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REVIEW ARTICLE

ECMO and adult mediastinal masses

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Abstract

The role of extracorporeal membrane oxygenation (ECMO) is expanding as surgeons look at its utility beyond rescue treatment and have started adopting it for high-risk procedures to provide temporary airway and hemodynamic stabilization. ECMO needs to be deliberated in all patients with mediastinal masses who have compromised airways as well as in those with compression of heart and great vessels. There is a dearth of literature highlighting the definitive role of ECMO in patients with mediastinal masses. This article reviews the available adult literature and highlights the possible situations where the use of ECMO would be supportive in the management of patients with mediastinal masses.

Keywords Extracorporeal membrane oxygenation · Mediastinum · Mass

Introduction

Large mediastinal tumors can compress major airways and vascular structures. It is imperative that biopsy and tissue diagnosis would be important to modify further management while the patient gets cardiorespiratory support during surgical biopsy and anesthetic induction and at times until clinical condition improves [1]. Acute fatal cardiopulmonary decompensation can occur when major airways and/or blood vessels become acutely compressed by the mass in a sedated patient, especially when these patients are positioned for sedation, biopsy, or intubation. The compression of the airways and blood vessels is further worsened by general anesthetics and neuromuscular blockers in a supine patient [1]. Distal airway obstruction can lead to inadequate ventilation despite securing airway and can lead to ventilation perfusion mismatch [2]. Endotracheal intubation and mechanical ventilation can lead to further increased intrathoracic pressure, which in turn reduces blood flow through the pulmonary vessels narrowed by the mediastinal mass leading to acute right heart dysfunction, rectified only by regaining spontaneous respiration [3]. Extracorporeal membrane oxygenation (ECMO) has been used in such emergent settings to control airway, prevent hemodynamic collapse, and provide cardiovascular stability [1, 2, 4, 5]. The indications for ECMO have been expanding rapidly even though the use of ECMO in the management of mediastinal masses is currently limited to case reports and single-center cohorts [6]. ECMO has also been successfully used in the management of large goiters with severe airway compression (> 50%) [7, 8]. We discuss the role of ECMO in the support of patients with mediastinal masses in this review article.

Classification of mediastinal masses

It is pertinent for the thoracic surgeon to have a basic knowledge on the anatomical classification of the mediastinum to establish a differential diagnosis of masses based on their location. This permits easier planning of the optimal approach for surgical biopsy as well as excision of mediastinal tumors, if necessary. The 3-compartment model and Shields' 3-zone classification appear to be the most important and useful clinical classifications in this context [9], whereas Fraser and Paré, Zylak, and Whitten models are used more often in radiologic practice [10–13]. The Shields model consists of three compartments: an anterior compartment, a middle (or visceral)

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compartment, and a posterior compartment (Fig. 1). The anterior compartment or pre-visceral zone extends from the thoracic inlet to the diaphragm and from the posterior sternum to the pericardium and contains the thymus, adipose, and mesenchymal tissues. The middle compartment or the visceral zone in this model extends from the anterior pericardium to the spinal anterior longitudinal ligament posteriorly and contains the heart and the great vessels along with the trachea, main bronchi, and lymph nodes. The visceral compartment occupies the entire thoracic inlet. The posterior compartment or the retro visceral zone refers to the area from the posterior pericardium and trachea to the ventral aspect of spine with the esophagus, descending aorta, and vagus nerve traversing through it. It also contains some lymph nodes [9]. Pathologically, lymphoma remains the commonest tumor of the anterior mediastinum in children, while thymoma is the most common occurring tumor in adults.

Early evaluation and risk stratification

Evaluation of at-risk patients involves clinical and radiological assessments which can be helpful in deciding the course of management and decide on the need for extracorporeal support. It would be prudent to have a stepwise pathway for selecting alternative tissues for diagnosis when available, using local anesthetic or ketamine for peripheral lymph node biopsy. Computerized tomography (CT)–guided biopsy would be another option while mediastinoscopic biopsy should be reserved where all of the above options are not feasible [14]. Clinical signs and symptoms of patients with mediastinal masses can vary from being asymptomatic to mild symptoms where patients can lie supine with some cough or pressure sensation. Patients with moderate symptoms can tolerate only supine position for a short period while those with severe symptoms cannot tolerate the position altogether [15]. Radiological corroboration with the clinical findings on a CT scan allows better assessment of the severity of the airway and vascular compression. Tracheal compression is best measured as the ratio of the smallest anteroposterior diameter of trachea on CT scan to that of the tracheal dimensions at the thoracic inlet. A decrease in the lumen diameter by more than 50% has been associated with complete airway obstruction during induction or emergence from anesthesia [16, 17]. Similar calculation using the tracheal cross-sectional area (TCSA) has been proposed by King et al. and a reduction in TCSA by more than 50% has been clinically correlated to have a higher association with significant respiratory complications even if the initial presentation is asymptomatic [16, 18]. Other indices like the mediastinal thoracic ratio and the mediastinal mass ratio have also been shown to correlate with risk of compression and perioperative complications [18, 19]. The CT thorax is also useful to identify compression of the major blood vessels (innominate veins, superior vena cava, pulmonary artery, and aorta) and together with a transthoracic echocardiography can help predict hemodynamic collapse perioperatively. Pericardial effusion on echocardiography has been shown to be a strong predictor of intraoperative cardiovascular collapse and may need emergent pericardiocentesis preoperatively prior to planning the biopsy [20].

Patients presenting with moderate to severe clinical symptoms as well as those with orthopnoea, stridor, or signs and symptoms of superior venacaval syndrome and those with radiological evidence of > 50% airway compression or cardiac

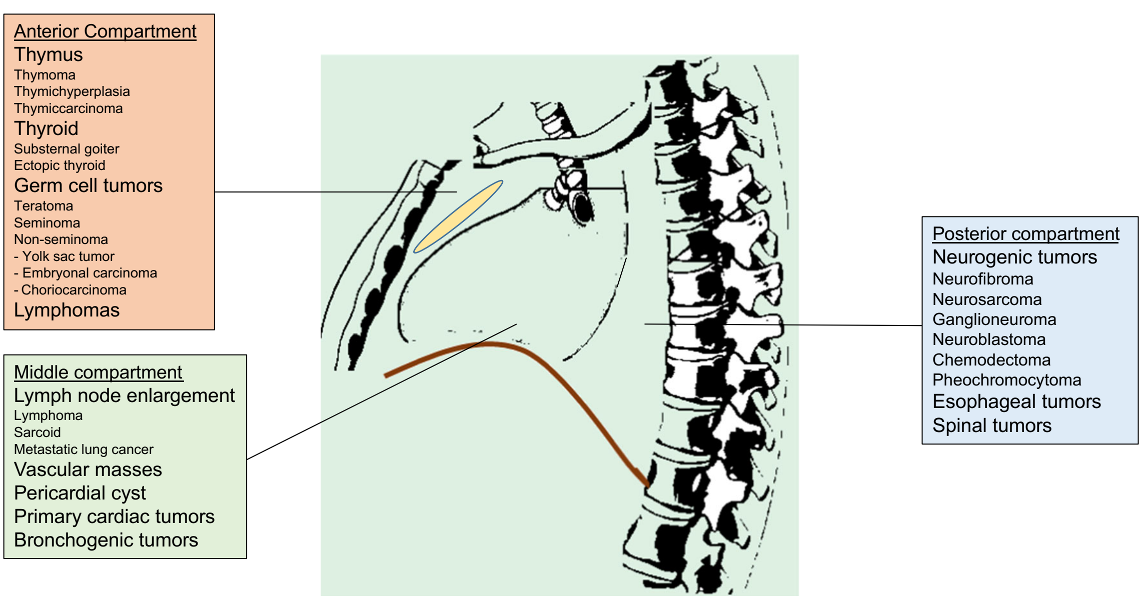

Fig. 1 Common etiologies for mediastinal masses in the three compartments

or great vessel involvement should be deemed as high-risk group and should be managed in a monitored environment. They would need a collaborative multidisciplinary approach involving anesthetists, intensivists, oncologists, and surgeons for airway control and planned interventions like biopsies with consideration of extracorporeal life support in specific scenarios [14]. If the thoracic surgeon deems Chamberlain procedure as impossible, the option of an emergent ultrasound-guided biopsy should be considered in liaison with an interventional radiologist in the operating room.

ECMO: role and management

ECMO needs to be considered in all patients with mediastinal masses who have significant compromised airways. In addition, ECMO would also be deemed prudent in patients with anticipated hemodynamic collapse during intubation or surgical interventions. It has also been used in the context of maintaining hemodynamic stability during the initial phase of curative or palliative chemotherapy treatment [4, 6, 21]. Malignant tumors expand initially during chemotherapy, worsening the compression, before the tumor size regresses. Patients also get referred for ECMO for severe cardiopulmonary failure secondary to infections or due to toxicity to chemotherapeutic agents during the course of treatment of mediastinal masses. The decision to use ECMO electively versus emergently in the first three scenarios has its own pros and cons. Elective ECMO based on clinical and radiological criteria may help patient selection appropriately and avoid catastrophic consequences and the necessity to cannulate in a peri-arrest scenario. Procedures including intubation and biopsies can then be carried out without interruption in a relatively stable patient. However, the risks of subsequent anticoagulation and secondary infections always remain. While patients with malignant mediastinal tumors would need chemo/radiotherapy, the risks of bleeding and the impact of immunosuppression are intensified if the patient remains on ECMO. The choice of ECMO mode is equally tricky and there are multiple case reports in literature on patients with mediastinal masses who were managed successfully either on venovenous or venoarterial ECMO [6, 22–24]. It would be prudent to initiate venoarterial ECMO in patients where extrinsic compression of the mass on the airways and vascular structures would be unpredictable as well as when ECMO is initiated in an emergent setting [6, 22]. In cases where the heart is involved or great vessel reconstruction intraoperatively is anticipated, the use of cardiopulmonary bypass may even be considered. Fixed airway obstruction from tracheal or bronchial tumors, which may be stented, may be managed on venovenous ECMO [23, 24]. Our hospital protocol for patients with anterior mediastinal masses identifies the presence of:

a Acute superior vena cava (SVC) syndrome
b Pulmonary artery or right ventricular outflow tract obstruction
c Airway compression > 50% and
d Cardiac or great vessel involvement/invasion with possible need for cardiac or vascular excision or reconstruction as "high" risk patients, who may need extracorporeal support as part of their ongoing management (Fig. 2). The need for airway control or a Chamberlain procedure in the high-risk group would entail having an ECMO pump primed in the operating room. In addition, we insert 5 Fr sheaths into the femoral vein and artery in the groin prior to attempted intubation, for speedy cannulation in the event of unstable hemodynamics. Venoarterial ECMO (VA ECMO) is initiated in all patients who need it emergently as well as in those with cardiac/vascular compression. Distal perfusion of the limb is achieved by using ultrasound-guided antegrade cannulation of the distal femoral artery or by retrograde cannulation of the posterior tibial artery [25]. We do not administer heparin boluses at the time of initiation even though the ECMO circuit would be primed with fluid containing 1000 U of heparin. Of the 74 patients who presented to National University Hospital, Singapore, with mediastinal masses in the last 5 years, 26 were deemed as high-risk patients. All of them had Chamberlain procedure done with vascular access of groin vessels and ECMO team on standby and 5 of them needed emergent cannulation to VA ECMO. (Fig. 3). All 5 patients were young (19–40 years) and had diagnosis of high-risk mediastinal leukemia, lymphoma, germ cell tumor, and retrosternal goiter, which compressed the airways and great vessels. They had to be cannulated for periprocedural hemodynamic stability. Three of them survived to ECMO explantation and hospital discharge; one of the survivors needed radiotherapy on ECMO as the tumor size did not shrink despite 2 cycles of chemotherapy. The remaining two patients died from hospital-acquired infection and septic shock on ECMO.

It is prudent that high-risk adult patients have their femoral vessels secured with a sheath or a central line guide wire inserted into the vessels for easy exchange, if required, prior to securing the airway. Patients with severe compression, as defined above, should receive awake fiber optic intubation in a controlled environment like the operating room under inhalational anesthetics, if required. Intubation should be done by an anesthetist experienced in difficult airway management and inability to intubate despite 2 attempts should be deemed as a failed intubation and as an indication to go electively on ECMO under local anesthesia. If there is tumor compression of the great vessels in the neck or mediastinum, internal jugular vein cannulation is best avoided. In patients where airway is not secured, even after initiation of VA ECMO, administration of oxygen by a non-breather mask or non-invasive

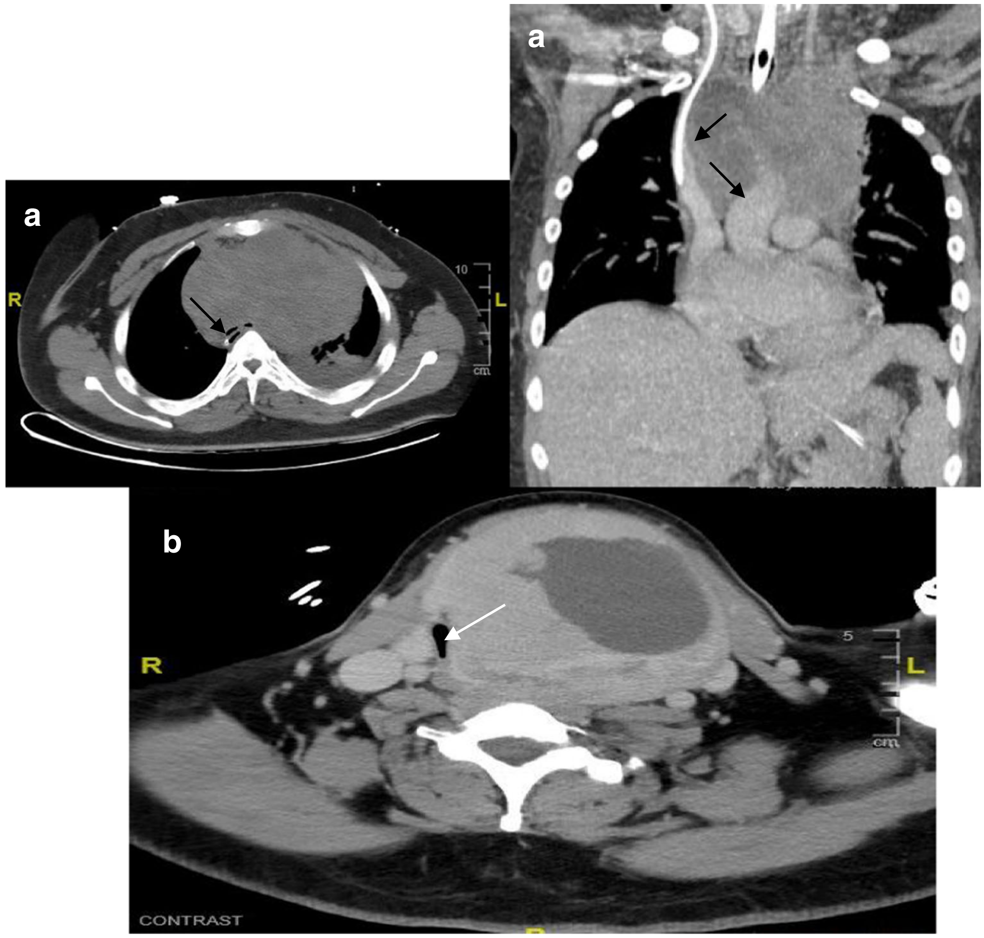

Fig. 2 CT images of patients with mediastinal masses who needed ECMO during management. Panel **a**: Large mediastinal mass in a 23-year-old male with compression of the main bronchi (left panel) and major vascular structures (right panel) shown in black arrows. Panel **b**: Large substernal thyroid mass in a 52-year-old female with a compressed slit-like trachea (white arrow)

ventilation face mask would help overcome differential cyanosis. The impact of compression is higher in the pediatric age group, given the smaller thoracic cavity size, more compressible cartilaginous structure of the airway, reduced cardiopulmonary reserve in children, and a higher incidence of neurogenic tumors in this age group. The need for ECMO in children with mediastinal masses is made more challenging by the fact that initiation under local anesthesia would be very difficult. Patients with altered airway anatomy from compression by the mediastinal mass on CT scan should be assessed for suitability to intubate [26, 27].

While ECMO initiation can be resource-intensive in patients with mediastinal tumors for anatomical reasons, the maintenance of ECMO for initial clinical stability has its own list of management challenges. Tumor lysis syndrome(TLS) most often occurs after the initiation of cytotoxic therapy in patients with clinically aggressive and highly aggressive tumors like lymphoma and T cell leukemia. TLS is also seen in tumor types with high proliferation and large tumor burden, or those with high sensitivity to cytotoxic therapy and it has been observed that the incidence of TLS has increased with the use of targeted antitumor drugs [28]. It is an oncologic emergency that is caused by massive tumor cell lysis with the release of large amounts of potassium, phosphate, and nucleic acids into the systemic circulation. About 5% of the patients, who receive cytotoxic therapy, are at high risk for TLS and care should be taken to address this while patients are on ECMO [29]. Adequate hydration and prophylactic rasburicase form the cornerstone of TLS prevention prior to initiation of definitive chemotherapy [30]. Effective management for patients with established TLS on ECMO involves the combination of treating specific electrolyte abnormalities, the use of rasburicase, loop diuretic, and intravenous fluids to wash out the obstructing uric acid crystals, and the appropriate use of renal replacement therapy on ECMO. While the pharmacokinetic distribution of chemotherapy agents and rasburicase is poorly understood while the patient is on ECMO, some patients often require more than one cycle of treatment before tumor regression happens and they get ready to be explanted.

Patients with mediastinal masses who receive ECMO are at risk of immunosuppression and secondary infections. Immunosuppression happens not just from the underlying malignancy but also from the chemotherapy that ensues. Patients

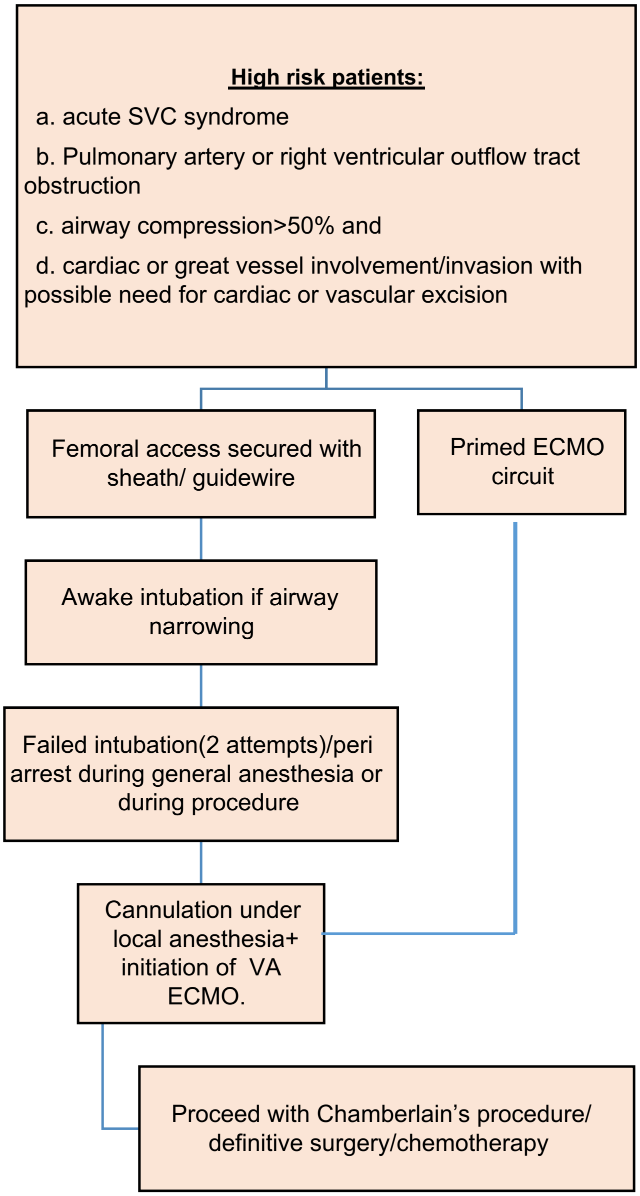

Fig. 3 Algorithm highlighting the role of ECMO in the management of high-risk mediastinal masses. Tumors that involve heart and great vessels may need cardiopulmonary bypass during reconstruction

get pancytopenic, needing colony-stimulating factors for treatment in addition to blood and blood products for correction of coagulopathy. This might also necessitate temporary cessation of heparin and close monitoring of the anticoagulation profile. While it is accepted that immunosuppressed patients have poor survival rates on ECMO, it is also commonly perceived that patients who are unwell enough to receive mechanical ventilation have outcomes comparable to those who then go on to receive ECMO [31]. About a fifth of the patients enrolled for the ECMO to Rescue Lung Injury in Severe Acute Respiratory Distress Syndrome (ARDS) trial (EOLIA) [32] were immunocompromised in one way or the other and the 60-day mortality was higher in the control group compared to the ECMO group (78% vs 56%) [33]. The pattern of survival in immunosuppressed patients needing ECMO shows pathophysiologic inhomogeneity amongst patients with solid tumors versus hematological malignancies versus pharmacologically induced immunosuppression (6-month survival rate: 20% vs 24% vs 37%). It has also been observed that a period of less than 30 days between diagnosis of immunosuppressed state and ECMO initiation has a better 6-month survival than the other immunosuppressed cohort, allaying fears of poor outcomes of ECMO in patients with newly diagnosed mediastinal masses who need a period of stability for their initial treatment [31].

While we have no full-fledged evidence on the duration of ECMO in individuals with mediastinal masses, it remains an open research ethical question as to when to switch to comfort care [33]. Treatment failure and futility would be difficult decisions by the bedside; however, the benefits and limitations of ECMO should be explained to the patient or their proxies during ECMO initiation and on a daily basis. Although the bridge to nowhere scenario is not unique to ECMO, it is a particularly challenging dilemma when using this advanced form of life support in young patients with preserved capacity. All aspects of patient's treatment plan should be reassessed appropriately, including the need to continue or terminate ECMO. The decision to stop ECMO should not be solely based on preset criteria but only after demonstrating no realistic recovery [34].

Conclusion

The role of ECMO in rescuing high-risk patients with mediastinal masses is gaining importance as trained clinicians look at it beyond the realms of salvage therapy and start adopting it as a bridge for high-risk procedures to provide temporary cardiopulmonary stabilization. While the role of elective versus emergent ECMO can be debatable in a group of select patients, who have clinical and radiological evidence for ECMO initiation, it would be prudent for ECMO centers to have clear-cut selection criteria and treatment guidelines for this group of patients. The guidelines should highlight management of anticipated complications like airway control, tumor lysis syndrome, immunosuppression, and futility while patients remain on ECMO. ECMO remains a viable option in select high-risk patients with mediastinal masses, not only at the point of diagnosis but also for maintaining hemodynamic stability during initial treatment.

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Compliance with ethical standards

Conflict of interest Nothing to declare.

Ethical committee approval Not applicable.

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