



## Impact of extracorporeal membrane oxygenation in lung transplantation

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### TO THE EDITOR:

Lung transplantation is a complex procedure that requires extracorporeal mechanical cardiopulmonary support in many situations. Such support can be provided preoperatively, intraoperatively, or postoperatively, depending on the patient's severity of illness and clinical status. This occurs in approximately 30-40% of lung transplants. The situations that most commonly require such support in the intraoperative period include pulmonary arterial hypertension (PAH), right ventricular dysfunction, and intolerance to single-lung ventilation.<sup>(1)</sup> The optimal strategy remains a matter of debate<sup>(2)</sup>; however, the use of extracorporeal membrane oxygenation (ECMO) has been shown to provide numerous benefits over the use of cardiopulmonary bypass. This is because ECMO support resulted in lower rates of primary graft dysfunction (PGD), bleeding, and renal failure requiring dialysis, as well as a lower rate of tracheostomy, less intraoperative blood transfusion, shorter durations of mechanical ventilation, and shorter hospital stays.<sup>(3)</sup>

Between January of 2017 and December of 2018, 24 lung transplants were performed at the Porto Alegre *Hospital de Clínicas*, located in the city of Porto Alegre, Brazil. The clinical and laboratory data from those transplant recipients were statistically analyzed by using the chi-square and Mann-Whitney U tests and are shown in Table 1. Of the 24 patients included in the analysis, 12 received ECMO for cardiopulmonary support, 11 (92%) of whom underwent bilateral lung transplantation, whereas 12 did not require ECMO, 7 (58%) of whom underwent unilateral lung transplantation. Suppurative lung diseases accounted for 50% of the cases of patients transplanted with ECMO support. In patients who did not require ECMO, a diagnosis of COPD was more prevalent. The first use of ECMO at our center was as a bridge to transplantation. Three of the patients in the ECMO group, given the impossibility of establishing single-lung ventilation, received venovenous (VV) ECMO only for ventilatory support. The remaining patients received venoarterial (VA) ECMO for ventilatory and hemodynamic support. Patients with significant PAH underwent peripheral cannulation under local anesthesia and sedation prior to induction of anesthesia. Patients without PAH or with mildly elevated pulmonary pressure underwent central arterial cannulation of the thoracic aorta and peripheral venous cannulation of the right femoral vein. At the end of the procedure, VA ECMO was continued in patients with PAH or was converted to VV ECMO if the patient was hemodynamically stable and did not have PAH. To that end, a single-lumen catheter previously positioned in the right internal jugular vein allowed placement of a guidewire and local cannulation.

Thus, the aortic arterial cannula was disconnected and removed after reconnection with the jugular vein cannula. Decannulation from VV ECMO was performed in the ICU after extubation and confirmation of absence of PGD. There was no difference in hospital or ICU lengths of stay between patients who received ECMO and those who did not, although the former were more severely ill, as demonstrated by the need to use a greater volume of crystalloids, the greater need for transfusion, the longer operative times, and the higher percentage of bilateral transplants. The estimated 36-month survival was 66.7% among patients who received ECMO, compared with 91.7% among those who did not. Although mortality was higher in the ECMO group, the difference was not statistically significant ( $p = 0.143$ ).

The first reports of the use of ECMO date back to the 1970s; however, they were limited to experimental strategies with unfavorable outcomes.<sup>(4)</sup> The use of ECMO in the pediatric population and in patients with ARDS<sup>(5)</sup> has resulted in technical progress and increased experience. Although the use of ECMO during lung transplantation was first described in 2001, it has only recently been introduced in Brazil.<sup>(6)</sup> VV ECMO provides ventilatory support by drawing deoxygenated blood from the venous system in order to oxygenate it and return it to the same system. In contrast, VA ECMO enables cardiopulmonary bypass by returning oxygenated blood to the arterial system.<sup>(7)</sup> Intraoperative ECMO, in addition to ensuring greater safety during cardiac manipulation, reduces the chance of reperfusion injury by allowing better control of blood flow after the pulmonary artery clamp is released, thereby preventing the first implanted graft from receiving the entire cardiac output during implantation of the second graft. In addition, intraoperative ECMO precludes the need for aggressive ventilation to maintain gas exchange and allows continued support in the postoperative period.<sup>(2)</sup> In patients with PAH or considerable hemodynamic instability, it is essential to maintain VA support in the postoperative period, since cardiac output has to be reduced to enable remodeling of the right ventricle, which is chronically hypertrophic.<sup>(8)</sup> In other patients, there is no consensus on the type of or need for postoperative support. As for our team, in cases in which it is possible to discontinue VA support at the end of the surgery, we prefer to avoid decannulation and carry out conversion from VA to VV support, which is continued in the postoperative period. Thus, mechanical ventilation at protective settings is delivered until early extubation is achieved and spontaneous ventilation begins. The use of VV ECMO for the treatment of severe PGD is well established, increasing survival and minimizing the deleterious effects of mechanical ventilation. There

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**Table 1.** Data from patients undergoing pulmonary transplantation between January of 2017 and December of 2018. Porto Alegre Hospital de Clínicas, Porto Alegre, Brazil.<sup>a</sup>

Data	Groups		p
	ECMO (n = 12)	No ECMO (n = 12)	
Gender (M/F)	7 (58%)/5 (42%)	6 (50%)/6 (50%)	0.68
Age, years	48 (17-60)	55 (22-65)	0.14
Type of transplant			0.027
- Unilateral	1 (8%)	7 (58%)	
- Bilateral	11 (92%)	5 (42%)	
Diagnosis			0.12
- Pulmonary fibrosis	2 (17%)	2 (17%)	
- Cystic fibrosis	3 (25%)	0 (0%)	
- COPD/emphysema	3 (25%)	7 (58%)	
- Bronchiectasis	3 (25%)	2 (17%)	
- PAH	1 (8%)	0 (0%)	
- Alpha-1 antitrypsin deficiency	0 (0%)	1 (8%)	
PASP ≥ 35 mmHg	7 (58%)	2 (17%)	0.09
MPAP, mmHg	28 (17-79)	22 (13-32)	0.16
FEV <sub>1</sub> , % predicted	21% (16-70%)	23% (17-42%)	0.63
FVC, % predicted	37% (13-78%)	40% (33-56%)	0.16
Operative time, h	11 (8-17)	6 (3-11)	< 0.001
Cold ischemia time of the first graft, min	432 (270-540)	400 (205-558)	0.45
Cold ischemia time of the second graft, min	632 (520-720)	635 (480-705)	0.82
Crystalloid, mL	6,500 (3,000-32,600)	2,800 (1,400-7,000)	< 0.001
Need for blood transfusion	9 (75%)	1 (8%)	0.001
ICU length of stay, days	12 (5-103)	7 (2-16)	0.17
Hospital length of stay, days	27 (20-117)	29 (17-76)	0.84
90-day mortality	3 (25%)	1 (8%)	0.27
Mean estimated 36-month survival, months	27	35	0.143*

<sup>a</sup>Values expressed as n, n (%), or median (minimum-maximum). ECMO: extracorporeal membrane oxygenation; M/F: male/female; PAH: pulmonary arterial hypertension; PASP: pulmonary artery systolic pressure; and MPAP: mean pulmonary artery pressure. \*Log-rank test comparing the Kaplan-Meier curves of the two groups.

is also evidence that the institution of ECMO within 2 hours of the diagnosis of grade 3 PGD results in increased survival, whereas delayed institution of ECMO is associated with very high mortality.<sup>(9)</sup> Other studies have shown that cases requiring ECMO for the treatment of PGD have a significantly reduced rate of long-term graft survival, as compared with cases not requiring such management.<sup>(10)</sup> Thus, institution of VA ECMO in the intraoperative period helps hemodynamic stability and provides protection for the graft, whereas continued VV support in the postoperative period

reduces the need for mechanical ventilation and provides preemptive treatment of possible reperfusion injury.

In our experience, we found that the use of ECMO to provide cardiopulmonary support in patients with suppurative lung disease with or without concomitant PAH resulted in good survival, although these patients were more severely ill than those who did not receive ECMO; however, hospital and ICU lengths of stay were similar in both groups of patients, making this strategy an important part of the therapeutic arsenal in the setting of lung transplantation.

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