Ex vivo lung perfusion of pediatric lungs for adult recipients

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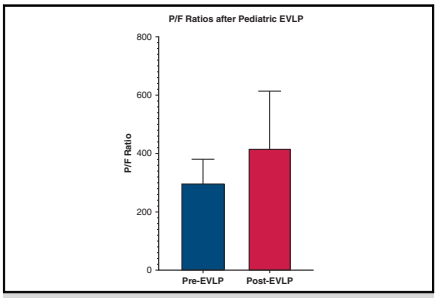
Pediatric lungs before ex vivo lung perfusion.

CENTRAL MESSAGE

Lungs from pediatric donors requiring ex vivo lung perfusion can be considered for adult recipients given the shortage of suitable lungs for transplantation.



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IRB approval was not required. Patients provided informed consent for inclusion in this report.

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Lung transplantation (LT) is limited by shortages in the donor organ pool, leading to a waitlist mortality of up to 21%.[1,2] To meet this demand, organs from deceased after circulatory death (DCD) donors and extended criteria donors are increasingly being utilized.[3] Ex vivo lung perfusion (EVLP) is routinely utilized to facilitate DCD and extended criteria LT[3,4]; perfusion of pediatric lungs on EVLP has not been described before, representing an untapped source of donor organs. Here, we present 3 cases of pediatric lungs placed on EVLP and successfully transplanted into adult recipients.

CASE DETAILS

Donor and recipient characteristics are presented in Table 1. Institutional review board approval was not required. Patients provided informed consent for inclusion in this report.

Case 1

A 61-year-old woman with a history of autoimmune hepatitis and scleroderma with associated idiopathic pulmonary fibrosis on 8 L home oxygen awaiting LT with a most recent lung allocation score of 44.9 was admitted to the hospital as a suitable DCD donor had been identified. The donor was a 9-year-old boy with no significant past medical history who died asphyxiation and was intubated for 23 days before donation.

On procurement, bronchoscopy and the Pao_2/fraction of inspired oxygen (P/F) ratio of 337 were favorable, and DCD donation commenced. After pronouncement, explant of lungs and cannulation for EVLP on the Organ Care System (OCS) platform (TransMedics) commenced (Figure 1, *A*).

Once flow was initiated, a mean pulmonary artery pressure of 8-13 mm Hg was targeted and achieved with 0.7 and 1.3 L/minute flow. Tidal volumes of 200 to 250 cc were delivered with peek end expiratory pressure (PEEP) of 4 to 5, and a consistent respiratory rate of 14.

After transport, the P/F improved to 638, and bilateral lung transplant proceeded uneventfully. On postoperative day (POD) 3, she underwent cannulation for venovenous extracorporeal membrane oxygenation (VV-ECMO) for primary graft dysfunction (PGD) but recovered and was decannulated on POD 8. She underwent tracheostomy on POD 7 and was decannulated on POD 41 before discharge on POD 76 with stable chest radiograph (Figure 1, *A*). She remains well now 1 year and 9 months postprocedure.

Case 2

A 73-year-old woman with a history of idiopathic pulmonary fibrosis on 8 L home oxygen, comorbid with type 2 diabetes, coronary artery disease, and osteoporosis, was admitted to the hospital with hypercarbic respiratory failure treated with noninvasive ventilation. She was subsequently listed for single left LT with a lung allocation score of 55.73. That admission, a suitable donor was identified in a 12-year-old boy with no significant past medical

TABLE 1. Donor and recipient characteristics and ex vivo lung perfusion (EVLP) parameters

Characteristic	Donor 1	Recipient 1	Donor 2	Recipient 2	Donor 3	Recipient 3
Age (y)	9	61	12	73	8	65
Sex	M	F	M	F	M	F
Height (cm)	121.92	154.9	150.0	149.9	127.0	157.5
Weight (kg)	25.85	59.11	43.0	48.2	25.0	56.6
Lung length, L/R (cm)	11.2/12.5	11.5/11.7	18.9	18.7	16.2/16.1	16.0/16.6
Systolic/diastolic/mean preoperative pulmonary artery pressures (mm Hg)		41/9/21		28/6/10		16/5/10
Laterality		Bilateral		Left single lung		Bilateral
Preoperative RVSP (mm Hg)		37		47		36
Postoperative RVSP (mm Hg)		25		22		28
Allograft cold ischemic time (min)		49		66		48
Pre-EVLP allograft warm ischemic time (min)		27		39		None
Duration on EVLP (min)		258		205		578
Post-EVLP allograft warm ischemic time (min)		60		37		62
P/F ratio after EVLP		638		267		357
Perfusate volume		1500 mL OCS lung solution 3 U pRBCs		1500 mL OCS lung solution 3 U pRBCs		1500 mL OCS lung solution 3 U pRBCs

M, Male; *F*, female; *L/R*, left/right; *RVSP*, right ventricular systolic pressure; *P/F ratio*, defined as the partial pressure of oxygen in the arterial blood gas divided by the fraction of oxygen in air delivered by the ventilator; *OCS*, Organ Care System (TransMedics); *pRBCs*, packed red blood cells.

history who died from a motor vehicle accident. Bronchoscopy at the donor hospital was favorable, P/F ratio was 358, and DCD procurement commenced. The lungs were cannulated for OCS and flow was initiated to target a pulmonary artery pressure of 8 mm Hg, achieved with flows ranging from 1.53 to 2.01 L/minute. Ventilator settings were set at a PEEP of 5, tidal volume of 200 cc, and respiratory rate of 14. At the conclusion of EVLP, bronchoscopy was reassuring, the lungs appeared healthy (Figure 1, *B*), and the P/F ratio was 267; off-pump, single LT proceeded uneventfully.

The recipient was extubated on POD 3 and was discharged home on POD 17 after an uneventful hospitalization with stable chest radiograph (Figure 1, *B*). She remains only on 1 L/minute oxygen at night and is otherwise well.

Case 3

A 65-year-old woman listed for bilateral LT due to a history of interstitial lung disease secondary to fibrotic hypersensitivity pneumonitis on 2 L home oxygen was admitted to the hospital when a suitable brain-dead donor was identified. Her most recent lung allocation score was 34.15. The donor was an 8-year-old boy with no significant past medical history who died from anoxic brain injury due to drowning.

Bronchoscopy at the donor hospital was favorable, and P/F ratio was 205 before procurement; the lungs were explanted and cannulated for EVLP due to extended donor distance. A short segment of ascending aorta was anastomosed in an end-to-end fashion to the trachea to fit the OCS ventilation cannula (Figure 1, *C*). After cannulation, perfusion was initiated with flows to target a pulmonary artery pressure of 6 mm Hg, and ventilation was initiated with a tidal volume of 300 cc, PEEP of 5, and a respiratory rate of 14. At the conclusion of EVLP, bronchoscopy and the P/F of 357 were favorable, and the patient underwent uneventful bilateral LT.

On POD 1 she had experienced PGD and was cannulated for VV-ECMO. She improved gradually with a furosemide drip, was extubated on POD 7, and decannulated from VV-ECMO on POD 9. She continued her recovery and was discharged POD 21 on 1 L oxygen via nasal cannula as needed, with improvement in her chest radiograph (Figure 1, *C*).

DISCUSSION

Barriers to perfusion of pediatric lungs on EVLP include anatomic, such as using cannulas and endotracheal tubes suitably sized to the donor lungs, and physiologic, surrounding uncertainty about the capacity to flow at rates that preserve allograft function. Our successful use of pediatric donor lungs perfused on EVLP demonstrates that these

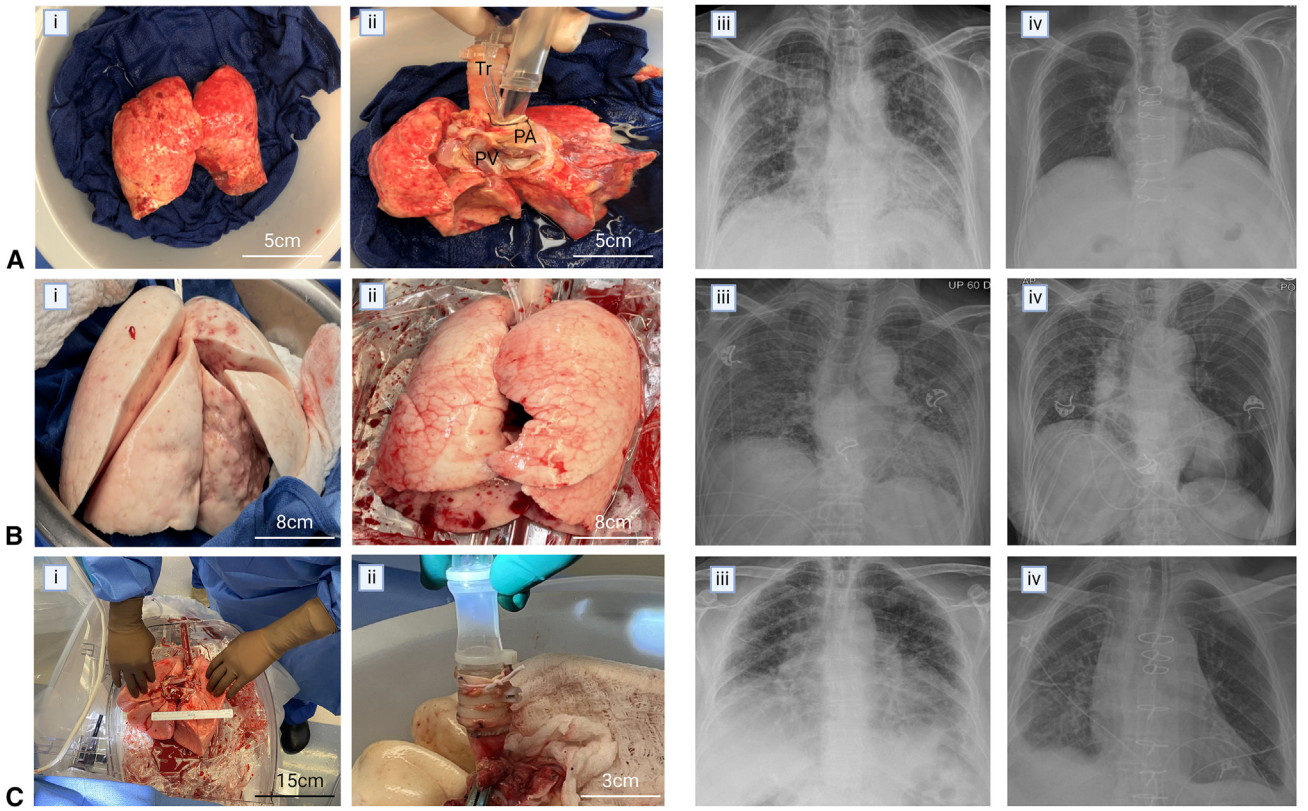

FIGURE 1. A, Pediatric lungs precannulation (i) and postcannulation (ii) (*left to right*), and preoperative (iii) and discharge chest radiograph (iv) of the first patient. B, Pediatric lungs before (i) and after ex vivo lung perfusion (*EVLP*) (ii) and preoperative (iii) and discharge chest radiograph (iv) of the second patient. C, Donor 3's trachea was too narrow to fit the ventilation cannula adaptor (i), so a short segment of ascending aorta was anastomosed to the end of the trachea for the duration of EVLP (ii). The anastomosis was airtight, and ventilation parameters were met without issue. Preoperative (iii) and discharge (iv) chest radiograph of recipient 3. *Tr*, Trachea; *PA*, pulmonary artery; *PV*, pulmonary veins.

challenges can be overcome safely and may offer additional avenues for donor pool expansion for both adult and pediatric recipients. This is particularly urgent because since 2004 when the first pediatric DCD thoracic transplant was performed, only 7 pediatric DCD donors have been utilized for LT.[5]

All patients in this series had restrictive lung disease, which was a factor in consideration of pediatric donors. In our experience, patients with restrictive lung disease have smaller chest cavities that can accommodate smaller lungs. However, all donor lungs in this series were within 1 cm of recipient lungs in length because we attempted to optimize size matching. Donor criteria for these patients with small chest cavities did not include age minimums, but rather prioritized size matching. All 3 patients had technically uncomplicated anastomoses and postoperative bronchoscopy did not demonstrate any stenosis or obvious signs of size mismatch.

Two of the 3 patients in this series experienced PGD requiring VV-ECMO. PGD is common in extended criteria or DCD donors given additional ischemia from the agonal period, or multiple bouts of ischemia reperfusion injury per results of the OCS Lung EXPAND trial.[6]

Because the use of pediatric lungs on EVLP is novel, challenges may arise during procurement. The use of aortic tissue to augment the size of the trachea and successfully facilitate airway cannulation demonstrated a useful technique with readily available donor tissue to facilitate EVLP. Other options, including custom making endotracheal tubes and adaptors, are possible, but require adequate lead time, which may not be available given the nature of organ donation. Additional considerations included alterations to flow parameters and ventilator settings to accommodate pediatric lung sizes. Lung-protective ventilation parameters were targeted with initial targets of 6 cc/kg tidal volumes, and then adjustment per arterial blood gas. Flow rates were used to target mean pulmonary artery pressures of 6 to 8 mm Hg over a steady state. We recommend using frequent assessment of arterial blood gas and perfusion parameters to inform goal-driven perfusion and ventilation parameters.

CONCLUSIONS

Three adult patients successfully underwent LT utilizing pediatric donor lungs preserved on EVLP, demonstrating that pediatric lung perfusion on EVLP and subsequent transplantation can safely be performed, potentially expanding the donor pool. Size-matched pediatric lungs may be considered for adult recipients despite the age differences between donors and recipients.

Conflict of Interest Statement

Dr Krishnan is supported by the National Heart, Lung, and Blood Institute (1T32HL098049). All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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