Special Article
The Year in Thoracic Anesthesia: Selected Highlights From 2020

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Selected highlights in thoracic anesthesia in 2020 include updates in the preoperative assessment and prehabilitation of patients undergoing thoracic surgery; updates in one-lung ventilation (OLV) pertaining to the devices used for OLV; the use of dexmedetomidine for lung protection during OLV and protective ventilation, recommendations for the care of thoracic surgical patients with coronavirus disease 2019; a review of recent meta-analyses comparing truncal blocks with paravertebral and thoracic epidural blocks; and a review of outcomes after initiating the enhanced recovery after surgery guidelines for lung and esophageal surgery.

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THIS SPECIAL ARTICLE is the fifth in an annual series for the Journal of Cardiothoracic and Vascular Anesthesia. The authors would like to thank the Editor-in-Chief Dr Kaplan, the Associate Editor-in-Chief Dr Augoustides, and the editorial board for the opportunity to expand this series, which includes the research highlights of the year that specifically pertain to the specialty of thoracic anesthesia. The major themes selected for 2020 are outlined in this introduction, and each highlight is reviewed in detail in the main body of the article.

Prehabilitation and Thoracic Surgery

In 2020, research on the preoperative assessment of patients undergoing thoracic surgery focused on prehabilitation and the publication of guidelines for the preoperative care of patients presenting for thoracic surgery. The current literature on prehabilitation includes a meta-analysis, randomized controlled studies, and a multidisciplinary consensus statement. A meta-analysis by Kamarajah et al. included 19 cardiothoracic surgery trials that examined the effect of prehabilitation compared with no prehabilitation on postoperative complications. Primary outcome measures included overall and grade III Clavien-Dindo complications, and secondary outcomes included...
cardiopulmonary complications, surgical-site infections, length of hospital stay, and in-house mortality. Because there was a significant heterogeneity in prehabilitation regimens and study outcomes, the authors concluded that prehabilitation reduced complications; but more standardized studies need to be performed to determine the exact benefit of prehabilitation in this patient population.

Laurent et al., using a randomized controlled trial (RCT), evaluated the benefit of prehabilitation with preoperative respiratory muscle endurance training (RMET) added to chest physiotherapy for three weeks before the resection of non–small cell lung cancer compared with their standard practice of chest physiotherapy in 26 patients. Their endpoints were respiratory muscle capacity and postoperative complications. They reported that the patients in the preoperative RMET group had improved respiratory muscle endurance, with a significantly lower rate of postoperative complications. However, their control group had an 83% incidence of pulmonary complications, leading to questions about validity and generalizability of that result. Liu et al. randomized 73 patients to two weeks of home-based exercise prehabilitation and respiratory muscle training. Their primary outcome measure, six-minute walk distance (6MWD), increased by 60.9 meters (95% confidence interval [CI], 32.4-89.5; p < 0.001) compared with controls, with no difference observed in complications or quality of life. Improvements in functional status persisted at 30 days after surgery (mean 21.5 meters from baseline). These findings, along with those of a recent meta-analysis, raise the question whether 6MWD is an acceptable surrogate endpoint for clinical outcomes compared with cardiopulmonary exercise testing (CPET).

Respiratory muscle training in the postoperative setting was examined in a single-center RCT by Taskin et al. in 40 lung resection patients receiving either standard chest physiotherapy or chest physiotherapy, with RMET on respiratory muscle strength, exercise capacity, and hospital length of stay. They found that respiratory muscle training significantly improved respiratory muscle strength as measured as maximal inspiratory and expiratory pressures, 6MWD, and reduced hospital length of stay (length of stay 9.1 v. 12.9 days in the control group).

To improve the perioperative care of thoracic surgical patients, a multidisciplinary group of experts from the Italian anesthesiology, surgical, and pneumonologist societies called the Perioperative Anesthesia in Thoracic Surgery (PACTS) group was established to develop recommendations for the anesthetic management of patients undergoing thoracic surgery, with a focus on lung resection for cancer. The first part of the consensus statement focused on preoperative evaluation and prehabilitation and recommendations are based on existing literature. The evidence was graded as good, in which the evidence comes from well-designed, well-conducted studies; fair, in which the evidence is sufficient to determine the effects of the preventive intervention on outcomes but there are issues with the number, size, or quality of the studies or there are conflicting results; poor, in which the available evidence is insufficient to assess effects on health outcomes and I, in which the evidence is insufficient to assess the effects on outcomes. The strength of the recommendations are graded as A, in which the benefit is substantial and the intervention is recommended; B, in which the intervention is recommended but there is a high certainty that the benefit is moderate or a moderate certainty that the benefit is moderate-to-substantial; C, in which the intervention can be offered to individual patients because the net benefit is small; D, in which there is no net benefit because the harm outweighs the benefits; and I, in which the current evidence is insufficient to make a recommendation. The grade-A recommendations included the consideration of age older than 70 years, American Society of Anesthesiologists (ASA) class ≥3, morbid obesity and chronic renal insufficiency as high risk for developing postoperative complications, alcohol and tobacco cessation four weeks before surgery, a thorough pre-operative cardiac evaluation, and the use of spirometry to calculate postoperative forced expiratory volume in one second (FEV₁) and diffusing capacity (DLCO). In patients with a postoperative FEV₁ or DLCO <40%, CPET testing is recommended. CPET identifies thoracic surgery patients at increased risk. Peak oxygen consumption (VO₂peak) frequently is used to determine operability for lung cancer. Preoperative care guidelines for cardiothoracic surgery recommend risk stratification using VO₂peak (class: A recommendation, level of evidence: fair) as follows; patients with a VO₂peak >20 mL/kg/min have a low risk of pulmonary complications and are deemed fit for surgery and patients with a VO₂peak <10 mL/kg/min are considered high risk and should be counseled about minimally invasive surgery, sublobar resections, or nonoperative treatment options. In patients with a VO₂peak between 10 and 20 mL/kg/min, further stratification is required. These patients may benefit from prehabilitation, which has been demonstrated to improve VO₂peak. Another CPET parameter, ventilatory efficiency or VE/VO₂ slope, has been suggested as a more accurate outcome predictor in heart failure and thoracic surgery patients. The VE/VO₂ slope is defined as the best-fit linear regression line relating minute ventilation (VE) and expired carbon dioxide (VO₂), and it usually is calculated from rest to the anaerobic threshold, in which the relationship between the two is linear. A slope of >35 has been associated with an increased rate of postoperative complications in thoracic surgery patients. Unlike VO₂peak, it is unknown whether prehabilitation can modify the VE/VO₂ slope. Gravier et al. reported on a cohort of 50 lung cancer patients who underwent CPET before and after prehabilitation. They concluded that median VE/VO₂ slope did not change despite an increase in median VO₂peak. An accompanying editorial by Srinathan questioned the validity of this conclusion, noting a significant correlation between changes in VO₂peak and VE/VO₂ slope, and pointing out heterogeneity in their patient cohort and prehabilitation program that was not standardized.

Because prehabilitation may reduce the incidence of postoperative pulmonary complications as well as hospital length of stay, besides the poor quality of evidence, the PACTS group issued a class A recommendation for a three-week course of multimodal prehabilitation, including early functional...
respiratory evaluation, smoking cessation, respiratory rehabilitation, nutritional status, and physical exercise before intervention for lung cancer.

Devices for One-Lung Ventilation

One-lung ventilation continues to be an important aspect of thoracic surgery. Although some consider the double-lumen endobronchial tube (DLT) to be the device of choice to achieve lung isolation, the armamentarium also includes bronchial blockers. Recently, Morris et al. compared the EZ-Blocker (n = 81) to the left-sided DLT (n = 82) in an RCT that predominantly involved robotic thoracoscopic surgery. The primary outcome examined rates of repositioning of the airway device during surgery, whereas secondary outcomes included the quality of lung isolation and postoperative dysphagia. Outcomes were calculated separately depending on the side of surgery. For left-sided surgeries, the repositioning rates per hour were similar, but the DLT had slightly better average isolation scores. Although there were similar degrees of dysphagia on postoperative day one, the dysphagia was worse in the DLT group on postoperative day two. For right-sided surgeries, the EZ-Blocker had higher repositioning rates per hour; however, the mean isolation scores and degree of postoperative dysphagia were similar. A limitation of this trial was that the surgeon was not blinded to the device used. Furthermore, the rightsided double-lumen tube was not studied in this trial.

Due to the recent studies comparing DLTs and bronchial blockers (BB) suggesting that the BBs are associated with fewer hemodynamic perturbations during insertion, improved oxygenation with lower airway pressures, with less trauma, and less risk of trauma to the airway than with a DLT, with a bronchial blocker.

Zhang et al. recently compared the Coopdech BB (Daiken Medical Co. Ltd, Osaka, Japan) (n = 27) and the DLT (n = 28) in minimally invasive esophagectomy patients to determine which device resulted in better isolation at one, five, and ten minutes after opening the pleura. Despite taking longer to place, the Coopdech was associated with slightly better isolation scores at five and ten minutes, with no difference at one minute. Analysis of secondary outcomes showed a higher incidence of postoperative dysphagia in the DLT group, but no differences in the number of patients experiencing hypoxia, pulmonary complications, or tube malposition, suggesting that a BB, in this case the Coopdech BB, is a viable alternative to a DLT in patients undergoing minimal invasive esophagectomy.

Although DLTs are a commonly used device for OLV, they are not without risk. One of the most serious complications is airway rupture. Liu et al. examined 187 cases of airway rupture in a systematic review. The most common sites of rupture were the trachea (52.4%), followed by the left mainstem bronchus (37.4%), but ruptures in other sites such as the right mainstem bronchus or a combination of sites also were reported. Interestingly, 24.5% of patients were asymptomatic; otherwise, the most predominant symptoms were subcutaneous emphysema, air leak, low arterial oxygen (PaO2), and air in the mediastinum. The majority of ruptures were found intraoperatively and treated surgically, and most patients ultimately survived. Possible risk factors for rupture include female sex, the use of a stylet, difficult intubations, multiple manipulations of the DLT, an inappropriately large DLT or overinflation of the device cuff(s), and chronic obstructive pulmonary disease (COPD).

Overall, although this review provided insight into a catastrophic complication, the quality of evidence was low given that these data originated from 22 case series and 105 case reports.

Although it is important to choose an appropriately-sized DLT, data are lacking to guide best practice. The current view is to use tracheal or left mainstem bronchus size to make an appropriate selection. Shiqing et al. conducted a trial in which the DLT size was selected based on measurements and calculations obtained from preoperative computed tomography (CT) scans related to the size of the cricoid ring and left mainstem bronchus, and reported this method to be superior compared with using the left mainstem bronchus size alone. The majority of DLT sizing studies have been focused on the left DLT. Liu et al. studied the feasibility of using cricoid ring diameter measurements to determine right DLT size in 100 women—50 undergoing right-sided thoracic surgery and 50 undergoing left-sided surgery. This patient population and the site measured were chosen based on previous work reporting that the cricoid measurement alone predicted left DLT size in more than 90% of female patients. Measurements of the cricoid ring diameter used to determine DLT size first were obtained by preoperative CT and then compared with those obtained by ultrasound, using a 5- to 10-MHz linear probe positioned in the horizontal plane on the midline of the neck with the neck extended. The authors reported 86% and 92% accuracy in determining the correct size for left- and right-sided DLTs, respectively, with good correlation between the ultrasound and CT measurements. Because both of these studies were performed in Asian women at a single institution, further research is necessary to determine the generalizability of these results.

Although DLTs commonly are used, intubation is not always straightforward. Given that video laryngoscopy has become an invaluable adjunct for intubation with single-lumen tubes, Risse et al. conducted an RCT to determine whether video laryngoscopy could also facilitate placement of a DLT. The protocol was completed on 31 patients in the direct laryngoscopy group using MacIntosh blade and 34 patients in the video laryngoscopy group using the Glidescope (Verathon Inc, Bothell, WA) titanium blade. The primary outcome, time to intubation, was longer in the video laryngoscopy group (median = 93 seconds) compared with the direct laryngoscopy group (median = 74 seconds) (p = 0.044). Interestingly, this occurred despite a higher incidence of grade I views in the video laryngoscopy group. The first attempt success rate and the frequency of tracheal intubation attempts did not differ between the two groups, but DLTs were more likely to be positioned correctly in the direct laryngoscopy group. Notably, only one type of video laryngoscope was used, which may limit generalizability to other systems. Also, the standard DLT stylet was used in all patients instead of the stylet that was...
designed specifically for the video laryngoscope, which may account for the prolonged time to intubation.

In addition to the traditional DLT, other endobronchial tubes, such as the three-cuff ANKOR DLT (Insung Medical, Wonjou, Republic of Korea), also exist. The additional cuff, which is located between the bronchial and tracheal cuffs, is designed to prevent advancement of the endobronchial tube into the right mainstem bronchus and to limit the insertion depth. Recently, Kim et al. published the results of an RCT comparing the depth of insertion and correct endobronchial placement of a traditional DLT versus the ANKOR DLT. A total of 190 patients were randomized to be intubated with a traditional DLT (n = 95) or the ANKOR DLT (n = 95).27 Patients in both groups were intubated using direct laryngoscopy. The traditional DLT was advanced to a depth of insertion calculated using the equation 12.5 + (0.1 x height(cm)). The position then was adjusted based on a combination of factors such as auscultation, chest movements, airway pressures, and lung compliance before and after clamping the DLT lumens. In contrast, after passing through the vocal cords, the tube was rotated 90˚, the carinal cuff of the ANKOR DLT was inflated, and the tube was advanced until it contacted the carina. Fiberoptic bronchoscopy then was performed to evaluate both groups for the primary outcomes, which were placement on the correct side as well as correct depth. The number of correct placements was similar between both groups. However, mean adjustments in depth after verification with bronchoscopy were higher in the traditional DLT group versus the ANKOR group (12.9 ± 9.7 mm v 1.8 ± 1.8 mm, p < 0.001), suggesting that the ANKOR DLT was more likely to be properly positioned on initial placement.

**Dexametomidine and Lung Protection During OLV**

Recently, the literature has focused on the benefits of the administration of dexametomidine (DEX), a selective α2 agonist, either intravenously or by inhalation, on oxygenation, lung mechanics, and postoperative outcomes in patients undergoing thoracic surgery. The favorable effects of dexametomidine that have been reported include bronchodilation, a reduction in intrapulmonary shunt during OLV, improving arterial oxygenation, and pulmonary artery vasodilation, making it useful in patients with preexisting pulmonary hypertension.27

During video-assisted thoracoscopic surgery (VATS), lung injury occurs through different mechanisms including oxidative and capillary shear stress in the dependent lung and in the operative lung, ischemia-reperfusion injury, dependent on the length of the procedure, the degree of surgical resection, and lung reexpansion.28 This can lead to the degradation of the endothelial glycocalyx, disruption of vascular permeability, and acute lung injury (ALI), as well as the release of pulmonary inflammatory cytokines, all contributing to the development of postoperative pulmonary complications (PPCs).29,30 The initiating event is a reduction in the expression of the proteins occludin and ZO-1, two proteins integral for maintaining the pulmonary epithelial barrier. This causes a breakdown of the epithelial barrier, leading to an upregulation of inflammatory mediators, increased vascular permeability, and pulmonary edema.31,32 One of the inflammatory mediators released, tissue necrosis factor alpha (TNF-α), an initiating cytokine in acute lung injury (ALI), is involved in the induction and prolongation of inflammatory reactions by recruiting neutrophils to the site of inflammation, leading to the release of other cytokines, such as IL-6.33,34

DEX has been shown to ameliorate lung injury by reducing pulmonary vascular ischemia-reperfusion injury and inflammatory cytokine release, including IL-6 and endothelin; but the mechanism for the protective effects on post- VATS lung injury is unclear.35 Previous animal studies demonstrated DEX-induced reductions in IL-6 and TNF-α through the phosphatidylinositol 3-kinase (PI3K)/Akt/hypoxia-inducible factor (HIF)-1α signaling pathway, a pathway known to suppress the inflammatory response.36,37 Zhu et al. studied the pulmonary effects of DEX on the inflammatory and clinical response in 67 ASA I and II patients undergoing VATS, in a blinded RCT.38 The DEX group received a 1-µg/kg loading dose before induction followed by an infusion of 0.5 µg/kg/min until 30 minutes before the end of the procedure; while the control group received saline. The investigators obtained arterial blood gases before anesthesia induction, 40 minutes after the initiation of OLV, and ten minutes after the resumption of two-lung ventilation (TLV) to evaluate oxygenation, measured with TNF-α and IL-6 levels in lung tissue and blood, and performed histopathologic and immunohistochemistry analyses to measure occludin, ZO-1, and phosphoinositide-3-kinase (PI3K)/AKT/hypoxia-inducible factor (HIF)-1α levels.39 Postoperative outcomes included thoracostomy tube duration, length of hospital stay, hospitalization expenses, and PPCs, defined as purulent sputum, low fever, prolonged air leakage, and pulmonary embolism. The investigators reported that in the DEX group there were higher Pao2 levels during OLV and at the initiation of TLV, reduced TNF-α and IL-6 in both the blood and lung tissue, and the histology revealed better- aerated alveoli, reduced neutrophil infiltration, intraalveolar congestion, exudates, and hemorrhage, and an increased expression of ZO-1, occludin, and p-PI3K, p-AKT/HIF/1α. Clinically, patients in the DEX group had lower incidences of PPCs and hospitalization costs, as well as shorter thoracostomy tube duration and hospital length of stay, suggesting that the activation of PI3K/Akt/HIF-1α signaling seen with DEX may be involved in lung protection in patients undergoing VATS. Because the patient population consisted of healthy patients, it is unknown if these effects would occur in patients with preexisting lung disease.

Meng et al. also evaluated the effect of DEX on postoperative lung injury in thoracic surgery patients. They conducted a double-blind RCT with 40 ASA class I and II thoracic surgical patients into a DEX and control group evaluating oxygenation, as measured by the oxygenation index and alveolar-arterial oxygen partial pressure difference (A-aDO2), plasma interleukin-8 (IL-8), the expression of aquaporin-1 (AQP-1) protein in lung tissue, and PPCs including atelectasis, pneumonia, and acute respiratory distress syndrome (ARDS).38 IL-8 was
measured because it is a sensitive marker for airway inflammation and can activate neutrophils to release cytokines, promoting and aggravating airway inflammation,39 and aquaporin-1 (AQP1), located mainly in the lung tissue, is responsible for removing fluid in the alveoli, interstitium, and capillaries, preventing fluid overload.40 The investigators reported that in the DEX group there were increases in oxygenation and in the expression of AQP1, a decrease in IL-8 levels but no difference in PPCs.

Consistent results similarly were reported during the same period in studies by Guo et al. and Liu et al.41,42 Both groups similarly demonstrated attenuation in the increase of inflammatory markers in the dexmedetomidine group compared with controls.

Xu et al., in a prospective clinical trial, evaluated the use of nebulized DEX versus placebo on pulmonary shunt and lung mechanics in 128 patients undergoing OLV for elective thoracic surgery.43 The patients were placed in one of four groups—saline, or 0.5 μg/kg, 1.0 μg/kg, or 2 μg/kg of nebulized DEX administered during TLV. Blood samples were taken 15 minutes after bronchial intubation during two-lung ventilation, after 30 and 60 minutes of OLV, and 15 minutes after return to TLV. Dynamic compliance also was calculated at each time point. The investigators found that inhaled DEX reduced the propofol requirement in a dose-dependent manner, at each time point. The investigators found that inhaled DEX reduced the propofol requirement in a dose-dependent manner, with considerable heterogeneity in results. Interestingly, the authors pointed out a trend toward greater improvement in oxygenation with the low-PEEP approach.

A meta-analysis examining the effect of applied PEEP revealed a significant mean increase in PaO2 of +3.0 mmHg (p = 0.01; 95% CI, 11.9-48.6 mmHg). Here a considerable heterogeneity among studies was noted. A subgroup comparison revealed a beneficial effect of PEEP with no PEEP (+35.3 mmHg; p < 0.01; 95% CI, 16.2-54.5 mmHg), but there was no significant increase in PaO2 when comparing individualized PEEP with control PEEP of 5 cmH2O. Further, a post-hoc analysis of high PEEP (8-10 cmH2O) versus low PEEP (3-5 cmH2O) showed no significant difference in oxygenation, with considerable heterogeneity in results. Interestingly, the authors noted that nearly all studies had a high risk of bias, mainly due to the absence of blinding. The studies also were limited in their protocols, sample size, intervention, and outcome measures, leading to marked heterogeneity in results.

In conclusion, Peel et al. advocated for a cautious approach to the interpretation of these findings. A significant limitation of the included studies was their narrow focus on physiologic parameters rather than clinical outcomes. A short-term gain in physiologic parameters does not guarantee clinical benefit. It may even be associated with harm, such as lung overdistention during recruitment that can improve oxygenation but lead to delayed inflammation and injury. The few included studies examining clinical outcomes did not report a significant difference between intervention and no intervention. The authors also noted that nearly all studies had a high risk of bias, mainly due to the absence of blinding. The studies also were limited in their protocols, sample size, intervention, and outcome measures, leading to marked heterogeneity in results.
Additional attention in the literature also was directed toward the choice of the optimal ventilation mode used during OLV. Two small-scale randomized studies individually examined the benefits of pressure-controlled ventilation-volume guaranteed (PCV-VG). Yao et al. performed a randomized comparison of PCV-VG versus volume-controlled ventilation (VCV) in 50 elderly patients undergoing thoracoscopic lobectomy with a tidal volume (TV) of 6 mL/kg and PEEP of 5 cm H₂O during OLV. Their data revealed that the use of PCV-VG mode resulted in significantly lower inspiratory pressure (PIP), improved dynamic lung compliance, higher mean arterial pressure, and a lower concentration of neutrophil elastase, one of the markers of inflammatory response. Notably, there was no difference in a limited set of examined clinical outcomes. A separate randomized study by Li et al. analyzed the combined effect of PCV-VG with standard protective OLV versus open-lung approach (OLA) that used stepwise recruitment maneuvers with an individualized PEEP application in 176 patients undergoing thoracoscopic surgery. The TV was set at 5-to-6 mL/kg, and the control level of PEEP was set at 5 cm H₂O. The results revealed the beneficial effect of PCV-VG combined with OLA on intrapulmonary shunt, deadspace fraction, and the concentration of neutrophil elastase. The use of OLA also was associated with improved oxygenation and dynamic compliance when applied to either PCV-VG and VCV strategy—these results also were consistent with a meta-analysis of Peel et al. previously noted. The only difference in measured clinical outcomes was a modest reduction in the length of intensive care unit (ICU) admission in the PCV-VG + OLA group (median 32 hours compared with 40 hours, p < 0.05).

In aggregate, studies published in the previous year examining protective strategies for OLV provided clinicians with a direction for future research but were limited in their immediate impact on clinical management. Although there may be a specific benefit in using different recruitment strategies, ventilation approaches, and the use of anesthetic adjuncts, caution is needed in the interpretation of primary clinical surrogate markers that were reported in the recent literature. Additional attention should be directed toward the study of meaningful clinical end-points.

COVID and Thoracic Anesthesia

The COVID-19 pandemic has changed the delivery of surgical care for thoracic malignancies and other urgent and elective thoracic procedures. The Society of Thoracic Surgeons (STS) and other organizations have created guidelines for triaging surgical cases. Deciding when to operate is dictated largely by (1) the availability of resources, which may be limited in the rapid escalation of COVID-19 hospital cases and (2) the acuity of the disease. The STS differentiated management by phases. Phase I is when there are few COVID-19 patients in the hospital and care is prioritized for patients whose survivorship is compromised by delaying surgery more than three months. Phase 2 occurs when there is an escalation of COVID-19 cases and hospital and ICU resources including physician availability are limited. In this situation all elective surgeries are delayed up to three months or transferred to facilities that are able to accommodate them and surgery is limited to patients who need surgery within three days. In phase 3, hospital resources are exhausted and only those patients in whom emergent surgical intervention is required can proceed (eg, perforated esophagus, surgical complications, surgically treatable sepsis).

The management of patients presenting for thoracic surgery during the COVID-19 pandemic is discussed thoroughly in reviews and expert consensus statements published within the past year. Previously published guidelines came from the Association for Cardiothoracic Anesthesia and Critical Care and the Society for Cardiothoracic Surgery in Great Britain and Ireland, the European Association of Cardiothoracic Anesthesiology Thoracic Subspecialty Committee, and Tryphonopoulos et al. from the Ottawa Hospital, who published a local expert consensus on the placement of double-lumen tubes.

There is expert consensus that the conduct of thoracic anesthesia is associated with several aerosol-generating procedures including bag-valve mask ventilation, tracheal intubation, lung isolation, OLV, tracheal tube exchange, airway suctioning, flexible bronchoscopy, and extubation. These necessary components of patient care place the anesthesiologist at elevated risk of COVID-19 transmission in the COVID-positive patient. Recommendations for airway management and the establishment of positive-pressure ventilation were well-described in multiple position statements from various worldwide organizations. The use of personal protective equipment, infection control practices, and the technical performance of intubation were consistent among these guidelines and were well-summarized by the European guidelines.

Thornton et al. pointed out that there are advantages and disadvantages to the different lung isolation modalities including double-lumen tubes and bronchial blockers, which were well-summarized in their statement. The various guidelines agreed that placement of a lung isolation device in a patient with known or suspected COVID infection is fraught with additional technical and nontechnical challenges. The most ideal lung isolation device to use in patients with known or suspected COVID-19 is the one that is most indicated for the specific clinical setting and with which the anesthesiologist is most familiar.

Patients should be screened carefully for possible infection. In the case of a positive response to screening (eg, fever, cough, sore throat, myalgia, shortness of breath, diarrhea, fatigue, eye pain), real-time polymerase chain reaction (RT-PCR) of respiratory tract material should be performed. Serologic tests revealing lymphopenia, thrombocytopenia, increased C-reactive protein, elevated lactate dehydrogenase, erythrocyte sedimentation rate, and D-dimer, as well as the presence of anemia, hypoalbuminemia, and transaminitis should warrant RT-PCR in those who screened negative. Findings such as consolidation and ground-glass opacities (GGO) in a peripheral and lower zone distribution on x-ray or computed tomography (CT) scans should be investigated.
If infection is diagnosed, surgery should be postponed at least seven-to-thirteen days from the end of symptoms and after a negative RT-PCR test, if possible. Postoperatively, it is important to ensure that hospital resources (eg, hospital bed, ICU, ventilators) are available to care for the patient.

A negative/neutral-pressure operating room (OR) is preferred, and appropriate personal protective equipment should be worn by all OR personnel according to individual institutional guidelines. The number of individuals present during airway manipulation should be minimized. The plan for airway manipulation should be discussed, and the most experienced operator should perform the tracheal intubation. HEPA filters should be applied to inspiratory and expiratory limbs, as well as between mask and circuit to help prevent colonization of the ventilator and breathing circuit.

Preoxygenation for three minutes or an end-tidal oxygen (ETO2) concentration greater than 0.9 is recommended to allow for apneic oxygenation. A modified RSI with high-dose rocuronium (1-1.2 mg/kg) and avoidance of bag-mask ventilation is suggested. Tracheal intubation using a video laryngoscope, preferably one with disposable blades, is performed followed immediately by cuff inflation, connection to the circuit, and ventilation of both lungs. If using a DLT, both cuffs should be inflated immediately to avoid aerosolization. Bronchial blockers should be considered for shorter procedures or when postoperative ventilation is anticipated to avoid changing a DLT to a single-lumen tube. After placement of the lung isolation device, maintaining a closed circuit is the best way to avoid aerosol generation in the OR. In many patients, it is possible to avoid flexible bronchoscopy and to confirm placement of the lung isolation device with auscultation, clinical examination, and with the use of ultrasound to assess the absence of lung sliding and presence of a lung pulse (subtle movement with cardiac oscillations) in the isolated lung.

In situations in which flexible bronchoscopy is necessary, the guidelines recommended depressurizing the circuit and using a disposable bronchoscope with an adapter that will limit aerosolization. If available, a DLT with an embedded bronchoscope should be considered. Bronchoscopes provide an opportunity for contamination and cross-infection and should be used with caution. With adequate denitrogenation of the surgical lung, it is possible to maintain a closed airway; however, if the airway must be opened to the atmosphere, an additional airway pressure (CPAP) device with a HEPA filter, as opposed to direct insufflation of oxygen.

Exutubation of the thoracic surgical patient is higher risk for aerosol generation due to a greater risk of reactive airways and airway secretions and the use of a larger-caliber tracheal tubes. Operating room staff present during extubations should be protected from airborne contamination in accordance with previously published guidelines. Reducing aerosols can be facilitated by suctioning airway secretions before neuromuscular blockade reversal, retaining the HEPA filter on the tracheal tube during extubation, considering a deep extubation, and the use of adjuncts such as lidocaine, propofol, or dexmedetomidine to prevent coughing. A clear plastic drape can be placed over the patient’s head to limit aerosolization and applying a surgical face mask over the oxygen mask once extubation is achieved.

Bronchoscopy is an aerosol-generating procedure that places staff at a greater risk of infection. Numerous international guidelines have been published to assist healthcare providers in the safe conduct of bronchoscopy. The review by Lentz summarized nicely the published guidelines related to bronchoscopy management. In procedures that cannot be delayed, the established principles for preventing transmission include airborne-protective precautions, maintaining a closed circuit, covering the patient’s mouth and nose with a surgical mask, and considering the use of a negative-pressure room. Some centers have elected to intubate all patients for elective bronchoscopy in an attempt to reduce aerosol generation.

The management of open airway surgery in patients with confirmed or suspected COVID-19 infection deserves attention as these procedures are associated with significant aerosol generation. Several multidisciplinary consensus statements have been published in this regard. Many critically ill patients with COVID-19 require tracheostomy to support recovery. Patient selection, location to perform the tracheostomy, the specific technique, and anesthetic considerations should all be guided by best practices, similar to how patients without COVID-19 are treated. Mitigation strategies for aerosol generation and staff exposure should be emphasized. In patients with COVID-19, tracheostomy should be performed only if there are signs of clinical improvement and ideally outside the infectious window, which many consider greater than ten-to-fourteen days after the first positive test. The ideal location for tracheostomy placement is different for particular healthcare settings and should balance patient and staff risk.

Regional Anesthesia in Thoracic Surgery

The recent literature in regional analgesia for thoracic surgery continues to focus on comparisons between neuraxial and truncal blocks in regard to analgesia, opioid consumption, and adverse effects. Yeap et al. compared the use of continuous thoracic epidural analgesia (TEA) to single-shot paravertebral block (PVB) and continuous PVB in 120 patients undergoing VATS and assessed pain scores for up to 72 hours after surgery, opioid
consumption, and patient satisfaction. Patients in the TEA group reported lower pain scores with movement compared with the two PVB groups at 24 and 48 hours. No differences in pain scores at rest and after 72 hours could be shown using mixed-model analysis of variance. Opioid consumption in the continuous-PVB group (as well as in the single-shot PVB group) was several-fold higher than in the TEA group at 24 and 48 hours. Patient satisfaction and side effects, as well as chronic postsurgical pain evaluated at six months, were similar among the three groups. Although the difference in opioid consumption between the TEA and the two PVB groups was remarkable and the time course of analgesic efficacy between single-shot and continuous PVB was unexpectedly similar (essentially no difference between the two), it is interesting to note that the differences in pain scores, although statistically significant, might not be clinically relevant because the absolute difference in pain scores was only one-or-two points on a ten-point scale. This result, together with the safety and paucity of side effects of PVB, led the authors to conclude that a single-shot PVB was a more-than-valid alternative to TEA in patients undergoing thoracic surgery. This new prospective, randomized study will add to the existing body of evidence, which led several meta-analyses to conclude that PVB provides similar analgesia to TEA in thoracic surgery patients.

Han et al. explored the effect of TEA on quality of life and neuroinflammation, rather than pain outcomes, in elderly patients undergoing laparoscopic esophagectomy. The patients who received a continuous epidural block during surgery displayed better quality-of-life scores on postoperative day seven, a reduction in side effects (nausea, constipation, sleep disorders, dysphagia, reflux, pain, and cough difficulty), as well as a lower plasma level of S100B, a protein associated with neuroinflammation.

In regard to intercostal blocks, Chen et al. compared the effects of adding what the authors called a “modified intercostal nerve block” (injection point between the serratus anterior muscle and rib) with 10 mL of 0.35% ropivacaine added to a general anesthetic to general anesthesia alone in 50 patients undergoing single-port thoracoscopic lobectomy. The authors showed reductions in intraoperative opioid consumption and time-to-first analgesic request, as well as total postoperative analgesic demands and a higher proportion of patients with visual analog score (VAS) 0-3 versus 4-6 (and v >7) 24 hours after surgery. This block targets the same plane of the deep serratus plane block as originally described by Blanco et al.

The erector spinae plane block (ESPB) has been a subject of interest this year. In the past few years, studies have confirmed that the ESPB is more effective than placebo in terms of pain scores and opioid consumption for the first 12-24 hours in VATS surgery. A meta-analysis of 14 RCTs conducted by Huang et al., involving patients undergoing thoracic and breast surgery, confirmed that the patients receiving the ESPB demonstrated lower pain scores and opioid consumption as well as reduced rates of postoperative nausea and vomiting. Prospective, randomized studies comparing ESP with other types of blocks included the one by Ekinci et al. who compared the ESPB to the serratus anterior plane block (SABP) in 60 patients undergoing VATS and reported lower zero- to 24-hour intra- and postoperative opioid consumption, as well as lower zero- to 48-hourpain scores in the ESPB group without any differences in adverse events. Finnerty et al. compared ESPB and SABP in 60 patients undergoing minimally invasive thoracic surgery and used the Quality of Recovery-15 questionnaire (QoR-15) to assess the quality of patient recovery at 24 hours, as well as verbal rating scale (VRS) scores and time-to-first opioid. All of these outcome variables were significantly better in the ESPB group except for opioid consumption at 24 hours, which was not different between the groups. Interestingly, the “comprehensive complication index” was significantly lower in the ESPB group, indicating that patients randomized to this group experienced fewer postoperative complications.

ESPB was compared with multiple intercostal blocks at the level of ports in 78 patients undergoing VATS, by Chaudhary et al. ESPB was found to be superior in terms of PACU length of stay, pain scores, and pulmonary function (FEV1, FEV1/FVC and FEF25-75%) within the first 24 hours. What is remarkable is that a significantly lower percentage of patients in the ESPB group experienced postsurgical pain at eight weeks at the port or chest tube sites (10.6% v 35.4%, p = 0.008), even though no other differences were observed in terms of complications or lengthofstay. Fiorelli et al. conducted a prospective randomized trial with 60 patients undergoing minithoracotomy, comparing ESPB with intercostal blocks (ICB), assessing peri-operative analgesic requirements, pain scores, patient satisfaction, and respiratory muscle strength (measured as “maximum inspiratory and expiratory pressure,” (MIP and MEP)) and reported that the assessed outcomes were better in the ESPB group for the first 48 hours.

Zhao et al. performed a prospective randomized noninferiority trial comparing ESPB with paravertebral blocks (PVB) at two different injection sites (T4 and T6, with a total of 30 mL of 0.4% ropivacaine) for each technique in 66 patients undergoing VATS. Postoperatively, patients received flurbiprofen and oxycodone, administered as patient-controlled analgesia, as part of a multimodal strategy for pain control. The primary outcome was postoperative oxycodone consumption at 48 hours, and the noninferiority limit was set at 10 mg for the total intravenous oxycodone dose received over 48 hours. Pain scores and QoR-15 scores also were recorded. Postoperative oxycodone consumption was 7.9 ± 8.7 mg in the ESPB group v 6.9 ± 6.3 mg in the PVB group at 48 hours, with a difference of 2 mg (95% CI, –1 to 5.6), well within the noninferiority limit set by the authors. No differences in QoR-15 or pain scores were noticed after 24 or 48 hours, and, therefore, the authors concluded that ESPB was noninferior to PVB in terms of analgesia and quality of recovery when used in combination with round-the-clock nonsteroidal anti-inflammatory drugs.

The SABP was a subject of interest in 2020. There were two meta-analyses and other studies comparing its analgesic effect with no block, placebo, or ICBs. Liu et al. performed a meta-analysis of five RCTs comparing SABP to either saline

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**References:**

1. A meta-analysis of five RCTs comparing SABP to either saline.
placebo or no block in patients undergoing thoracic surgery, and found that the SAP in this patient population reduced pain and opioid consumption for the first 24 hours, as well as reduced postoperative nausea and vomiting. The meta-analysis performed by Zhang et al. also showed reduced pain scores and opioid consumption in the immediate postoperative period (within 60 minutes from emergence) and better patient satisfaction with the analgesic regimen, but there were no statistically significant differences in time-to-catheter removal, length of stay, or side effects.

Viti et al. performed a prospective trial with 94 patients undergoing VATS, who were randomized to either SAPB or systemic analgesia, and measured pain scores and postoperative respiratory recovery, as assessed by incentive spirometry. They found that the SAPB group had a reduction in pain scores and improved respiratory function, and these effects still were significant on postoperative day two. Reyad et al. evaluated the effectiveness of SAPB compared with systemic analgesia in reducing post-thoracotomy pain syndrome (PTPS). A total of 89 patients were randomized and then evaluated postoperatively at eight and 12 weeks for PTPS. Additionally, the authors assessed pain, quality of life, and activity level. At eight (24%) and 12 (22%) weeks, the incidence of PTPS was significantly lower in the SAPB group compared with the control group (45% and 43%, respectively). Interestingly, although pain scores were not significantly different in the immediate postoperative period, they were significantly lower in the SAPB group at eight and 12 weeks. No differences were found in quality of life or activity level. Two other studies comparing SAPB with intercostal nerve block for “traditional” for single-port VATS have not been able to show any meaningful difference in terms of pain and opioid consumption.

Research on PVB focused on the effect on stress response and inflammation, as well as its effects on postoperative pain. Chu et al. randomized 54 patients undergoing VATS lobectomy to PVB versus no block and evaluated the effects on pain and plasma level of matrix metalloproteinase (MMP). Matrix metalloproteinases comprise a family of zinc-dependent endopeptidases that, when increased, are direct evidence of cancer progression. They have a significant overexpression in every type of human cancer, and this expression often is associated with reduced survival. Increased levels of MMP-9 have been found in non—small cell lung cancer patients. Not only did patients have lower pain scores, their MMP-9 concentration, although similar in both groups preoperatively, postoperatively it was significantly lower. Zhang et al. randomized 120 patients undergoing lung cancer surgery into three groups—those receiving general anesthesia alone, those receiving GA with PVB, those receiving GA with PVB, and those receiving GA with PVB and DEX—and found that the GA-PVB group had reduced postoperative pain, enhanced recovery, and reduced markers of lung injury and inflammation, which were increased further by DEX.

Although the clinical and prognostic significance of these studies is yet to be determined, they add to the mounting evidence of the effects of analgesia on the mechanisms involved in cancer progression and recurrence.

An interesting noninferiority study published by Hanley et al. compared PVB placed by the surgeon at the end of the procedure with ultrasound-guided SAPB performed by the anesthesiologist in 40 patients undergoing VATS. The researchers reported that the patients in the SAPB group had lower pain scores with comparable opioid consumption, but issues with this study included no description of the performance of the surgical blocks and that the majority of patients in the SAPB group displayed a sensory block in the PACU and there was no evidence of a dermatomal block in any patient in the PVB group. Even though the study was underpowered to determine the primary outcome, there was a greater standard of deviation than expected, limiting the generalizability of these findings.

Furthermore, even if this is not considered among “traditional” regional anesthetic techniques, a phrenic nerve block ipsilateral to the surgical site has been shown to decrease the severity of postoperative shoulder pain and the frequency of postoperative analgesic use compared with placebo. When evaluating these studies, it is important to realize that the vast majority used statistically significant difference in pain scores and opioid consumption as the outcome for their analysis and there is a question whether these effects actually are clinically relevant.

Enhanced Recovery After Surgery for Lung Resection: 2020 Update

Since the release of the European Society of Thoracic Surgeons (ESTS)/Enhanced Recovery After Surgery (ERAS) Society guidelines for lung resection surgery in 2018, interest and evidence for enhanced recovery after thoracic surgery (ERATS) have steadily increased. The majority of literature related to ERATS continues to be comprised of retrospective, single-center studies related to institutional experiences with pathway implementation. However, 2020 saw the release of notable manuscripts related to (1) overall compliance with ERATS elements and (2) evaluation of several individual pathway components, namely prehabilitation, lung-protective ventilation, and regional blockade in lung resection surgery.

Compliance

Although the elements of an ERATS pathway have been well-described, overall compliance with such pathways continues to be a challenge. As Forster et al. described in their retrospective analysis of 192 patients undergoing VATS pulmonary resection, high compliance was associated with better postoperative outcomes and decreased rate of delayed discharge. In this study, “high compliance” was defined as ≥75% of the components achieved. The majority of adverse outcomes (85%) were postoperative pulmonary complications, and 16 ERAS pathway elements were included. The importance of compliance in ERATS has been described previously by Rogers et al. and outlined in several recent editorials.
Prehabilitation

Ferreira et al. performed a prospective, randomized trial comparing four weeks of “prehabilitation” before lung resection surgery to eight weeks of traditional postoperative rehabilitation in the context of an ERAS pathway. For both groups, the strategies included nutritional counseling/supplementation, exercise, and anxiety reduction techniques. The two groups were virtually indistinguishable during the perioperative period, and by eight weeks both had returned to their baseline functional capacity.109

Lung-Protective Ventilation

The quest for optimal ventilatory parameters in thoracic surgery and within an ERATS pathway has yielded important guidance regarding minimization of driving pressure, as well as the provision of moderate tidal volumes and some level of PEEP.45,110 A recent meta-analysis of 16 articles concluded that recruitment maneuvers and PEEP were advantageous (improving oxygenation and compliance, decreasing deadspace fraction), but the optimal value of PEEP remains elusive.43

Locoregional Anesthesia/Opioid Reduction

There has been significant attention paid to the advent and comparison of regional blockade techniques in thoracic surgery. As mentioned previously, Finnerty et al. compared the SAPB to the ESPB and concluded that the ESP block provided higher quality recovery at 24 hours, as well as a lower complication rate and improved analgesia.89 Similarly, Turhan et al. performed a prospective, single-blinded study of 106 patients undergoing VATS who were randomized to receive either PVB or ICB. Although they deemed each effective, the TPV group had lower morphine requirements and lower dynamic pain scale scores at 24 hours.111 A randomized, double-blinded trial comparing multiple-level PVB to ICB and ESP blocks concluded that PVB was superior for analgesia, similar to the other two blocks.112 With the continued emphasis on opioid reduction, some centers are turning to an opioid-free approach to thoracic surgery. Described to be feasible and safe by Devine et al., this thought-provoking technique warrants prospective evaluation and further description.113

Patient-Centered Outcomes

Traditionally, the efficacy of an ERAS pathway was measured by the hospital length of stay. However, more recently, attention has shifted toward patient-reported outcomes and quality of recovery.114 However, these data can be difficult to collect. To be effective, the patient interface must be user-friendly and efficient. To this end, Kneuertz et al. described the effective implementation of a mobile device application to support patient-centered care and to collect data related to patient-reported outcomes in the context of ERATS.115

ERAS Esophagectomy 2020

ERAS pathways are multidisciplinary, multimodal perioperative care paradigms that incorporate evidence-based best practices focused on decreasing the impact of surgical stress, expediting functional recovery, improving patient outcomes, and reducing cost.116 Initially used in the management of patients undergoing colorectal surgery, early published successes of implementing these pathways led to the development and implementation of ERAS protocols for a broad range of surgical procedures.117

During the past decade, there has been increasing interest in applying ERAS principles to the management of esophagectomies, which are technically complex, highly morbid procedures performed in a physiologically fragile patient population. Reported morbidity rates have been as high as 59%, with 30- and 90-day mortality rates of 5% and 13%, respectively.118,119 Although initial outcomes improvements were not consistently as robust as those reported from other surgical disciplines, this likely was due to the variability of the ERAS components implemented among institutions.120-122 Formal guidelines ultimately were developed and published in 2019 by the ERAS Society, with the goal of a more standardized approach to ERAS protocol use for patients undergoing esophagectomy.123 Since its publication two years ago, there have been a few (largely retrospective) studies published examining specific elements of the ERAS esophagectomy guidelines.

With regard to analgesic techniques, the guidelines included strong recommendations for multimodal, opioid-sparing analgesic techniques including thoracic epidurals (first-line approach) and paravertebral blocks (alternative to thoracic epidural). Given the proven benefits of epidurals for this patient population, a well-functioning epidural is key to successful outcomes. A small retrospective review of 67 patients evaluated the level of epidural catheter placement with regard to numeric pain scores for McKeown esophagectomy (tri-incisional esophagectomy: laparotomy, thoracotomy, neck incision).124 In this study, T7/T8 placement demonstrated better postoperative pain control than T6/T7 or T8/T9 placement. Although a small study, it underscored the importance of refining the guideline’s preferred analgesic technique to match surgical incision(s). Along these lines, a recent retrospective review by Boshier et al. evaluated the role of epidurography for select esophagectomy patients who had features concerning for incorrect epidural catheter placement (eg, difficult insertion, inadequate pain control, lack of sensory level).125 Fifty-two of 192 patients during a seven-year period underwent epidurography, which served to “rescue” inadequate pain control by expediting changes in management, such as catheter replacement or withdrawal.

The literature on the use of ketamine, lidocaine infusions, gabapentanoids, and magnesium did not support a strong or moderate recommendation in the 2019 ERAS esophagectomy guidelines. However, the guidelines did support the perioperative use of acetaminophen and nonsteroidal antiinflammatory drugs. A recent retrospective review of 1,019 esophagectomy
patients attempted to correlate perioperative ketorolac use with anastomotic leak. A total of 686 (67%) of patients received ketorolac during a 12-year period, with interval increases in use throughout the defined study period. The overall rate of anastomotic leak was 9% (n = 87), with interval decrease in leak rate during the defined study period. On multivariate analysis of the data, ketorolac administration was not associated with anastomotic leak either as a categorical variable (odds ratio 0.99, p = 0.958) or continuous variable using dose (odds ratio 1.0, p = 0.843). This study adds to the body of literature supporting the safety of this widely used nonsteroidal antiinflammatory drugs for multimodal pain management.

With regard to fluid management, the guidelines gave strong recommendations to avoid volume overload using a balanced crystalloid approach. The overall goal for fluid management was to avoid more than 2 kg/d of weight gain for this patient population. Goal-directed fluid therapy (GDFT) for esophagectomy was given only a weak recommendation given the lack of high-quality studies supporting its use in this specific patient group. A multicenter randomized trial published in December 2020 sought to evaluate the impact of intraoperative GDFT on morbidity and mortality in patients undergoing Ivor-Lewis esophagectomy. A total of 232 patients were randomized to receive (1) intraoperative GDFT using stroke-volume variation interpretation plus systolic blood pressure maintained higher than 90 mmHg by vasopressors as necessary (n = 115), or (2) conventional hemodynamic and fluid management (n = 117). The primary outcomes were incidence of death or major complications including reoperation for bleeding, anastomotic leak, pneumonia, reintubation, or >48 hours ventilator dependence. Major morbidity and mortality were lower in patients randomized to GDFT (19.1% v 35%, absolute risk reduction 15.9%, p = 0.0006). GDFT was associated with decreased postoperative atrial fibrillation (odds ratio [OR], 0.18), respiratory failure (OR, 0.27), and readmission to the ICU (OR, 0.09). Although this RCT was small, it supported the use of intraoperative GDFT for ERAS esophagectomy.


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