ORIGINAL ARTICLE

OTHERWISE, INOPERABLE. THE ROLE OF ECMO IN THORACIC SURGERY – FOCUS ON THE MEDIASTINUM

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Abstract

The use of extracorporeal membrane oxygenation (ECMO) in surgery is expanding as the medical community started adopting it, with good results, for procedures with high risk of respiratory and hemodynamic instability. This technique provided the possibility to reduce the number of patients previously considered inoperable because of these limitations.

Thymic epithelial tumors (TETs) are rare neoplastic mediastinal lesions, with a reported incidence of 0.3 per million. They are indolent and associated with a delayed diagnosis, as symptoms arise late. Some can reach such dimensions that surgery without ECMO support would render these patients at risk of heart/great vessels or/and respiratory compression of prohibitive surgical risk or even inoperable.

This report aims to update information on ECMO support in surgery for prevascular mediastinal masses, focusing on pre-operatory assessment, ECMO implantation, patient selection and surgical results.

Keywords: *Mediastinal tumor; ECMO; mediastinal mass syndrome; inoperable*

INTRODUCTION

Mediastinal tumors are rare. In some cases, the mediastinal tumor growth can result in the clinical and radiological compromise of the circulatory and respiratory systems. Some of these mediastinal tumors are resectable, but otherwise, inoperable, given the prohibitive anesthesia and surgical risks, so only palliative treatment (chemotherapy and radiotherapy) is considered. The use of extracorporeal membrane oxygenation (ECMO) for thoracic neoplasm has expanded and became a feasible curative treatment opportunity with acceptable risks in this specific patient subgroup[1]. It is associated with a lower survival rate compared with the overall cohort of ECMO patients (for example non-surgical), although its outcome varies depending on clinical factors, associated procedures and timing of implantation. We aim to analyze the role of ECMO support in the treatment of mediastinal masses, with a focus on pre-operatory evaluation, ECMO implantation, and surgical results.

Oncological diseases in the mediastinum

The pre-vascular mediastinum is the most common compartment for developing tumors (54%), followed by retrovisceral (26%) and visceral (20%). Two-thirds of the mediastinal masses are benign, the predilection for malignancy is greater in the pre-vascular zone.[2] In the malignant group, thymic epithelial tumors (TETs) are the most frequent. They represent a heterogeneous group of rare thoracic tumors, with an annual incidence of 1.3-3.2 per million. The World Health Organization [ESMO guidelines 2015] considers two histological types with distinct clinical features and survival: thymomas and thymic carcinomas.

As slow-growing tumors, thymomas can have an indolent disease course, with symptoms arising just when a conflict of space becomes evident, allowing a significant dimension to be reached. The same behavior can be found in thymic carcinomas, although the disease course is associated with a more aggressive progression and earlier diagnosis.

As surgery is the only potentially curative treatment for TETs (chemotherapy and radiotherapy reserved for extensive disease, with non-optimal results)[3] and considering resectability (absence of visceral zone invasion) the only contra-indication for surgery, the focus is frequently on operability. This depends not only on the patient's condition but also on the anesthetic risk. The clinical presentation might include superior vena cava syndrome, esophageal narrowing with dysphagia, pericardial effusion and cardiac compression, and dynamic tracheal stenosis. The anesthetic risk is mainly associated with the compression of the airway and vascular structures during the induction of anesthesia and surgical manipulation.

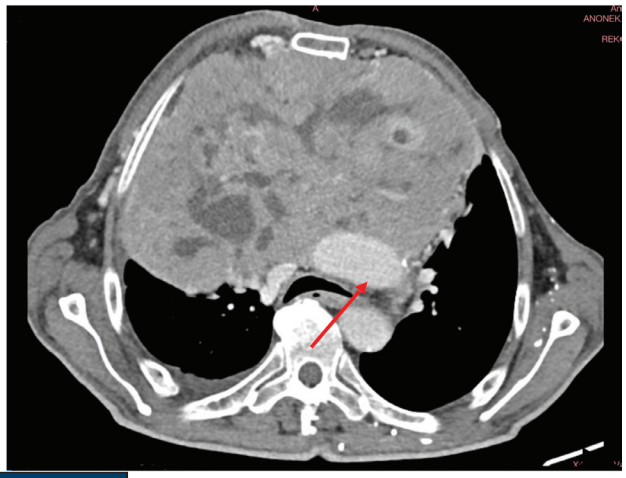

Figure 1 *Respiratory compression*

Mediastinal mass syndrome in the operating room setting - pre-operatory evaluation

The implications in the anesthesiology approach of the mediastinal mass have led to the identification of a so-called mediastinal mass syndrome (MMS), which represents the various changes in physiology (especially respiratory (image 1) and circulatory (image 2)) associated with the presence of the intrathoracic mass, when an anesthetic procedure, such as sedation or more (such as general or regional) is started. MMS is characterized by acute respiratory and cardiovascular decompensation on initiation of positive pressure ventilation[4], as it impairs cardiac output by increasing intrathoracic pressure and blunting venous return, already limited by the mediastinal mass, which is often associated with a pericardial effusion, or it may exert direct compression of the superior vena cava, right ventricle, or its outflow tract, resulting in tamponade-like physiology[5]. Wide venous return is critical for maintaining adequate cardiac output in the setting of extrinsic cardiac compression, and positive pressure ventilation may result in refractory hypotension and cardiovascular collapse[6]. Hypercoagulability from an underlying malignancy may also contribute to cardiovascular collapse in patients

MMS may also cause tracheal or bronchial compression, especially the anterior mediastinal masses, resulting in poor ventilation, V/Q mismatching, refractory hypoxemia, and cardiac arrest. Double-lumen endotracheal tubes may stent open areas of tracheal and bronchial compression, ensure adequate ventilation, correct hypoxemia, and reverse hypoxemic cardiac arrest in such cases[7], although its insertion could be challenging in these patients. ECMO in patients with high risk for MMS has shown to be the solution for diagnosis or treatment purposes, reducing the risk associated with such procedures.

ECMO use in thoracic disease

These patients, who need a diagnosis or are entitled to treatment for their mediastinal mass, in which clinical and radiological features point to the risk of cardiorespiratory collapse, should be discussed in a multidisciplinary collaborative approach involving anesthetists, intensivists, oncologists, and surgeons.

The first cases of ECMO support in this niche of patients were in catastrophic/emergent contexts as a bridge to decision[8-11]. The initial favorable results expanded the application of such support, namely as pre- and peri-operative adjuvant support for patients previously not considered for radical treatment. The number of case reports is higher in pediatric age, related to hematopoietic disease. It is associated with a lower survival rate compared with the overall cohort of ECMO patients (comparing to non-surgical), although its outcome varies depending on clinical factors such as the tumor site (worst for lung and esophageal, better for bronchial, intermediate mediastinum)[1].

ECMO should be considered for surgical treatment in all patients with mediastinal masses who have significant proven or suspected airway and/or cardiovascular compression[12], to account for cardiorespiratory collapse associated with anesthetic induction and surgical manipulation.

Some debate exists about the setting in which ECMO support is initiated (pre-operative vs rescue) and the type (veno-venous vs veno-arterial), as all scenarios have specific

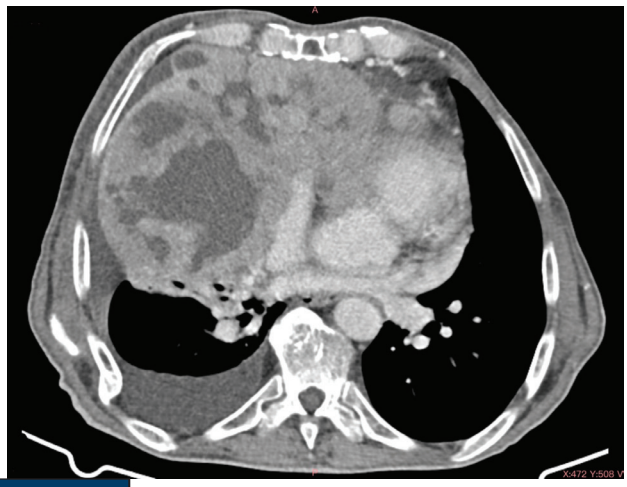

Figure 2 *Cardiac compression*

indications and contraindications. Overall rescue cases have worst prognosis[1].

Pre-operative ECMO is usually decided based on clinical and radiological criteria (compression) and potentially avoids the catastrophic consequences during anesthesia induction and the need for peri-arrest cannulation. Procedures such as sedation, intubation, and biopsies can then be carried out without interruption. However, risks such as hemorrhage or infection associated with ECMO support should also be considered. To mitigate the hemorrhagic risk, no systemic anticoagulation is used during ECMO support.

When there are doubts regarding the need for ECMO support, introducer sheaths are placed preoperatively in the femoral vessels to facilitate ECMO cannulation if intraoperative cardiopulmonary complications occurs.

The choice of ECMO configuration is also challenging with multiple case reports of mediastinal masses successfully managed either using veno-venous or veno-arterial ECMO[13-15]. Veno-arterial ECMO should be considered in the emergent setting or preoperatively whenever extrinsic compression of the mass on the airways and vascular structures is present or anticipated. In cases of intrinsic (from tracheal or bronchial tumors) or extrinsic (mediastinal masses) airway compression, veno-venous ECMO should be considered.

ECMO cannulation is usually restricted to the femoral vessels, therefore avoiding jugular vein cannulation. As part of surgical preparation, a vascular eco-Doppler and a thoracic-abdominal-pelvic CT scan should be performed, with careful evaluation of vessel atherosclerotic disease, dimensions, and anatomy. To evaluate cardiovascular compression, an echocardiogram and contrasted CT can predict possible hemodynamic complications, especially in the presence of a superior vena cave syndrome. Hemodynamic instability can also complicate the post-operative period due to type 2 myocardial infarction associated with anemia and prolonged hypotension as well as due to hypovolemia after removal of a heavy and compressing mediastinal mass. Although needed for surgery, respiratory fiberoptic tracheobronchoscopy and pulmonary function tests, are usually avoided, as the first one, in the presence of MMS can cause respiratory collapse and the second usually is altered (restrictive curve), but should not be a reason for surgical inoperability, except on cases of bilateral phrenic neoplastic suspected involvement.

Intra-operatively, the use of pads for external defibrillation should be the first choice instead of internal pads, as in most cases the heart is not accessible. This could occur during sternal opening and during sudden compression of the heart and great vessels occurs after the separation of the mediastinal mass from the posterior part of the sternum. Surgical complexity, such as other procedures beyond excision (for example venous bypass), are associated with worst prognosis[1].

Patient selection – frailty as a cause of failure

Immunosuppression and its associated factors (exacerbated risk of infection (usually with atypical agents)), need for large-spectrum antibiotics, transfusion of blood and its derivates, high inotropic support, and renal insufficiency are important determinants of survival after mediastinal surgery under ECMO. Some authors, extrapolating data from other settings in which ECMO is the standard of care, suggest that survival inversely correlates with the period between the diagnosis of immunosuppression and ECMO support16. To mitigate this risk, the multidisciplinary team could consider forgoing chemotherapy so as not to aggravate immunosuppression in patients with mediastinal masses that are resectable using ECMO[17]

Another topic that deserves consideration is the duration of ECMO in the postoperative period in cases of hemorrhagic or infectious complications[18]. The benefits and complications associated with ECMO use for mediastinal mass surgery should be anticipatedly explained to the patient and family. Whenever the probability of a meaningful recovery is not possible, ECMO support should be withdrawn[19].

CONCLUSION

This article presents a review of the potential role of ECMO in the surgical treatment of mediastinal masses, namely by extending surgical indications in resectable but inoperable patients.

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. We believe it is a viable option not only at the point of diagnosis but also for maintaining stability during and after surgical treatment. We present its strengths and limitations and possible ways of reducing its associated morbidity and mortality.

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