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Lung Transplantation From Donation After Brain Death Donors on Extracorporeal Support

Alessandro Palleschi, MD,[1,2] Ilhan Inci, MD,[3] Dirk E. Van Raemdonck, MD, PhD,[4,5] Jonas Ehrsam, MD,[3] Laurens J. Ceulemans, MD,[4,5] Valeria Musso, MD,[1,2] Paula Moreno, MD,[6] Davide Tosi, MD,[2] Giuseppe Citerio, MD,[7] Mario Nosotti, MD,[1,2] and Arne Neyrinck, MD, PhD[8]

Shortage of lung donors has led transplantation programs to work on new approaches to getting potential donors. In contrast, lung transplant surgeons face the advances in treatments for critically ill patients, including the increased use of extracorporeal membrane oxygenation (ECMO) support. The use of donors on ECMO raises some concerns: endothelial injury and pulmonary edema because of extracorporeal circulation-induced systemic inflammatory response syndrome; pulmonary congestion, caused by increased left ventricle afterload (venoarterial ECMO); alveolar hemorrhage induced by pulmonary edema; and anticoagulation therapies.[1] Also, the criteria for determination of death and the assessment of graft quality are challenging in potential donors on ECMO.[2] We report the experience of lung recipients from donors after neurological determination of death (DBD) while on ECMO support from 3 centers of the European

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[1] University of Milan, Milan, Italy.

[2] Thoracic Surgery and Lung Transplantation Unit, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy.

[3] Department of Thoracic Surgery, Zurich University Hospital, Zurich, Switzerland.

[4] Department of Thoracic Surgery, University Hospitals Leuven, Leuven, Belgium.

[5] Department of Chronic Diseases and Metabolism, Laboratory of Respiratory Diseases and Thoracic Surgery (BREATHE), KU Leuven, Leuven, Belgium.

[6] Thoracic Surgery and Lung Transplantation Unit, University Hospital Reina Sofia, Cordoba, Spain.

[7] School of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy.

[8] Department of Cardiovascular Sciences, KU Leuven, Leuven, Belgium.

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Correspondence: Alessandro Palleschi, MD, Thoracic Surgery and Lung Transplantation Unit, Università degli Studi di Milano, Via Francesco Sforza 35, Milan 20122, Italy. (alessandro.palleschi@unimi.it).

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TABLE 1.

Donor and recipient characteristics

Variables	Value
Patients, N	4
Fondazione IRCCS Ca' Granda-Ospedale Maggiore Policlinico, Milan, Italy	2
Zurich University Hospital, Switzerland	1
University Hospitals Leuven, Belgium	1
Donor	
ECMO indication	
Cardiac arrest	3 (75)
Cardiogenic shock	1 (25)
Venoarterial ECMO	4 (100)
ECMO duration (h)	32–137
Sex: male	4 (100)
Age (y)	30–59
BMI (kg/m^2)	25–33.9
Cause of brain death	
Anoxia	3 (75)
Vascular	1 (25)
Mechanical ventilation (d)	1–8
Smoking habit: never smoker	3 (75)
Chest x-ray	
Clear	2 (50)
Minor opacity	2 (50)
Opacity ≤1 lobe	0 (0)
Opacity >1 lobe	0 (0)
Secretions at bronchoscopy	
None	2 (50)
Minor	0 (0)
Moderate	2 (50)
Major	0 (0)
Medical history: previous cardiac surgery	2 (50)
Organs retrieved	
Lung only	1 (25)
Lung + abdominal organs	3 (75)
Lung + heart	0 (0)
Lung + heart + abdominal organs	0 (0)
Transplantation	
Machine perfusion evaluation	
Yes, EVLP	3 (75)
Not used	1 (25)
Cold ischemia time (min)	
First lung	258–606
Second lung	607–795

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TABLE 1. (Continued)
Donor and recipient characteristics

Variables	Value
Type: bilateral	3 (75)
Intraoperative ECMO (VA/VV)	3 (75) (1/2)
Recipient	
Sex: male	2 (50)
Age (y)	16–42
Indication	
Cystic fibrosis	2 (50)
Interstitial lung disease	1 (25)
Pulmonary vascular disease	1 (25)
Bridge to transplantation	
Yes, ECMO (VA/VV)	3 (75) (1/2)
No	1 (25)
Bridge duration (d)	3–69
$PGD_{(72h)}$ grade 3	3 (75)
Postoperative MV duration (d)	1–25
Postoperative ECMO (VA/VV)	3 (75) (1/2)
Postoperative ECMO duration (d)	1–22
Postoperative ICU stay (d)	4–58
Postoperative hospital length of stay (d)	29–58
30-d mortality	0 (0)
Best FEV_1 (%)[a]	70–107
Airway complications	0 (0)
CLAD	2 (50)
Retransplantation	0 (0)

Values are expressed as number (%), range.
[a]1 missing data.
BMI, body mass index; CLAD, chronic lung allograft dysfunction; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; FEV1, forced expiratory volume in 1 s; ICU, intensive care unit; IRCCS, Istituti di Ricovero e Cura a Carattere Scientifico; MV, mechanical ventilation; PGD (72 h), primary graft dysfunction in the first 72 h after transplantation; VA, venoarterial; VV, venovenous.

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From 2013 to April 2019, 4 patients were transplanted with grafts from DBD donors on ECMO (Table 1). All donors were supported with venoarterial-ECMO for cardiovascular failure; 3 recipients needed a bridge to transplant. Early postoperative course was characterized by grade-3 primary graft dysfunction in 3 cases. Postoperative respiratory function was satisfactory; no airway complications occurred. The very first patient had a dramatic clinical course with a single lung retransplantation after 69 d of venoarterial-ECMO bridge.

To our knowledge, only 3 cases of lung procurement from DBD donors on ECMO have been reported because of major challenges connected to this kind of donation.[3-5] For intensivists, the management of patients on ECMO and the determination of death are complicated. In this setting, the apnea test is not standardized. It should be performed by lowering to 0 (usually 1 L/min) the sweep gas flow to the oxygenator; therefore, ventilation and oxygenation are completely dependent on the ventilator and hypercapnia is induced. In some cases, additional CO_2 can be added to the gas exchanger to further reach the thresholds for hypercapnic stimulation of the control centers for respiration. Ancillary tests can be of aid for death determination.

Lung transplant surgeons also face a great challenge because of graft evaluation. Lung suitability is assessed according to usual parameters. As always, macroscopic inspection after opening the pleurae is of primary relevance; a careful and complete recruitment of all parenchyma under direct vision is mandatory. In these cases, pulmonary vein blood gas analysis could provide objective data on lungs functionality. Finally, because an in situ assessment of this type of donor may be partial and particularly demanding, ex situ evaluation becomes crucial: ex vivo lung perfusion can be used for lung evaluation and reconditioning.

This study is limited by its small population size and the severe conditions of the recipients, which should also be considered when interpreting our results. Considering this and the challenging assessment of lungs, our multicenter case series suggests that the outcomes of transplantation using DBD donors on ECMO support are encouraging. We advocate for systematic consideration of these as potential donors and not an a priori contraindication; nevertheless, these findings need to be confirmed in larger series.

REFERENCES

1. Roumy A, Liaudet L, Rusca M, et al. Pulmonary complications associated with veno-arterial extra-corporeal membrane oxygenation: a comprehensive review. *Crit Care.* 2020;24:212.
2. Bein T, Müller T, Citerio G. Determination of brain death under extracorporeal life support. *Intensive Care Med.* 2019;45:364–366.
3. Dewei R, Abu Saleh WK, Al Jabbari O, et al. Lung procurement from a donor on ECMO support. *ASAIO J.* 2015;61:e40–e41.
4. Bronchard R, Durand L, Legeai C, et al. Brain-dead donors on extracorporeal membrane oxygenation. *Crit Care Med.* 2017;45:1734–1741.
5. Lee H, Cho YH, Sung K, et al. The use of extracorporeal circulation in suspected brain dead organ donors with cardiopulmonary collapse. *J Korean Med Sci*. 2015;30:1911–1914.