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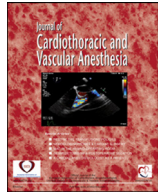
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Case Conference

Perioperative Approaches to the Anterior Mediastinal Mass—Principles and Pearls From a Ten-Year Experience at an Experienced Referral Center

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Key Words: anterior mediastinal mass; thymoma; airway compression; echocardiography; spontaneous ventilation; neuromuscular blockade; general anesthesia; superior vena cava

MEDIASTINAL MASSES represent a heterogeneous spectrum of disease that may present unique perioperative challenges in the operating room.¹⁻⁵ They may arise in the anterior mediastinal compartment, with origins that include the thymus and thyroid, and with pathologies that include germ cell tumors and lymphomas.^{1,2} Anterior mediastinal masses may be malignant and, consequently, may invade adjacent cardiovascular or respiratory structures. Even with careful multidisciplinary planning, perioperative cardiopulmonary collapse still may occur in the perioperative period.³⁻⁵

Given the relative rarity and clinical heterogeneity of mediastinal masses, there remains an evolving understanding of

perioperative outcomes. This case conference begins with a large single-center report of patients undergoing surgical intervention for anterior mediastinal masses. The findings from this report then are discussed and framed in the context of the current literature by two expert commentaries.

Background for the Study*

Surgery for anterior mediastinal masses may be indicated for either diagnostic or therapeutic purposes.^{4,5} Surgical biopsy is often the standard of care for histologic diagnosis of mediastinal lesions because larger specimens are required for accurate diagnosis of many lesions, such as lymphoma.^{1,2} The parasternal anterior mediastinotomy, first described by Chamberlain and McNeill in 1966, typically provides adequate exposure for biopsy of large masses in the anterior mediastinum, particularly those adjacent to the posterior sternum or

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chest wall.³ At some centers, awake, video-assisted thoracoscopic biopsy has been advocated for patients with complex anterior mediastinal masses to avoid the risks of general anesthesia and to minimize the incidences of perioperative airway and hemodynamic compromise.^{4,5}

Advances in perioperative care and multimodal oncologic therapy have made surgical resections a possibility for more aggressive or advanced tumors that previously would have been deemed unresectable.¹⁻⁵ These lesions, which may involve or abut adjacent mediastinal structures, such as the great vessels, lung, and heart chambers, often are approached through a median sternotomy because of advantages such as favorable exposure and decreased postoperative pain compared with thoracotomy.²⁻⁵ Further resection and, if needed, vascular reconstruction or pulmonary resection, also typically can be performed safely through this approach. Alternative surgical approaches, such as a clamshell incision or thoracotomy, also may be used in appropriate circumstances.^{1,2}

The anesthetic approach to a mediastinal mass often will stratify the clinical risk of cardiopulmonary compromise based on criteria such as preoperative symptomatology and chest imaging, including proximity to and compression of crucial structures in the mediastinum.^{6,7} Additional perioperative considerations include maintenance of spontaneous ventilation, avoidance of neuromuscular blockade, invasive hemodynamic monitoring, adequate intravenous access, patient positioning, and the possibility of cardiopulmonary bypass.⁶⁻⁹

The purpose of the present case series was to assess the safety and efficacy of perioperative management at the University of Pennsylvania for patients with anterior mediastinal mass over a ten-year period. The clinical outcomes for this surgical cohort also were examined, including in-hospital and 30-day mortality.

Study Methods

The study population included all patients who presented for surgical management of an anterior mediastinal mass, by a single senior thoracic surgeon at the University of Pennsylvania from June 2008 to June 2018. The study protocol was approved by the Institutional Review Board and was granted a waiver of patient consent. Exclusion criteria included patients with middle or posterior mediastinal masses, patients who did not have surgery during this timeframe, and patients who were treated by another surgeon. The demographic, anesthetic, and remaining perioperative data were collated from prospectively maintained institutional databases.

The anesthetic clinical data included anesthesia type, induction method, airway management, use of neuromuscular blockade, and evidence of significant preoperative tracheal compression, as defined by a $\geq 50\%$ decrease in the cross-sectional area on preoperative chest imaging. All data were archived in a secure research electronic database. Descriptive and analytical statistics were undertaken for both continuous and categorical variables with Stata software, version 15.1 (StataCorp, College Station, TX).

Study Results

During the study period, 151 patients presented with an anterior mediastinal mass. After all exclusions (Fig 1), the study cohort for further analysis comprised 57 patients.

The patient demographic data are presented in Table 1. The majority of patients presenting for resection were male, with an average age of 53.4 ± 14.2 years at the time of surgery. Most were symptomatic at the time of presentation, and the minority (17.5%) underwent neoadjuvant treatment before surgery. A history of tobacco use (42.1%) was common, but only 3.6% of the trial cohorts had clinically diagnosed chronic obstructive pulmonary disease.

The perioperative variables are summarized in Table 2. The most common approach was via median sternotomy, although thoracotomy and parasternal anterior mediastinotomy (Chamberlain procedure) also were used. Overall, the surgical procedure was well-tolerated in this cohort, with an incidence of atrial fibrillation and pneumothorax in the 3%-to-5% range. Perioperative cardiac arrest was observed in only one patient who was successfully resuscitated. Rarer complications included vocal cord paralysis, phrenic nerve injury, pericarditis, deep vein thrombosis, respiratory distress, and enteral intolerance. The average length of hospital stay was 4.2 ± 4.5 days. The readmission rate at 30 days was 10.5%, and nearly three-quarters of the study cohort ($n = 40$ [71.4%]) were alive at the end of the study period.

The histopathologic data are summarized in Table 3. Nearly half of the patients (45.6%) had biopsy-proven thymoma, followed by lymphoma as the next most common etiology (19.3%). Invasion of adjacent mediastinal structures was noted in about half of the study cohort ($n = 24$ [43.6%]). On average,

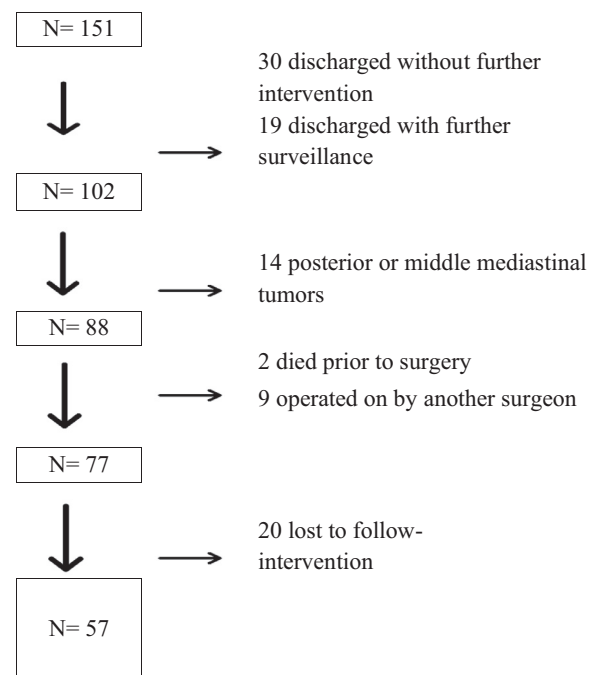


Fig 1. Study flow diagram: patient selection and enrollment.

Table 1
Patient Characteristics and Demographics

Characteristic	n	Percentage (%)	Mean	Standard Deviation
Age at surgery (y)			53.4	14.2
Weight at surgery (kg)			85.7	20.8
Body mass index (kg/m ²)			29.1	7
Male sex	31	54.4%		
Race				
White	44	77.2%		
African-American	10	17.5%		
Other	3	5.3%		
Preoperative factors				
Symptomatic	34	59.6%		
Chemotherapy/radiation	10	17.5%		
History of COPD	2	3.6%		
Tobacco exposure	24	42.1%		
Pack-years smoked*			20.3	32.4

Abbreviation: COPD, chronic obstructive pulmonary disease.

* Data for 23 patients.

Table 2
Perioperative Factors and Outcomes

Characteristic	n	Percentage (%)	Mean	Standard Deviation
Surgical approach				
Sternotomy	39	68.4%		
Thoracotomy	7	12.3%		
Chamberlain	7	12.3%		
Other	4	7.0%		
Length of stay (d)			4.2	4.1
Readmitted within 30 d	6	10.5%		
Interval to readmission (d)			14.3	10.7
Postoperative complications				
Pneumothorax	2	3.5%		
Vocal cord paralysis	1	1.8%		
Cardiac arrest	1	1.8%		
Phrenic nerve injury	1	1.8%		
Pericarditis	1	1.8%		
Atrial fibrillation	3	5.3%		
Deep vein thrombosis	1	1.8%		
Respiratory distress	1	1.8%		
Enteral intolerance	1	1.8%		
Vital status as of June 1, 2018				
Alive	40	70.2%		
Dead	3	5.3%		
Unknown	14	24.5%		

the larger specimen size was 5.9 ± 3.4 cm, although some larger lesions (particularly lymphomas) were biopsied and not completely resected.

The majority of patients (98.2%) underwent routine intravenous anesthetic induction, as outlined in Table 4. Of these 56

Table 3
Pathology Findings

Characteristic	n	Percentage (%)	Mean	Standard Deviation
Tumor type				
Thymoma	26	45.6%		
Hodgkin's lymphoma	6	10.5%		
Large B cell lymphoma	5	8.8%		
Thymic carcinoma	4	7%		
Benign cyst	4	7%		
Other carcinoma	2	3.5%		
Schwannoma	2	3.5%		
Other	8	14%		
Mediastinal invasion	24	43.6%		
Mass size (cm)			5.9	3.4

cases, only one patient (1.8%) had a mask induction, with the preservation of spontaneous ventilation before intubation, after which, neuromuscular blockade was commenced. Most intravenous inductions included neuromuscular blockade before endotracheal intubation (92.9%), except in two cases of myasthenia gravis for which bolus remifentanyl was added to optimize intubating conditions. The entire study cohort underwent positive-pressure ventilation during anesthetic maintenance. A successful tracheal intubation was possible with direct or video laryngoscopy in almost all patients (96.4%). Complex airway management with flexible fiberoptic bronchoscopy was required in a single patient. Tracheal compression >50% was noted on preoperative chest imaging in only 1.8% of the entire cohort. None of the study patients required mechanical circulatory support before or during their procedures.

Discussion

This retrospective trial has demonstrated that the described techniques of perioperative management in this ten-year, single-center experience are safe and effective compared with the recent literature.⁹⁻¹³ Because of the heterogeneous nature of anterior mediastinal masses, there are limited large experiences published from the perioperative perspective. However, investigators have noted excellent results with surgical resection for invasive anterior mediastinal tumors. In a series of patients undergoing surgical resection of advanced thymic tumors (N = 45), the major complication rate was 6.7% (3/45 cases), without any surgical mortality.¹⁰ The success of surgery in the contemporary era has been achieved within the framework of a balanced multimodal oncologic approach.^{10,11} A potent predictor of long-term survival in this patient population is the ability to achieve complete resection; incomplete resection or debulking procedures do not appear to modify disease-free survival.^{12,13} Unfortunately, some patients may present at advanced stages of disease, making it unlikely to completely complete resection unlikely. For this patient group, neoadjuvant therapy may be of benefit to alleviate disease burden before surgical resection.^{1,2}

Table 4
Anesthetic Data

Characteristic	n	Percentage (%)
Anesthesia type		
General anesthesia	57	100%
Induction type		
Mask	1	1.80%
Intravenous	56	98.20%
Ventilation type		
Positive pressure	57	100%
Airway management		
Routine intubation	55	96.40%
Fiberoptic/complex/awake	1	1.80%
No airway documented	1	1.80%
Tracheal compression >50%	1	1.80%

Despite an emphasis in the literature on the maintenance of spontaneous ventilation (and therefore avoiding neuromuscular blockade and positive pressure ventilation), the anesthetic plan for nearly every case in this series included positive pressure ventilation and neuromuscular blockade.^{5,6} There were no untoward effects of this anesthetic practice, including an absence of major respiratory or hemodynamic compromise. Neuromuscular blockade was minimized in patients with known myasthenia gravis. Of note, the anesthetics during this study period were used before sugammadex was available routinely in the operating room environment at the University of Pennsylvania. A recent report demonstrated that there may be minimal diminishment of airway caliber with the institution of neuromuscular blockade and positive-pressure ventilation in the setting of a large anterior mediastinal mass.¹⁴ The lack of neuromuscular blockade may contribute to interference with the surgical approach and allow coughing that can lead to a decrease in venous return secondary to an increase in intrathoracic pressure and precipitate hemodynamic collapse in patients with less reserve.^{5,6}

There are, however, certain precautions that have been recommended in the literature when considering an anesthetic approach to these patients.¹⁴⁻¹⁷ Patients should be assessed on an individual basis to determine a safe and effective anesthetic approach, including review with the multidisciplinary team.¹⁵⁻

¹⁷ A rescue position, such as left lateral decubitus, should be identified so that presenting symptomology may be ameliorated by patient repositioning in the operating room.^{5,6} An arterial line should be considered for intensive hemodynamic monitoring during anesthetic induction, especially in patients susceptible to cardiovascular collapse because of proximity between the mass and great vessels.^{16,17} Adequate intravenous access should be secured, with consideration for placement of lower extremity and/or femoral access if there is concern about compression of the superior vena cava.¹⁵⁻¹⁷

In patients with large masses that compress the major airways and great vessels with/without significant symptomatology, consideration should be given to mechanical cardiopulmonary support, whether extracorporeal membrane oxygenation or cardiopulmonary bypass.^{5,6} If there is concern about cardiopulmonary collapse with the induction of anesthesia, femoral arterial and venous access may be required before induction to facilitate prompt mechanical cardiopulmonary support.¹⁵⁻¹⁷ In these cases, cardiac surgical and perfusion personnel should be immediately available with a primed circuit to minimize delays.^{5,6}

This retrospective trial had its limitations. Even though it was performed at a tertiary care center with a large catchment area, the study population and outcomes may not be generalizable to all-comers because it was a single-center analysis of a senior surgical practice. Furthermore, some records were incomplete at times and the study population was limited to adults.

Despite these limitations, the reported complications were similar to those in the published literature.¹⁷ In an analysis of perioperative cardiorespiratory complications in adults with mediastinal mass (N = 98), no patients had intraoperative airway collapse.¹⁷ Cardiovascular collapse occurred in 3.1% of the trial cohort and was significantly associated with pericardial effusion, a known risk factor in the development of cardiovascular complications with initiation of positive-pressure ventilation.¹⁷ As in the case series presented for this case conference, most complications in this adult observational trial were postoperative.

The trials to date have demonstrated that, although mediastinal masses present perioperative challenges, they can be

Table 5
Reports of Perioperative Outcomes for Patients with Mediastinal Mass

Author	Year	Population	Cohort Size	Respiratory Complications (%)	Cardiovascular Complications
Bechard et al. ¹⁷	2004	Adult	98	0%	3.1%
Azarow et al. ¹⁹	1993	Adult/pediatric	257 (192 adults)	3.5%	0%
Angheliescu et al. ¹⁸	2007	Pediatric	118	9.3%	0%
Azizkham et al. ²⁰	1985	Pediatric	50	18.0%	Not reported
Ferrari et al. ²¹	1990	Pediatric	44	9.1%	0%
Freud et al. ²²	2002	Pediatric	27	Not reported	Not reported
King et al. ²³	1997	Pediatric	51	9.8%	2.0%
Malik et al. ²⁴	2019	Pediatric	44	0%	0%
Shamberger et al. ²⁶	1995	Pediatric	31	0%	0%
Stricker et al. ²⁷	2010	Pediatric	46	10.9%	0%
Reddy et al. ²⁵	2020	Pediatric	25	0%	0%

managed successfully with a thoughtful multidisciplinary approach that can minimize perioperative complications.¹⁷⁻²⁷ The preponderance of data in the literature comes from the pediatric population, as summarized in Table 5. The adult case series in the present case conference, therefore, adds to the limited literature concerning perioperative outcomes in adults presenting with anterior mediastinal mass. Although this area requires additional study, the current data suggested that complications can be minimized at an experienced center.

Even though relatively uncommon, mediastinal masses present significant challenges in the perioperative period. In order to ensure the best outcome for each patient, patients presenting for surgical management of a mediastinal mass should be managed in a comprehensive multidisciplinary fashion.¹⁵⁻²⁸ The perioperative strategy should be coordinated and framed within a holistic oncologic model.¹⁵⁻²⁸

Commentary 1†

†R. Ibrahim and J. Sanders

The anesthetic management of patients with mediastinal masses is challenging. In the mediastinum, a significant mass effect may compress cardiopulmonary structures, leading to airway and/or hemodynamic instability.¹⁻⁴ Expert consensus has recommended avoiding general anesthesia when possible; but if indicated, then to consider preserving spontaneous respiration in order to minimize the risks of airway compression and hemodynamic collapse.¹⁻⁷ Even though special considerations must be made for each patient because of unique presenting features, recent studies also have evaluated perioperative management of these challenging cases.¹⁻⁷ In this presented case series, the experience of a single surgeon at a tertiary care center in the management of anterior mediastinal masses over the past decade has been described to further clarify the factors that can guide this complex decision-making process.

The mediastinum can be divided into anterior, middle, and posterior compartments.^{1,2} Even though all three compartments are bound superiorly by the thoracic inlet and inferiorly by the diaphragm, the anterior mediastinum lies anterior to the heart and great vessels.^{1,2} Anterior mediastinal masses include thymomas, germ cell tumors, lymphomas, and thyroid-derived lesions, as illustrated in Table 3. Although anterior mediastinal masses frequently are benign; there are, however, malignant etiologies that typically require biopsy for definitive diagnosis.^{1,2}

In this case series, the investigators assessed the safety and efficacy of the perioperative management of patients who underwent resection or biopsy of an anterior mediastinal mass by a single senior surgeon over ten years from 2008 to 2018. The investigators also assessed factors that may contribute to perioperative morbidity and mortality. The data were collected from a pool of patients who presented to the thoracic surgery outpatient clinic at the University of Pennsylvania and include demographics, anesthetic details, surgical specifics, and clinical outcomes, as outlined in the accompanying Tables 1 through 4.

An important step in the management of patients with mediastinal masses is the appropriate preoperative assessment of the patient.^{28,29} A symptomatic presentation is very suggestive that there may be high risk for anesthetic complications.^{6-8,17,18} The symptoms in this setting may be a result of mass effect of the tumor, direct extension of mass into neighboring structures, and/or paraneoplastic syndromes.^{1,2,17-25} The spectrum of presenting symptoms includes cough, shortness of breath, orthopnea, hoarseness, wheezing, stridor, cyanosis, facial edema, and syncope.¹⁷⁻²⁹ It remains important to assess for changes in severity of symptoms with body position because these dynamic presentations may be a result of significant compression of vital mediastinal structures.⁵⁻⁹

The perioperative management of these patients is complex because of these factors and, therefore, frequently requires a multidisciplinary approach.^{17-20,28,29} Some patients may be candidates for chemotherapy and/or radiotherapy to decrease tumor size, with clinical improvement and decreased perioperative risk, as outlined in Table 1 of this case series.¹⁰ Chest imaging, including echocardiography, often guides the delineation of disease extent as a platform for perioperative planning.^{1,2} The level of perioperative risk can be stratified into low, intermediate and high risk depending on symptomatology and imaging.¹⁷⁻¹⁹ In this presented study, 60% of patients were symptomatic at the time of presentation, with only one patient showing tracheal compression >50%, as outlined in Table 1. These factors suggested that this trial cohort included low- and intermediate-risk groups, rather than exclusively focusing on high-risk patients.

In the trial by Bechard et al., the presence of cardiopulmonary signs and symptoms at initial presentation were predictive of postoperative life-threatening respiratory complications, with an odds ratio of 6.2.¹⁷ Even though they also found that the presence of combined obstructive and restrictive patterns on pulmonary function testing was associated with perioperative pulmonary complications with an odds ratio of 3.9, pulmonary function testing has not become an essential preoperative test because there may be a weak correlation between the severity of major airway obstruction and the findings from pulmonary function testing in patients with anterior mediastinal masses.^{15,30} Furthermore, in the trial by Bechard et al., the presence of a preoperative pericardial effusion on chest imaging correlated very strongly with intraoperative complications, with an odds ratio of 19.8.¹⁷

In a clinical trial by Ng et al. of 63 children with mediastinal masses, tracheal compression, vascular involvement, and respiratory symptoms/signs all were strongly predictive for significantly increased risk of general anesthesia.³¹ In another study conducted by Lam et al. on 29 pediatric patients, the factors associated with acute airway compromise included airway narrowing/displacement on imaging, anterior location of tumor, histologic diagnosis of lymphoma, symptoms/signs of superior vena cava obstruction, radiologic evidence of vessel compression, pericardial effusion, and pleural effusion.³² The findings from these two trials were in keeping with the literature, although the level of perioperative risk appeared to vary across the reports, as outlined in Table 5.¹⁷⁻²⁸

Even though the preservation of spontaneous ventilation has been emphasized in the anesthetic management of patients with anterior mediastinal mass, the safety of positive-pressure ventilation also has been demonstrated, as in the present case series.^{5-7,14-16} This emphasis may have stemmed from trials that were conducted mostly on pediatric patients who may display a higher likelihood of airway compromise and hemodynamic instability in the presence of mediastinal masses.^{27-29,33,34} Furthermore, spontaneous ventilation does not guarantee successful airway management and clinical stability in this setting, with reports also indicating that patient positioning and associated coughing may be more related to cardiopulmonary compromise than positive-pressure ventilation and neuromuscular blockade.^{5-7,33-35} The safety of general anesthesia and positive-pressure ventilation also has been highlighted in the present case conference, in which all 57 patients had this anesthetic approach with good clinical outcomes. Of note, only one patient in the presented study had tracheal compression >50%, and the mediastinal mass size averaged 5.9 ± 3.4 cm. These clinical outcomes must be considered in light of these factors because mass size and significant tracheal compression >50% significantly predict perioperative complications.^{1-7,15-17}

A report described serial bronchoscopic evaluation during general anesthesia of a patient with a mediastinal mass compressing the tracheobronchial tree and superior vena cava.¹⁴ The anesthetic management included awake endotracheal intubation followed by general anesthesia with positive-pressure ventilation and neuromuscular blockade.¹⁴ The bronchoscopic findings were that although airway calibers were diminished with anesthetic induction, positive-pressure ventilation and neuromuscular blockade led to a slight increase in airway area.¹⁴ These observations suggested that positive-pressure ventilation may not always compromise cardiopulmonary stability in patients with an anterior mediastinal mass.

As an alternative to endotracheal intubation in this setting, a recent study by Liu et al. demonstrated the safety and efficacy of laryngeal mask ventilation in 96 cases of uniportal thoracoscopic thymectomy.³⁶ In contrast to endotracheal intubation, the anesthetic approach with laryngeal mask ventilation was associated with a faster perioperative recovery and fewer complications such as sore throat, nausea, cough, and urinary retention.³⁶ For select patients, this approach to airway management may serve as an alternative less-invasive option.

The adequate preparation with a multidisciplinary team is important for the successful management of patients with mediastinal masses.^{14-16,37,38} Several studies also have highlighted, in selected cases, the feasibility of successful surgical intervention with the patient under local anesthetic and sedation.^{37,38} The literature also has emphasized the roles for cardiopulmonary bypass in this setting for clinical rescue and for aggressive mediastinal resection.^{5-9,12,13} No patients in the present case conference required mechanical circulatory support. In high-risk patients, the multidisciplinary approach included invasive monitoring and thorough preparation for clinical rescue, including cardiopulmonary bypass. The availability of thoughtful planning, communication, and additional

resources can be life-saving in the event of cardiopulmonary collapse.³⁹ These additional measures are especially relevant in patients with large symptomatic masses causing significant compression of neighboring mediastinal structures.¹⁴⁻¹⁶

Even though the present case series focused on anterior mediastinal masses, management of middle and posterior masses also can be challenging.^{8,9} In a retrospective study by Shen et al. of 44 cases of surgical intervention on posterior mediastinal masses, the incidence of perioperative cardiopulmonary complications was 16%.²⁹ These complications included severe hypoxemia, hemodynamic instability, and postoperative respiratory distress.²⁹ They noted that complications correlated with large masses and clear evidence of mediastinal compression.²⁹

A significant limiting factor in the research regarding the perioperative management of mediastinal masses is sample size. This was a feature of the present case series due to factors such as the rarity of the disease, a focus on anterior mediastinal masses, and collected data from a single center. With only 60% of the patients being symptomatic, as well as almost all but one showing <50% tracheal compression, a significant percentage of this trial cohort would not be considered high risk. Although this data bias has contributed to the favorable reported results, the trial described herein nevertheless challenged the previous generalizations for anesthetic management of mediastinal masses. The investigators have demonstrated that with appropriate patient selection, general anesthesia with positive-pressure ventilation and neuromuscular blockade can be performed safely in this clinical setting, with an emphasis on a multidisciplinary approach and thorough consideration and preparation for clinical rescue.

Commentary 2‡

‡N. Kumar and M. Capdeville

The anterior mediastinal mass can be a major perioperative challenge because of concomitant encroachment and/or invasion of vital mediastinal structures such as the heart, major vessels, and central airways.¹⁻⁸ The recommended approaches to anesthetic management in this setting include important goals such as maintenance of airway control and hemodynamic stability, even with the introduction of newer anesthetic options such as dexmedetomidine.³⁷⁻⁴⁰ Major limitations in the current evidence base include a pediatric focus and a preponderance of case reports and case series, with an absence of large registry data to inform contemporary anesthetic management in adults. This case-based approach has, however, facilitated the identification of best practices, recognizing that there still will be cases that challenge these recommendations.³²⁻³⁵ The major messages from the literature to date include the importance of meticulous preoperative preparation, high-quality communication within a multidisciplinary approach, and clear plans for clinical rescue.⁹⁻²⁹

A unique feature of the present case conference is the contemporary presentation of a ten-year experience in adults from a reputable and experienced tertiary care center. The authors

investigated the safety and efficacy of perioperative approaches to anterior mediastinal mass at the University of Pennsylvania in Philadelphia. They also examined perioperative outcomes after resection, including surgical mortality. All the surgical interventions were performed by a single experienced thoracic surgeon, eliminating possible bias with regard to surgical techniques and level of experience. A total of 57 patients were included in the study after all exclusion criteria were applied (see Fig 1). A total of 68% underwent median sternotomy, with thymoma being the most common diagnosis. There was tumor invasion of adjacent structures in nearly half of all patients, and the larger surgical specimen dimension averaged 5.9 ± 3.4 cm. Most patients underwent standard induction of general anesthesia, including neuromuscular blockade, as outlined in Table 4. Neuromuscular blockers deliberately were avoided in patients with myasthenia gravis. All the trial patients were managed uneventfully with positive-pressure ventilation during anesthetic maintenance. Importantly, no patients required mechanical circulatory support. This case series demonstrated the safety and feasibility of standard anesthetic techniques in general anesthesia in properly selected patients. This does not imply, however, that this approach is safe in all patients.

The complex pathology of anterior mediastinal masses necessitates a multidisciplinary diagnostic approach, including multimodal imaging for the assessment of neighboring vital structures and consideration of cannulation strategies for possible extracorporeal support.²⁵⁻³⁴ Detailed computed tomographic imaging of the chest will characterize mass location and involvement of neighboring structures and often is considered a high-yield diagnostic study.²⁶⁻³⁶ High-resolution computed tomography with angiography and multiplanar reconstruction will delineate involvement of vascular structures and facilitate airway reconstruction to evaluate obstruction and/or displacement. It should be noted, however, that this detailed assessment of the airway may be limited by changes in airway diameters during the respiratory cycle.^{41,42} Magnetic resonance imaging may facilitate further the differentiation of surrounding tissues and has enhanced sensitivity for identifying invasion into neighboring neurologic structures.²⁸⁻³⁵ Both types of cross-sectional imaging can be used to assess for mediastinal cardiovascular involvement including dynamic compression during the cardiac cycle, with optimal spatial resolution and limited temporal resolution.

Once considered an important part of a patient's preoperative assessment, pulmonary function testing in the setting of a mediastinal mass with flow-volume loops to differentiate intrathoracic versus extrathoracic obstruction is of questionable benefit in contemporary practice.^{15-17,28-30} In addition to radiographic cross-sectional imaging and spirometry, real-time echocardiography also can aid in the assessment of a given mediastinal mass and its relationship to the heart and great vessels.^{43,44} Transesophageal echocardiography can be used to evaluate unusual presentations, including large aortic pseudoaneurysms developing after cardiac surgery and can be used to assess the dynamic compression of the great vessels in the mediastinum that may follow changes in patient position and

surgical dissection.⁴³⁻⁴⁵ The mediastinal risks of transesophageal echocardiography, such as esophageal injury and compression of the posterior trachea, must be assessed in this setting.⁵⁻⁷

Perioperative risk stratification has been framed by the concept of a "mediastinal mass syndrome."⁵⁻⁷ This syndrome is characterized by acute hemodynamic and/or respiratory decompensation from compression of mediastinal structures by the mass.⁵⁻⁷ Low-risk patients are asymptomatic or have mild symptoms without any postural component and no radiographic evidence of impingement on adjacent structures. Intermediate-risk patients may have mild or moderate postural symptoms or symptoms related to an associated secondary disease such as myasthenia gravis and tracheal compression <50%. High-risk patients have stridor, cyanosis, severe postural symptoms, with tracheal compression >50% or tracheobronchial compression, pericardial effusion, or superior vena cava syndrome.⁵⁻⁷ Based on these risk profiles, the perioperative team can plan accordingly in a stratified fashion.⁵⁻⁷

Bechard et al. described 98 adult patients with mediastinal masses who were administered 105 anesthetics from 1994 to 2000.¹⁷ They reported four intraoperative cardiorespiratory complications and 11 postoperative respiratory complications.¹⁷ Even though no instances of airway collapse occurred intraoperatively, seven of the 11 postoperative respiratory complications were life-threatening.¹⁷ After multivariate logistic regression analysis, perioperative complications were predicted when cardiorespiratory signs and symptoms were present at initial presentation (odds ratio 6.2) and in the presence of mixed pulmonary syndrome on pulmonary function testing (odds ratio 3.9).¹⁷ The presence of a pericardial effusion on preoperative imaging was predictive of intraoperative complications (odds ratio 19.8), and postoperative respiratory complications occurred in the presence of either tracheal compression >50% (odds ratio 7.4) or mixed pulmonary syndrome (odds ratio 15.1).¹⁷

The anesthetic assessment for anterior mediastinal mass should focus on the presence of signs and symptoms associated with mediastinal compression and/or invasion of the major airways, great vessels, and heart chambers. A multidisciplinary team-based approach sheds light on the underlying pathology of anterior mediastinal masses and allows for an appropriate perioperative treatment plan to be established in both adults and children.^{28-34,43-47} This multidisciplinary team may include the disciplines of oncology, surgery, anesthesiology, perfusion, radiology, and critical care.¹⁷⁻²⁸ In adults, thymomas are the most common neoplasms of the anterior mediastinum requiring surgical intervention, as illustrated in the present case series. One-third of these tumors demonstrate capsular invasion into surrounding structures, including the heart and great vessels, and myasthenia gravis is present in up to 50% of patients, adding to the anesthetic complexity for these patients.^{1,2,48}

Surgical approaches to anterior mediastinal masses have been a process in evolution; minimally invasive thoracoscopic and robotic techniques have gained increasing appeal in recent years.^{36-38,49} In a retrospective analysis of 262 patients without

myasthenia gravis who underwent thymectomy via video-assisted thoracoscopic surgery (n = 125) versus transsternal (n = 137) approaches, Ye et al. demonstrated that the minimally invasive technique offered multiple advantages, including superior pain control, less blood loss, shorter surgical times, and shorter length of stay.⁴⁹ Minimally invasive approaches, however, are limited by mass size, quality of exposure, and tumor extension into adjacent structures. Median sternotomy has remained the reference standard for thymectomy.^{1,2} Either full or partial upper sternotomy offers optimal access to the superior mediastinum, lungs, and hilum. Moreover, surgeons can achieve central cannulation rapidly in the event that extracorporeal support becomes necessary. The classic clamshell or hemi-clamshell incision also can be considered for more inferiorly located tumors while still providing access to the central vessels. At the Cleveland Clinic, minimally invasive approaches are used whenever possible, including thoracoscopic techniques with or without robotic assistance.

The anesthetic choice in patients with anterior mediastinal masses is highly dependent on characteristics and location of the mass, its pathology, and the selected surgical technique. There is typically an individualized anesthetic approach depending on these aforementioned considerations.⁵⁻⁷ Of utmost importance is patient symptomatology.¹⁵⁻¹⁷ Patients who present with superior vena cava syndrome, pericardial effusions, syncope, dyspnea at rest, and positional intolerance should be deemed very high risk, and extreme measures, such as institution of cardiopulmonary bypass or extracorporeal membrane oxygenation before anesthetic induction, may be necessary.⁵⁻⁷ Ideal rescue positioning also should be determined before anesthetic induction when applicable.⁵⁰ In patients with airway obstruction who can tolerate lower inspired concentrations of oxygen, heliox, a helium-oxygen mixture, can enhance laminar gas flow and alleviate respiratory symptoms.⁵¹

Anesthetic induction in patients with anterior mediastinal masses generally is dictated by the following two major challenges: safely securing the airway and avoiding hemodynamic derangements.³²⁻³⁵ Airway management may be complicated by tracheal compression at baseline.¹⁷⁻²⁷ There are multiple approaches to securing the airway in patients with an anterior mediastinal mass.³⁸⁻⁴⁰ Awake fiberoptic intubation with airway topicalization has been described as an optimal technique.^{27,28} Deep inhalation induction with maintenance of spontaneous ventilation is an alternative method when deemed appropriate.¹⁵⁻¹⁷ A technique used at the Cleveland Clinic for deep inhalation has included the following steps: prepping the airway with 4% nebulized lidocaine followed by bilateral glossopharyngeal nerve blockade; inhalation induction with sevoflurane; insertion of a laryngeal mask airway; bronchoscopy via the laryngeal mask airway with an Aintree airway exchange catheter (Cook Medical, Bloomington, IN); and subsequent endotracheal intubation with the assistance of the airway exchange catheter. Ultimately, the approach to securing the airway will be dictated by airway anatomy, including displacement and compression; symptomatology; and the ability of the patient to cooperate during awake intubation.⁵⁻⁷

In the present case series, more than 90% of patients received neuromuscular blockade during anesthetic induction, with no untoward effects. This was likely because of meticulous patient selection, with only one patient in the series having >50% tracheal compression. Neuromuscular blockade was used in all patients during anesthetic maintenance, without incident. Should there have been any type of compromise secondary to the use of muscle relaxants, although there are no documented reports, the administration of sugammadex for rapid reversal of neuromuscular blockade could be considered, assuming rocuronium or vecuronium was the selected paralytic agent. In instances of severe airway obstruction, rigid bronchoscopy and an experienced operator should be available immediately at the time of induction for possible clinical rescue.¹⁻⁷

Many of the published adverse airway outcomes in patients with mediastinal masses have been in pediatric practice, an age group with smaller diameter and more compressible airways, and greater difficulty in eliciting specific symptomatology to gauge risk, particularly in the youngest patients (see Table 5).¹⁷⁻²⁷ These pediatric reports generally should not be extrapolated to adults because there are distinct anatomic and physiologic differences, with the former group being at potentially greater risk.¹⁷⁻²⁷ In general, neuromuscular blockade and positive-pressure ventilation have been avoided, particularly in higher-risk patients, with spontaneous ventilation offering the advantage of maintaining transpleural gradients and large airway patency.⁵²

Hemodynamic derangements during anesthetic induction may be caused by compression of the heart or major vascular structures.³¹⁻³⁵ Decreased systemic vascular resistance from anesthetic agents, decreased chest wall muscle tone with reduced lung volumes, and airway smooth muscle relaxation, resulting in greater airway compressibility, all can exacerbate these effects. It is essential, therefore, for the team to discuss and plan the safest approach to anesthetic induction and maintenance for a given patient, including contingency plans. Intraoperative concerns beyond airway and hemodynamic management include the following: potential for blood loss in superior vena cava syndrome with large venous collaterals, displacement of the airway and other mediastinal structures, phrenic nerve involvement with associated hemidiaphragmatic paralysis, hoarseness from recurrent laryngeal nerve involvement, airway edema and cerebral edema that can be associated with the superior vena cava syndrome, hypoxemia from pulmonary artery compression, tracheomalacia and/or bronchomalacia from chronic external airway compression, and effects of supine positioning on central blood volume.⁵⁻⁷ As a consequence, intensive monitoring with an arterial line and generous intravenous access for volume resuscitation are essential. Lower extremity intravenous access is necessary in the setting of superior vena cava obstruction. Emergency sternotomy, with manual displacement of the mass away from underlying structures and various means of stenting the airway, has been described for clinical rescue in this setting.⁵⁻⁷

In the present case series, 20% of patients underwent anterior mediastinotomy (Chamberlain procedure).¹⁻³ Many

diagnostic procedures can be performed with the patient under local anesthesia with monitored anesthesia care, including lymph node biopsy and mediastinoscopy in appropriately selected patients.^{57-58,53} The potential consequences of coughing in this setting include injury from the rigid mediastinoscope and/or patient decompensation, with the need to induce general anesthesia.⁵⁻⁷ In extreme cases in which the risk of anesthetic induction is deemed prohibitive, the use of mechanical circulatory support for respiratory or hemodynamic reasons should be strongly considered with planned cannulation of the femoral vessels.^{54,55} Groin exposure may be more prudent than simply inserting percutaneous guidewires into the femoral vessels because the latter approach does not guarantee the ability to advance a cannula into what might be a small, tortuous, or diseased vessel. Preemptive groin access is particularly important when patients are in a lateral decubitus position. Preoperative vascular imaging should be given consideration in extremely high-risk patients for whom the possible need for mechanical circulatory support is anticipated. At the Cleveland Clinic, there is a low threshold for institution of extracorporeal membrane oxygenation in patients who are deemed high risk, as part of the necessary precautions before anesthetic induction in these challenging scenarios.

Despite the unpredictability of intraoperative complications, outcomes in the immediate postoperative period generally are favorable. The more common postoperative complications include pneumonia, airway edema with obstruction, and atelectasis, and they generally manifest within the first 48 hours.¹⁷⁻²⁷ Longstanding compression of the major airways can lead to bronchomalacia that may have adverse effects in the postoperative period. In severe cases, tracheobronchial suspension may be required after resection of large mediastinal masses in patients with tracheomalacia.⁵⁶

Conclusion

A comprehensive multidisciplinary approach can minimize the risk of catastrophic hemodynamic and airway compromise in the anesthetic management of patients with an anterior mediastinal mass. The current evidence base, including the present case conference, can guide perioperative planning to maximize safety and strategy for clinical rescue. The perioperative management of these patients steadily has improved.^{5-7,15-17,54-57} Furthermore, there is general agreement that in low-risk patients, conventional anesthetic techniques with neuromuscular blockade and positive-pressure ventilation are well-tolerated, as outlined in this case conference. Conversely, intermediate- or high-risk patients may best be served by maintaining spontaneous ventilation at the beginning and possibly throughout the case. Although maintenance of spontaneous ventilation has been encouraged, clinical experience at high-volume tertiary care centers has suggested that neuromuscular blockade and positive-pressure ventilation can be safe in selected patients. Mechanical cardiopulmonary support should be reserved for patients at greatest risk of respiratory and/or hemodynamic collapse,

and serious consideration should be given to femoral access with the patient under local anesthesia with light sedation.

Conflict of Interest

None.

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