Transplantation of initially rejected donor lungs after ex vivo lung perfusion

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Objective: Ex vivo lung perfusion has the potential to increase the number of patients treated with lung transplantation. Our initial clinical experience with ex vivo lung perfusion is reviewed as well as early clinical outcome in patients transplanted with reconditioned lungs.

Methods: Six pairs of donor lungs deemed unsuitable for transplantation underwent ex vivo lung perfusion with Steen solution mixed with red blood cells to a hematocrit of 10% to 15%. After reconditioning, lung function was evaluated and acceptable lungs were transplanted. Technical experience with ex vivo lung perfusion as well as clinical outcome for patients transplanted with ex vivo lung perfusion-treated lungs were evaluated.

Results: Donor lungs initially rejected either as a result of an inferior partial pressure of arterial oxygen/fraction of inspired oxygen ($n = 5$; mean, 20.5 kPa; range, 9.1-29.9 kPa) or infiltrate on chest radiograph ($n = 1$) improved their oxygenation capacity to a mean partial pressure of arterial oxygen/fraction of inspired oxygen of 57 ± 10 kPa during the ex vivo lung perfusion (mean improvement, 33.6 kPa; range, 21-51 kPa; $P < .01$). During evaluation, hemodynamic (flow, vascular resistance, pressure) and respiratory (peak airway pressure, compliance) parameters were stable. Two single lungs were not used for lung transplantation because of subpleural hematoma or edema. Six recipients from the regular waiting list underwent single ($n = 2$) or double ($n = 4$) lung transplantation. One patient had primary graft dysfunction grade 2 at 72 hours. Median time to extubation was 7 hours. All patients survived 30 days and were discharged in good condition from the hospital.

Conclusions: The use of ex vivo lung perfusion seems safe and indicates that some lungs otherwise refused for lung transplantation can be recovered and transplanted with acceptable short-term results. (*J Thorac Cardiovasc Surg* 2012;144:1222-8)

Lung transplantation (LTx) is the treatment of choice for end-stage lung disease, but the shortage of donor lungs remains the limiting factor. Recent national data from the United States reports use of 22% of lungs from multiorgan donors; corresponding U.K. data indicate 17%.^{1,2} After improvements in donor management and implementation of extended donor criteria, lungs from as many as 30% to 40% of multiorgan donors in Sweden have been transplanted during the past few years.

Reconditioning and evaluation of lungs initially rejected for transplantation with ex vivo lung perfusion (EVLP) has been used to differentiate reversible from irreversible pathology.³⁻⁵ In 2007, Steen and colleagues⁶ reported the first transplantation of an ex vivo reconditioned lung. Thereafter, transplantations of initially rejected but EVLP reconditioned lungs from brain dead donors have been reported in 32 patients from 4 centers.^{4,5,7,8} We present our early clinical experience with EVLP management of initially rejected donor lungs with subsequent LTx.

MATERIALS AND METHODS

Patients

The Ethics committee of the University of Gothenburg approved this study. All recipients on the LTx waiting list were eligible for transplantation with lungs reconditioned with EVLP. Recipients were matched for compatible blood group, size, and urgency, and were brought to the transplantation center during the organ retrieval procedure. Recipient characteristics are presented in Table 1.

Donor Selection and Characteristics

Between January 2011 and October 2011, lungs from 107 brain dead donors were offered to our center; 27 were accepted for transplantation and 80 were rejected because of no matching recipient (26%); advanced smoking history (18%); high donor age (14%); inferior blood gases despite efforts such as recruitment maneuvers, bronchial suction, and diuretic

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Abbreviations and Acronyms

CO ₂	= carbon dioxide
EVLP	= ex vivo lung perfusion
FiO ₂	= fraction of inspired oxygen
LTx	= lung transplantation
PA	= pulmonary artery
PaO ₂	= partial pressure of arterial oxygen
PEEP	= positive end-expiratory pressure
P/F	= ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen
PO ₂	= partial pressure of oxygen
PVR	= pulmonary vascular resistance

treatment (8%); aspiration of gastric content (8%); and other signs of inferior lung function, trauma, macroscopic abnormalities, or unclear reasons (19%). Six pairs of the rejected donor lungs were subjected to EVLP. Criteria for EVLP evaluation were (1) best ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (P/F) in the intensive care unit <40 kPa; and/or (2) radiologic signs of extensive lung edema; and/or (3) radiologic signs of infiltrates suggestive of pneumonia, lung infarction, or aspiration.

The lungs were harvested in a standard fashion with antegrade Perfadex (Vitrolife AB, Gothenburg, Sweden) flush, cold storage in Perfadex and were kept on ice during transport. If the heart was harvested, an additional piece of the ascending aorta was brought for elongation of the pulmonary artery (PA) to facilitate connection of the lung to the EVLP artery cannula. For detailed donor characteristics see Table 2.

Ex Vivo Lung Perfusion

EVLP was performed with the CE-marked Vivoline LS1 (Vivoline Medical AB, Lund, Sweden) (Figures 1 and 2). The system was primed with 2.0 L of Steen Solution (Vitrolife AB) mixed to a hematocrit level of 10% to 15% with bank blood, compatible and cross-checked to the selected recipient. Meropenem 100 mg (AstraZeneca AB, Sodertälje, Sweden) and 10000E Heparin (LEO Pharmaceutical, Copenhagen, Denmark) were added to the perfusate. Before the lungs were connected to the EVLP unit, the pH in the solution was corrected to between 7.35 and 7.45 with isotonic trometamol (Addex-THAM, Fresenius Kabi AB, Uppsala, Sweden).

To perform a safe cannulation of the PA, a 3- to 4-cm graft of the ascending aorta from the donor was used to elongate the PA in 3 cases. The trachea was connected to the mechanical ventilator via a silicon tube size matched for the tracheal diameter. The remnant of the left atrium was opened widely to prevent pulmonary vein outflow obstruction and to keep left atrial pressure near 0 mm Hg. A temperature probe was sutured inside the left atrium. All perfusion was performed in an antegrade fashion. Figure 1 illustrates the setup of the lung in the EVLP system.

The different EVLP phases (Figure 3) were as follows:

Reconditioning phase. Initially, the lungs were perfused at a flow rate of 0.5 L/min. The shunt from the inflow cannula was closed when the perfusate was de-aired. The lungs were warmed to a target of 36°C, and the temperature difference between lung blood inflow and outflow was not allowed to exceed 8°C. The flow rate was increased gradually to a target level of 70 mL/min per kilogram donor weight, during which the PA pressure was measured continuously and limited to 15 mm Hg. If initial perfusion was uneventful, the PA pressure limit was increased to 20 mm Hg. When the temperature reached 32°C, mechanical volume-controlled ventilation was started at an initial minute-volume of 1.5 times the PA

flow, a positive end-expiratory pressure (PEEP) level of 5 cm H₂O, a rate of 12 breaths/min, and an FiO₂ of 0.5. If uneventful, ventilation was increased gradually to a maximum of 100 mL/min per kilogram donor weight. At 36°C, an incremental PEEP trial was performed to recruit atelectatic lobes/segments. Blood samples for gas analysis were drawn from the left atrium and, if deemed acceptable, EVLP was shifted to the evaluation phase. If blood gases were suboptimal, further treatment was performed in the reconditioning phase.

Evaluation phase. The oxygenator was now used to deoxygenate the perfusate and to add carbon dioxide (CO₂). Ten minutes after the start of the evaluation phase, samples for blood gas analysis were drawn from the left atrium and from the circuit after the oxygenator in the EVLP system (the latter to make sure that the perfusate was deoxygenated adequately). FiO₂ was then decreased to 0.21 and, after another 10-minute period, new blood samples were drawn. FiO₂ was finally set to 1.0 followed by a third set of blood gas analyses. A collapse test was performed at FiO₂ 1.0 by disconnecting the tracheal tube at the end of inspiration. Recoil of the lungs was evaluated subjectively. Pulmonary mechanics as well as end-tidal CO₂ concentrations were monitored continuously (Datex-Ohmeda Anesthesia Monitor; GE Health Care, Chalfont St. Giles, UK). Physiologic dead space was calculated as (PaCO₂ – End-tidal CO₂)/PaCO₂. Static lung compliance was defined as Tidal volume/(Inspiratory plateau pressure – PEEP). Left atrial pressure was assumed to be 0 mm Hg, and pulmonary vascular resistance (PVR) was consequently defined as Mean PA pressure/PA flow × 80.

Acceptance of EVLP-evaluated lungs for transplantation. The decision to transplant the lungs was based on (1) a lung oxygenation capacity with a P/F ratio of >40 kPa during the evaluation phase, (2) stable hemodynamic and respiratory variables (PVR, peak airway pressures, and lung compliance) during EVLP, (3) absence of macroscopic signs of pneumonic infiltrates or lung infarctions, and (4) a normal collapse test.

After the evaluation test, the lungs were cooled in the EVLP system (core cooling) to 12°C. The ventilator was disconnected at 32°C and the trachea was clamped when 50% of the tidal volume was exhaled. In the first 2 pair of lungs, the PA was clamped after an antegrade flush of 1 L Perfadex with additives at 12°C, and thereafter stored in Perfadex on ice. The subsequent donor lungs (n = 4) had surface cooling instituted with the EVLP perfusate continuously flowing over the compress-immersed lungs. Temperature of the donor lungs during surface cooling were kept at 8°C. In case of double LTx, the second lung was kept cold by continuous surface cooling as the first lung was transplanted.

Lung Transplantation

When possible, surgery was performed as bilateral sequential thoracotomies without extracorporeal circulation. Postoperatively, the patients who underwent LTx received treatment according to our standard protocol for LTx. Lung spirometry was performed at the time of discharge from the hospital.

Statistical Analysis

Data were collected prospectively. Continuous data are presented as mean and range. Categorical data are presented as frequency and percentage. Early mortality was defined as hospital mortality, which is all-cause death within any time interval after the LTx. Differences between values before and after treatment were calculated with the Wilcoxon signed-rank test. A *P* value of <.05 was considered as statistically significant.

RESULTS

Six pair of lungs were evaluated with EVLP. The evaluated lungs were initially rejected for LTx as a result of inferior blood gases in the intensive care unit (n = 5) or advanced bilateral infiltrates on chest radiograph (n = 1).

TABLE 1. Recipient characteristics

Variable	Recipient						Mean
	1	2	3	4	5	6	
Age, y	56	55	29	17	51	69	46
Height, cm	160	170	171	151	178	168	166
Weight, kg	55	61	52	41	84	78	62
Blood group	A	A	A	A	B	B	
Diagnosis	COPD	COPD	CF	KS	COPD	Fibrosis	
FVC, L/% of predicted	1.7/62	1.9/59	2.0/43	2.0/58	2.7/59	1.4/51	1.95
FEV 1.0, L/% of predicted	0.5/22	0.5/26	1.1/31	1.0/32	0.8/22	1.2/52	0.85

COPD, Chronic obstructive pulmonary disease; CF, cystic fibrosis; KS, Kartagener syndrome; FVC, forced vital capacity; FEV 1.0, forced expiratory volume in 1 second.

Rejections were based on the best recorded blood gas after optimization of lung function. After EVLP, 2 single lungs were still deemed unsuitable as a result of consolidation or edema and were not used for LTx. Donor characteristics are described in Table 2.

EVLP Outcome

In EVLP no. 1, the lungs were rejected at a P/F ratio of 16.7 kPa. Chest radiography showed basal infiltrates. After 134 min of EVLP, the P/F ratio improved to 67.4 kPa. A PA flow of 77% of the estimated was reached at a PA pressure of 20 mm Hg. PVR was stable around 580 dynes · sec · cm⁻⁵. Double LTx was performed and the recipient had an uneventful recovery.

In EVLP no. 2, the lungs were rejected at a P/F ratio of 17.0 kPa. Chest radiography showed edema. After 220 min of EVLP, the P/F ratio improved to 40.6 kPa. A PA flow of 55% of the estimated was reached at a PA pressure of 20 mm Hg. PVR was reasonably stable around 650 dynes · sec · cm⁻⁵. The lung weight decreased from 2550 g to 1950 g. The intended double LTx was converted to single LTx because of complicated recipient lung adhesions. It was also assumed that transplantation of the second lung

would result in the need for extra corporeal circulation during or after the procedure because of severely impaired blood gases after transplantation of the first lung. The decision to not transplant the second lung was supported by the fact that the patient was planned for either single or double LTx. Indeed, the transplanted lung showed immediate signs of dysfunction in terms of extensive lung edema. The recipient had primary graft dysfunction grade 2 at 36 hours and was dependent on mechanical ventilation for 24 days.

In EVLP no. 3, the lungs were rejected at a P/F ratio of 29.8 kPa. Chest radiography showed localized infiltrate and edema. After 116 min of EVLP, the P/F ratio improved to 56.8 kPa. PA flow was not restricted by the PA pressure limit. PVR was stable around 300 dynes · sec · cm⁻⁵. Double LTx was performed and the recipient had an uneventful recovery.

In EVLP no. 4, the lungs were rejected at a P/F ratio of 41.8 kPa. Chest radiography showed extensive bilateral infiltrates. After 93 min of EVLP, the P/F ratio improved to 70.2 kPa. PA flow was not restricted by the PA pressure limit. PVR was stable around 370 dynes · sec · cm⁻⁵. Double LTx was performed and the recipient had an uneventful recovery.

In EVLP no. 5, the lungs were rejected at a P/F ratio of 29.9 kPa. Chest radiography showed bilateral basal infiltrates. After 112 min of EVLP, the P/F ratio improved to 49.9 kPa. PA flow was not restricted by the PA pressure limit. PVR was stable around 245 dynes · sec · cm⁻⁵. Double LTx was performed and the recipient had an uneventful recovery.

In EVLP no. 6, the lungs were rejected at a P/F ratio of 9.1 kPa. Chest radiography showed extensive infiltrate on the right side. After 295 min of EVLP, the P/F ratio improved to 59.6 kPa in the left lung and remained at 13.6 in the right lung, which was severely consolidated. PA flow was not restricted by the PA pressure limit. PVR was stable around 320 dynes · sec · cm⁻⁵. The lung weight decreased from 1650 g to 1250 g. Single LTx was performed and the recipient had an uneventful recovery.

TABLE 2. Donor characteristics

Variable	Donor no.						Mean
	1	2	3	4	5	6	
Age, y	22	52	42	52	59	19	41
Height, cm	170	168	172	145	180	175	168
Weight, kg	80	66	62	61	102	55	71
Blood group	A	A	A	A	B	B	
Cause of death	SAH	SAH	SAH	SAH	SDH	IBI	
P/F ratio (in donor when accepted for EVLP)	16.7	17	29.8	41.8	29.9	9.1	24.1
Radiographic findings	Bilateral basal infiltrate	Edema	Infiltrate, edema	Bilateral infiltrate	Bilateral basal infiltrate	Extensive infiltrate	
Transport, min; cold flush to start EVLP	143	217	216	191	221	336	220

SAH, Subarachnoid hemorrhage; SDH, subdural hemorrhage; IBI, ischemic brain injury; P/F, ratio of partial pressure of arterial oxygen/fraction of inspired oxygen; EVLP, ex vivo lung perfusion.

FIGURE 1. Schematic drawing of the ex vivo lung perfusion unit. The blood enters the open reservoir via the remnant of the left atrium. Samples for blood gas analyses are drawn from the left atrium (LA) and from a port after the oxygenator where drugs can also be administered. PA, Pulmonary artery; HCU, Heater-cooler unit.

Detailed data from EVLP are presented in Tables 3 through 5. Mean duration of EVLP was 231 min. The mean reconditioning time was 104 min before initiation of the evaluation phase. Two pairs of lungs (nos. 2 and 6) were heavy with edema and reconditioned for 162 and 242 minutes, respectively. These 2 pairs of lungs had the lowest P/F ratios and the lowest lung compliance (both 53 mL/cm H₂O).

FIGURE 2. Picture of a setup of the lung in the Vivoline ex vivo lung perfusion circuit. Cannula to pulmonary artery in top. Cannula to trachea in bottom. Shunt closed with plastic clamp in upper right corner. White temperature probe crossing the lung.

During EVLP, the P/F ratio improved, with a mean of 33.6 kPa (range, 21.0-50.7 kPa) compared with the donor P/F ratio (range, 9.1-41.8 kPa).

Mean peak airway pressure was 15.3 cm H₂O at FiO₂ 1.0 and did not exceed 18 cm H₂O in any pair of lungs. Mean static lung compliance at the end of EVLP was 59 mL/cm H₂O (range, 53-65 mL/cm H₂O). Mean dead space fraction was 35% (range, 17-45%). In 2 pairs of lungs (nos. 1 and 2), PA flow was limited (77% and 50% of target, respectively) by the preset upper PA pressure limit of 20 mm Hg. These 2 pairs of lungs had a high dead space fraction (43% and 44%). In the remaining 4 pairs of lungs (nos. 3-6), the target flow of 70 mL/min per kilogram donor weight was reached. These 4 pairs of lungs had a considerable lower mean dead space fraction of 30%. PVR were stable during the reconditioning and evaluation phases, even beyond 4 hours of perfusion (Figure 4). Hematocrit increased during EVLP from a mean of 11.8 to 12.8 ($P = .03$), and blood glucose decreased from a mean of 12 mmol/L to 9.3 mmol/L ($P = .03$).

Early Clinical Results

All LTx were performed without the use of extracorporeal circulation. There was no 30-day or hospital mortality and all patients were discharged from hospital after a mean stay of 31 days (range, 25-44 days). Early lung function test prior to discharge showed that the patients, on average, had 70% of anticipated forced expiratory volume at 1 second (FEV 1.0). Data are presented in Table 6.

DISCUSSION

Our results indicate that lungs initially rejected for donation because of impaired function can be recovered during EVLP and eventually transplanted without compromising early clinical results. Six patients underwent successful LTx with initially rejected donor lungs. In 5 donors, blood gases were impaired to the extent that the lungs were deemed unusable. In 1 donor, bilateral infiltrates disqualified the lungs for transplantation, although the P/F ratio was >40 kPa. All donors had varying extent of pathologic findings on chest radiography. In our program, none of the lungs would normally have been used for transplantation prior to the introduction of EVLP.

Two different EVLP protocols for human lungs have been applied for clinical use. The Toronto group has developed an EVLP technique with low PA flow (40% of estimated cardiac output), low PA pressure (10-15 mm Hg), and acellular Steen solution.⁵ We have adopted the EVLP protocol initially described by Steen and colleagues⁶ that allows higher PA flow and pressures. Perfusion is performed with Steen solution mixed with banked blood to a hematocrit of 10%-15%. In an animal study of lungs from nonheart-beating donors with warm ischemic times of more than 1 hour, it was shown that PVR increased

FIGURE 3. The practical, circulatory, and ventilatory settings of the different phases during ex vivo lung perfusion. *FiO₂*, Fraction of inspired oxygen.

over time when evaluated in an EVLP model with red blood cells in the perfusate.⁹ Based on that study, it has been questioned whether perfusion with red blood cells can be performed safely for longer than 2 hours,¹⁰ which is sometimes needed for proper ex vivo reconditioning. However, in our series, lungs underwent EVLP for up to 5 hours with no marked increase of PVR over time, with the exception of temporary elevations seen in conjunction with lung recruitment maneuvers. During the end of EVLP, when the cooling phase is instituted, and the lung becomes cold and less compliant, PVR tends to increase (Figure 3). Cypel and associates¹¹ suggested that low flow is essential for successful EVLP. This might hold true when extended perfusions are anticipated, for example, in experimental organ treatment purposes. In our opinion, however, the evaluation of the lung function ex vivo should always be performed using as normal physiologic conditions as possible with respect to PA flow and pressure, blood corpuscle-containing perfusate, as well as ventilatory settings. Functional testing at low flow and low PA pressure during EVLP is not

congruent with the environment in which the lung should later function.

The duration of EVLP was, in the current study, in the range of 157 to 393 minutes. A range of 53 to 98 minutes of this time was used for cooling. The seemingly large time differences are a consequence of the time needed to reach acceptable lung performance. In concurrence, with Aigner and coworkers,⁸ we believe that no further time needs to be spent on EVLP if blood gas values and circulatory and ventilatory data are satisfactory. On the other hand, if the initial physiologic variables are suboptimal, the reconditioning phase should be prolonged to provide time for the oncotic effect of the hyperoncotic perfusate to reduce lung water. All lungs reconditioned during EVLP increased their oxygenation capacity compared with donor blood gas recordings at time of acceptance. In this series, we believe that the most important reason for improvement of lung function is recruitment of atelectasis together with extensive clearance of bronchial secretion.

TABLE 3. Ex vivo lung perfusion duration data

Variables	EVLP duration data						Mean
	1	2	3	4	5	6	
From start to 32°C, min	30	40	27	27	23	23	28
From start to 36°C, min	44	79	50	37	43	60	52
Reconditioning	61	162	58	55	50	242*	104
Evaluation	61	32	58	42	62	53	51
Core cooling	59	85	53	60	62	98	70
Total EVLP, min	193	305	169	157	174	393	231
Cooling method, after EVLP	Ice	Ice	SC	SC	SC	SC	—
Duration, post-EVLP cooling, lung 1, min	299	285	328	303	237	260	285
Duration, post-EVLP cooling, lung 2, min	438	N/A	537	480	455	N/A	478
Total time lung 1, harvest to recipient perfusion, min	643	807	713	701	632	1049	758
Total time lung 2, harvest to recipient perfusion, min	782	N/A	923	878	850	N/A	858

EVLP, Ex vivo lung perfusion; SC, surface cooling; N/A, not applicable. *A first evaluation was done after 68 minutes. As a result of suboptimal partial pressure of arterial oxygen in the right lung, the phase was shifted back to reconditioning. After a total EVLP time of 242 minutes, another evaluation was performed for which data are presented.

TABLE 4. Ex vivo lung perfusion hemodynamic and respiratory data

Variables	EVLP no.						Mean
	1	2	3	4	5	6	
P/F ratio, 0.5	29.8	15.8	29.3	37.7	22	25.7L, 7.7R	26.7
P/F ratio, 0.21	11.4	MD	14.9	18	9.7	9.9L, 5.9R	12.8
P/F ratio, 1.0	67.4	40.6	56.8	70.2	49.9	59.6L, 13.6R	57.4
Ventilation, L/min, at FiO ₂ 1.0	4.3	4.7	6	6	6	3.8	5.1
PawP, mm Hg, at FiO ₂ 1.0	12	15	17	16	15	13	15
Compliance at FiO ₂ 1.0	56	53	65	64	63	53	59
DSF, %, at FiO ₂ 1.0	44	43	45	17	32	28	35
PaO ₂ improvement from donor to EVLP FiO ₂ 1.0 (best lung)	50.7	23.6	27.1	28.4	21.0	50.5	33.6
PA flow, L/min, at FiO ₂ 1.0	4.3	2.4	4	4.2	6	3.9	4.1
PA maximum flow, % of predicted, at FiO ₂ 1.0	77	55	100	100	100	100	
PA pressure, mm Hg, at FiO ₂ 1.0	19	20	15	19	18	16	18
PVR, dynes · s · cm ⁻⁵ , at FiO ₂ 1.0	576	682	308	371	240	330	418

EVLP, Ex vivo lung perfusion; P/F, ratio of partial pressure of arterial oxygen/fraction of inspired oxygen; L, left lung; R, right lung; MD, missing data; PawP, peak airway pressure; DSF, dead space fraction; PVR, pulmonary vascular resistance.

Glucose levels decreased and lactate levels increased during EVLP, as reported by others.^{12,13} We do not believe these are signs of impaired lung function. On the contrary, we find them congruent with normal lung metabolism as described previously.¹⁴ The pairs of lungs (nos. 2 and 6) with the poorest function were subjected to a longer EVLP time, and consequently developed lower glucose and higher lactate levels than the others.

In theory, one of the main objectives of EVLP is to mobilize extensive interstitial and/or alveolar fluid to the hyperoncotic perfusate. However, because 3 of 6 lungs gained weight during EVLP, we are not convinced that this is the main reason for improvement of the lung function. On the other hand, in lungs heavy with fluid prior to EVLP, as in 2 pairs of our lungs (nos. 2 and 6; weight, >1500 g), fluid shift from the lung to the perfusate seems a likely explanation for some of the improved lung function. One of these pairs of lungs (no. 2) was by far the heaviest and had the worst oxygenation capacity of all donor lungs. Although improvement was seen during EVLP, the

oxygenation capacity just reached the preset requirements for transplantation. The recipient operation was complicated and, therefore, lungs with very extensive edema and oxygenation capacity just reaching 40 kPa after EVLP should be considered carefully before transplantation. A lesson learned from this suboptimal outcome, with postoperative morbidity as well as a less-than-ideal postoperative lung function, is that either transplantation should not have been performed in this patient or both donor lungs should have been implanted with postoperative extracorporeal membrane oxygenation. All other patients had an acceptable outcome with no mortality, low morbidity, and good lung function at discharge from hospital.

The yield of transplantation after EVLP was 100% in this series, which is higher than that reported by others.^{4,5,8} Two single lungs, however, were deemed unsuitable for transplantation in our series. We continue to evaluate selected, rejected donor lungs with EVLP.

TABLE 5. Ex vivo lung perfusion laboratory data

Variable	EVLP no.						Mean
	1	2	3	4	5	6	
Hct start, %	12.3	10.9	11.1	10.7	12.4	13.3	11.8
Hct final, %	12.9	11.7	11.6	11.4	13.2	16	12.8
ΔHct, %	0.6	0.8	0.5	0.7	0.8	2.7	1.0
B-glucose start, mmol/L	11.3	10.1	12.6	12.5	13.6	11.8	12.0
B-glucose final, mmol/L	10.0	4.3	11.7	9.8	10.7	<0.1	7.8
Weight start, g	MD	2550	600	500	750	1650	1210
Weight final, g	MD	1950	1050	1000	1000	1250	1250
ΔWeight, g	MD	-650	450	500	250	-400	10

EVLP, Ex vivo lung perfusion; Hct, hematocrit; MD, missing data; ΔWeight, change in lung weight before and after EVLP core cooling.

FIGURE 4. PVR over time in 6 lungs during ex vivo lung perfusion. PVR, Pulmonary vascular resistance.

TABLE 6. Patient outcome after ex vivo lung perfusion and lung transplantation

Variable	Recipient no.					
	1	2	3	4	5	6
Procedure	DL	SL	DL	DL	DL	SL
ECC, Y/N	N	N	N	N	N	N
Time to extubation, h	3	574	6	7	5	7
ICU stay, h	40	625	73	54	152	40
PGD grade at 72 hours*	0	2	0	1	1	0
Hospital stay, d	27	44	39	27	25	25
Spirometry at discharge						
FEV 1.0, % expected	1.7 L, 75%	1.1 L, 40%	2.2 L, 64%	2.1 L, 76%	3.2 L, 88%	1.7 L, 74%
FVC, % expected	2.2 L, 82%	1.8 L, 56%	3.0 L, 76%	2.2 L, 69%	3.8 L, 83%	1.8 L, 66%

DL, Double lung; SL, single lung; ECC, extracorporeal circulation; Y, yes; N, no; ICU, intensive care unit; PGD, primary graft dysfunction; FEV, force expiratory volume; FVC, force vital capacity. *PGD was defined as grade 0, PaO₂/FiO₂ ≥ 40 kPa with a clear chest radiograph; grade 1, PaO₂ ≥ 40 kPa with infiltration on chest radiographs; grade 2, PaO₂/FiO₂ ≥ 27 but < 40 kPa; and grade 3, PaO₂/FiO₂ < 27 kPa.

Limitations

We believe that this EVLP concept is safe, and that proof-of-concept has been shown by others. In our experience, the Vivoline system has been reliable; however, this case series is small and has no control group. Moreover, the included lungs are heterogeneous and therefore conclusions have to be drawn very cautiously.

CONCLUSIONS

In conclusion, the use of EVLP seems safe and indicates that lungs otherwise refused for LTx can be recovered and used subsequently for transplantation with acceptable results. However, the system comes with a considerable cost. Larger series of patients as well as long-term data are required before EVLP can be determined as an important adjunct to LTx.

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