, many continue to modify these devices to make placement easier. In a randomized trial, Hsu et al. studied the Trachway (Biotronic Instrument Enterprise Ltd) device. The Trachway serves as a stylet for the DLT that is placed into the tracheal lumen and also has a camera at the tip.[26] After intubation, the stylet can be connected to a monitor to facilitate visual confirmation of DLT placement or guide any necessary adjustments, thereby obviating the need for a separate fiberoptic bronchoscope. In this study, randomization occurred in 3 groups, each with 36 patients. All patients initially were intubated using video laryngoscopy. The patients in the conventional group had the DLT advanced until resistance was met, with fiberoptic bronchoscopy to confirm placement. In the fiberoptic bronchoscopy group, the DLT was advanced over the bronchoscope into the mainstem bronchus. The third group had placement into the bronchus guided by the Trachway device. The time between when the vocal cords were first seen to the DLT being properly positioned was shortest in the Trachway group (47.8 $\pm$ 11.2 seconds) when compared to the fiberoptic group (72.0 $\pm$ 22.1 seconds) or the conventional group (122.1 $\pm$ 28.7 seconds) ($p < 0.001$).[26]

Another innovation reported this year was a Y-connector that rotates and has a valve to control the direction of air-gas flow, thereby minimizing the need for disconnection or clamping of the traditional Y-connector to institute OLV.[27] The authors noted that the rotational connector was associated with better preservation of inspired and expired sevoflurane, possibly because of a decrease in the amount of volatile anesthetic lost compared to the traditional connector. The "switching time" was shorter with the use of the rotational connector; although this parameter did not seem to be explained clearly in terms of how it was defined, it presumably related to the time required to change from two-lung ventilation (TLV) to OLV.[27] However, whether this is clinically significant is questionable because the switching time in both groups was <10 seconds. Furthermore, this study may have been biased because the authors were involved in the invention of the device, and the trial was not blinded, which suggested that further research be done to see whether this device will be useful when switching to OLV.

Protective OLV

Patients undergoing thoracic surgery have a higher incidence of PPCs than those undergoing other types of surgeries. This is multifactorial and due to perioperative changes in physiologic parameters combined with mechanical ventilation-induced lung injury. Although choosing intraoperative ventilator settings is crucial, no universal protocol exists to help ameliorate these complications. Airway driving pressure (DP), defined as the difference between the plateau and positive end-expiratory pressures (PEEPs), indicates alveolar stress and strain. It is the only ventilation parameter independently associated with adverse outcomes in ventilated patients. Park et al., by conducting a multicenter, randomized, controlled, and patient- and evaluator-blinded trial, examined the effect of a targeted reduction in DP on the incidence of PPCs in a total of 1,170 patients undergoing lung resection surgery.[28] These patients were randomized into 2 groups: the DP group

(n = 576), which received alveolar recruitment and individualized PEEP to deliver the lowest DP, and the conventional protective ventilation group (n = 594) with a fixed PEEP of 5 cmH_2O. The primary outcome was a composite of PPCs within 7 days postoperatively. Secondary outcomes included intraoperative arterial oxygen level (PaO_2), arterial to inspired oxygen ratio (P-F) ratio, static lung compliance 15 minutes after initiation of OLV, C-reactive protein on POD 1, postoperative transfusion within the first 3 PODs, extrapulmonary complications within the first 7 PODs, intensive care unit (ICU) and hospital LOS, readmission, and 30-day mortality. The DP group had significantly lower DP values (7.1 cmH_2O *v* 9.2 cmH_2O) than the protective ventilation group (mean difference [95% CI]; 2.1 [2.4-1.9] cmH_2O; $p < 0.001$). Intraoperatively, the DP-guided ventilation group had increased static lung compliance, including during OLV (mean SD, 42.7 [12.4] *v* 33.5 [11.1] mL cmH_2O; $p < 0.001$). Similarly, the PaO_2 (median [IQR], 21.5 [14.5-30.4] *v* 19.5 [13.5-29.1] kPa; $p = 0.03$) and P-F ratios (median [IQR], 27.7 [18.5-38.5] *v* 24.4 [16.8-37.5] kPa; $p = 0.03$) were higher after the initiation of OLV in the DP-guided group. Finally, the need for intraoperative rescue ventilation was less frequent (39 of 576 [6.8%] *v* 64 of 594 [10.8%]; $p = 0.02$) in the DP group. Postoperatively, the incidences of PPCs were similar between the 2 groups, (DP group [40.5%] *v* protective ventilation group (42.8%) (risk difference 2.3%; 95% CI, 8.0%-3.3%; $p = 0.42$)]. They concluded that although DP-guided ventilation improved intraoperative pulmonary mechanics, there was no difference in the development of PPCs.[28]

Yu et al.[29] performed a similar study investigating the effect of DP on the incidence of PPCs in patients undergoing selective lung resection surgery. A single-center, randomized trial was performed on 207 patients. For adjusting PEEP during OLV, patients were divided into 2 groups. In group D, PEEP was titrated to the lowest DP. In group C, a conventional low level of PEEP (4 cmH_2O) was set. In both groups, respiratory rate was adjusted during OLV for end-tidal CO_2 ($ETCO_2$) between 30-45 mmHg. The DP was significantly lower in group D than in group C (10 *v* 13 cmH_2O, $p < 0.001$), with a median PEEP of 7 cmH_2O in group D. During OLV, in group D, the peak pressure ($p = 0.023$) and $PaCO_2$ ($p = 0.003$) were reduced, whereas the PaO_2 ($p = 0.037$) and dynamic lung compliance ($p < 0.001$) were increased compared with group C. After restarting TLV, the peak pressure was significantly lower in group D than in group C (13 *v* 14 cmH_2O, $p = 0.002$). Postoperatively, the primary outcome was measured using the Melbourne Group Scale for the first 3 days after surgery. If a patient developed at least 4 Melbourne Group Scale variables, they were considered positive for PPC. Four patients (4%) had PPCs in group D, whereas 13 patients (13%) had PPCs in group C (RR, 0.32 [95% CI, 0.10-0.90]; $p = 0.021$). Secondary outcomes included major pulmonary complications occurring within 7 days postoperatively, ICU and hospital LOS, and blood gas analysis at POD 1. No significant differences were found between the 2 groups, including major PCCs (RR, 1.00 [95% CI, 0.95-1.06]; $p = 1.000$). The incidences of major PPCs on the ventilated lung within 3 PODs or hospital days were lower in group D than in group C (40 of 104 [39%] *v* 54 of 103 [52%]; RR, 0.73 [95% CI, 0.54-0.99]; $p = 0.044$). In summary, titration to the lowest DP significantly reduced PPCs within the first 3 PODs, but not for the first 7 PODs.[29] A third study examining the DP during OLV was performed by Li et al.[30] This was a systematic review and meta-analysis of 7 studies totaling 640 patients that compared the effects of DP-oriented ventilation with other ventilation strategies on patients undergoing OLV. The primary outcome, the P-F ratio, was higher during OLV in the DP-oriented ventilation group (mean deviation [MD]: 44.96; 95% CI, 24.22-65.70; I^2: 58%; $p < 0.0001$). Secondary outcomes included PPCs during follow-up, respiratory system compliance, and mean arterial pressure (MAP) during OLV. In comparison with the control group, the DP-oriented group had a lower incidence of PPCs (OR 0.58; 95% CI 0.34-0.99; I^2: 0%; $p = 0.04$) and higher respiratory system compliance (MD: 6.15; 95% CI, 3.97-8.32; I^2: 57%; $p < 0.00001$). There were no significant differences in the MAP between the 2 groups (MD 0.51; 95% CI, −2.85 to 3.87; I^2: 28%; $p = 0.77$).[30]

To estimate the risk for PCC, lung function is evaluated preoperatively. Godbole et al.[31] performed a prospective observational study to determine the utility of measuring the volume of deadspace ventilation (VD) and the ratio of deadspace to tidal volume (VD-VT) ventilation at rest in predicting PPCs, including pneumonia, respiratory failure, and atelectasis requiring bronchoscopy in patients undergoing robotic-assisted lung resection for lung malignancy. Thirty-five patients with preoperative pulmonary function testing were included in the study. Postoperative pulmonary complications occurred in 14 (40%) patients. The most common PPCs were postoperative pneumonia and atelectasis requiring therapeutic bronchoscopy. At rest, in comparison with the non-PPCs group, the PPCs group had increased VD (average was 0.318 L versus 0.230 L, $p < 0.006$), VD-VT ($p = 0.051$). $PetCO_2$ and other ventilatory variables had similar arterial blood gas measurements. With exercise, the peak VO_2, VO_2 at lactate threshold, peak power, VE/VCO_2 slope, and nadir VE/VCO_2 were similar between the 2 groups. As a conclusion, resting VD is a potential predictor for PPCs.[31]

Even though low-tidal-volume ventilation and PEEP are well-established in critical care as lung- protective strategies, they can cause significant hypoxemia and auto-PEEP during OLV. Peel et al.[32] performed a systematic review and meta-analysis of 18 studies (3,693 patients) to determine how tidal volume during OLV affects oxygenation, compliance, and clinical outcomes. The mean tidal volume in the "low"-tidal-volume groups was 5.6 (0.9) mL/kg versus 8.1 (3.1) mL/kg in the control groups. No significant difference was observed between "low" and "conventional" tidal volumes in PaO_2 (15.64 [88.53-57.26] mmHg; $p = 0.67$), P-F ratio (14.71 [7.83-37.24]; $p = 0.20$), compliance (2.03 [5.22-9.27] mL/cmH_2O; $p = 0.58$), hospital LOS (0.42 [1.60-0.77] days; $p = 0.49$) or mortality (pooled OR, 1.30 [0.38-4.41]; $p = 0.68$). Nevertheless, "low" tidal volume was associated with significantly lower odds of PPC (pooled OR, 0.40 [0.29-0.57]; $p < .0001$).[32]

During OLV in thoracoscopic lobectomy, lung-protective ventilation usually is adopted. Unfortunately, lung-protective

strategies are defined poorly in the field of thoracic surgery. However, there are few studies on the selection of PEEP values during OLV in patients 65 years or older. Yao et al.[33] performed a single-center RCT to evaluate the best PEEP titration method for these patients. Fifty patients, from 65-78 years old, were divided randomly into the following 2 groups (n = 25 each): the optimal oxygenation titration group (group O) and the optimal compliance titration group (group C). The PEEP value of the optimal oxygenation titration group (11.24 ± 1.71 cmH_2O) was significantly higher than that of the optimal lung compliance titration (7.68 ± 1.28 cm H_2O; $p < 0.05$). In addition, in group C, the DP and peak inspiratory pressure (PIP) decreased, whereas dynamic lung compliance increased 10 minutes after the completion of OLV titration. This indicated that PEEP titration by dynamic lung compliance can have a positive effect on respiratory mechanics. Finally, both groups had a similar significant increase of VD-VT after OLV.[33] Leonardi et al.[34] investigated whether obesity affected peri- and postoperative outcomes in patients undergoing VATS lobectomy for lung cancer. They performed a retrospective single-center study with 111 patients, from whom 26 (23%) were included in the obese group and 85 (77%) were included in the nonobese group. Comparing the 2 groups for peri- and postoperative outcomes or mortality, there were no statistically significant differences, even though the obesity group had nonstatistically significant higher incidences of hypoxemia (35% *v* 20%, p = 0.12) and lower incidences of prolonged air leaks (22% *v* 8%; p = 0.09). Double-lumen endobronchial tube placement was preferred in the nonobese group (61% *v* 39%; p = 0.02), whereas a single-lumen tube with a BB was preferred in the obese group (81% *v* 19%, p = 0.001). Intergroup comparison also showed statistical significance (p = 0.02). Patients in the obese group had longer intubation times (94.0 ± 6.1 *v* 85.0 ± 7.0 seconds; p = 0.0004) and higher failure rates of first intubation attempts (23% *v* 5%; p = 0.01).[34]

It is established that mechanical ventilation increases the risk of ventilator-induced lung injury (VILI). There is a higher incidence of VILI with OLV, with the hypothesis that the main risk factors for OLV-induced VILI are iatrogenic. Bruinooge et al.[35] performed a scoping review of 29 papers in an attempt to identify biomarkers of VILI during surgeries requiring OLV. Blood (45%, n = 13), bronchoalveolar lavage fluid (BAL) (41%, n = 12), and tissue (41%, n = 12) were the most common sample types used. Most of the markers investigated in blood were proinflammatory (81%, n = 22 markers), and only 3 were antiinflammatory markers. Studies using BAL fluid tested for proinflammatory markers (90%, n = 26). The most studied analytes were tumor necrosis factor-alpha (TNF-α) (n = 14), followed by interleukin (IL)-6 (n = 13), IL-8 (n = 9), and IL-10 (n = 7). Across all sample types and studies, 84% (n = 66) of the 79 inflammatory markers and 75% (n = 6) of the 8 antiinflammatory markers tested were found to be increased after OLV. Approximately one-half (48%) of all studies showed an increase in TNF-α or IL-6. As a conclusion, those markers potentially can serve as outcome measures for studies on OLV.[35]

Since the introduction of VATS, surgical artificial pneumothorax by CO_2 insufflation has been used to improve surgical exposure in various thoracic surgeries. Recently, interest has focused on comparing OLV to TLV for different thoracic surgeries using VATS. Yun et al.[36] performed a retrospective study comparing OLV versus TLV in patients with myasthenia gravis undergoing bilateral VATS-extended thymectomy with capnothorax in 54 patients. These patients were divided into the following 2 groups: the DLT (D) group, with 26 patients who underwent OLV, and the single-lumen tube (S) group, with 28 patients who underwent TLV during the surgery. They set 9 anesthesia time points; T0 was intubation, T1 was a right-sided incision, T2 was 10 minutes after CO_2 insufflation of the right lung, T3 was 30 minutes after right-lung CO_2 insufflation, T4 was the transition from the right-to-left and in group D, TLV, T5 was a left-sided incision, T6 was 10 minutes after CO_2 insufflation, T7 was 30 minutes after left-sided CO_2 insufflation, and T8 was the end of the left-sided surgery. The endpoints measured included $ETCO_2$, PIP, respiratory rate, SpO_2, fraction of inspired oxygen (F_IO_2), MAP, heart rate, cardiac index, P-F ratio, PPCs, and hospital and ICU LOS. They reported that the SpO_2 at time points T1 to T3 and T8 was significantly lower in group D than in group S. The F_IO_2 was lower in group D than in group S at all time points. The $ETCO_2$ was higher for group D at T1-T3 and T7 points. The number of P-F ratios ≤300 and ≤200 was significantly higher in group D than in group S. There were no significant differences in PIP, respiratory rate, or any of the hemodynamic variables. Finally, the duration of surgery and anesthesia was longer in group D than in group S, but with no difference in the duration of ICU or hospital LOS. Overall, TLV during bilateral VATS-extended thymectomy with capnothorax is safe, with improved lung oxygenation and a reduction in anesthesia time.[36]

Daghmouri et al.[37] also performed a study comparing the safety and advantages of TLV over OLV in minimally invasive esophagectomy (MIE) in the prone position. A systematic review of 7 trials was completed, totaling 1,710 patients (765 patients with TLV *v* 945 patients with OLV). The primary outcome was the assessment of respiratory parameters between OLV and TLV. Secondary outcomes were intraoperative surgical characteristics (such as estimated blood loss and surgical time), 30-day mortality, clinical and biologic postoperative inflammatory parameters (according to the Systemic Inflammatory Response Syndrome criteria), and POCs defined by the Berlin criteria. When compared between the 2 groups, there were no differences observed in intraoperative respiratory parameters (P-F ratio, DP), overall surgical duration, thoracoconversion rate, the number of harvested lymph nodes (16 [4-40] *v* 18 [3-37], p = 0.072 and 42.1 ± 17.0 *v* 40.9 ± 17.5, p = 0.77), or postoperative PaO_2 (231.6 ± 46.25 mmHg *v* 230.44 ± 47.8 mmHg, $p > 0.05$). Postoperative complications were similar in both groups, including rates of pneumonia, ARDS, and anastomotic leak. Thirty-day mortality was comparable in both groups. The TLV group had a higher intraoperative PaO_2 (207.1 ± 28.3 mmHg *v* 124.45 ± 10.6 mmHg, p = 0.002) during the thoracic portion of the MIE, decreased

blood loss, and duration of surgery. Postoperatively, the TLV group had superior oxygenation and reduced inflammatory response as measured by a lower temperature on day 1 (36.8 ± 0.25 8˚C *v* 37.4 ± 0.4 8˚C, $p < 0.005$), lower white blood cell count at day 7 (9,850 ± 200 cells/m^3 *v* 10,100 ± 500 cells/m^3, $p < 0.05$) and lower C-reactive protein at day 7 (6.2 ± 1.4 mg/L *v* 10.0 ± 3.5 mg/L, $p < 0.005$)]. In conclusion, TLV for MIE in the prone position is safe when compared to OLV.[37]

Anesthetic Management of OLV

The current literature in the anesthetic management of OLV includes updates ranging from pulmonary drug delivery, anesthetic choice and lung injury, cerebral oxygenation, and monitoring modalities. Pengyi et al., in an RCT, evaluated the effect of prostaglandin E1 (PGE1) nebulization on oxygenation during OLV.[38] A total of 90 patients with esophageal cancer were randomized into the following 3 groups: group A, who received 60% F_IO_2 and PGE1 at 0.1 ug/kg/min; group B, who received 40% F_IO_2 and PGE1 at 0.1 ug/kg/min; and group C, who received 40% F_IO_2 with PGE1 at 0.2 ug/kg/min. The primary outcomes were oxygenation and pulmonary shunt during OLV, and the secondary outcome was oxidative stress after OLV, as measured by IL-6 and malondialdehyde levels. They reported lower oxygenation, MAP, and pulmonary shunt in groups B and C compared with group A, but with less oxidative stress, suggesting that a lower F_IO_2 with the addition of PGE1 can be used to maintain oxygenation while reducing oxidative stress on the lung.

Selective-lobe ventilation as a novel pulmonary drug delivery platform also was highlighted by Maracaja et al.[39] Citing lobar mechanical heterogeneity and dependence on gravity in ARDS and ventilation-perfusion regional changes in diseases such as COVID-19, a device allowing selective lobar ventilation, lobe recruitment, and inhaled drug delivery, invented by the authors, was introduced. This endotracheal tube (ETT), called a "shuttle tube", allows selective lobe mechanical ventilation using 2 different modes (differential PEEP and asynchronous reverse-cycle ventilation of the upper and lower lobes), and 2 different types of alveolar recruitment (selective-lobe recruitment and continuous positive airway pressure of lower lobes, with continuous ventilation of the upper lobes). This tube is single or DLT, with a special contour and collapsed sheath in the posterior wall of the tube. This sheath forms an internal channel to allow the placement of a bronchoscope and a distal lobar tube. The authors then tested their tube using a mannequin, and found that the difficulty level was similar to that of a single-lumen tube, and that both the bronchoscope and lobar tube were placed successfully through the sheath. They then evaluated this tube in an ex vivo swine model to evaluate placement and differential ventilation, and found that not only could the shuttle and lobar tubes be properly positioned, but the authors successfully could perform regional ventilation in separate lobes. The last part of the study was in vivo testing performed in swine with ARDS. After successfully placing the shuttle and lobar tubes, they reported improved ventilation and oxygenation with a selective lobe strategy. The shuttle tube has potential uses in the ICU to provide protective ventilation in patients with ARDS, and the operating room in patients undergoing segmentectomy, where it can be used to isolate the affected segment, or in those patients who require but cannot tolerate OLV.

The effect of anesthetic choice on PPCs was discussed in multiple articles this year. A meta-analysis of 8 RCTs out of China reviewed the effects of sevoflurane versus propofol on the inflammatory response in lung resection.[40] The primary outcome was the concentration of the inflammatory cytokines TNF-α and IL-6 in blood, and the secondary outcome was the concentration in BAL of both the operative and nonoperative lungs. They reviewed a total of 488 patients undergoing lung resection, and reported that there was no difference between propofol or sevoflurane in the level of systemic inflammatory markers, but the use of sevoflurane was associated with a minor reduction in IL-6 in the BAL of both the operative and nonoperative lungs, suggesting a reduction in the local alveolar inflammatory response. Li et al., in an RCT, compared the effects of propofol, sevoflurane, and desflurane on PPCs in 555 patients undergoing lung resection, and found no difference in their primary outcome.[41] Citing no consensus for volatile anesthetics versus total intravenous anesthesia (TIVA), Lee et al. tackled this same question by comparing TIVA versus volatile anesthetics in a retrospective study of 579 patients undergoing pulmonary resection.[42] Again, no difference was seen in the rate of PPCs, although patients on TIVA had shorter LOS, ICU time, prolonged air leak, and time to chest tube removal.

The role of dexmedetomidine in thoracic surgery was examined in 2 studies. The first study by Ran et al. was a double-blind RCT of 102 patients that examined the role of dexmedetomidine in reducing the incidence of early postoperative cognitive decline.[43] A loading dose of 0.5 μg/kg was administered upon entering the operating room, then an infusion of 0.5 μg/kg was administered until the end of OLV, and then 200 μg were administered as patient-controlled analgesia (PCA). Cognitive decline was then compared with hydromorphone PCA. They found no difference between the 2 groups. Approximately one-third of patients in both groups experienced cognitive decline, but the dexmedetomidine group experienced less postoperative pain and reduced hospital LOS. A separate meta-analysis by Bai et al. concluded that dexmedetomidine significantly attenuated OLV-associated lung injury via decreased inflammatory responses.[44] The meta-analysis examined 20 clinical trials and 870 patients. The use of intraoperative dexmedetomidine resulted in decreased IL-6, TNF-α, and other inflammatory cytokines, and ameliorated oxygenation issues, although various component studies displayed heterogeneity in their results. Dexmedetomidine also was used in an RCT by An et al. investigating the use of opioid-free anesthesia (OFA) in patients undergoing lung resection requiring VATS.[45] In this study, 2 groups of 50 patients received thoracic paravertebral peripheral nerve blocks (PVB) with either intraoperative dexmedetomidine 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.

There were a few studies on the use of cerebral oximetry monitoring during OLV. Sato et al. examined the effects of desflurane, propofol, and remifentanil on regional cerebral oxygenation changes in an RCT that included 50 patients undergoing lung resection.[46] They reported that the effects of desflurane and propofol on cerebral oxygenation were equivalent. A separate prospective cohort study by Cui et al. examined the association between cerebral desaturation and postoperative delirium in thoracotomy patients requiring OLV.[47] Delirium was assessed through POD 5, in relation to minimum cerebral saturation during the case, as measured by forehead oximetry, with secondary analysis examining the area under the curve of hypoxemic events. Delirium occurred in 20% of 175 patients, and desaturation <90% for left and <85% for right oximetry, but not the nadir in value itself, may be associated with increased risk for delirium.

Nonopioid-Based Techniques

Nonopioid analgesic techniques were another focus in thoracic surgery this year. Pain in thoracic surgery is multifactorial, and generally due to the wound itself, the pain caused by the traction of the drainage tube, and the active pain caused by routine atomization inhalation, back buckle, deep breathing, and effective cough to prevent pulmonary infection.[48] Therefore, a considerable amount of research is being spent on managing pain after thoracic surgery, particularly as uncontrolled pain can lead to worsening lung function and/or acquisition of pulmonary pathologies. Due to the limited respiratory reserves of this patient population, opioids may place them at particular risk of sedation, altered sensorium, pneumonia, atelectasis, and respiratory failure, resulting in prolonged ICU LOS, duration of mechanical ventilation, and prolonged postoperative ileus.[49-51] The development of opioid-sparing techniques has the ability to reduce these complications.

Opioid-free anesthesia or opioid-sparing analgesia is the multimodality use of neuraxial or plane blocks in the thoracic nerve distribution, along with an array of pharmacologic agents that act on multiple receptors, including N-methyl-D-aspartate agonists, sodium-receptor blockers, alpha-2-agonists, non-steroidal antiinflammatory drugs, steroids, and the serotonin, dopamine, and norepinephrine-reuptake inhibitors. D'Amico et al. performed a systematic review and meta-analysis of 6 studies of 904 patients comparing the outcomes of patients receiving opioids to those receiving OFA.[52] Five of the 6 studies were retrospective, whereas only 1 was an RCT. All OFA groups did not receive any intraprocedural opioid in favor of "locoregional" techniques—neuraxial, PVB, and various plane blocks, as well as non-opioid adjuncts, including dexmedetomidine, nonsteroidal antiinflammatory drugs, acetaminophen, gabapentin, lidocaine, magnesium, and nefopam. Comparing OFA with opioid-based anesthesia (OBA), OFA was associated with a lower rate of any complication (74 of 175 [42%] *v* 200 of 294 [68%] $p < 0.001$), lower 48-hour morphine equivalent consumption ($p = 0.05$), and lower pain scores at 48 hours ($p = 0.02$). Despite the statistical significance, the average difference was 3 cm on a 100 cm visual analog pain score, and a total of 0.7 mg of morphine consumptive difference. Similar pain scores were reported at 24 hours. Length of stay was shorter in the OFA group. One of the studies evaluated OFA in patients undergoing thoracotomy. When that study was excluded, there were no statistically significant differences in pain or complications of LOS, suggesting that OFA is more beneficial in open procedures. Similarly, a retrospective propensity-matched analysis was performed by Selim et al., evaluating the benefit of OFA in VATS.[53] The OFA group (48 patients) received dexmedetomidine, lidocaine, ketamine, and acetaminophen, whereas the OBA control (33 patients) received remifentanil and morphine. Both groups received either a serratus anterior plane block (SAPB) or PVB, along with ketoprofen and nefopam. Postoperative pain and complications were assessed for up to 48 hours. Morphine consumption was reduced in the OFA group (28.5 mg *v* 55 mg, $p = 0.002$). Reduced pain scores were seen in the OFA group at 24 hours (2 *v* 3. $p = 0.064$) and at 48 hours (0 *v* 2.5, $p = 0.034$). No differences in respiratory or hemodynamic complications were noted. Sadowska et al. used skin-conducting algesimetry (SCA) to provide a quantitative and/or numerical assessment of opioid-sparing benefits. In this study, a PVB was performed and compared to the routine use of opioids in VATS procedures. The SCA uses the sympathetic response to pain-induced diaphoresis to detect changes in electrical resistance at the skin surface. The aim of the study was to determine the safety and effectiveness of OFA and the nociceptive response. They used $T_{3\text{-}4}$ PVB using 0.5% bupivacaine, in addition to ketamine and lidocaine infusions. As expected, intubation in the OFA group showed a greater response than in the opioid group, clarifying that the opioid-sparing techniques play their primary role in the thorax and not systemically. However, during the surgical opening, pleural drainage, and after anesthesia, the OFA group had a reduction in SCA nociceptive input, suggesting greater analgesic control. Equally important, this SCA data in 3 patients revealed that the PVB was inadequate and required the addition of opioids, which could be useful in determining the efficacy of these blocks in patients requiring thoracic surgery. Jiang et al. published a similar article comparing OFA to OBA from 2019 to 2021, looking at multiple outcomes—intraoperative blood loss, urine output, postoperative nausea and vomiting (PONV), shivering, postoperative pain, rates of atrial fibrillation, and postoperative pulmonary infection in patients requiring VATS.[54] The OFA group received dexmedetomidine, and the standard group received remifentanil. Both groups received opioids for anesthesia induction, and all patients could receive NSAIDs. Both groups received a T4-T5 PVB, SAPB block, pectoralis block, or thoracic epidural analgesia (TEA) at T4 to T5. In total, 1,975 patients were studied. In the OFA group, PONV was reduced significantly (14.7% *v* 18.9%, $p = 0.041$), rescue antiemetic was lower (7.5% *v* 12%, $p = 0.002$), but postoperative care unit (PACU) duration was longer though clinically insignificant (70.8 *v* 67 minutes; $p = 0.016$). In addition,

postoperative fever was reduced in the opioid-sparing group (11% *v* 7.7%, p = 0.032). No differences were found in the following postoperative symptoms: urinary retention, shivering, atrial fibrillation, pulmonary infection, hypoalbuminemia, or hypoxemia, nor intraoperative urine output, blood loss, postoperative pain, or the use of rescue analgesia at 48 hours. A retrospective study by Larue et al. compared OFA with dexmedetomidine and OBA with sufentanil in 151 thoracic surgical patients, and found that there were no differences in vasoactive agent requirements, total opioid consumption, or postoperative pain within the first 48 hours, but patients receiving OFA had a lower pain score at day 30, suggesting a reduction in hyperalgesia due to opioids.[55]

The use of novel pharmacologic agents has been studied in the thoracic surgical population in an attempt to reduce the incidence of postthoracotomy pain. Racemic ketamine, both S and R enantiomers, provide a well-established N-methyl-D-aspartate receptor antagonism, contributing to anesthesia and analgesia, though with numerous disadvantageous side effects. Esketamine, the S-form of ketamine, has been studied as an adjunct in OFA due to its lower incidence of side effects such as hallucinations, faster recovery, and the maintenance of hypoxic pulmonary vasoconstriction during OLV.[56] Additionally, it has a more substantial analgesic effect. Subanesthetic doses of S-ketamine can reduce acute opioid tolerance,[57] inhibit nociceptive hypersensitivity,[58] and, in this regard, show promise in opioid-sparing effects; however, this has not been examined in thoracic surgery. Yuan et al. performed a randomized, double-blinded, placebo-controlled study evaluating esketamine in thoracic surgery for the following endpoints: reducing perioperative opioid consumption, side effect rates from both esketamine and opioids, and 3-month postsurgical follow-up for the development of chronic pain.[59] Both groups received opioids intraoperatively in the form of hydromorphone, sufentanil, and remifentanil, and hydromorphone PCA postoperatively. A total of 82 patients were allocated to either esketamine 0.25 mcg/kg/h (K2 group), 0.15 mcg/kg/h (K1 group), or a placebo group after intubation. The authors reported that the K2 group had significantly reduced hydromorphone consumption in the first 24 and 48 hours postoperatively, as well as reduced extubation time and PACU stay, compared with the K1 and placebo groups. Comparing the K1 to the K2 group, the K2 group had a statistically significant reduction in opioid usage, with a shorter time to extubation, and higher patient satisfaction. The incidences of hallucinations (p = 0.198), drowsiness (p = 0.209), and itching (p = 0.264) did not differ among the 3 groups. Although both esketamine groups showed a reduction in chronic pain compared to the control group, there was no significant difference in the incidence of postoperative pain among the 3 groups at 3 (p = 0.187) and 6 months (p = 0.286) after surgery. The authors concluded that their study demonstrated the opioid-sparing effect of esketamine as a pain adjuvant in thoracoscopic surgery while contributing to postoperative recovery, confirming its value in patients requiring thoracic surgery. Another trial evaluated the role of S-ketamine in postoperative pain and perioperative neurocognitive disorder (PND) after VATS.[60] They divided patients into the following 3 groups: 1 group received general anesthesia (GA); the second group received GA + PVB; and the third group received GA + PVB + S-ketamine. All patients received intraoperative opioids (sufentanil and remifentanil) and a sufentanil PCA postoperatively. Cognitive function was measured using the Mini-Mental State Examination 1 day preoperatively, 1 day postoperatively, and 3 months postoperatively. A visual analog scale (VAS) score of 1 to 10 was used for pain comparison. The intraoperative heart rate and MAP were lower in the GA + PVB and GA + PVB + S-ketamine groups than in the control group. Patients in the GA + PVB + S-ketamine group exhibited significantly lower pain scores at 30 minutes and 24 hours (p = 0.001 and p = 0.004) postoperatively, as well as significantly lower rates of PONV and pulmonary complications ($p < 0.05$). The incidences of PND at 3 months in the GA + PVB and GA + PVB + S-ketamine groups were lower than in the control group; however, there were no significant differences in the incidence of PND among GA + PVB and GA + PVB + S-ketamine groups ($p > 0.05$). Furthermore, the results of this study indicated that the remifentanil dose used in the GA + PVB + S-ketamine group was significantly lower than that in the control and GA + PVB groups. Therefore, PVB combined with S-ketamine can maintain intraoperative hemodynamic stability while reducing acute postoperative pain.

Nefopam, a nonopioid, nonsteroidal, centrally-acting analgesic drug that is derivative of the non-sedative benzoxazocine, developed and known in the 1960s as fenazocine, is a multireceptor antagonist at the serotonin, norepinephrine, and dopamine receptors. Additionally, it reduces glutamate signaling via modulation of sodium and calcium channels.[61] Therefore, it was theorized that its use may help reduce opioids in thoracic surgery. Chen et al. studied the effect of nefopam compared to saline in 83 patients undergoing VATS. The nefopam group received 20 mg of nefopam preoperatively and 60 mg during the first 24 hours postoperatively.[62] Postoperative opioid usage and adverse effects, quality of recovery, hospital LOS, and the development of chronic pain were assessed. The nefopam group showed significantly lower cumulative opioid consumption during the first 24 hours (median difference: −270 μg [95% CI: −400 to −150 μg], $p < 0.001$) and 48 hours (median difference: −365 μg [95% CI: −610 to −140 μg], $p < 0.001$) postoperatively. The nefopam group did show a significantly lower pain score during coughing. However, there were no differences in the other postoperative outcomes, including quality of recovery, the occurrence of analgesic-related side effects, hospital LOS, or the development of chronic pain. Perioperative nefopam, although having a significant opioid-sparing effect in patients undergoing VATS, could be a feasible option for multimodal analgesia in these patients, but more data would be necessary to confirm this.

Research also has focused on modulating the inflammatory pathway, using the antiinflammatory agents ulinastatin and flurbiprofen, with the goal of optimizing lung function via the reduction of parenchymal damage. Hwang et al. designed a randomized, prospective study to evaluate the effect of the urinary trypsin inhibitor (UTI) ulinastatin on the inflammatory

response after VATS lobectomy in patients with lung cancer.[63] During OLV, inflammatory cytokines are released during lung damage caused by OLV and reexpansion ischemia-reperfusion that can promote further local and contralateral lung damage through systemic circulation. The anesthetic consisted of propofol remifentanil TIVA. A total of 14 patients in the UTI group received 300,000 units of ulinastatin, whereas 14 patients in the control group received saline. Inflammation was measured using the ratio of interferon-γ (IFN-γ)−IL-10, which is reduced during surgery. The baseline (time-0) IFN-γ−IL-4 ratio was not different between the groups (6,941.3 ± 2,778.7 *v* 6,954.3 ± 2,752.4 pg/mL, $p > 0.05$), but the IFN-γ−IL-4 ratio was significantly higher in the ulinastatin group at 30 minutes after entering the recovery room than in the control group (20,148.2 ± 5,054.3 *v* 6,674.0 ± 2,963.6, respectively; adjusted $p < 0.017$). The authors concluded that administering UTI attenuated the antiinflammatory response, and assumed a beneficial effect of UTI with respect to preventing cancer metastasis and recurrence and preserving the postoperative immune balance. Although OFA was not used and metrics in analgesia were not the aim of the trial, it may be a source of future trials to look into the antiinflammatory effects of UTI as it relates to reduction in analgesia requirements.

Flurbiprofen has been a component in some of the above studies as a part of multimodal analgesia for OFA and/or opioid-sparing analgesia in thoracic surgery. Shen et al. evaluated the effect of flurbiprofen on cerebral saturation ($rScO_2$), PaO_2 and postoperative delirium in 120 patients undergoing VATS lobectomy; 60 received the drug, and 60 received a placebo.[64] Compared to the placebo group, flurbiprofen treatment significantly improved both the intraoperative $rScO_2$ and PaO_2 and was associated with a reduced incidence of postoperative delirium.

In summary, opioid-free and opioid-sparing techniques using regional anesthesia and nonopioid adjuncts are being examined for their potential benefits in thoracic surgery. It is likely they may reduce overall opioid consumption and the untoward side effects, including PONV, decreased hospital and PACU LOS, and development of chronic pain. Research continues to focus on improving perioperative management through opioid-sparing modalities in this patient population.

Regional Anesthesia

Neuraxial Blockade

The use of ultrasound-guided nerve blocks continues to be increasingly popular for postoperative analgesia after thoracic surgery. Most notably, the thoracic PVB (TPVB), which is compared to other nerve blocks due to the safety and efficacy for the management of postthoracotomy pain. The studies this year focused on the use of ultrasound and the TPVB effects on coagulation, analgesia, and inflammation.

Ultrasound-guided needle placement has revolutionized TPVB placement. Zhang et al. conducted a study investigating the median effective volume (EV50) of an ultrasound-guided single shot of 0.3% ropivacaine TPVB for the thoracoscopic resection of lung cancer in 27 patients.[65] They administered differing doses of ropivacaine to determine an adequate block and reported that 14 (51.8%) patients had a successful block. The EV50 of 0.3% ropivacaine was 18.46 mL (95% CI 17.09-19.95 mL), and the EV95 was 20.89 mL, suggesting that approximately 21 mL of 0.3% ropivacaine was the optimal dose for a TPVB.

Kawase et al. set out to validate whether a higher dose of bupivacaine administered in continuous PVB (CPVB) provided a greater analgesic effect after VATS.[66] In this double-blind RCT, they hypothesized that levobupivacaine administered at 8 mL/h in CPVB after VATS provides a greater analgesic effect than 0.125% levobupivacaine at the same rate. The primary outcome was the VAS score during coughing on the morning of POD 1. The secondary outcomes were the VAS scores at rest and during coughing on POD 2, the number of anesthetized dermatomes, the frequency of rescue analgesics, PONV, patient satisfaction, and adverse events and complications. There were no significant differences in VAS scores during coughing on the morning of POD 1 between the low and high groups (median, 37.5 [IQR 21-50] *v* 40.0 [IQR 21-50], respectively; $p = 0.79$). Similarly, there were no significant differences in any secondary outcomes between the 2 groups. Levobupivacaine at 0.25% 8 mL/h in CPVB did not provide greater analgesia after VATS over the lower concentration.

Studies also focused on how to administer local anesthetics in the TPVB catheter. Programmed intermittent bolus infusion (PIBI) is thought to provide a more rapid and wider dermatomal spread of the sensory block compared to continuous infusion, but there is a concern that rapid infusion using the PIBI approach may cause increased absorption of local anesthetics into the bloodstream, which may lead to some side effects, including local anesthetic toxicity. There were 3 studies in the recent literature to answer that question.

Liu et al. performed an RCT to compare the effects of PIBI, continuous thoracic paravertebral infusion (CTPI), and continuous intravenous infusion (CII) of an opioid on postoperative analgesia in patients undergoing VATS.[67] The primary outcome was the numeric rating scale (NRS) score at rest and during coughing at 1, 4, 24, and 48 hours after surgery. Secondary outcomes included PCA use, ropivacaine use, Ramsay Sedation Scale score, quality of recovery-15 (QoR-15) score, values of hemodynamic parameters at different periods, intraoperative consumption of anesthetic drugs, and postoperative adverse events. They reported that postoperatively, the NRS score was reduced in the PIBI group compared with the CTPI and CII groups at rest and during coughing ($p < 0.05$). Patient-controlled analgesia use was reduced, and the QoR-15 score increased in the PIBI group compared with the CTPI and CII groups ($p = 0.001$ and $p = 0.000$, respectively). A study by Lee et al. aimed to investigate the effects of programmed intermittent versus continuous epidural bolus administration for controlling night-time pain and improving sleep quality within the first 48 hours after thoracotomy.[68] They assessed the degree of analgesia using the VAS and the patients' sleep condition on PODs 0 and 1, as well as other adverse events. They found that the programmed intermittent epidural bolus technique of

patient-controlled epidural analgesia reduced postoperative night-time pain and improved sleep quality in patients undergoing thoracotomy. In the third study, using the NRS at multiple time points, Yang et al. compared the analgesic effects among PIBI, continuous infusion, and PIBI + continuous infusion in an RCT of 112 patients who underwent VATS.[69] They reported that patients with the PIBI + continuous infusion combination had lower NRS scores than the continuous infusion group at 12, 24, and 48 hours postoperatively ($p < 0.05$), both during resting and when coughing ($p < 0.01$). The PIBI + continuous infusion group had lower NRS scores than the PIBI group at 24 hours when patients were coughing ($p < 0.01$). Additionally, the 2-day cumulative dosage of PCA in the PIBI + continuous infusion group was lower than both the continuous infusion and PIBI groups ($p < 0.01$), and the number of blocked dermatomes in the PIBI and PIBI + continuous infusion groups were comparable and were both wider than the continuous infusion group at 24 hours ($p < 0.01$).

Yuan et al. designed a prospective, randomized, double-blind, placebo-controlled trial to investigate the effect of TPVB (T) compared to saline on blood coagulation in 60 patients after thoracoscopic lobectomy.[70] The primary outcome was thromboelastogram parameters before anesthesia (T0), at the end of surgery (T1), and on PODs 1 (T2) and 2 (T3). Compared with the placebo group, the TPVB group had significantly longer R and K values, and the α-angle and maximum amplitude values were significantly reduced at the T2 and T3 time points, suggesting that TPVB is beneficial to improve postoperative hypercoagulability and to promote postoperative rehabilitation of patients after thoracoscopic lobectomy.

Liu et al. compared the analgesic, tumor marker, and immunologic effects of TPVB, SAPB, and no block in 132 patients undergoing single-portal thoracoscopic surgery of lung cancer in a prospective randomized trial.[71] They reported that patients in the TPVB and SAPB groups had lower intraoperative opioid requirement, later time to PCA requirement, and reduced PCA doses than the control group. The TPVR and SABP groups had lower VAS scores and lower T suppressor cell and serum tumor markers than the controls, suggesting that regional anesthesia positively affects healing and tumor recurrence. There were no differences in adverse events and no difference in the analgesic or immunologic effects of TPVB and SAPB. Okuda et al. tested the hypothesis that TEA could attenuate systemic and local inflammatory cytokine production in patients undergoing lung cancer surgery.[72] They performed a prospective RCT of 60 patients with lung cancer who were allocated randomly into the following 2 groups (n = 30 each group): the epidural group (group E), in which anesthesia was maintained with propofol, fentanyl, rocuronium, and TEA with 0.25% levobupivacaine, or the remifentanil group (group R), in which a remifentanil infusion replaced TEA. Lung epithelial lining fluid (ELF) and blood sampling were collected before OLV at OLV initiation (T1) and 30 minutes after the end of OLV (T2). The concentrations of TNF-α, IL-6, and IL-10 in the ELF at T2 were increased significantly compared with those at T1 in both groups. The ELF concentration of IL-6 in group E was significantly lower than that in group R at T2 (median [IQR]: 39.7 [13.8-80.2] *v* 76.1 [44.9-138.2], p = 0.008). Plasma IL-6 concentrations of IL-6 and TNF- α were not significantly different between the 2 groups. This RCT suggested that TEA could attenuate local inflammatory responses in the lungs during lung cancer surgery.

Tong et al. performed a retrospective study to determine whether the addition of TPVB to GA could reduce the incidence of adverse outcomes.[73] They studied 13,966 patients who received VATS for lung cancer, and compared GA to GA + TPVB using propensity score matching. They reported that TPVB was placed in 14.8% of patients and that the GA + TPVB group had lower incidences of PPCs (30.4% *v* 33.5%, p = 0.005), postoperative atrial fibrillation (2.1% *v* 2.9%, p = 0.041), and shorter hospital LOS (median [IQR]; 5 [4-5] *v* 5 [4-6]) days, $p < 0.001$) compared to GA alone, suggesting a benefit for TPVB.

Postoperative delirium is a relatively common and serious complication associated with longer hospital stays, morbidity and mortality, the need for long-term care amenities, and increased healthcare resource expenditure.[74] Wei et al. performed an RCT on 338 older adult patients aged 65-80 years undergoing VATS lobectomy to study the effect of GA with TPVB on the incidence of postoperative delirium. In this cohort, delirium occurred in 47 (28%) of 168 patients in the opioid group, and 28 (16.5%) of the 170 patients in the TPVB group (RR 1.7, p = 0.03). This was associated with smaller increases in surgery-induced TNF-α and neurofilament light levels, suggesting that the antiinflammatory and analgesic properties of the TPVB can reduce postoperative delirium in the older population. Although TPVB was associated with earlier chest tube withdrawal (4.53 ± 1.71 *v* 5.92 ± 2.03 days, $p < 0.01$) and a higher rate of overall recovery at POD 7 (27.1% *v* 17.3%, p = 0.013), there was no significant difference in hospital LOS.

Vijitpavan et al. conducted an RCT comparing intrathecal morphine (ITM) to intravenous PCA for analgesia after VATS in 38 patients.[75] The ITM group received a single shot of 0.2 mg of ITM before GA, and the control group received only GA. For 48 hours postoperatively, the patients received a morphine PCA and oral acetaminophen 4 times daily. Postoperative pain scores, PCA morphine requirement, side effects, sedation at 1, 6, 12, 24, and 48 hours, and overall treatment satisfaction scores were assessed. The ITM group had reduced postoperative pain scores (p = 0.006), a lower PCA requirement, and a higher incidence of pruritis. Although there were no significant differences in PONV, sedation scores, and satisfaction scores between the 2 groups, the opioid requirement and pain scores in both groups were high, suggesting that opioids alone may be inadequate to fully treat post-VATS pain.

Fascial Plane Blocks

Research this year focused on the comparison of the different fascial blocks to neuraxial blocks and to each other in an attempt to determine the optimal block for the different

thoracic surgical procedures. Sertcakacilar et al. performed a retrospective analysis comparing single-shot erector spinae plane block (ESPB) to single-shot PVB for single-port VATS in 250 patients.[76] The primary outcome was morphine consumption in 24 hours, with secondary outcomes being static and dynamic pain scores at several time points over the first 24 hours. The analysis of morphine consumption over the first 24 hours demonstrated a reduction in morphine requirement favoring the PVB group, 11 versus 20 mg. Both static and dynamic pain scores remained relatively low at all time points, not exceeding an NRS of 4 at any time. Although this study did demonstrate a statistically significant benefit of PVB over ESP block, the clinical significance of the reported outcomes was likely minimal.

A study by Dikici et al. evaluated the use of preoperative SAPB to preoperative infiltration of the trochar sites from the depth of the pleura to the skin in patients undergoing VATS.[77] Results of this study demonstrated a significant delay in the time until the first PCA dose, heavily favoring the SAPB group, 160 versus 7 minutes. It also demonstrated statistically and clinically significant decreases in both rest and dynamic pain scores up to 12 hours postoperatively. Morphine consumption also was found to be reduced in the SAPB group at all time points out to 48 hours. Zengin et al. compared the use of single-shot SAPB to that of ESPB, and aimed to assess static and dynamic pain scores.[78] Evaluations of rest and dynamic pain out to 24 hours were evaluated, and they reported no difference between the 2 approaches regarding NRS at any time point. Pain scores remained low in both groups, VAS <3, denoting good analgesia in both groups. Hassan et al. compared single-shot ESPB, SAPB, and a control.[79] A total of 90 patients were randomized to equal-sized groups, and opioid consumption, rest and dynamic pain scores, and postoperative pulmonary function were recorded. This study demonstrated the superiority of ESPB blocks to SAPB and to control, with morphine consumption of 8.5 *v* 19.5 *v* 36 mg, respectively. Group characteristics also demonstrated preserved respiratory function, favoring the ESPB group over the SAPB and control cohorts. A similar pattern also was observed when evaluating pain scores up to 24 hours, with the ESPB group averaging an NRS score of 3, SAPB averaging 4, and the control group averaging 4.5. Equally important to the postoperative pain scores, the authors evaluated forced vital capacity (FVC) and forced expiratory volume at 1 second (FEV_1), and found that the ESPB group best maintained pulmonary function at 24 hours compared to the control.

Another block that has been gaining in popularity is the rhomboid intercostal block (RIB). Deng et al. attempted to identify the optimal dose of local anesthesia required for this block by evaluating patients in the following 4 groups: control and ropivacaine 0.2%, 0.3%, and 0.4%.[80] The primary outcome, the QoR-40, found statistically significant improvements favoring the 0.3% and 0.4% groups. Rest and dynamic pain scores were also statistically improved in these 2 groups compared to the control and 0.2% ropivacaine groups, leading to the conclusion that 0.3% ropivacaine is the ideal concentration for this block. Zhang et al. recently published a prospective RCT comparing the use of ESPB, RIB, and SAPB regarding postoperative pain scores, opioid consumption, and patient satisfaction.[81] A total of 90 patients undergoing VATS were randomized to 1 of each ultrasound-guided regional plane block, and followed for 48 hours postoperatively. The study demonstrated a statistically significant decrease in sufentanil consumption at 0-12 hours and 12-24-hour time frames, favoring the ESP and RIB blocks over SAPB. This trend was continued at the 12-24-hour time frame, demonstrating a more modest decrease in opioid consumption. Although the results reached statistical significance, the clinical differences remained minimal, and this would support the use of any of the regional techniques. Reported pain scores at rest failed to reveal a difference among the different study blocks, but there was an improvement in dynamic pain scores from 6-24-hour time points, favoring ESP and RIB blocks over the SAPB block.

Most studies evaluating facial plane blocks for thoracic surgery procedures primarily focused on single-shot blocks, which likely limited their efficacy to 24 hours. It is possible to insert an indwelling catheter during block placement, but the utility of these catheters is limited by pumps with only continuous infusion abilities. Fascial plane blocks typically rely on volume to provide adequate spread of the local anesthetic, thus spreading to a larger anatomic coverage. Xin et al. conducted a small retrospective analysis comparing ESP catheters placed preoperatively by an anesthesiologist to extrapleural catheters placed intraoperatively by the thoracic surgeon.[82] They reported that the rest and dynamic pain scores of patients with ESP catheters were superior for the first 24 hours postoperatively. Taketa et al. compared the dosing of ESP catheters and randomized patients to either a continuous infusion of 8 mL/h of 0.2% ropivacaine versus intermittent boluses of 8 mL of 0.2% ropivacaine every 2 hours.[83] The dermatomal anesthesia was evaluated at 5 and 21 hours, and the authors found that the intermittent-bolus group maintained a wider area of anatomic coverage at both time points in the paraspinal, midclavicular, and anterior axial regions, averaging 1-2 additional dermatomes covered. This study also found a statistically significant but clinically insignificant decrease in morphine consumption over the first 24 hours, which was not replicated in the second 24-hour period. Intermittent boluses allowed for greater coverage area despite using only half of the volume of local anesthetic over the same period, likely providing an improved safety profile, especially in patients at higher risk of local anesthetic systemic toxicity. Moorthy et al. published an RCT comparing ESP catheters to PVB catheters, with the primary outcome being the QoR-15 and secondary outcomes, including pain scores, opioid consumption, pulmonary function, and the incidences of chronic postsurgical pain.[84] Patients were evaluated at 24 and 48 hours postoperatively, and the QoR-15 was found to favor the ESP group at both time points. No differences in postoperative pain scores, opioid consumption, or peak inspiratory flows were noted at any time point; however, there was less PONV in the ESPB group. The existing body of evidence evaluating fascial plane blocks demonstrates good efficacy in decreasing pain scores and opioid consumption while

maintaining respiratory parameters after VATS. Current literature likely favors ESPB over RIB and SAPB, although the latter still maintains a significant decrease in NRS and analgesic consumption. The current evidence evaluating indwelling fascial plane catheter requires further evaluation before routinely adapting this analgesic technique. Although indwelling catheters show promise up to 24 hours, the evidence for later time frames remains scant. This lack of reported evidence may be secondary to limited perfusion pumps with intermittent bolus ability, or disruption of the fascial planes during surgery, which could affect the spread of the local anesthetic instilled by the infusion pump.

Special Techniques in Thoracic Anesthesiology

This year, the research included a focus on unconventional anesthetic management for special thoracic procedures. Namely, researchers explored alternative ventilation and oxygenation strategies for risky procedures involving the airway, as well as exploring regional anesthetic techniques to optimize patient outcomes and avoid the use of GA in risky patient populations. As the evolution of thoracic and airway procedures unfold, so do anesthetic management strategies.

Management Strategies in Airway Resection Procedures

Airway management during tracheal resection presents challenges for both anesthesiologists and surgeons. Besides maintaining ventilation and gas exchange, the anesthetic technique should provide optimal conditions to perform the procedure. Standard management involves endotracheal intubation, with the ETT placed at the vocal cords during tracheal resection. Once the trachea is discontinuous, a sterile ETT is inserted into the distal trachea to maintain gas exchange (cross-field intubation). Once the anastomosis is completed, the ETT in the proximal trachea is advanced. This presents potential challenges—the introduction of the ETT after completion of the anastomosis presents a trauma risk, and the cuff may exert pressure on a fresh anastomosis, potentially stunting the healing process.

Defosse et al. addressed these issues in a single-center prospective study assessing the feasibility of laryngeal mask airway (LMA) use with positive-pressure ventilation (PPV) in conjunction with high-frequency jet ventilation (HFJV) in 10 patients undergoing tracheal resection.[85] High-frequency jet ventilation was introduced via an airway exchange catheter during the resection of the trachea, then PPV with LMA resumed once the anastomosis was completed. Arterial blood gasses were drawn throughout the perioperative setting. The average HFJV time was 25.0 (20.5-27.8) minutes, with the lowest PaO_2 during HFJV of 93 mmHg. There were no significant differences in arterial blood gasses values preoperatively and postoperatively, and no one required emergency cross-field intubation, demonstrating the feasibility of this technique during tracheal resection. This strategy improves visualization for surgeons, may promote anastomotic healing, and reduces the risk of ETT-induced trauma.

A similar strategy was employed by Qui et al. for patients undergoing carinal resection.[86] They hypothesized that HFJV, administered by an exchange tube through an ETT or LMA, would improve surgical exposure, decrease operating time, and decrease airway trauma by avoiding repetitive intubations to the distal airway. The authors conducted a retrospective analysis comparing HFJV to the conventional approach, with a primary outcome of hypoxemic events (SpO_2 <90% for >1 minute). They included 32 patients in their analysis (10 HFJV and 22 cross-field ventilation). The median area under the curve for the cross-field ventilation group and the HFJV was 21.92 and 28.93 minutes ($p = 0.366$), respectively. There were no significant differences in cumulative hypoxemia or hospital LOS. The cross-field ventilation group had 1 death and 1 continuous air leak, whereas the HFJV group had no severe complications. The median operating time in the HFJV group (240 minutes) was about 40 minutes longer than the cross-field ventilation group; authors attributed this to a higher incidence of VATS in the HFJV group rather than the cross-field ventilation group (6/10 *v* 1/22). Nonetheless, this study again demonstrated the safety and efficacy of HJFV use in airway resection surgery.

The use of HFJV in airway resection received much attention in the past year. Given the complexity of these procedures, HFJV can be administered through various devices. Ly et al. conducted a prospective single-center study with 16 subjects, comparing outcomes with HFJV administration via ETT, LMA, and airway-exchange catheters.[87] Contingent on the degree and location of stenosis, patients were assigned to intubation with an ETT proximal to the lesion in 4 patients, ETT distal to the lesion in 6, LMA in 3, tracheostomy in 2, and airway-exchange catheter in 1 patient. Arterial blood gasses were analyzed at various time points throughout the perioperative setting. Results showed an average apnea time of 20.91 ± 2.53 minutes, with both PaO_2 and $PaCO_2$ increasing significantly during the apnea−HFJV period (PaO_2: 186.19 ± 60.14, $PaCO_2$: 79.63 ± 13.39), resulting in a subsequent transient decrease in pH (7.17 ± 0.05). All arterial blood gasses values normalized postoperatively once ventilation resumed. One patient required cross-field intubation and ventilation due to hypoxia. Researchers, again, demonstrated that the use of HFJV is a feasible option for tracheal resection procedures in patients who can tolerate transient acute respiratory acidosis.

In a single-center retrospective analysis, Zhou et al. described an anesthetic technique that allows for spontaneous ventilation during tracheal resection.[88] A total of 51 patients were anesthetized using an LMA, TIVA with propofol and remifentanil, and regional anesthesia using bilateral cervical plexus blocks (CPB) with or without TEA. Before resection, a hollow tube was placed in the distal airway during the resection for possible HFJV. Any hypoxemia or hypercapnia was treated with HFJV initially, and cross-field intubation was used for intractable hypoxia, hypercarbia, bleeding, pneumothorax, persistent cough, and changes in the surgical approach. Of the 51 patients, 2 (3.9%) required HFJV, but spontaneous ventilation was maintained. Three patients required cross-field intubation, 2 for pneumothoraces, and 1 for persistent cough

that interrupted the surgery. The LMA was removed in all patients once they were fully awake. The median hospital stay was 6.31 ± 4.30 days. Postoperative complications included 6 pneumothoraces (11.8%), 1 pleural effusion requiring drainage (2%), 1 atrial arrhythmia (2%), and 1 death during the follow-up period (2%). The authors demonstrated that spontaneous ventilation through LMA is a useful alternative to mitigate the risks associated with ETT intubation and HFJV while permitting adequate surgical exposure.

Analgesic Strategies in Thoracic Procedures

Emergence agitation (EA) can be manifested by excitement, disorientation, and inappropriate behavior during awakening from anesthesia. It is commonly associated with GA, and has a higher incidence among patients undergoing thoracic procedures. In a prospective RCT, Meng et al. attempted to address EA and minimize its incidence in 602 subjects undergoing VATS for segmentectomy and/or lobectomy with the use of preoperative butorphanol infusion, which may reduce EA through its actions on kappa and delta receptors.[89] These patients were assigned randomly to receive a butorphanol infusion (0.02 mg/kg over 1 minute) or control (normal saline) before the induction of anesthesia. Peripheral nerve blocks were performed after induction. Emergence agitation was present 5 minutes after extubation in 29 out of 296 patients (9.8%) in the butorphanol group, and 75 out of 306 (24.5%) in the control group ($p = 0.0001$). The NRS pain score also was assessed as a secondary outcome; NRS >5 15 minutes after arrival to the PACU was significantly lower in the butorphanol group (23/296 [7.8%] compared to the control group [56/306 (18.3%)]; [$p = 0.03$]). The authors concluded that butorphanol appears to be a safe and effective agent in reducing EA in the VATS patient population.

The invasive nature of thoracic lung surgeries and subsequent stress encountered render many patients ineligible for surgery or places them at significant risk. Local thermal ablation therapy for lung tumors has distinct advantages over traditional surgical resection—less trauma, faster recovery, fewer complications, ease, and convenience. This technique, administered primarily with the use of radiofrequency ablation (RFA) or microwave ablation, tends to be more suitable for higher-risk patients. However, a conventional anesthetic management strategy has not been established with this procedure. In a prospective single-arm study, Cheng et al. aimed to assess the efficacy and safety of TPVB in patients undergoing lung ablation therapy.[90] They performed TPVB using 15 mL of 0.375% ropivacaine in 30 patients 20 minutes before RFA or microwave ablation, and assessed pain using the VAS. Their results were promising, with no patient requiring conversion to GA—93.9% of patients had significant pain relief (VAS ≤2), and 78.8% had complete relief (VAS ≤1). Contralateral segmental sensory blockade was reported in 5 subjects (15.2%), suggesting possible epidural or paravertebral spread. Thoracic PVB is a safe and efficacious anesthetic strategy for lung ablation procedures that mitigates risks associated with sedation and GA. In a separate retrospective cohort analysis, Garcia et al. conducted a similar assessment of the efficacy of TPVB in patients receiving thoracic RFA.[91] A total of 17 patients received a TPVB 20 minutes before RFA, between T4 to T8, with 20 mL of 2% lidocaine and 2 mg of midazolam as sedation. As with the previous study, no patients required conversion to GA. Two patients required an alfentanil bolus during the procedure for pleuritic pain. No patient required rescue analgesia in the PACU. Their results also demonstrated that TPVB is a safe and effective anesthetic strategy for the RFA procedure; it reduces respiratory complications associated with GA and provides adequate analgesia.

The use of regional techniques to avoid GA was reiterated in an RCT performed by Sahin et al.[92] Although tracheostomies traditionally are performed under GA with an ETT, there are some patients who present challenges in securing the airway. These include patients with maxillofacial trauma, angioedema, and upper airway tumors. These authors aimed to assess the procedural comfort of bilateral CPB in adjunct with translaryngeal blocks in patients requiring tracheostomy for large tumors. They randomized 29 subjects scheduled for elective or emergent tracheostomy into 2 groups. Group 1 received bilateral superficial CPB with 15 mL of 0.5% bupivacaine (n = 14), and group 2 received bilateral superficial CPB with 15 mL of 0.5% bupivacaine and a translaryngeal block with 5 mL of 2% lidocaine (n = 15). The providers were blinded to the groups. Midazolam, 0.03 mg/kg, was administered to each patient. Tolerance (assessed by a tracheostomy cannula comfort score) was higher in group 1 when compared to group 2 ($p < 0.001$). There were otherwise no significant differences between the 2 two groups with regard to total analgesic consumption, NRS pain score related to the incision, at rest, and with mobilization, time to first analgesic demand, and the presence of nausea and vomiting, demonstrating that superficial CPB, in conjunction with translaryngeal blocks in patients undergoing tracheostomy, is an adequate alternative to GA and may be favorable in patients with difficult airway access. In addition to avoiding oral ETT intubation of a difficult airway, this technique provides the added benefit of patient comfort.

Mediastinal masses often present challenging airway and hemodynamic risks during anesthetic management. The induction period is particularly high-risk, with the dreaded potential complication of airway collapse. Classically, it is taught that the use of neuromuscular blockade (NMB) and PPV should be avoided in this patient population. However, there is a lack of evidence for this, and the mechanism is ill-defined.[93] Hartigan et al. aimed to challenge this theory by investigating the anesthetic induction in patients with mediastinal masses with moderate to severe tracheobronchial compromise while using NMB and PPV under bronchoscopy.[93] The authors analyzed data from 17 patients. After the placement of preinduction arterial and venous catheters, the airway was anesthetized with 2% lidocaine. Airway management included an awake fiberoptic placement of an 8.5 mm oral ETT or a supraglottic airway. A continuous bronchoscopic recording of the airway stenosis was attained during inhalation induction with sevoflurane, PPV with bag-mask ventilation, and the administration of NMBs (either succinylcholine or nondepolarizing agents). The

authors scored the airway caliber (−2 to +2) throughout this period as follows: unchanged = 0; 25% to 50% larger = +1, >50% larger = +2, 25% to 50% smaller = −1, >50% smaller = −2. The mean airway patency scores after induction with GA were not associated with clinically significant airway change (0 [95% CI, 0-0]; p = 0.953). Airway caliber increased after the administration of PPV (0 [95% CI, 0-1]; p = 0.024), followed by a subsequent increase after NMB administration (1 [95% CI, 0-1]; p < 0.001). This study found an increase in airway patency after initiation of PPV and administration of NMB compared to awake, spontaneously breathing patients, ultimately challenging traditional dogma adopted by anesthesiologists.

ECMO in Thoracic Surgery

Complex thoracic surgical procedures, including the reconstruction of major airways and the resection of large mediastinal tumors, especially those that compromise major vascular structures, are undertaken with great perioperative risk. The airways and major cardiovascular structures can be compromised at any time, making the maintenance of normal oxygenation, ventilation, and cardiac output a tricky endeavor. Historically, these procedures have been supported with advanced ventilation techniques, including jet ventilation or the use of cardiopulmonary bypass. The use of ECMO increasingly is being used as an important supportive tool during complex thoracic surgery.[6]

In 2022, there was an expansion of the literature on the use of venovenous (VV) and venoarterial ECMO to support cardiorespiratory function during complex thoracic surgery, including novel applications of ECMO, and reviewing data on the use of ECMO to support patients after thoracic surgery. Unfortunately, the quality of data remained limited to large retrospective reviews, registry data, and case series as opposed to prospective controlled trials. ECMO continues to be regarded as the preferred modality of mechanical circulatory support for thoracic surgery because of documented reductions in the incidences of massive hemorrhage and major systemic inflammatory response, and has largely replaced cardiopulmonary bypass. Extracorporeal membrane oxygenation continues to be used most frequently for the resection of obstructing tracheal and carinal lesions, large thoracic masses, including those invading the heart and great vessels, and caval reconstruction. Extracorporeal membrane oxygenation is an important supportive measure in patients with pulmonary hypertension and right ventricular dysfunction, and recently has been recognized by the ASA in their difficult airway guidelines.[94]

Zhang et al. conducted the largest case series, highlighting 15 patients who underwent complex thoracic surgery, with a 1-year follow-up.[95] Consistent with previous case series, they demonstrated a 1-year survival >80%, and all patients were decannulated successfully from ECMO postoperatively. As is the case in many high-volume ECMO centers, they have created a systematic process for managing these patients, highlighting the need for expert personnel to be available in the operating room. They captured what they considered to be the most salient aspects of ECMO management into the 5 A's—adequate tissue perfusion, accurate protective pulmonary ventilation, appropriate anticoagulation, available anti-inflammation, and accurate evaluation for ECMO weaning.

Venovenous ECMO appears to be most frequently used in the thoracic operating room for major airway surgery. It was shown recently to facilitate a successful tracheal reconstruction with a uniportal approach.[96] There was also a report from Lee et al. of an obstructing tracheal mass managed successfully with VV ECMO. This report highlighted the need for expert personnel to always be available for these cases for cannula troubleshooting and repositioning. In this patient, there was hypoxemia on VV ECMO, likely from recirculation due to a malpositioned inflow cannula.[97]

Besides complex thoracic surgery, there are reports of ECMO use to support patients with advanced comorbidities, such as cardiomyopathies or end-stage lung disease. Rocha et al. described a patient with severe emphysema, after multiple unsuccessful attempts at endoscopic lung volume reduction, who was supported successfully on VV ECMO for robotic-assisted lung volume reduction.[98] Venovenous ECMO allowed for the maintenance of baseline oxygenation and ventilation, allowing for a successful decannulation at the end of the procedure and an uneventful recovery and discharge on Day 5. Novellis et al. reported on a patient who initially was deemed unfit to undergo VATS lobectomy for NSCLC because of advanced congestive heart failure and an ischemic cardiomyopathy with an ejection fraction of 23%.[99] This patient was supported successfully on venoarterial ECMO for the duration of the procedure, was extubated immediately postoperatively, and discharged on POD 3. These reports highlighted the utility and improved safety profile of ECMO support for high-risk patients with advanced cardiorespiratory disease who would otherwise not be deemed a candidate for life-sustaining surgery.

Although the use of ECMO as an intraoperative support device during complex thoracic surgery is well- established, the data are less clear on the benefits of ECMO postoperatively in patients who develop cardiorespiratory failure after thoracic cancer resection. The incidence of acute respiratory failure after lung resection surgery is low; however, the mortality rate in these patients is upwards of 40% to 60%. It is unclear whether ECMO support in these patients improves their prognosis. Suzuki et al. examined the Extracorporeal Life Support Registry from 2000 to 2019 to assess the outcomes of patients requiring ECMO support after lung cancer resection. They analyzed 498 patients receiving postoperative ECMO after surgery for cancer of the airways, lung and pleura, heart, mediastinum, and esophagus. Survival to hospital discharge occurred in 39.8% of patients. Upper airway neoplasms were associated with better survival (73.5%; p = 0.005), whereas lung neoplasms were associated with worse survival (30.0%; p < 0.001). Survival in patients requiring rescue ECMO for postoperative respiratory failure was 71.4% after tracheal procedures, but only 13.3% after pneumonectomy, 23.7% after any lung resection, and 21.4% after esophageal procedures.[100]

In these patients, ECMO was likely to be a futile measure.[101] Feeney et al. published their results on outcomes for their postoperative patients who received VV ECMO for ARDS from 2011 to 2019.[102] In 40 patients receiving postoperative VV ECMO after thoracic surgery, 62% underwent esophagectomy, and 28% underwent lung resection. Their 30-day survival was 62.5%, where 52.5% were discharged from the hospital, and of those discharged, the 90-day survival was 80%. Patients in their cohort were more likely to survive if they did not suffer an ECMO-related complication; however, they were unable to find any association between benign versus malignant processes, cancer staging characteristics, the use of chemotherapy, or intraoperative versus postoperative cannulation. These 2 studies reported conflicting data with respect to outcomes and, unfortunately, could not delineate any prognostic factors, which may portend a favorable outcome in this highly complex and heterogeneous population. Extracorporeal membrane oxygenation use in this setting should be highly individualized based on the likelihood of recovery from the disease process and the oncologic prognosis of the patient.

Enhanced Recovery After Surgery in Thoracic Surgery

Since enhanced recovery after surgery (ERAS) protocols in thoracic surgery have been developed, research has focused on improvements to the technique and outcomes. Mena et al. analyzed the impact of ketamine and dexmedetomidine infusions as an opioid-free option from single-center data of 1,630 patients, of whom 117 matched pairs received ketamine and dexmedetomidine.[103] Although the raw analysis demonstrated lower pain scores and less opioid usage in the dexmedetomidine and ketamine group, there were no differences in the PACU or hospital stay after adjusting for multiplicity. Both groups had similar rates of pulmonary complications (5.9% *v* 9.4%, p = 0.326), ileus (0.9% *v* 0.9%, p = 1.00), and 30-day readmission (2.6% *v* 4.3%, p = 0.722), suggesting that ketamine and dexmedetomidine infusions can be opioid-sparing with no increase in complication rate. Most of the ERAS pathways provide short-term benefits of reduced opioid usage in the perioperative period. To evaluate the effect of ERAS on long-term postoperative opioid use, Turner et al. analyzed 240 patients who required pulmonary resection, of which 85 were performed using an ERAS protocol, and demonstrated that long-term opioid use of up to 1 year postoperatively, and new persistent opioid use remained the same in both groups. No differences in opioid usage were seen from POD 14 in their multivariate analysis.[104] A single-center retrospective cohort study by Kodia et al. evaluated outcomes after modifying their ERAS protocol by replacing the saline diluent for liposomal bupivacaine with 0.25% bupivacaine and adding tramadol, as needed.[105] They observed a significant reduction in overall opioid usage without a change in the hospital stay or pain control. Modifications in the ERAS protocol can help to reduce opioid usage in this patient population.

Other literature this year focused on outcomes. Tiberi et al. compared the use of uniportal to multiportal incisions using an ERAS protocol.[106] They analyzed 1,167 patients, of whom 185 were enrolled for uniport VATS, and observed shorter hospital stays (3.13 *v* 4.19 days, $p < 0.001$) for patients who had uniportal lobectomy, segmentectomy, and wedge resection. There were no differences in cardiopulmonary complications and readmission rates between the 2 groups. Yang et al. analyzed data from 272 patients who required ERAS, of whom 91 underwent noninvasive VATS, and the outcomes were comparable with conventionally intubated parents in their cohort.[107] Qi et al., in their single-center study of 100 patients, observed less intraoperative remifentanil dosage, less fluctuation in the hemodynamic parameters, lower postoperative pain scores, and reduced medical expenses, along with fewer increases in C-reactive protein in the nonintubated group compared to the conventionally intubated group ($p < 0.05$).[108] Merritt et al. performed a single-center retrospective analysis of 574 patients who underwent robotic-assisted lung resection, using an ERAS protocol in 259 of them. They demonstrated significant reductions in the ERAS group regarding weight-adjusted mean direct hospital costs ($p < 0.001$) and mean indirect costs ($p = 0.018$) for the total hospital stay, as well as a significant decrease in prescribed opioid medication on discharge.[109] Thomson et al. evaluated the impact of introducing an ERAS protocol in 704 patients in a single-center study.[110] They demonstrated that the implementation of this protocol resulted in shorter hospital stays (4.7 *v* 6.2 days, post- versus pre-ERAS), expedited feeding, ambulation, and chest tube removal, higher 6MWD test scores (402 *v* 371 meters, post- versus pre-ERAS, $p < 0.05$) without an increase in readmissions, at the same time maintaining a high level of patient satisfaction and overall quality of life. The adoption of ERAS led to improvements in multiple process-of-care measures, which eventually achieved the optimization of clinical outcomes. Enhanced recovery after surgery alone in VATS has shown a significant reduction in overall cost, and combining it with robotic surgeries further reduced total cost ($p = 0.004$) and LOS ($p < 0.001$). Enhanced recovery after surgery implementation and the robotic approach were independently associated with LOS reduction and cost savings in patients undergoing minimally invasive lobectomy.[111]

Days alive and out of hospital (DAOH) integrates hospitalization, readmissions, and mortality, and is one of the newer ways of reporting outcome measures in the perioperative setting. There are limited data using DAOH in thoracic surgeries. Huang et al., in their single-center retrospective study of 316 lobectomy patients, analyzed outcomes based on DAOH, and observed that DAOH was reduced by 6 median days with an already successfully implemented ERAS program.[112] Air leak, adjuvant chemotherapy, and recurrence of tumor were considered potential contributing factors for a reduction in DAOH. Days alive and out of hospital may be considered an important patient-centered outcome to define future improvement strategies, especially in ERAS pathways. Although ERAS pathways facilitate early discharge from the hospital, Huang et al. evaluated the quality-of-life and pain scores in 32 patients undergoing VATS lobectomy using an ERAS protocol.[113] They reported a reduction in quality-of-life scores even after discharge due to fatigue in 43% and pain in 33% of patients;

however, there were no changes in the sedentary activity or sleep duration. Despite compliance with ERAS after VATS lobectomy, functional recovery was not achieved within 7 days after hospital discharge. Managing fatigue and appropriate control of pain are of the utmost importance for a better quality of life after discharge from the hospital.

ERAS for Esophagectomy

Research on ERAS for esophagectomy has focused on outcome measures. Shen et al. conducted a single-center RCT in 60 patients, comparing outcomes of patients undergoing esophagectomy with and without an ERAS protocol.[114] They observed lower incidences of pulmonary-related complications in the ERAS group (16.7% *v* 32.8%; p = 0.04), with comparable anastomotic leaks (11.7% *v* 15.5%; p = 0.54). Although early ambulation was achieved in the ERAS group, there were no significant differences in the total hospital LOS. Another single-center retrospective data with a propensity-matched cohort from 243 patients comparing outcomes between ERAS and non-ERAS procedures demonstrated significant differences in LOS (7.40 *v* 11.17 days, p < 0.001) and hospitalization cost (p < 0.001).[115] The time to chest tube removal (4.91 *v* 7.16 days, p < 0.001) and first bowel movement (2.87 *v* 3.97 days, p < 0.001) were also shorter in the ERAS group. However, there was no significant difference in overall postoperative complication morbidity (20.2% *v* 25.1%, p = 0.193). Although ERAS has shown some benefits in esophageal surgeries, Puccetti et al. analyzed overall compliance with ERAS protocols in patients undergoing esophagectomy. Their retrospective cohort showed that 82.7% of patients were compliant with the ERAS protocol for the first 48 hours, and after 48 hours, there was significant deviation from the protocol, possibly contributing to an increased incidence of POCs. It is recommended to review ERAS protocols periodically at the institutional level to maximize use and improve overall patient outcomes.[116]

Nonintubated VATS

Nonintubated VATS (NIVATS) is an evolving surgical technique that allows for minimally invasive thoracic surgery without mechanical ventilation. Many studies in 2022 added to the growing body of research on the feasibility and benefits of NIVATS. Liu et al. published a multicenter RCT that compared spontaneous-ventilation VATS (SV-VATS) via LMA to traditional intubated, mechanically-ventilated VATS (MV-VATS) in patients undergoing blebectomy for spontaneous pneumothorax.[117] The SV-VATS group had similar perioperative complication rates to the patients who required MV-VATS (19.90% *v* 22.09%; RR 0.81; 95% CI 0.52-1.26; p = 0.346); however, the SV-VATS group required fewer postoperative opioids and had a faster PACU recovery, as well as decreased anesthesia costs, compared to MV-VATS. Elkhouly et al. performed a propensity-matched analysis of NIVATS and intubated VATS (IVATS) for patients with spontaneous pneumothorax. Comparable results were found, with shorter operative times and decreased hospital LOS for the NIVATS group, with no differences in mortality.[118] Notably, both studies were in relatively young populations. Additional studies analyzing NIVATS for older populations yielded similar results, with no differences in complication rates or mortality, and a reduction in hospital LOS with NIVATS.[119,120] Interestingly, NIVATS was not found to alter the incidences of postoperative cognitive dysfunction.[121]

Most studies on NIVATS used a supraglottic airway device (SAD) with spontaneous ventilation. However, NIVATS with a native airway using a high-flow nasal cannula (HFNC) has been investigated. A recent case series of 18 patients undergoing NIVATS with HFNC during the COVID-19 pandemic found that this could be done safely, with results comparable to IVATS.[122] However, in a retrospective study comparing SAD to HFNC during NIVATS, the authors noted differences in the lowest pulse oximeter reading (SAD 95.9% ± 4.1 *v* HFNC 93.8% ± 5.2; p = 0.0053) and hospital LOS (SAD 3.6 days ± 0.6 *v* HFNC 4.1 ± 0.8; p < 0.0001 between the 2 groups.[123]

Multiple studies observed increased incidences of hypercapnia and acidemia with NIVATS.[117,120,121] Pathonsamit et al. showed a marginal, though statistically significant, increase of end-tidal carbon dioxide (mean difference 4.56 mmHg; 95% CI 1.85-7.27) in patients receiving NIVATS compared to IVATS.[120] Moreover, Huang found significant elevations in blood carbon dioxide levels (64 mmHg *v* 40 mmHg) and a reduction in pH (7.20 *v* 7.35) in patients receiving NIVATS compared to IVATS.[121] Although the perioperative complication rates appeared unaffected by these changes, most of the patients in these studies were relatively healthy. Patients with extensive comorbidities may not tolerate the hypercapnia and acidemia induced by NIVATS, precluding them from the technique.

Nonintubated VATS allows for spontaneous ventilation, which may benefit patients with poor lung function. In a retrospective study by Wang et al., in 93 propensity-matched patients with poor lung function (defined as FEV_1 and/or FVC <70%), NIVATS was compared to IVATS.[124] The authors found no significant differences in anesthesia duration (241.84 minutes ± 56.99 *v* 258.47 minutes ± 78.13; p = 0.66) and hospital LOS (7.74 days ± 5.41 *v* 9.97 days ± 7.95; p = 0.20) between the 2 approaches. Likewise, another retrospective propensity-matched study compared patients who required NIVATS and IVATS with more severe lung dysfunction (IVATS FEV_1 47.21% ± 8.84, NIVATS FEV_1 47.94% ± 13.10).[125] They found no differences in the length of surgery, anesthesia duration, or increases in the incidence of PPCs.

Nonintubated VATS has been evaluated as an alternative to IVATS in specific disease states. Two studies reviewed outcomes for patients with lung cancer undergoing NIVATS. Both studies concluded that NIVATS did not influence OS, though the number of nodes sampled was slightly reduced compared to patients receiving IVATS.[119,124] The authors concluded that NIVATS was a feasible alternative to IVATS in this population. For patients with interstitial lung disease, a small prospective observational study found that NIVATS

may better maintain diaphragmic function after surgery, perhaps due to the maintenance of spontaneous ventilation.[126] Notably, they did not demonstrate any benefit to gas exchange or pulmonary function tests, leaving the clinical importance unknown. Likewise, a comparison between patients with interstitial lung disease and obesity (BMI ≥30), versus patients without obesity, showed no differences in outcomes, which may broaden the selection criteria for NIVATS in the future.[127] In a recent case series, patients with myasthenia gravis undergoing subxiphoid thymectomy with NIVATS achieved excellent outcomes and rapid recovery.[128] Though this involved a small number of patients, it showed the feasibility of this approach for a new patient population.

Although the growing body of NIVATS-related literature suggests expanding the use of this technique, there are 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 address the topic of NIVATS.[129]

In 2019, a survey was conducted in Italy by the multidisciplinary INFINITY group (Italian Network for Investigation of Nonintubated Thoracic Surgery) to review the use, techniques, and outcomes of NIVATS for parenchymal disease in 55 Italian centers that performed >100 thoracic surgeries per year. Of the responding centers, 78% reported that NIVATS was most commonly performed for pleural effusions (86% of responding centers) and pleural pathologies (81%), and less commonly for parenchymal pathologies (38%). Nonintubated VATS was performed primarily in patients with severe comorbidities or preexisting respiratory impairment (67%), and less frequently in patients without comorbidities (38%). Reported contraindications to NIVATS 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.[130] Preoperative management and intraoperative sedation strategies were similar at most institutions performing NIVATS for parenchymal pathology, but a range of regional anesthetic techniques were used. Most of these centers (90%) reported performing preoperative counseling for patients before NIVATS, with most using a multidisciplinary team. A variety of intraoperative management strategies were used, including aerosolized lidocaine (52%), vagal block (14%), and pleural nebulized lidocaine (14%). Intraoperative sedation largely was provided by anesthesiologists, and included propofol and opioids. Regional techniques were used commonly at experienced centers, and included paravertebral blocks (37%), SAPB (32%), epidural catheters (32%), and intercostal nerve blocks (32%). Thirty-one percent of centers reported converting to GA at least once, and 79% reported transitioning to GA when a minimally invasive procedure required conversion to an open technique.[130] The advantages of NIVATS 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 NIVATS, as the authors noted 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 nonintubated patient (68%). However, reported advantages appeared to bolster ongoing interest in pursuing NIVATS, with 72% of centers reporting a belief that case volume will continue to grow.[130]

The results of this survey indicated that NIVATS is being performed currently for parenchymal disease at a limited number of experienced thoracic surgical centers in Italy; however, the generalizability of these survey findings may be limited, as other published studies demonstrated different practice patterns and primary indications for NIVATS in other countries, such as China and Taiwan.[131] Additional multicenter investigation is required to better define the scope, appropriate patient population, advantages, and limitations of this technique.

Pediatric Thoracic Anesthesia

This year, the literature focused on techniques to achieve OLV, ventilatory and fluid management, and regional anesthesia in pediatric patients. In small children, BBs are used commonly to provide OLV. As age diminishes, intraluminal BBs are impractical due to BB impairment of tidal volume, leading to the placement of extraluminal BBs. Templeton and colleagues described a new technique to place an extraluminal BB in children <3 years old.[132] After induction and intubation, using fiberoptic bronchoscopy, they endobronchially intubated the operative lung. Then, an Arndt BB or Fogarty catheter (Edwards Life Sciences) was inserted into the ETT.

Once in place, the child was extubated, leaving the BB in place. Then, the child was reintubated with an ETT that was 0.5 mm smaller than the original ETT. Fifteen patients (median age 8 months) were included in the study, with 11 out of 15 successful lung isolation attempts on the first attempt. Six out of 15 did experience transient hypoxemia during BB placement. All were mask-ventilated successfully with the BB in place. The advantage of this approach is not needing to "steer" the BB into place, as the endobronchial tube guides bronchial blocker placement. The disadvantage of this technique is periods of apnea during fiberoptic and ETT manipulation. Where to place the BB was also a subject of study.

Placing the BB in the mainstem bronchus can lead to inadvertent migration of the blocker into the trachea, or can produce hypoxia in patients with poor lung function. Yu et al. conducted a retrospective case-control study in which patients roughly 6 months old had either mainstem or selective lobar BBs placed.[133] The lobar BB was either placed in the left lower lobe or right middle and/or lower bronchus, depending on the operative side. Each group consisted of 60 patients. The lobar bronchial group had lower peak airway pressures, higher P-F ratios, and lower alveolar-arterial oxygenation differential

pressures at time points of 10 minutes after OLV, and 10 minutes after resuming TLV.

Furthermore, incidences of hypoxemia, atelectasis, and BB adjustments were lower in the lobar blockade group, without any noticeable difference in the degree of lung collapse or surgical exposure. This led the authors to conclude that selective lobar bronchial blockade may be a reasonable alternative to mainstem bronchial blockade. The appropriate position of a small BB is an ongoing challenge in pediatric thoracic anesthesia. Some centers use BBs, whereas others use mainstem intubation for lung isolation. Kaplan et al. performed a retrospective review of 32 patients <2 years old comparing endobronchial intubation versus bronchial blockade.[134] Mainstem intubation patients were slightly younger (6.3 *v* 10 months old). Four out of 17 patients for whom a BB was used for isolation required conversion to mainstemintubation. When compared with the BB group, mainstem intubations were associated with shorter operative times (139 *v* 209 minutes), shorter anesthesia times (259 *v* 328 minutes), and less intraoperative blood loss (14 *v* 47 mL). Surgeons reported more inadvertent lung expansion in the BB group. Six out of 17 patients in the BB group experienced hypoxemia compared to only 1 in the mainstem-intubation group. The differences in outcomes were nearly universally due to abrupt loss of working space and poor surgical visualization. Thus, if BB placement is challenging, one option may be to simply perform a mainstem intubation to achieve lung isolation. Mainstem intubation is an attractive method for lung isolation given the ease; however, lung collapse due to carbon dioxide insufflation pressures may pose hemodynamic and oxygenation issues.

To study this concern, Wang et al. conducted a study comparing lung isolation by bronchial blockade versus lung isolation by mainstem intubation and CO_2 insufflation.[135] A total of 68 patients were enrolled, with a median age of approximately 6 months. Lung collapse was superior in the BB group at 10 and 30 minutes after starting OLV. Although the pre- and post-OLV MAPs were not different, MAPs in the CO_2 pneumothorax group were significantly lower at 10 minutes after starting OLV (42 mmHg *v* 57 mmHg) and 30 minutes after OLV (41.9 *v* 52.6 mmHg) when compared to the BB group. During OLV, both groups exhibited a significantly higher lower alveolar-arterial oxygenation gradient and significantly lower P-F ratio. Lung deflation via CO_2 insufflation resulted in higher rates of hypotension and less surgical field exposure when compared to BB. Thus, when determining the method of lung isolation, one must consider both the ease of achieving lung isolation with the resulting hemodynamic fluctuations.

Once a child is intubated, determining adequate lung collapse and successful OLV can be challenging. Auscultation has proven to be inaccurate, and bronchoscopy can be invasive. Ultrasound is evolving into a highly used imaging modality for its lack of radiation and ease of use. Tognon et al. studied the ability to use ultrasound to confirm OLV in 22 patients roughly 16 months old.[136] After intubation and lung isolation, a lung ultrasound was performed to identify lung collapse by observing either no lung sliding or the presence of lung pulse in the collapsed lung. Lung pulse is heartbeat-synchronous movement transferred to the pleural line, found to be 93% sensitive and 100% specific for lung collapse. All but one patient who displayed the ultrasound findings were able to achieve appropriate lung isolation, and no patients required bronchoscopy. The authors noted that the clinician should perform prelung isolation examinations as a baseline before imaging the collapsed lung. A limitation of ultrasound use is the presence of lung parenchymal disease.

One imaging modality not terribly impacted by lung parenchymal disease is fluoroscopy. Ponde et al. described an interesting retrospective case series using C-arm to confirm lung isolation in 15 patients with a mean age of 43 months.[137] An advantage of C-arm in right mainstem intubations is the ability to see movement of the right upper lobe, indicating ventilation. All 8 right mainstem intubations were achieved on the first pass, and 4 out of 7 left mainstem intubations were successful on the first pass via C-arm guidance. Certainly, one would need to weigh the risks and benefits of radiation exposure in a child before using C-arm guidance.

Once the airway is secure and OLV is achieved, fluid therapy is a nuanced aspect of thoracic surgery. Xie and researchers used MostCare (Vygon, Vytech), a computer program that studies the hemodynamic effects of a fluid bolus in children undergoing VATS.[138] Thirty-nine children, approximately 2.5 years old, were enrolled and received a volume load of 5 mL/kg of hydroxyethyl starch. Patients were grouped into fluid responders and nonresponders based on changes in hemodynamic measurements. Thirteen patients were classified as fluid responders by having a cardiac index elevation >10%. Pulse-pressure variation and stroke-volume variation were then measured as an ability to predict which patients would be responsive to a fluid bolus. Stroke-volume variation accurately predicted fluid responsiveness in 73% of patients when using a cutoff value of 22%. Unfortunately, pulse-pressure variation showed a poor ability to predict fluid responsiveness, with an accuracy of 46%. Limitations to the study noted by the authors rested with inaccuracies and confounders in calculating pulse-pressure variation unique to the high lung and arterial compliance found in children compared to adults.

One common ventilator strategy used in adults is pressure-controlled ventilation volume-guaranteed (PCV-VG). This modality is unique because airflow decreases during the inspiratory phase, allowing airway pressure to achieve maximum value early in inhalation sustained throughout the inhalation phase. This allows for improved oxygen diffusion. Zhu and colleagues studied PCV-VG versus volume-controlled ventilation (VCV) in 62 patients aged 5-40 months.[139] Peak inspiratory pressures were lower, static compliance was higher, and $PaCO_2$ was lower in the PCV-VG group than the VCV during OLV. However, PIP and static compliance only differed by 2-3 mmH_2O and 2-3 mL/cmH_2O, respectively, and $PaCO_2$ differed by 9 mmHg, suggesting possible minimal clinical impact.

Postsurgical thoracotomy pain is known to be severe and can be an issue for both children and parents. Grap et al. conducted a retrospective chart review comparing epidural catheters with local anesthetic infusion and parental opioids to

parental opioids alone.[140] They studied pain scores and total morphine equivalents in children aged 1 month to 18 years. Children in the epidural group were noted to be significantly older than the opioid-only group. There were no differences between the groups with regard to intraoperative or postoperative morphine equivalents or in postoperative pain scores out to 48 hours. Of note, the bupivacaine concentration was low at 0.1%, which the authors attributed as a possible explanation of similar opioid requirements. The authors chose this concentration to allow for more volume infused when infusing at 0.4 mg/kg/h. Whereas Grap et al. looked at TEA for VATS surgery, newer techniques have emerged as potential alternatives, Yuan et al. conducted a similar study in children undergoing VATS procedures by comparing GA alone to GA with ESPB.[141] Intraoperative opioids included a remifentanil infusion, with a single dose of 0.2 mcg/kg of sufentanil administered 30 minutes before the end of the surgery. Postoperative analgesia included scheduled acetaminophen and sufentanil, 0.05-0.1 mcg/kg, for rescue for a face, legs, activity, cry, and consolability score >4. Children receiving the ESPB received 0.5 mL/kg of 0.25% levobupivacaine. Sixty-five patients were studied, with a mean age of 2 years. They reported that the intraoperative remifentanil and postoperative sufentanil requirements were significantly lower in the ESPB group compared to the GA-only group. The time to first analgesic rescue was significantly longer (5.15 *v* 2.79 hours), parental satisfaction was higher, and the face, legs, activity, cry, and consolability scores in the first 24 hours were significantly lower in the ESPB group (7.23 *v* 4.77) compared to the GA-only group. The incidence of PONV was lower in the ESPB compared to GA alone (6 *v* 20 patients). A potential explanation for the success of ESPB effectiveness in pediatrics is drug diffusion. A local anesthetic may diffuse throughout spinal segments and into the epidural and paravertebral space due to thinner fascia found in children than adults. ESPBs have gained attention as a potential, less risky, yet equally efficacious substitute to epidural analgesia in children. Singh et al. compared TEA versus unilateral ESPB catheters in 42 children aged 2-7 years undergoing left-sided thoracotomy.[142] The authors used the same mL/kg of 0.25% bupivacaine block bolus dose and the same infusion dose of 0.25% bupivacaine at 0.1 mL/kg/h for 24 hours for both techniques. Total intraoperative and postoperative fentanyl administration and number of patients requiring rescue analgesia were similar in both groups. The pain scores did not reach statistical significance at 0, 2, 4, 8, 12, and 14 hours postoperatively. The time to complete the block was faster in the ESPB group (4.43 *v* 7.14 minutes), and side effects were more common in the TEA group (20% urinary retention, 40% hypotension *v* 0% for the ESPB). Both groups required additional intraoperative fentanyl administration; however, the total dose was not >4 mcg/kg. The authors noted that for patients requiring thoracotomy, ESPB catheters can be a viable option for postoperative analgesia compared to TEA. Finally, Hung et al. retrospectively reviewed perioperative outcomes between intubated and non-intubated patients undergoing VATS surgery.[143] Seventeen intubated and 64 nonintubated patients, with a median age of 16 years, were included in this study. Nonintubated patients were sedated with propofol either with LMA or natural airway, and received intercostal nerve blocks from the thirdto eighth intercostal spaces, with 0.5% bupivacaine up to 2.5 mg/kg. Intubated patients had a left-sided DLT placed. Nonintubated patients who required VATS had reduced LOS and shorter chest tube days. However, the reduction in LOS by 0.75 days may not be clinically significant. Of note, though, patients enrolled later in the study showed shorter chest tube days, indicating chest tube days may be more related to the enrollment time frame instead of the choice of airway. None of the nonintubated patients required conversion to tracheal intubation. The authors concluded that VATS via a nonintubated route is a feasible anesthetic choice for children undergoing wedge or bullae resection for tumors.

Postoperative Management

This year, literature on postoperative management after thoracic surgery focused on identifying anesthetic management and interventions to decrease postoperative acute pain, chronic postsurgical pain (CPSP), PPCs, and cancer recurrence.

Mori et al. compared the incidence of chronic pain after thoracotomy in patients who received a PVB versus TEA for postoperative pain.[144] This observational cohort study was conducted via a telephone survey of 48 patients who had undergone thoracotomy 1.5-2 years prior. The measures used to assess the primary outcome were quality-adjusted life years and the NRS. The results showed that there was no difference in the incidence of chronic postthoracotomy pain between patients who received PVB versus TEA. Lu et al. conducted a double-blind RCT studying the effect of perioperative lidocaine infusion on CPSP after thoracoscopic radical pneumonectomy.[145] Patients were randomized into either lidocaine or control (normal saline) groups. The primary outcome was the incidence of CPSP at 3 months, and secondary outcomes included the incidence of CPSP at 6 months, the effect of lidocaine infusion on acute postsurgical pain, and opioid requirements in the first 48 hours after surgery. The study found that patients in the lidocaine group had a reduced incidence of CPSP at 3 months, and had decreased opioid requirements in the first 48 hours after surgery. There was no significant difference between the 2 groups with respect to all other outcomes measured. Two meta-analyses focusing on postoperative pain were published, one looking at PVB versus TEA for acute postoperative thoracotomy pain, and the other looking at the effect of PVB versus no block or other regional technique on CPSP after thoracic surgery. Xu et al. identified RCTs comparing PVB and TEA for thoracotomy.[146] The outcomes studied were pain at rest and with movement at 12, 24, and 48 hours postoperatively, as measured by VAS, rescue analgesic consumption, and adverse effects, including hypotension, urinary retention, and vomiting. This meta-analysis included 16 clinical trials with a total of 1,000 patients. There was no statistically significant difference in acute postoperative pain at all time points between the patients who received PVB versus TEA. Patients with TEA required significantly less rescue

analgesia, but had significantly higher incidences of all adverse effects. The meta-analysis conducted by Na et al. included RCTs with a total of 1,028 patients who underwent thoracic surgery, comparing the incidence of CPSP in those who received PVB versus other regional anesthesia (mainly TEA) versus no block.[147] The primary outcome of the meta-analysis was the incidence of CPSP at 3 months. Secondary outcomes were CPSP at 6 months and postoperative pain at 24 and 48 hours. At 3 months and 6 months postoperatively, there was no significant difference in CPSP in patients who received a PVB versus no block or a different regional anesthetic. Regarding acute postoperative pain at rest, patients who received PVB had significantly less pain than patients with no block at both 24 and 48 hours. Although there was no difference in pain at rest between PVB and other blocks at 24 hours compared to other blocks, patients who received PVB reported more pain with movement at 24 hours and more pain at rest at 48 hours. Based on the data published this year, the use of PVB or other regional anesthesia techniques does not reduce the incidence of CPSP in patients requiring thoracic surgery. However, the use of regional anesthetic techniques seems to provide better pain relief in the immediate postoperative period.

Wang et al. conducted an RCT analyzing the incidence and severity of dysphagia in patients intubated with DLTs who received a postoperative ultrasound-guided block of the internal branch of the superior laryngeal nerve versus no block.[148] A total of 180 patients were randomized to either receive the block or no block. The primary outcome was the presence and severity of dysphagia at 2 hours and 24 hours postoperatively. Secondary outcomes were rates of hoarseness, dyspnea, nausea and/or vomiting, and dysphagia with swallowing saliva 2 hours postoperatively. In the experimental group, the total incidences and severity of sore throat were reduced at both 2 and 24 hours postoperatively compared to the control group. There was no difference in secondary outcomes between the experimental and control groups.

A small pilot study by Millard et al. examined the use of measuring preoperative peak alpha frequency on the electroencephalography to predict postoperative pain sensitivity in patients undergoing surgery for lung cancer.[149] A total of 16 patients had peak alpha frequency and baseline pain levels assessed 4 weeks before lung resection. During the immediate postoperative period (72 hours), patients were asked to report present, average, and worst pain levels. The main finding was that preoperative peak alpha frequency was negatively correlated with postoperative pain levels, with patients with lower frequency peak alpha frequency reporting more severe postoperative pain. The main limitation of this study was that it was a pilot study with a very small sample size (n = 16), and this work is yet to be replicated in a larger population.

A multiinstitutional observational study by Okamoto et al. examined the intersection between intraoperative pain control and POCs in patients undergoing VATS for primary lung cancer.[150] Postoperative complications were defined as any deviation from the expected postoperative course that required treatment or interventions of any kind, life-threatening complications, and death. Intraoperative pain control was measured using the Nociceptive Response Index, a scale quantifying the physiologic response to surgery by measuring hemodynamic variables (heart rate, systolic blood pressure, and perfusion index). In addition to the Nociceptive Response Index, other intraoperative variables were measured and incorporated into the analysis, including the extent of lung resection, use of regional anesthesia, intraoperative dose of opioids, duration of surgery and anesthesia, intraoperative urine output, and blood loss. A total of 536 patients were enrolled in the study, and multivariate analysis and ROC curve analysis demonstrated that a higher Nociceptive Response Index, longer duration of surgery, higher blood loss, and lower urine output were significantly associated with higher incidence of POCs.

Several studies were published this year addressing PPCs in patients having lung resection. Li et al. published an RCT of 1,224 patients analyzing the effect of intraoperative ventilation modes during thoracic surgery requiring OLV on PPCs.[151] The 3 modes of ventilation were PCV, VCV, and PCV-VG. The primary outcome was the incidence of PPCs in the first 7 days after surgery. The secondary outcomes were PPCs during PODs 7 to 30, unplanned admission to ICU, reintubation, hospital LOS, and degree of pulmonary complications. Pulmonary complications were defined as respiratory infection, respiratory failure, pneumothorax, pleural effusion, and bronchospasm. There were no differences among the 3 groups in either primary or secondary outcomes. Baar et al. conducted a multicenter retrospective study through the German Thorax Registry looking at PPCs in 1,426 patients undergoing open thoracotomy for primary lung cancer.[152] The outcomes investigated were the incidence of PPCs, risk factors for PPCs with a focus on anesthesia-related risk factors, and in-hospital mortality rate. Postoperative pulmonary complications were defined as pneumonia, need for invasive or noninvasive ventilation, need for chest tube, fistula with an air leak for >7 days postoperatively, and an ECMO requirement. The overall incidence of PPCs was 33%. The risk factors associated with PPCs were either patient-specific, surgery-related, or anesthesia-related. Patient-specific risk factors significantly associated with PPCs were male sex, age $\geq$60, ASA physical status $\geq$3, and no previous smoking history. Following multivariate analysis, surgery-related risk factors significantly associated with PPCs were the duration of surgery $\geq$195 minutes and the need for partial ligation of a pulmonary artery. Anesthesia-related risk factors in the multivariate logistic regression analysis significantly associated with PPCs were intraoperative fluid administration that exceeded 6 mL/kg/h, continued endotracheal intubation in the immediate postoperative period, and epidural or paravertebral analgesia, which significantly reduced the incidence of PPCs. Patients with 1 PPC had a similar in-hospital mortality compared to those who did not experience PPCs. Patients with 2 PPCs had significantly increased mortality compared to patients with 1 or no PPCs. Patients with 3 or more PPCs had significantly increased mortality compared to all of the groups. Pastene et al. performed a case-control study to assess whether the initiation of rehabilitation within the first hour of extubation in the PACU would primarily decrease the

incidence of PPCs and secondarily decrease hospital LOS, ICU admission, readmission, and mortality.[153] This case-control study was performed in patients undergoing elective lung resection at a single center. The intervention group had ultra-early initiation of rehabilitation in the PACU, and the control group, consisting of contemporary and historical patients, received usual care. The ultra-early initiation of rehabilitation consisted of respiratory rehabilitation with incentive spirometry, deep breathing exercises, and, when possible, ambulation in the PACU. A total of 1,528 patients were included in the study; 243 patients were allocated to the intervention group. The rates of postoperative atelectasis, pneumonia, LOS, and postoperative ventilation were significantly lower in the intervention group compared to the control group, suggesting early rehabilitation may be helpful. Shelley et al. conducted a multicenter retrospective cohort study in the United Kingdom assessing the outcomes of patients requiring unplanned ICU admission after lung resection.[154] The study's goals were to estimate the incidence of unplanned ICU admissions in this patient population, identify characteristics of patients requiring these admissions, and track mortality and post-ICU outcomes. Of the 11,208 patients included in this analysis, 253 patients required unplanned ICU admission. The predominant indication for ICU admission was PPCs, and almost all the patients required mechanical ventilation at some point during their ICU stay (94.7%). Patient demographics associated with ICU admission were female sex, older age, more extensive lung resection, and an open surgical procedure. Of the 253 patients experiencing unplanned ICU admission, 89 (35.9%) died during the same hospital admission. Out of the 151 patients who survived to hospital discharge, 121 (80.1%) were discharged to home, and 30 (19.9%) were discharged to a facility. The critical care mortality in this cohort was similar to historic data. The main finding of this study was that a favorable outcome is possible for thoracic surgery patients experiencing unplanned critical care admission; 65.6% of the patients survived to hospital discharge.

Two studies developed nomograms aimed at predicting PPCs in patients who undergo lung and minimally invasive esophageal surgery. Wang et al. developed and validated a nomogram for predicting PPCs in patients requiring lung surgery. This single-center retrospective cohort analysis included 1,501 patients who were observed for PPCs for the first 7 days after lung surgery.[155] The primary outcome was postoperative pulmonary infection within a week of surgery, and the secondary outcomes were a need for ICU admission, in-hospital mortality, hospital LOS, and other in-hospital complications. Data on preoperative, intraoperative, and postoperative variables were gathered. Univariate and multivariate logistic regression analysis was used to formulate the nomogram based on selected variables. The nomogram is based on 4 variables that were predictors of postoperative pulmonary infection. The 4 predictors identified by this study were surgical procedure (extent of resection, open surgery), OLV duration, and postoperative pain. The performance of the nomogram was validated using the ROC curve, calibration plots, and detrended correspondence analysis.

Tong et al. developed a nomogram for predicting PPCs after minimally invasive esophageal cancer surgery. Postoperative pulmonary complications in this study were defined as atelectasis, pneumonia, respiratory insufficiency, and failure.[156] The study was a retrospective analysis of 969 patients at a single center. This study identified 10 predictors for PPCs, and found that patients who developed PPCs also had a higher incidence of other poor outcomes such as anastomotic leakage, ICU readmission, and prolonged ICU and hospital stay. The 10 predictors identified by the study were older age, higher BMI, heavy smoking, squamous cell carcinoma, FEV_1 and/or FVC $<105\%$, chemoradiation, intraoperative blood loss ≥ 400 mL, operative time ≥ 240 minutes, conversion to thoracotomy, and GA without a combined regional anesthetic.

There were 3 papers published this year specifically focusing on the potential impact of anesthetic and analgesic management on cancer recurrence in patients with NSCLC. Rosbach et al. retrospectively analyzed the records of 382 patients who underwent lung resection for stage 1 NSCLC.[157] The study's primary objective was to determine whether the use of TEA versus intravenous analgesia was associated with differences in the incidence of cancer recurrence and OS. Results showed no differences in outcomes between patients who received TEA versus intravenous analgesia with respect to 5-year recurrence rates and survival. Watanabe et al. retrospectively explored the impact of anesthetic and analgesic techniques on inflammation, quantified with laboratory data, and subsequent recurrence of NSCLC in patients undergoing lung resection.[158] A total of 396 patients with stages I through IIIB NSCLC were included in the study, and the median follow-up period was 42 months. Of the 396 patients, 118 experienced recurrence, and two-thirds of the patients who experienced recurrence did so within 2 years after surgery. Inflammation was quantified by measuring serum C-reactive protein; serum albumin; and neutrophil, platelet, and lymphocyte counts. The results of this study showed that increased markers of inflammation independently predicted recurrence, and that patients with increased inflammatory markers who received volatile anesthetics had worse RFS. In patients with low inflammatory markers, there was no association between timing of recurrence and anesthetic technique. Patients with low inflammatory markers had delayed recurrence compared to patients with high inflammatory markers, regardless of whether they received TIVA versus volatile anesthesia. Seo et al. carried out a retrospective cohort study on the effect of propofol-based TIVA versus inhalation anesthesia on long-term outcomes in patients undergoing curative resection of NSCLC.[159] The primary outcomes measured were RFS and OS. A total of 1,508 patients with stage I and II NSCLC were included in the study, and none of the patients received regional anesthesia. The TIVA group (n = 980) had better RFS and OS than the inhalation anesthesia group (n = 528). The RFS in the TIVA group was 7.7 years versus 6.8 years in the inhalation group ($p = 0.003$). The OS in the TIVA group was 8.4 years versus 7.3 years in the inhalation group ($p <$

0.0001). Prospective randomized studies need to be done to validate these findings.

Economics of Thoracic Surgery

With the current emphasis on value-based care, it is essential for physicians and health systems to evaluate drivers of perioperative and postoperative costs to identify both cost- and quality-based optimization opportunities. Two recent articles evaluated costs associated with thoracic surgery—one evaluated drivers of costs associated with MIE, whereas the other explored both costs and outcomes associated with the surgical start time for elective lung surgery.

Multiple published studies have compared cost differences between MIE versus open esophagectomy for esophageal cancer.[160,161] A unique cost analysis performed by Panda et al. retrospectively evaluated drivers of operative and postoperative costs for patients undergoing either Ivor Lewis or 3-incision McKeown esophagectomy at a single institution from December 2008 until March 2020.[162] Fixed and variable direct costs were tabulated in the perioperative and postoperative periods, whereas human and indirect costs were excluded. Cost data were adjusted over time, and ultimately converted to relative measures to account for hospital-level variation. The authors sought to identify clinicopathologic variables that contributed to differences in cost. Financial data for 254 patients were reviewed. All but 3 patients underwent an Ivor Lewis esophagectomy. There were no postoperative deaths, but 45% of patients experienced at least 1 postoperative complication. Patient, pathologic, and procedural factors associated with higher mean operative costs included a Zubrod score $\geq$1, and performance of intraoperative jejunostomy, with the largest contribution associated with BMI $\geq$30 (+43%, $p < 0.001$). Clinical, pathologic, and postprocedural factors associated with higher mean postoperative costs included male sex and Zubrod score $\geq$1, with the largest increase associated with prior cardiothoracic surgery (+66.7%, $p = 0.035$), increased LOS (56.2% for each additional inpatient day, $p < 0.001$), and occurrence of major complications (+501.9%, $p < 0.001$). Demographic and patient-related risk factors that contributed to differences in total operative costs included age, BMI $\geq$30, FEV_1, and year of surgery. Clinical, pathologic, and postprocedure factors associated with increased postoperative costs included reoperation (+60.5%, $p = 0.001$), renal failure (+91.6%, $p = 0.022$), pneumonia (+136.1%, $p < 0.001$), and respiratory failure (+414.6%, $p < 0.001$). The authors further emphasized the importance of evaluating drivers of cost in identifying care optimization strategies, prioritizing quality improvement initiatives, implementing programs focused on modifiable risk factors (such as nutrition and prehabilitation), and formulating appropriate reimbursement models. A retrospective observational study published by A-Lai et al. sought to determine whether surgical start time impacted cost and patient outcomes.[163] In particular, the authors highlighted safety and efficiency concerns related to fatigue and sleep deprivation. All patients who underwent elective lung surgery during the 3-month study period were enrolled. Patients in whom incision occurred between 8 AM and 4 PM were characterized as 'early start,' with patients undergoing incision after 4 PM were characterized as 'late start.' Primary outcomes included postoperative LOS and cost, and secondary outcomes included operative duration, chest tube duration, intraoperative blood loss, ICU LOS, POCs, and 30-day operative mortality. A total of 389 patients were reviewed, with 295 early-start cases and 103 late-start cases. Baseline demographic and comorbidity factors were similar between the groups. The authors found no statistically significant differences in postoperative LOS or hospital cost, though the latter trended higher in the early-start group ($p = 0.07$). Additionally, no significant differences in secondary outcomes were noted between the groups. Although previously published studies on this topic offered variable conclusions,[164-166] it is important to note that this study was performed at a single institution, evaluated only elective lung surgeries performed by a group of experienced high-volume surgeons, and described a workflow that may vary significantly from other health systems.

Although the results of these retrospective studies may not be universally generalizable, they highlight the importance of ongoing review of practice paradigms to ensure balanced optimization of cost, safety, quality, and outcomes.

Declaration of Competing Interest

None.

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