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LETTER TO THE EDITORS

Successful transplantation of extended criteria lungs after prolonged *ex vivo* lung perfusion performed on a portable device

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Dear Sirs,

Lung transplantation (LTx) remains the only treatment for end-stage lung disease regardless of etiology. A profound lack of donor organs remains the greatest challenge in providing LTx, resulting in stagnant rates of transplantation at many large centers [1]. As more patients are being referred for LTx, there is a growing rate of deaths on the recipient waitlist [2]. Technologies that increase use of the scarce donor pool remain the best option of increasing rates of LTx, and decreasing rates of death on the recipient waitlist [3].

Ex vivo lung perfusion (EVLP) was initially developed as a method of assessing lung function at normothermia from donors after cardiocirculatory death prior to successful transplantation [4]. The technique evolved to demonstrate that extended criteria lungs could be assessed and treated using EVLP to achieve similar early outcomes as conventionally selected lungs when transplanted [5]. The development of the Transmedics Organ Care System (OCS) lung device brings the first portable EVLP system [6]. The Leuven group recently reported a case of extended EVLP of 11.5 h in the *American Journal of Transplantation*, demonstrating the feasibility of such a lengthy perfusion on the OCS: lung [7].

Herein, we report a prolonged *ex vivo* perfusion of over 10 h for lungs previously deemed unacceptable for transplantation by other centers performed on a portable device with successful transplantation and discharge from hospital.

The donor was a 69-year-old female who had been in a motor vehicle accident (MVA). The MVA had caused multiple contusions and a parenchymal laceration leading to air leak requiring wedge resection. Hemorrhagic secretions were noted on bronchoscopy and there was evidence of contusions on chest X-ray (CXR) and CT. Consequently, these lungs were deemed to be extended criteria [8] and had a best PaO_2/FIO_2 (P/F) ratio of 267 mmHg.

These lungs were chosen as the prospective recipient, a 65-year-old female with idiopathic pulmonary fibrosis, had recently deteriorated and was in imminent need of mechanical ventilation after being on the recipient waitlist for over 2 years. The recipient had a complex dissection resulting from previous thoracic surgery leading to an extended operative time. The recipient consented to an off-label use of the OCS: Lung device to perfuse extended criteria donor lungs and underwent bilateral LTx.

The *ex vivo* lung perfusion run lasted 638 min. The decision to transplant the lungs was made based on the P/F ratio rising to over 400 mmHg, lung function parameters such as pulmonary artery pressure, pulmonary vascular resistance and peak airway pressure remaining stable and improved ventilation evidenced by increasing recruitment of lung tissue. Table 1 summarizes the critical donor and recipient information.

Lung function parameters are continuously monitored on the OCS: lung device. Physiologic stability was attained after the first 30 min of perfusion and remained stable throughout the 638-min perfusion. Bronchoscopy pictures of the airways at 72-h post-transplant reveal proximal airway excoriation potentially from epithelial desiccation due to the absence of a humidifier on the device. Substantiation of this observation, however, requires rigorous preclinical investigation. A CXR taken within hours after transplantation shows an acceptable immediate postoperative appearance following bilateral LTx, with marked improvement shown on another CXR taken just prior to discharge.

The P/F ratio 72 h postoperatively was 185, defined as primary graft dysfunction (PGD) grade 3. The aforementioned extended nature of the donor lungs coupled with the recipient's requirement of cardiopulmonary bypass contributed to the development of PGD 3 at 72 h. The recipient's recovery was complicated by recurrent hemothorax and pleural effusion as well as thoracosternal incision dehiscence requiring aggressive debridement. These factors all prolonged the time spent intubated in ICU and the overall length of stay in hospital. By 30 days post-transplant, the PGD had resolved and the recipient had P/F ratios over 300 mmHg.

Table 1. Donor and recipient characteristics.

Variable	Characteristic
Donor	
Age (years)	69
Gender	Female
Cause of death	Motor vehicle accident
Active pneumonia	No
Best P/F ratio	267
Recipient	
Age (years)	65
Gender	Female
Diagnosis	Idiopathic pulmonary fibrosis
Procedure	Bilateral lung transplant
ECMO	No
Cardiopulmonary bypass	Yes
Total ischemic time (min)	159
P/F ratio at 72 h	185
PGD grade at 72 h	3
P/F ratio at 30 days	370
PGD grade at 30 days	0
Days on mechanical ventilation	22
ICU length of stay (days)	26
Hospital length of stay (days)	70
Lung function at 1 year	FEV1 = 97% predicted FVC = 97% predicted
Status	Alive at 14 months

PF, PaO_2/FIO_2; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

The recipient continued to improve and was successfully discharged home after 70 days in hospital. Additionally, pulmonary function at 1-year post-transplantation is excellent, with an FEV1 of 97% predicted and an FEV1/FVC of 97% predicted. The recipient continues to function well at home 14-month post-transplantation.

There are many reasons for the prolonged nature of this EVLP run. The catchment area of our center represents over 6 million km^2, making it the most geographically isolated thoracic transplant program in the world, and in this case, the donor was located approximately 2 h away by plane at a remote site. As previously mentioned, an air leak was repaired by wedge resection and the recipient had a complicated explantation, contributing to the length of the case. Serial bronchoscopies for lavage of secretions and blood to improve airway compliance and oxygenation were also performed on the device. EVLP was used in this case primarily because of the extended criteria nature of the donor lungs. The aim of this EVLP was to recondition the donor lungs to make them suitable for transplantation. However, because of the aforementioned recipient factors, the strategy shifted to preservation once reconditioning had been achieved. There were no deleterious effects on the lungs from the prolonged preservation, as were also demonstrated by the Leuven group's 11.5-h perfusion on the same device [7].

The benefits of portable EVLP were of great use in this case, with the ability to continually monitor lung function and perform interventions such as resections and bronchoscopies directly on the device allowing for a more informed decision-making process and ultimately leading to maximizing the utility of available organs.

This case report adds to the growing literature on the value of EVLP, as *ex vivo* perfusion was possible with successful transplantation after 10.5 h on the OCS: lung device. This example of extended lungs placed on EVLP is an encouraging advance in increasing our limited donor lung pool. EVLP will likely develop into the gold standard of donor lung management, and the boundaries of marginal organs and length of *ex vivo* perfusion runs will continue to increase over time. This provides optimism for improved rates of transplantation for our growing recipient waitlists of patients requiring LTx, also providing new areas of investigation of *ex vivo* lung function and physiology.

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