Special Article

The Year in Thoracic Anesthesia: Selected Highlights from 2016

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Key Words: extracorporeal circulation; pulmonary transplantation; tracheal resection; pulmonary embolectomy; pulmonary hypertension guidelines; nonintubated video-assisted thoracic surgery; robotic esophagectomy; ROBOT trial; regional techniques for thoracic surgery; uniport video-assisted thoracic surgery; subxiphoid approach for video-assisted thoracic surgery; tubeless video-assisted thoracic surgery; intercostal block; thoracic epidural anesthesia; paravertebral block; serratus anterior block

This special article is the first in an annual series for the Journal of Cardiothoracic and Vascular Anesthesia. The authors 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 major themes selected for 2016 are outlined in this introduction, and each highlight is reviewed in detail in the main body of the article. The literature highlights in the specialty for 2016 begin with the advancement of the indications for thoracic surgery and surgical techniques and early results of nonintubated video-assisted thoracic surgery (NIVATS), followed by a discussion of regional techniques in thoracic surgery, including serratus anterior blocks (SABs) and methods to improve the success of established regional blocks. The third section reviews the role of extracorporeal membrane oxygenation (ECMO) in thoracic surgery, particularly in patients undergoing pulmonary transplantation, pulmonary artery embolectomy, and repair of critical airway stenosis or disruption. The fourth section details the 2015 European Society of Cardiology/European Respiratory Society guidelines for the diagnosis and treatment of pulmonary hypertension and how they differ from the 2009 guidelines, and the last section is an update on robotic esophagectomy and how it compares with both standard open esophagectomy and minimally invasive esophagectomy.

Nonintubated Video-Assisted Thoracic Surgery

The first NIVATS for lobectomy was reported in 2007.1 The use of this technique has been expanded from simple thoracic procedures, such as the management of pleural effusion, spontaneous pneumothorax, pleural empyema, bullectomy, mediastinal biopsy, and wedge resection, to major procedures, including lung-volume reduction, thymectomy, segmentectomy, lobectomy, pneumonectomy, and more recently, carinal reconstructions and tracheal resections. The rationale for the use of NIVATS is to minimize the detrimental effects of tracheal intubation, mechanical ventilation, and general anesthesia, especially in the critically ill, in high-risk patients with pre-existing pulmonary disease, and in elderly patients.

The anesthetic management described for this surgical technique is just as varied as the indications themselves. “Nonintubated” implies that an endotracheal tube is not used, and depending on the invasiveness of the procedure, the
anesthetic techniques range from serratus anterior or intercostal blocks to thoracic epidural anesthesia (TEA) with minimal-to-no sedation to general anesthesia with laryngeal mask airway placement. The proposed benefits of NIVATS include the avoidance of trauma to the trachea, esophagus, and hypopharynx from double-lumen endobronchial tube placement; mechanical ventilator-induced lung injury; and the effects of residual neuromuscular blockade and general anesthetic agents. Other disadvantages of video-assisted thoracoscopy with general anesthesia and endotracheal intubation (GAVATS) include compromised cardiac performance and impaired early postoperative respiratory function due to residual paralysis; postoperative pain; nausea and vomiting; and the inability to cough, increasing the risk of pneumonia. With NIVATS, the patient is ventilating spontaneously, with efficient diaphragmatic contraction that, along with lateral decubitus positioning, results in optimal ventilation perfusion matching to the dependent lung. This translates into faster recovery times, reduced costs and hospital length of stay, and lower morbidity. Theoretical advantages include a reduced need for intensive care unit stay, improved respiratory function in the early postoperative period, and reduced perioperative morbidity and mortality than with the same procedures performed using GAVATS.

During NIVATS, the lung collapse produced by surgical pneumothorax is similar to that of intubated single-lung ventilation. In the majority of procedures, the lung volume will decrease to functional residual capacity, allowing for space for surgical maneuvering. The pneumothorax-induced reduction in oxygenation can be corrected with supplemental oxygen. Permissive hypercapnia can develop due to pendular ventilation, generated by the development of pressure gradients after the creation of the pneumothorax. This hypercapnia usually is well tolerated and resolves immediately after surgery. The main drawbacks of NIVATS include coughing, which may hinder lymph node dissection around the hilum and trachea; poor maneuverability of instruments due to diaphragmatic and/or lung movement; and patient factors, including movement and the inability to tolerate being awake. Coughing can be mitigated by intraoperative vagal blockade. Depending on the procedure and the experience of the surgeon, the conversion rate to general anesthesia is between 2.3% to 10%. Contraindications to NIVATS include morbid obesity, hemodynamic instability, dense or extended pleural adhesions, noncompliant patients, and large, centrally located tumors.

According to a survey of members of the European Society of Thoracic Surgeons, the preferred type of anesthetic management for NIVATS was the use of intercostal blocks with no or minimal sedation, followed by laryngeal mask airway and TEA for more invasive procedures. The advantages of TEA include an increased minute ventilation, peak expiratory flow rate, decreased pulmonary vascular resistance, improved diaphragmatic contractility, and postoperative analgesia. TEA also decreases myocardial oxygen demand; improves myocardial blood flow and left ventricular function; and reduces heart rate, arrhythmia formation, and thrombotic complications. Sedation strategies include dexmedetomidine, remifentanil, propofol, and midazolam.

In 2004, a uniportal technique was developed in an attempt to make video-assisted thoracic surgery (VATS) more minimally invasive. Due to technologic improvements in instrumentation, its use has been increasing steadily and it is the surgical approach of choice for NIVATS. The potential advantages of this approach include less access trauma, improved cosmesis, and the ability to access both thoracic cavities using a subxiphoid approach, which may reduce the risk of intercostal nerve injury. Because of the limited incision, less-invasive regional techniques are required. One of the newest developments combines the uniportal technique with NIVATS, in an approach called the "tubeless" VATS. With tubeless VATS, the patient undergoes NIVATS without placement of a chest tube. Cui et al randomly assigned 173 patients undergoing uniportal VATS for sympathectomy, bullae resection, and mediastinal tumor resection to either tubeless VATS or VATS with a postoperative chest tube. They found that the tubeless VATS group had a more rapid recovery of respiratory muscle function, a lower incidence of systemic complications, decreased inflammatory cytokine levels, earlier postoperative oral intake, decreased pleural effusion, decreased postoperative infection and pain, earlier time to postoperative activity and functional exercise. There were no differences between the 2 groups with respect to surgical time, intraoperative blood loss, or complications. In select populations, minor procedures using tubeless VATS have been managed as day surgery.

The largest unicenter randomized trial comparing NIVATS with GAVATS recently was published by Liu et al. They enrolled 354 patients with diverse thoracic diseases and found that the NIVATS group had a statistically significant decrease in postoperative morbidity rate, most notably a reduction in postoperative respiratory complications. A recent meta-analysis by Tacconi et al reviewed 1,441 patients undergoing NIVATS and GAVATS to determine the benefits and disadvantages of NIVATS. They found an overall conversion rate of 2.4%, with the majority of conversions occurring in patients undergoing major procedures. In low-risk patients with peripheral pulmonary nodules, there appeared to be no difference in morbidity between the NIVATS and GAVATS groups, but in high-risk patients, GAVATS was associated with a higher incidence of pulmonary complications. Specific patient populations that appear to benefit from NIVATS include the elderly, in whom there is a lower incidence of postoperative delirium; in patients undergoing lung volume reduction surgery, in which NIVATS was associated with lower morbidity and a statistically significant reduction in the incidence of prolonged air leak; and in high-risk patients experiencing interstitial lung disease with a diffusing capacity of carbon monoxide < 40%. Other findings included an attenuated postoperative stress hormone response and procedure-related costs, but hospital length of stay was dependent on the procedure itself and not the technique used.

The use of NIVATS recently has been successful in procedures in which tracheal intubation may be less than ideal, including tracheal mass resection and carinal reconstruction. The indications, advantages, and limitations of NIVATS still need to be elucidated, but with experienced
surgeons, NIVATS appears to be the technique of choice in elderly patients and patients with multiple comorbidities, poor pulmonary function, and previous pulmonary resections and those in whom intubation is deemed detrimental.

Regional Anesthesia for Thoracic Surgery

Historically, TEA has been the gold standard for the management of post-thoracotomy. The dense sympathetic block provided by an epidural has been shown to decrease postoperative pulmonary complications and prevent long-term chronic post-thoracotomy pain syndromes. Despite these advantages, the risks, including hypotension, urinary retention, epidural abscess, and epidural hematoma, and the resource-intensive nature of TEA management have resulted in the investigation of alternative regional techniques and how to improve thoracic epidural placement to be safer, more efficient, and potentially more effective. According to Hernandez et al, an experienced hands, the thoracic epidural failure rate has been reported to be high as 50%. Recently, 2 randomized controlled trials examined imaging modalities to reduce the failure rate. Parra et al compared fluoroscopy with the loss of resistance to saline/air, and Auyong et al compared preprocedure ultrasound with palpation to facilitate thoracic epidural catheter placement. Both studies confirmed that the use of an imaging modality improved the number of successful placements with less trauma and improved patient satisfaction, suggesting a role for imaging in the future.

The paravertebral block (PVB) continues to show promise as a safe and equally efficacious analgesic technique for thoracic surgery. Yeung et al evaluated 698 patients in 14 studies comparing PVB with TEA for elective thoracotomy, with respect to analgesic efficacy, the incidence of major and minor complications, length of hospital stay, and cost-effectiveness. The conclusion from this review was that PVB was equally as effective as TEA for acute thoracotomy pain and that PVB reduced the risks of minor complications commonly associated with TEA. El Tahan reviewed 76 studies that examined analgesic techniques for thoracic surgery comparing TEA with PVB, intercostal nerve blockade (ICB), wound infiltration, and patient-controlled systemic analgesia. The summary of evidence suggested that PVB may be equally efficacious to TEA, especially when higher concentrations of local anesthetics are used, with reduced incidences of hypotension and urinary retention, and that TEA is superior to infiltrative analgesia and ICB. Pace et al retrospectively evaluated the safety of single-injection paravertebral blocks performed using ultrasound guidance in patients undergoing breast surgery and found that out of 856 patients, there were no accidental pleural punctures or pneumothorax, suggesting that the use of ultrasound increased the success of PVB placement.

There has been a renewed interest in ICB for thoracic analgesia with the advent of long-acting liposomal bupivacaine (Exparel; Pacira Pharmaceuticals, Parsippany, NJ) and the growing popularity of enhanced recovery the after surgery pathways for thoracic surgery. The advantages of ICB include ease of block placement, placement of the block under direct visualization by the surgeon, low risk of hemodynamic issues, and a good safety profile. Exparel adds yet another advantage to the list because it does not require placement or management of an indwelling catheter while providing up to 96 hours of analgesia. The Food and Drug Administration has not approved the use of Exparel for peripheral nerve blockade, but several studies using Exparel for ICB in thoracic surgery are emerging and are demonstrating a promising safety profile. A retrospective study of 108 patients compared TEA (n = 54) with ICB with Exparel (n = 54) for lung resection surgery. The authors found no differences in mean or maximal pain scores or in opioid consumption between ICB with Exparel and TEA. Of note, there was significant heterogeneity in surgical approach because the study included patients who underwent VATS, robotic, and open thoracotomy approaches. Reported pain scores were higher in the thoracotomy patients in each group. A second retrospective study of 85 patients compared TEA with ICB with Exparel specifically for thoracotomy patients. Patients in the Exparel ICB group had lower pain scores on postoperative days 1 and 3, and there was no difference in pain scores on postoperative day 2 or in supplemental opioid usage between the groups. Interestingly, there was a decrease in hospital length of stay in Exparel ICB patients (7.4 v 9.3 d) and fewer pulmonary complications in this group compared with the TEA group. Even though these results are promising, larger prospective studies need to be performed to further assess these findings.

The new nerve block technique of interest for thoracic surgery is the SAB, which is an interfascial plane block that targets the lateral cutaneous branches of the intercostal nerve as they pass through this fascial plane before dividing into anterior and posterior branches to innervate the chest wall. The block is performed by injecting local anesthetic either superficially or deep to the serratus muscle under ultrasound guidance. The advantage of this block is that the autonomic symptoms, such as hypotension and bradycardia, seen with TEA or PVB, are avoided. The disadvantages of this block are that the posterior primary rami, the anterior cutaneous branches of the intercostal nerve, and the supraclavicular nerves may be missed. A randomized controlled trial by Khalil et al compared TEA with SAB with local anesthetic infusion in 40 thoracotomy patients, 20 in each group. The authors found no difference in pain scores or morphine consumption between groups for the first 24 hours after surgery, but the SAB group experienced fewer episodes of hypotension. Even though this study was promising, larger studies that follow patients for longer periods are needed to demonstrate the effectiveness and safety profile of the SAB.

Use of Extracorporeal Membrane Oxygenation in Thoracic Surgery

As the indications for ECMO continue to expand in the intensive care and cardiac surgical arenas, thoracic surgeons
are beginning to use this technique in their practices. Although mechanical circulation has been used in the past for complex tracheobronchial construction and for the resection of complex thoracic malignancies, ECMO more recently has been used as an adjunct in the treatment of airway stenosis and massive pulmonary embolism and as a bridge to both pulmonary transplantation and retransplantation. Kim et al published a case series in which ECMO support was used for a range of tracheal procedures, including tracheal stenosis, tracheomalacia, tracheal tumors, and a tracheal compressing mediastinal mass. They were able to perform these procedures successfully and had no bleeding complications from ECMO. The advantages of ECMO are that it avoids hypercapnia, does not require tracheal intubation, and when veno-arterial ECMO (VA-ECMO) is used, provides hemodynamic stability. Recently, Biancosino et al and Bellier et al described the successful use of ECMO in the repair of bilateral bronchial disruptions and a resection of a glomus tumor.

The use of VA-ECMO has been increasing in the treatment of massive pulmonary embolism, particularly in patients who require hemodynamic support with vasoactive agents and respiratory support for poor oxygenation or when the initial presentation is cardiac arrest. VA-ECMO provides cardiopulmonary support for patients to tolerate catheter thrombolysis or surgical pulmonary endarterectomy. Dolmatova et al retrospectively reviewed 5 cases of massive pulmonary embolism supported with the use of VA-ECMO. Eighty percent of these patients presented in cardiac arrest, and there was a mortality rate of 40%, the same rate as with standard therapy, suggesting that VA-ECMO may be useful as a salvage therapy in patients who present in cardiac arrest.

Veno-venous ECMO (VV-ECMO) continues to be an emerging technology in the management of patients presenting for pulmonary pretransplantation and retransplantation. In the bridge-to-transplantation population (BTT), spontaneously breathing ECMO is an emerging strategy to reduce ventilator-induced diaphragmatic dysfunction and to permit withdrawal of sedation and neuromuscular blockade. In a large retrospective analysis of the United Network for Organ Sharing national database, awake ECMO as a BTT was associated with improved long-term survival after transplantation compared with bridging with mechanical ventilation alone or mechanical ventilation plus ECMO. Interestingly, 3-year survival in patients bridged with only ECMO was not significantly different from that of patients who required no bridging at all (invasive ventilation or ECMO), suggesting that older studies linking pretransplantation ECMO with worse outcomes post-transplantation probably were confounded by late initiation of ECMO and historically near-universal use of mechanical ventilation concomitant with ECMO. These findings may not apply to lower volume centers, which, in another analysis of United Network for Organ Sharing data, showed worse outcomes in ECMO BTT at lower volume centers compared with higher volume centers. Ambulatory ECMO as BTT is being used in an increasing number of centers, facilitated by technologic advances in circuit miniaturization, centrifugal pump design, and dual-lumen single cannulation, which simplify patient mobilization during ECMO support. Active rehabilitation mitigates deconditioning in critical illness and, even though labor intensive, the cost-effectiveness of such programs was illustrated in a report demonstrating a 22% reduction in total hospital costs and a 73% reduction in post-transplantation intensive care unit costs in ECMO patients who received active rehabilitation.

Collaud et al analyzed data from their institution and from 13 published studies to identify selection criteria for using ECMO as a bridge to pulmonary retransplantation. Of 21 patients, 18 underwent retransplantation after a total of 2- to-86 days, with a median of 11 days. The intertransplantation interval was between 0 and 168 months, with a median interval of 37 months. The types of extracorporeal circulation included extracorporeal carbon dioxide removal, VV-ECMO, and VA-ECMO. The reasons for graft failure most commonly were rejection or primary graft dysfunction. The 90-day postoperative mortality was 28% and the 1-year survival was 48%. Patients on extracorporeal carbon dioxide removal, awake ECMO, or VV-ECMO and those who experienced an intertransplantation interval > 2 years were the only statistically significant factors affecting survival after pulmonary retransplantation.

**Pulmonary Hypertension Guidelines**

Pulmonary hypertension (PH), seen in multiple clinical conditions, exerts a significant epidemiologic burden on the cardiovascular health of many patients. In the United States, the standardized death rate associated with PH ranges between 4.5 and 12.3 per 100,000 population. The new guidelines, as developed by the European Society of Cardiology and the European Respiratory Society, focus on the classification, diagnosis, precipitating factors, and treatment updates. PH is defined as a mean pulmonary artery pressure (mPAP) of ≥25 mmHg at rest as assessed using invasive techniques, namely direct right-heart catheterization. Changes in the classification of PH include the addition of pediatric causes of PH in the different clinical groups, the addition of recently identified gene mutations to the heritable pulmonary arterial hypertension subgroup of clinical group I, precapillary pulmonary hypertension has been moved to clinical group V, the pulmonary veno-occlusive disease and/or pulmonary hemangiomatosis subcategories have been expanded, and group IV has been renamed as chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions.

Updates in diagnosing the etiology and the extent of PH from the 2009 guidelines include the use of transthoracic echocardiography as an initial measure for determining the probability of the presence of PH and the use of genetic testing. The current algorithm for the diagnosis of PH is shown in Figure 1. Echocardiography remains a key noninvasive tool to detect and evaluate the diagnosis of PH in contemporary practice. It allows for an evaluation of direct and indirect signs of elevated pulmonary arterial pressure. Performing transesophageal echocardiography in patients with PH allows the
following: (1) assessment and confirmation of congenital systemic-to-pulmonary shunts, (2) evaluation of mitral valve disease, (3) characterization of intracardiac masses not otherwise well-defined by other imaging modalities, and (4) a means to guide other interventional and intraoperative procedures.50

Several echocardiographic indices of pulmonary hemodynamics exist. In the absence of pulmonary flow obstruction or pulmonic stenosis, tricuspid regurgitation peak velocity (TRV) has a positive linear correlation with systolic pulmonary artery pressure, as measured using right-heart catheterization. TRV is used to determine the right ventricular (RV) systolic pressure gradient, and when added to the right atrial pressure (RAP) as estimated by inferior vena caval diameter, is a measure of systolic pulmonary artery pressure.48,50 The 2015 European

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Fig 1. Diagnostic algorithm for PH. From Galiè et al.48 CHD, congenital heart diseases; CT, computed tomography; CTD, connective tissue disease; CTEPH, chronic thromboembolic pulmonary hypertension; DLCO, carbon monoxide diffusing capacity; ECG, electrocardiogram; HIV, human immunodeficiency virus; HRCT, high-resolution CT; mPAP, mean pulmonary arterial pressure; PAH, pulmonary arterial hypertension; PAWP, pulmonary artery wedge pressure; PFT, pulmonary function tests; PH, pulmonary hypertension; PVOD/PCH, pulmonary veno-occlusive disease or pulmonary capillary hemangiomatosis; PVR, pulmonary vascular resistance; V/Q, ventilation/perfusion; RHC, right-heart catheterization; RV, right ventricular. A computed tomography pulmonary angiogram alone may miss diagnosis of chronic thromboembolic PH.
guidelines for PH suggested a low probability of PH with a nonmeasurable or TRV \( \leq 2.8 \text{ m/s} \) with no additional echocardiographic signs of PH, intermediate probability of PH with a nonmeasurable or TRV \( \leq 2.8 \text{ m/s} \) with the presence of additional echocardiographic signs of PH or with a TRV of 2.9-to-3.4 m/s without additional signs of PH, and high probability of PH with a TRV of 2.9-to-3.4 m/s with the presence of additional echocardiographic signs of PH or with a TRV > 3.4 m/s regardless of whether additional signs exist.  

Additional signs include a right-to-left ventricular basal diameter ratio > 1.0, flattening of the interventricular septum with a left ventricular eccentricity index > 1.1, RV outflow Doppler acceleration time < 105 ms and/or midystolic notching, early diastolic pulmonary regurgitation velocity > 2.2 m/s, pulmonary artery diameter > 25 mm, inferior vena cava diameter > 21 mm with decreased inspiratory collapse, and right atrial area at end-systole > 18 cm\(^2\). mPAP may be estimated by calculating the peak pulmonary regurgitant pressure gradient if pulmonic regurgitation exists and then adding an assumed or calculated RAP. Similarly, diastolic pulmonary arterial pressure may be determined by calculating the end-diastolic pulmonary regurgitant pressure gradient and adding RAP. Pulmonary vascular resistance may be estimated by dividing TRV (in m/s) by the time-velocity integral of the RV outflow tract. This may be beneficial in differentiating PH due to increased pulmonary blood flow from PH secondary to increased pulmonary vascular resistance. In addition, this may prove beneficial in patients with clinically severe PH with no change or a decrease in mPAP due to a progressive decrease in RV ejection fraction. 

Pulmonary capillary wedge pressure is estimated to be > 15 mmHg when E/E′, as derived from the transmital early inflow (E) and tissue Doppler early excursion of the mitral valve anulus velocities (E′), is > 15. Indices of impaired RV systolic pressure also may be determined by an evaluation of the tricuspid annular plane systolic excursion, which often is reduced in PH to > 16 mm, suggesting decreased RV function. This may be accompanied by an RV fractional area change < 35% and basal RV free-wall S′ wave velocity by tissue Doppler imaging < 10 cm/s. Together these indices suggest a clinical diagnosis of PH. Indirect signs of PH may include RV hypertrophy, dilated right-sided cardiac chambers, or a pericardial effusion. 

A growing emphasis exists on developing other reliable noninvasive techniques of quantifying PH, including the use of high-resolution contrast-enhanced computed tomography and cardiac magnetic resonance imaging. Structural anatomic anomalies such as increased pulmonary artery diameter > 29 mm, pulmonary artery-to-aortic diameter ratio > 1.0, segmental artery-to-bronchus ratio > 1.1, reduced pulmonary arterial distensibility, and retrograde flow raise the suspicion of PH. 

The new guidelines suggest a risk stratification assessment based on symptomatology, 6-minute walk distance (6MWD), cardipulmonary exercise testing, N-terminal pro-b-type natriuretic peptide (NT-proBNP) plasma levels, imaging, and hemodynamics. Patients with PH who have a low risk of 1-year mortality (< 5%) include those with no signs of right heart failure, progression of symptoms, or syncope; a 6MWD > 440 meters; a peak oxygen consumption (VO\(_2\)) > 15 mL/min/kg; a BNP < 50 ng/L or NT-proBNP < 300 ng/L; right atrial (RA) area > 18 cm\(^2\); RAP > 8 mmHg; cardiac index (CI) ≥ 2.5 L/min/m\(^2\); and mixed venous oxygen saturation (SvO\(_2\)) > 65%. Those at intermediate risk (5%–10%) include patients with no signs of right heart failure, slow progression of symptoms, occasional syncope, a 6MWD between 165 and 440 meters, peak VO\(_2\) between 11 and 15 mL/min/kg, a BNP of 50-to-300 ng/L or NT-proBNP between 300 and 1,400 ng/L, an RA area between 18 and 24 cm\(^2\) with no to minimal pericardial effusion, a RAP 8-to-14 mmHg, CI between 2.0 and 2.4 L/min/m\(^2\), and an SvO\(_2\) between 60% and 65%. Patients at the highest risk (> 10%) are those with symptoms of right heart failure, rapidly progressing symptoms, repeated episodes of syncope, a 6MWD < 165 meters, a peak VO\(_2\) < 11 mL/min/kg, a BNP ≥ 300 ng/m or NT-proBNP ≥ 1,400 ng/L, RA area > 26 cm\(^2\) with a pericardial effusion, RAP > 14 mmHg, CI < 2.0 L/min/m\(^2\), and an SvO\(_2\) < 60%. 

With the development of new therapeutic agents, the management of patients with PH has been divided into 3 approaches. The initial approach includes general measures such as supervised rehabilitation; supportive therapy, including oral anticoagulants, diuretics, digoxin, and supplemental oxygen; and referral to centers for vasoactivity testing. The second step includes calcium channel blocker therapy in vasoreactive patients and single therapy with endothelin-receptor antagonists—ambrisentan, bosentan, or macitentan—and phosphodiesterase-5 inhibitors—sildenafil, tadalafil, or vardenafil—or the guanylate cyclase stimulator riociguat in patients who are not vasoreactive. The third step is combination therapy or pulmonary transplantation in patients who do not respond to a single therapeutic regimen. 

Robotic Esophagectomy

Esophageal cancer, primarily adenocarcinoma and squamous cell carcinoma, is the 8th most common malignancy worldwide and the 6th most common cause of malignancy-associated mortality. Esophagectomy with mediastinal lymphadenectomy remains the cornerstone of curative therapy and is often performed in conjunction with perioperative chemotherapy and/or neoadjuvant chemoradiation. Open techniques are associated with relatively high postoperative complication rates, specifically cardiopulmonary morbidity and mortality. Minimally invasive esophagectomy (MIE) techniques were developed with the goal of reducing surgical trauma and morbidity. Evidence suggested that MIE techniques lower postoperative morbidity, reduce blood loss, and decrease hospital length of stay while yielding noninferior oncologic outcomes compared with open esophagectomy. However, these techniques have technical challenges, most notably with regard to limited visualization of and access to the upper mediastinum, and restricted range of motion associated with laparoscopic/thoracoscopic instruments that...
may limit lymph node harvest or impair intrathoracic anastomoses. Recently, there has been growing interest in robotically assisted minimally invasive esophagectomy (RAMIE), which offers several distinct advantages over traditional MIE techniques. Specifically, RAMIE offers superior 3-dimensional imaging that closely mimics open surgery and articulated instruments with enhanced range of motion and depth compared with laparoscopic instruments. These features are particularly useful in facilitating visualization and dissection of lymph nodes in the upper mediastinum and precise suturing of the intrathoracic anastomosis.

Given the relative infancy of robotic esophagectomy, data comparing RAMIE with open esophagectomy are lacking, and there is limited literature comparing RAMIE with nonrobotic MIE. The preponderance of early literature consists of case series, single-center feasibility studies, and small-scale comparisons. Even though these early studies demonstrated feasibility, oncologic noninferiority, and short-term oncologic equivalence of RAMIE compared with other esophagectomy techniques, the consistencies largely end there. There are conflicting data regarding the impact of robotic techniques on metrics such as hospital length of stay, degree of resection, duration of mechanical ventilation, and other postoperative complications; some studies suggested improvements, whereas others observed no difference with MIE. Surgical times for RAMIE also varied, depending on approach, experience, and technique: some centers noted longer duration, whereas other experienced centers observed no difference between RAMIE and MIE. The small number of cases; the heterogeneity in surgical technique, experience, and terminology; and the incorporation of partially open hybrid procedures collectively restrict comparison and generalization. Few conclusions can be drawn from this early literature beyond the feasibility and oncologic noninferiority of RAMIE.

Two newly published case series added to the existing feasibility and safety data for RAMIE. Weksler et al evaluated 20 patients who underwent robotically assisted thoracoscopic esophagectomy, noting an average surgical time of 499.5 ± 70.1 minutes, estimated blood loss (EBL) of 355.7 ± 329.6 mL, and conversion to open surgery in 2 patients. Intensive care unit length of stay was 1.7 ± 1.2 days, and 1 patient developed postoperative pneumonia. In a larger series of 114 patients, Park et al noted a surgical time of 419.6 ± 7.9 minutes, EBL of 208.7 ± 25.8 mL, median intensive care unit stay of 1 day, recurrent laryngeal nerve palsy in 30 patients, and a 9.6% postoperative pulmonary complication rate that they deemed comparable with open and standard MIE techniques given the extent of mediastinal lymphadenectomy performed. In both series, the authors determined that RAMIE was feasible and safe at their respective institutions but acknowledged the need for long-term data.

In 100 patients, Sarkaria et al published a series that highlighted the importance of a standardized technique and a dedicated surgical and anesthesia team to optimize safety and outcomes while developing proficiency with RAMIE. The authors observed improvement over the course of the study period in surgical duration, EBL, and the number of conversions to open thoracotomy, corroborating earlier data from Puntambekar et al that surgical duration decreased with experience and a dedicated surgical and operating room team.

Two studies comparing aspects of RAMIE with open esophagectomy. Whereas neither technique demonstrated clear superiority, RAMIE was associated with several favorable postoperative metrics. Mori et al compared short-term outcomes of transhiatal RAMIE and conventional transthoracic surgery. Robotic transhiatal surgery was associated with longer surgical duration (524 vs 428 min, \( p < 0.0001 \)) but shorter hospital length of stay (18 vs 24 d, \( p = 0.0013 \)). The authors noted surgical equivalence and similarities in postoperative pulmonary morbidity between the groups. Jeong et al compared the incidence of postoperative delirium in 88 patients who underwent RAMIE with 159 patients who underwent open esophagectomy. The robotic group had longer surgical duration (4.8 vs 4.5 h, \( p < 0.001 \)) but lower rates of postoperative delirium (42% vs 30%, \( p = 0.035 \)); decreased EBL (200 vs 200 mL, \( p = 0.024 \)); and reduced incidences of chylothorax, wound dehiscence, and supraventricular tachycardia.

Two studies comparing RAMIE with conventional MIE did not demonstrate clear superiority of either approach. Park et al compared 62 patients undergoing robotic esophagectomy with 43 patients undergoing thoracoscopic esophagectomy for squamous cell carcinoma. The authors observed similar surgical duration and rates of early postoperative complications and mortality between the groups, even though the robotic group exhibited a trend toward a lower incidence of vocal cord paralysis that was not statistically significant. The robotic group had longer duration of one-lung ventilation (185.2 vs 120 min) and higher lymph node retrieval, which did not translate into a long-term survival or recurrence benefit. However, the authors concluded that robotic esophagectomy was superior on the basis that previously published studies demonstrated improved long-term survival with higher lymph node retrieval. In a retrospective comparison of open and MIE procedures from the National Cancer Database, Yerokun et al performed a subgroup analysis comparing MIE with RAMIE, observing surgical equivalence between the groups, with no differences in hospital length of stay or 30-day mortality. Of note, however, subgroup analysis did reveal a statistically significant survival benefit in patients with squamous cell carcinoma who underwent RAMIE (84% vs 56% at 2 years; \( p = 0.034 \)).

Recently published reviews reflected the existing literature with regard to the perceived benefits of robotic esophagectomy and the impact on short- and long-term outcomes. Martinek et al described the benefits of enhanced visualization and reach of robotic instruments in facilitating resection of cancer from the upper third of the esophagus, an area previously avoided due to technical difficulty. DeLong et al suggested that a transhiatal robotically assisted approach was superior to an open approach in patients with underlying lung disease and mid-to-distal esophageal tumors. However, reviews published
by Rodriguez et al., Giugliano et al., and Hammoud found no compelling evidence to suggest perioperative or long-term benefits of RAMIE over MIE.

Despite high cost and relative ambiguity regarding the benefits of robotically assisted esophagectomy, the purported surgical advantages and the development of more cost-effective robotic platforms continue to foster interest in developing RAMIE techniques. Long-term data and large-scale prospective, randomized controlled trials are required to determine the clinical benefits of RAMIE. At present, there is great anticipation in the thoracic oncology community for the clinical benefits, safety, and cost. 6

References


