New horizons of non-emergent use of extracorporeal membranous oxygenator support

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Abstract: The expansion of the extra corporeal membrane oxygenation (ECMO) use and its indication is strikingly increased in the past few years. ECMO use expanded to lung transplantation, difficult general thoracic resections, transcatheter aortic valve replacement (TAVR) and LVAD implantation. Here we will discuss the indications and the outcomes of non-emergent use of ECMO.

Keywords: Extra corporeal membrane oxygenation (ECMO); transcatheter aortic valve replacement (TAVR); TAVI; LVAD; lung transplant

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Introduction

Indications extra corporeal membrane oxygenation (ECMO) and its usage have rapidly expanded over the last 20 years; it has usually been applied in rescue situations and has become essential tool in the care of patients with severe cardiac and/or pulmonary dysfunction refractory to conventional management (1). These indications have been extended to more prolonged use in intensive care unit (ICU), bridge to cardiac and lung transplant. Venoarterial ECMO (VA ECMO) can also be used to stabilize the patient in emergency situations (1-5), however, it can also be used emergently or complications and as prophylaxis in very high risk patients undergoing transcatheter aortic valve replacement (TAVR) (6-8), LVAD implantation (9), and also used as support for lung resections in unstable patients (10,11). Several centers have now replaced conventional cardiopulmonary bypass (CPB) by ECMO for patients with respiratory and/or cardiac failure during transplantation (12-14). Here we will be discussing all possible usages of ECMO other than emergent use for respiratory tor cardiac failure.

Extra corporeal membrane oxygenation (ECMO) *vs.* cardiopulmonary bypass (CPB)

CPB is associated with undesirable effects well documented in the literature, including activation of inflammatory mediators, increased pulmonary vascular resistance, platelet activation, coagulopathy and impaired renal function (15-18).

In theory, the advantages of ECMO concept is a relatively miniaturized circuit that has lower priming volumes and the absence of both air-blood contact and cardiotomy suction. This leads to lesser anticoagulation requirement, potentially lesser coagulopathy, and attenuated systemic inflammatory response (19-22). The use of a miniaturized CPB circuit in cardiac surgery procedures has been shown to be associated with lower transfusion requirement, a reduction in peak troponin, and a lower incidence of neurologic injury in comparison with conventional CPB (20,23). Miniaturized circuits have been shown to have decreased inflammatory response, less hemodilution, less need for inotropic support, lower peak creatinine level, and a lower incidence of atrial fibrillation. These advantages were reflected in a decreases requirement for mechanical ventilation, shorter

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ICU and hospital stay, and ultimately decreased hospital mortality (9). In cases of major vessel injury or severe bleeding, conventional CPB with a venous reservoir allows safe cardiopulmonary support. Conventional CPB remains essential when opening the cardiac cavities and during surgery of the aortic arch or the lung artery trunk.

Using extra corporeal membrane oxygenation (ECMO) with TAVR

TAVR has emerged as a less-invasive alternative in high-risk patients with severe aortic valve stenosis. TAVR is a complex procedure and is often associated with complications that may result in hemodynamic instability. Recent published data reported the use of CPB ranging from 1.2% to 6% of TAVR cases (6-8).

Intraoperative emergent use of CPB is an effective strategy to rescue patients from myocardial collapse as a consequence of the most severe TAVR complications which allows time to perform a thorough diagnostic evaluation and facilitate a safe definitive treatment of the complication (7). These complications include severe paravalvular leak in patients with depressed left ventricular function, severe diastolic dysfunction, or significant mitral regurgitation. The ability of these patients to compensate for acute severe aortic insufficiency may be compromised (6,8,24). The use of CPB allows time for a full assessment of the leak and either reballooning of the prosthesis or preparation of a second device for valve-in-valve treatment, CPB also can be used in cases of coronary malperfusion, or severe bleeding at the apex of the left ventricle which allows decompression of the ventricle to facilitate a safe primary repair.

ECMO could replace CBP in both conditions as prophylaxis in very high risk patients undergoing TAVR insertion, used to stabilize patients in cases of hemodynamic instability with, or without ischemic changes. While there currently no data on systemic use of VA ECMO as prophylactic support, there are some reports which support this concept, as this strategy might potentially minimize the effects of procedural complications in these high risk patients (6,7,24,25).

Emergency implantation of VA ECMO for circulatory support appears to be safe and feasible to stabilize the patient for further treatment (6), in the sitting of severely impaired left ventricular function, slow recovery from rapid left ventricular pacing during testing of pacemaker, high vasopressor requirement during general anesthesia or concomitant high risk PCI might warrant the use of this prophylactic strategy (6). Banjac *et al.* (8) reported using ECMO in 10 patients (4.3% of all TAVR cases) as an emergent rescue strategy after TAVR complications with improved outcomes.

Using extra corporeal membrane oxygenation (ECMO) with LVAD implantation

Ventricular assist devices (VADs) implantation is typically performed with the use of CPB. The patient population that requires VAD implantation often has evidence of end-organ dysfunction, including hepatic congestion, renal insufficiency and pulmonary edema. VAD placement under CPB often exacerbates pre-existing conditions, resulting in post-operative coagulopathy, bleeding and worsening right heart failure. VAD implantation without the use of CPB could help to minimize these post-operative complications without hemodynamic compromise, or excessive bleeding during implantation (26,27). By minimizing the needs for blood transfusions, patients have decreased exposure to blood antigens which ultimately reduces the risk of sensitization in transplant candidates (28).

Anastasiadis *et al.* (9) has reported successful insertion of Jarvik 2000 device by using ECMO in spite of CPB for cardiac support during the procedure. This technique was associated with decreased duration of operation, reduction in blood transfusion, less inotropic support, shorter duration of mechanical ventilation, and length of hospital stay.

ECMO is also used as a bridge to LVAD insertion in patients with profound cardiogenic shock; bridging allows time for end-organ recovery from cardiogenic shock, thereby reducing the mortality rate in this critically ill group of patients (29-31). ECMO support also allows more time for adequate assessment of patients, and thus assists in choosing a management pathway (29). Haneya *et al.* (32) reported series of 6 patients with profound cardiogenic shock; provided on an emergency basis with a percutaneous ECMO via the peripheral vessels. After stabilization, LVAD was implanted using ECMO without switching to a conventional CPB system. These patients were compared with another 11 patients in whom the LVAD was placed with the aid of an additional CPB system. They demonstrated that the blood loss and blood product transfusions were lower in patients operated using ECMO. And the subsequent need for mechanical ventilation and inotropic support was shorter and the survival rate was higher when compared with patients who were operated using CPB.

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ECMO has also been used to temporarily support for right ventricular failure in patients with recently inserted LVAD (31-34).

Using extra corporeal membrane oxygenation (ECMO) for thoracic surgery support

The first case of non-cardiac surgical application of CPB was reported by Woods *et al.* in 1961 (35) for resection of the carina and both main stem bronchi for a bronchial adenoma. Since then conventional CPB has been used for intraoperative respiratory support during lung resections of tumors invading the great vessels and/or the left atrium where both respiratory and circulatory support are needed. CBP use is also needed when one-lung ventilation is impossible like single lung or hypoxemia after lung exclusion where respiratory reserve is insufficient (36), or in large mediastinal tumors invading the great vessels, compromising the heart and trachea (37).

Little has been reported in the literature about using ECMO support during general thoracic procedures. Horita reported using venovenous ECMO (VV ECMO) for 2 cases of carina and sleeve lobectomy in 1996 (10). Several cases have been reported using ECMO for carinal resection-reconstruction (11,38), segmentectomy for cancer in a patient with single lung (39). Limited resection of the lung (wedge or segmentectomy) for aspergillosis or lung abscess was performed under one-lung ventilation thanks to ECMO (40,41), mediastinal tumor resection, due to compression of the trachea (42). VV ECMO was also used for emphysematous bulla resection in single lung by video assisted thoracoscopy (VATS) (43). Peripheral VA ECMO was used as well for cases of lung volume reduction surgery for severe pulmonary emphysema (44), trauma conditions including tracheo-bronchial plasty for traumatic break (45,46), iatrogenic tracheal necrosis after radiation, traumatic intubations, during carinal injury during esophageal resection, or stentings (36) in a postoperative setting. ECMO has been demonstrated to improve survival in patients with post-pneumonectomy ARDS (47). Rinieri *et al.* (36) reported French experience with using ECMO for thoracic surgery procedures as an alternative to conventional CPB. ECMO allowed median duration interruption of ventilation of 78 and 65 min with VV ECMO and VA ECMO respectively. They also reported over 3 h of apnea duration.

In summary, ECMO can be an alternative to CPB in complex ventilatory situations, for major tracheo-bronchial surgery and single-lung procedures without in-field ventilation. Intraoperative ECMO can ensure good hemostasis and allows better surgical exposure than mechanical ventilation. The choice of ECMO type (VV *vs.* VA) depends on the relative need for circulatory support and pulmonary support, as well as the degree of urgency. The site of cannulation also depends on surgical access utilized (sternotomy *vs.* thoracotomy); the cannulation could be central cannulation when sternotomy is used and peripheral when thoracotomy is used.

Using extra corporeal membrane oxygenation (ECMO) in Lung transplantation

CPB historically is the most used modality for intraoperative cardiorespiratory support during lung transplantation (48). The use of CPB can lead to coagulopathy, increased blood product transfusions; complement activation, activation of the systemic inflammatory response syndrome which ultimately leads to endorgan injury (49). Early graft dysfunction in clinical lung transplantation is well described in association with lung transplant supported by CPB (50-55). The use of CPB was cited as an independent factor associated with primary graft dysfunction (56). ECMO might present as an alternative to CPB. The benefits of preoperative ECMO support as a bridge to transplantation (57,58) and the positive impact of ECMO support on outcomes following graft failure after lung transplantation is well documented (50,55,59,60).

Ius *et al.* (61) in retrospective study, reported using intraoperative ECMO in 46 patients who underwent lung transplantation, and compared to 46 patients who underwent lung transplantation with the use of CBP, and concluded that the patients with ECMO support lung needed less requirement for mechanical ventilation, had shortened ICU and hospital length of stay, and required less blood product transfusions during the perioperative period when compared with matched recipients who were supported with conventional CPB. Patients who underwent CPB support had higher requirements for dialysis and had a higher in hospital mortality (39% *vs.* 13%). No differences were found with regard to time on mechanical ventilation and ICU stay. They concluded that ECMO may be considered to be the preferred choice for intraoperative cardiopulmonary support for lung transplant. Conventional CPB will certainly remain an essential support tool for patients undergoing lung transplant and concomitant cardiac repair procedures, cases of complex atrial anastomosis requiring

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heart arrest, and in emergency situations such as massive intraoperative bleeding (62).

Summary

In the contemporary practice of cardiothoracic surgery, ECMO is emerging as a powerful tool in non-emergent applications, such as for lung transplant, TAVR, LVAD insertion, and general thoracic surgery resections. The successful clinical outcomes and improvement of minimized CPB support warrant further exploration of additional innovative applications as well as continue development of clinical experience. Future directions may provide improved patient outcome and reducing medical costs.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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