International Clinical Experiences with Ex Vivo Lung Perfusion

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Abstract Ex vivo lung perfusion has been proposed as a method to identify good quality organs from the suboptimal donor pool, and as a method to reduce cold ischemic times by using a transportable system. As lung transplant centers adopt this new technology, encouraging reports are being published. In addition, single center experiences are now being validated by prospective and multicenter clinical trials. In the present report, we will summarize the rationale behind the use of ex vivo lung perfusion, the current different methodologies, and the published international experiences with its use.

Keywords Lung transplantation · Lung preservation · Ex vivo lung perfusion · Lung transplant outcomes · EVLP

Introduction

In the U.S., nearly 2,000 lung transplants are performed every year; however, many patients still die waiting for an organ [1]. More patients could be saved if more lungs met transplantation criteria.

Lung quality is the major limitation in the utilization of donated lungs [2]. The donor lung is subjected to significant physiological and biochemical stresses during brain death, often compounded by trauma, aspiration of gastric contents, and even embolization of trauma-fragmented brain tissue

[3]. Tissue injury during this process results in a systemic innate inflammatory response that compromises the homeostasis of the alveolo-capillary membrane leading to poor oxygenation [4]. Improving organ quality while suppressing this deregulated response before transplantation is highly desirable. Ex vivo lung perfusion (EVLP) provides us with the opportunity to re-evaluate and recondition lungs before transplantation [5].

The use of EVLP has generated great enthusiasm. Several centers around the world have presented encouraging results when using EVLP as a platform to screen organs from the substandard donor pool [6–9]. In addition, data from these centers have demonstrated equivalent outcomes when transplanting standard criteria lungs or lungs selected using EVLP.

The goal of this review is to summarize the rationale, background, and the current published clinical experiences with the use of ex vivo lung perfusion.

Rationale for the Use of EVLP

In the last decade, more aggressive pharmacological management has led to an increase in the number of organs placed per donor. But still only up to 20 % of lungs offered are transplanted in most countries [10]. Cold ischemia, the current preferred method of lung preservation, reduces tissue metabolism limiting the opportunity for interventions after the lungs are explanted [11].

Ex vivo normothermic (37 °C) lung perfusion has been proven by our group and others as a reliable platform to screen lungs that had been previously rejected for transplant because of poor quality [12–15]. The ongoing NOVEL Trial has demonstrated that about 60 % of the lungs evaluated improve their quality during EVLP [16•].

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This quality improvement seems to be related to the low stress conditions of EVLP allowing the lung cells to regain a more physiological status before transplantation [17•]. Other favorable aspects of EVLP are the dehydration of the lung tissue by re-establishing Starling forces that may have been altered during brain death, and the re-expansion of atelectatic lung areas, which improve the ventilation/perfusion ratio leading to better gas exchange.

Clinical EVLP Methodologies

Contemporary clinical applications of EVLP could be summarized as: a method to increase the number of transplantable lungs by reconditioning unused/rejected lungs from the donor pool (Lund and Toronto's methods) [6, 9], and a method to replace cold preservation by using a transportable lung perfusion system (Organ Care System method) [18•]. Table 1 summarizes the differences and

similarities between the steps followed by these methods during EVLP initiation and EVLP stable-reconditioning modes.

When following the Lund or Toronto method, lungs are procured in the standard fashion and transported cold to the recipient center where they are rewarmed for EVLP assessment. When following the OCS method, the lungs are procured in the standard fashion, cold flush, but immediately placed in the EVLP system for normothermic transport to the recipient center. Any of these methodologies requires a stepwise rewarming and an increase of flow in order to maintain pulmonary artery pressures under 15–20 mmHg. During the rewarming period, the vasculature is particularly fragile and elevated pressures can result in worsening edema by increased capillary filtration or by the irreversible loss of the alveolo-capillary barrier integrity [19]. Ventilation is started when the outflow reaches a temperature of 32 °C. The ventilatory strategy is to maintain low airway pressures by using low tidal volumes, which, in combination

Table 1 Initiation and stable-reconditioning modes in current EVLP methodologies

	Lund's protocol [25]	Toronto's protocol [6]	Organ Care System [18•]
Application	Re-evaluation, reconditioning after procurement	Re-evaluation, reconditioning, treatment after procurement	Replace cold ischemia
Transportable	No	No	Yes
Flow			
Pump type	Roller	Centrifugal	Pulsatile
Start perfusion	100 mL/min	150 mL/min	200 mL/min
Target total	100 % cardiac output (70 ml/kg donor ideal weight)	40 % cardiac output CO = 3 × bsa	2.5 L/min
Ventilation			
Mode	Volume control	Volume control	Volume control
VT	3–8 mL/kg (1.5 × PA flow)	7 mL/kg	6 mL/kg
Frequency	12 bpm	7 bpm	10 bpm
PEEP	5 cmH ₂ O	5 cmH ₂ O	5 cmH ₂ O
FiO ₂	50 %	21 %	21 %
Pressure			
Pulmonary artery	<20 mmHg	<15 mmHg	<20 mmHg
Left atrium	0 mmHg	3–5 mmHg	0 mmHg
Temperature			
Start perfusion	25 °C	25 °C	32 °C
Start ventilation	32 °C	32 °C	32 °C
Start evaluation	37 °C	37 °C	37 °C
Perfusate	Steen solution®+red cells (Hto 10–15 %)	Steen solution®	Steen solution®+red cells (Hto 15–25 %)
Time to stability	1 h	1 h	10–15 min
Total time perfusion	2–7 h (92–393 min)	Up to 12 h	Transport time (188–622 min)

Hto hematocritum, *cmH₂O* centimeters of water, *P_{O₂}* partial pressure of oxygen, *bpm* breath per minute, *bsa* body surface area, *CO* cardiac output, ® trade mark, *PA* pulmonary artery, *FiO₂* fraction of inspired oxygen, *PEEP* positive end expiratory pressure, *VT* tidal volume

Table 2 Evaluation phase in current EVLP methodologies

	Lund's protocol [27]	Toronto's protocol [6]	Organ Care System [18••]
Temperature	37 °C	37 °C	37 °C
Flow	100 % cardiac output (70 ml/kg donor ideal weight)	40 % cardiac output CO = 3 × bsa	2.5 L/min
Ventilation			
Mode	Volume control	Volume control	Volume control
VT	1.5 x PA Flow	10 ml/kg	6 ml/kg
Frequency	12 bpm	10 bpm	10 bpm
PEEP	5 cmH2O	5 cmH2O	5 cmH2O
FiO ₂	50 %–21 %–100 %	100 %	NR
Recruitment maneuver	Incremental PEEP	Inspiratory hold (max peak pressure 20 mmHg)	NR
Pressure			
Pulmonary artery	<20 mmHg	<15 mmHg	<20 mmHg
Left atrium	0 mmHg	3–5 mmHg	0 mmHg
Deoxygenating gas	7 % CO ₂ –93 % N ₂	8 % CO ₂ –6 % O ₂ –86 % N ₂	NR
Deoxygenating gas (L/min) titrated PA pCO ₂	34–38 mmHg	35–45 mmHg	NR
Tx acceptance variables	PO ₂ /FiO ₂ >300 mmHg stable PVR Airway pressures Lung compliance Absence of consolidation lung collapse test	PO ₂ /FiO ₂ >400 mmHg stable: PA pressure PVR Airway pressures Lung compliance Clear chest X-ray bronchoscopy	PO ₂ /FiO ₂ ratio When system stable at donor site Before Tx at recipient site

Hto hematocritum, *cmH2O* centimeters of water, *PO2* partial pressure of oxygen, *bpm* breath per minute, *bsa* body surface area, *CO* cardiac output, ® trade mark, *PA* pulmonary artery, *FiO₂* fraction of inspired oxygen, *PEEP* positive end expiratory pressure, *PVR* pulmonary vascular resistance, *VT* tidal volume, *NR* not reported, *Tx* transplant

with low vascular pressures, reduces the possibility of damaging the lungs by inducing stress failure [20–22].

A sweep gas flow is also initiated at 32 °C. EVLP contains an oxygenator that works as a deoxygenator by using a sweep gas formulation of 7 % CO₂+93 % N₂ (Lund) or 8 % CO₂+6 % O₂+86 % N₂ (Toronto). The flow rate is titrated to maintain a pulmonary arterial PCO₂ of 34–38 (Lund) [9] or 35–45 mmHg (Toronto) [6]. Toronto recommends a 0.5-L/min starting flow rate, and we have found that the final flow typically stabilizes at 2–4 L/min.

Once the outflow temperature reaches 37 °C, the system can be considered stable and the lungs can be evaluated. When following the Lund or Toronto methodology, lungs are re-evaluated every hour until they meet acceptability criteria for transplantation. If the lungs do not meet quality criteria, the system is placed back into a reconditioning mode and the lungs are re-evaluated an hour later. Given the low pressures and tidal volumes, alveolar recruitment maneuvers may be necessary through the perfusion time to ensure an adequate ventilation/perfusion ratio.

When using the Organ Care System for transport, a PO₂/FiO₂ ratio is normally obtained at the donor site when the lungs are stable in the system and a second PO₂/FiO₂ ratio once in the recipient operating room before making the decision to transplant. Table 2 summarizes the evaluation mode and variables used to reassess lung quality during EVLP.

Clinical Experiences with EVLP

A review of www.clinicaltrials.gov revealed nine clinical trials studying the use of EVLP. Most of these trials are focused on the expansion of the usable lung donor pool, however one trial is looking at the effects of using a transportable EVLP system to replace cold ischemia as the standard of care. Table 3 shows the most relevant aspects of the clinical trials studying the use of EVLP.

Published literature, both in the form of abstracts and full reports, reveals that many centers are using different EVLP

Table 3 Clinical trials registered at www.clinicaltrials.gov evaluating the use of EVLP

Name	Code	Status	Study variable	Inclusion criteria	Primary endpoint	Center	Sponsor
HELP	NCT01190059	Completed	Transplant suitability	High risk donors	PGD scores in the first 72 h, 30-day mortality	Toronto	XVIVO Perfusion
NOVEL	NCT01365429	Recruiting	Transplant suitability	High risk donors	30-day mortality	Multicenter (U.S centers)	XVIVO Perfusion
EXPAND	NCT01963780	Not yet open	Transplant suitability	High risk donors	Composite: 30-day mortality and absence of PGD 3 in the first 72 h	Multicenter (International)	TransMedics
Evaluation and reconditioning of marginal lung donors to transplantation	NCT01353105	Not yet open	Transplant suitability	High risk donors	30-day mortality resp. complications 12-month survival	Sao Paulo, Brazil	InCor Heart Institute
Ex vivo lung perfusion to increase the number of organs for transplantation	NCT01967953	Completed	Transplant suitability	High risk donors	PGD scores in the first 72 h, 30-day mortality	Milan, Italy	Policlinico Hospital
STRESS INDEX in lung reconditioning	NCT01729637	Completed	Transplant suitability	High risk donors	Presence of mechanical stress as assessed by analysis of the “Stress Index”	Turin, Italy	University of Turin
Phase 2 study of ex vivo perfusion and ventilation of lungs to assess transplant suitability	NCT01241942	Suspended	Transplant suitability	High risk donors	30-day mortality	University of North Carolina	University of North Carolina, Chapel Hill
Ex vivo perfusion and ventilation of lungs recovered from non-heart-beating donors	NCT01615484	Recruiting	Transplant suitability	Non-heart-beating donors	30-day mortality	University of North Carolina, Duke University	University of North Carolina, Chapel Hill
INSPIRE	NCT01630434	Recruiting	Lung preservation	Lung donor	Composite: 30-day mortality and absence of PGD 3 in the first 72 h	Multicenter (International)	TransMedics

PGD primary graft dysfunction

methods to increase the number of usable lungs by screening the high risk donor pool. In addition, these reports demonstrate equivalent outcomes when using EVLP selected or standard criteria lungs, suggesting that EVLP is a safe method to increase the number of lung transplants.

Transportable EVLP as a Method to Reduce Cold Ischemic Time

In November 2012, the groups from Hannover and Madrid reported their initial experience using the Organ Care System as a method to reduce cold ischemia [18•]. Twelve patients received lungs from 12 donors whose lungs had been transported under normothermic ex vivo

lung perfusion conditions. The mean running time of transportable EVLP was 303 min, range 188–622 min. Lungs underwent a period of cold ischemia (i.e. time from harvest to start of EVLP and stop of EVLP to reperfusion after transplant), the mean cold ischemic time was 134 min for the first lung and 249 min for the second lung. The 30-day survival was 100 %, one patient died at day 140 after transplant from cardiomyopathy of unknown origin.

In 2013, the INSPIRE trial investigators (NCT01630434), presented their interim results after 60 lung transplants at the International Society of Heart and Lung Transplantation Society meeting in Montreal [23]; unfortunately, the published abstract does not provide information other than the number of lungs preserved using this methodology.

Table 4 International clinical experience with EVLP as a method re-assess and or recondition lungs

Center	EVLP method	Donors	EVLP conversion rate to Tx	PGD 3 72 h	LOS	30-day mortality (%)	90-day survival (%)	12-month survival (%)
Toronto [6]	Toronto	BDD = 32 DCD = 26	50/58 (86 %)	2 %	20 (7–156)	4	NR	87
NOVEL Trial [16]	Toronto	BDD = 47	31/54 (57 %)	9.6 %	13 (4–198)	3	NR	NR
U. Maryland		DCD = 7						
U. Colorado								
Columbia								
Duke								
UPENN								
Brigham and Women's								
Harefield [8]	Toronto	BDD = 10 DCD = 3	6/13 (46 %)	NR	38 (25–67)	0	0	NR
Madrid [28]	Toronto	DCD(I) = 8	4/8	0 %	NR	0	0	50
Vienna [7]	Toronto	BDD = 13	9/13 (69 %)	0 %	20 (14–59)	0	88	NR
Newcastle [29]	Toronto	BDD = 14 DCD = 4	7/18 (39 %)	14 %	12–43	0	100	NR
France [30]	Toronto	BDD = 21	20/21 (95 %)	10 %	37	5	NR	95
Hospital Foch								
Hospital Marie								
Milan [31]	Toronto + red blood cells	BDD = 2	NR	NR	34 ± 20 ^a	0	50	NR
Turin [32]	Toronto	BDD = 9	7/9 (78 %)	0 %	NR	NR	NR	NR
Three center [33]	Toronto	BDD = 90 DCD = 35	103/125 (82 %)	5 %	23 (7–120)	4	NR	88
Toronto								
Vienna								
Hospital Foch								
Lund [9]	Lund	BDD = 8	6/8 (75 %)	NR	NR	0	100	66
Gothenburg [27]	Lund	BDD = 11	6/6 (100 %)	9 %	28 (25–93)	0	100	NR
Brisbane [34]	Lund	BDD = 5	4/5 (80 %)	0 %	NR	0	0	NR

NR not reported, LOS length of hospital stay, BDD brain dead donor, DCD donation cardiac dead, DCD (I) donation cardiac dead category 1, PGD primary graft dysfunction

^a Data expressed as median and range # data expressed as mean and standard deviation

EVLP as a Method to Re-assess and or Recondition Organs from the Unused Lung Donor Pool

In 2001, Stig Steen [24] reported the first successful use of EVLP when a 54-year-old woman with COPD received a right lung from a 54-year-old donor who underwent cardiac arrest after myocardial infarction. Although initially the method was conceived to evaluate grafts from donors after cardiocirculatory arrest (DCD), Steen's group identified the potential of EVLP as a method to re-evaluate grafts originally rejected for transplantation based on their poor oxygenation. Subsequently in 2006, Wierup et al. [25] described their initial experience reconditioning six donors previously rejected by Scandia-transplant, Eurotransplant, and UK transplant organizations.

After his report, several centers recognized the value of EVLP in identifying good quality lungs within the donor pool that were not accepted for transplantation. One of these groups was the University of Toronto that not only identified the potential of EVLP for re-assessing and reconditioning lungs but also as a platform to deliver therapies looking to improve outcomes after transplantation. To achieve this, the Toronto group developed a low stress perfusion/ventilation strategy in order to maintain lungs ex vivo at a physiological body temperature for long periods of time, i.e. 12 h. In 2011, the results from the first prospective clinical trial using EVLP, the HELP trial, conducted by the Toronto group were published [26•]. The results from this publication were expanded in 2012 when the group presented the outcomes after 50 transplants using lungs selected by EVLP [6]. Table 4 summarizes the most relevant outcome data for this experience.

Our group at the University of Maryland, in collaboration with five other lung transplant centers in the United States (Duke, Columbia, UPenn, University of Colorado, and Brigham's and Women), presented in 2013 the first multicenter and prospective clinical trial, the NOVEL Lung Trial, evaluating the safety of EVLP as a tool to screen the unused lung donor pool for good quality grafts [16•]. This report included 31 lung transplants using lungs selected from the marginal donor pool using EVLP and compared to 31 lung transplants using standard criteria donors. No significant differences in outcomes were observed between the groups as seen in Table 4.

To date, several centers around the world have used this technique to re-evaluate organs from the substandard lung donor pool looking to increase the number of transplants. Table 4 summarizes the published data with the use of EVLP as a method to re-assess or recondition organs from the unused lung donor pool.

Conclusions

Published reports from different centers using EVLP, show a growing body of evidence that favor its use to screen the

suboptimal donor pool. Safety concerns regarding its ability to recognize good quality grafts from the high-risk donor pool are diminishing as data from large multicenter and prospective trials are published. As for the effects of reducing cold ischemic time by using a transportable EVLP system, the ongoing INSPIRE trial may bring some clarity once the data is published.

EVLP promises a new era in lung transplantation, providing investigators with a reliable platform to translate new therapies to improve graft quality.

Compliance with Ethics Guidelines Disclosure The University of Maryland is one of eight centers conducting the NOVEL trial, an FDA trial sponsored by XVIVO Perfusion looking at the safety of EVLP to screen the donor pool. Pablo G. Sanchez and Bartley P. Griffith declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

References of interest which have been published recently are noted as:

- Of importance
- Of major importance

1. McCurry KR, Shearon TH, Edwards LB, et al. Lung transplantation in the United States, 1998–2007. *Am J Transpl.* 2009;9(4 Pt 2):942–58.
2. Van Raemdonck D, Neyrinck A, Verleden GM, et al. Lung donor selection and management. *Proc Am Thorac Soc.* 2009;6(1):28–38.
3. Rosendale BE, Keenan RJ, Duncan SR, et al. Donor cerebral emboli as a cause of acute graft dysfunction in lung transplantation. *J Heart Lung Transpl.* 1992;11(1 Pt 1):72–6.
4. Land WG. Emerging role of innate immunity in organ transplantation part III: the quest for transplant tolerance via prevention of oxidative allograft injury and its consequences. *Transpl Rev (Orlando).* 2012;26(2):88–102.
5. Sanchez PG, D'Ovidio F. Ex-vivo lung perfusion. *Curr Opin Organ Transpl.* 2012;17(5):490–5.
6. Cypel M, Yeung JC, Machuca T, et al. Experience with the first 50 ex vivo lung perfusions in clinical transplantation. *J Thorac Cardiovasc Surg.* 2012;144(5):1200–6.
7. Aigner C, Slama A, Hotzenecker K, et al. Clinical ex vivo lung perfusion—pushing the limits. *Am J Transpl.* 2012;12(7):1839–47.
8. Zych B, Popov AF, Stavri G, et al. Early outcomes of bilateral sequential single lung transplantation after ex vivo lung evaluation and reconditioning. *J Heart Lung Transpl.* 2012;31(3):274–81.
9. Ingemansson R, Eyjolfsson A, Mared L, et al. Clinical transplantation of initially rejected donor lungs after reconditioning ex vivo. *Ann Thorac Surg.* 2009;87(1):255–60.
10. Rosendale JD, Kauffman HM, McBride MA, et al. Aggressive pharmacologic donor management results in more transplanted organs. *Transplantation.* 2003;75(4):482–7.
11. Haniuda M, Dresler CM, Hasegawa S, et al. Changes in vascular permeability with ischemic time, temperature, and inspired oxygen

- fraction in isolated rabbit lungs. *Ann Thorac Surg.* 1994;57(3):708–14.
12. Inci I, Hillinger S, Arni S, et al. Reconditioning of an injured lung graft with intrabronchial surfactant instillation in an ex vivo lung perfusion system followed by transplantation. *J Surg Res.* 2013;184(2):1143–9.
 13. Sanchez PG, Bittle GJ, Williams K, et al. Ex vivo lung evaluation of prearrest heparinization in donation after cardiac death. *Ann Surg.* 2013;257(3):534–41.
 14. Yeung JC, Wagnetz D, Cypel M, et al. Ex vivo adenoviral vector gene delivery results in decreased vector-associated inflammation pre- and post-lung transplantation in the pig. *Mol Ther.* 2012;20(6):1204–11.
 15. Dong B, Dong B, Stewart PW, Stewart PW, Egan TM. Post-mortem and ex vivo carbon monoxide ventilation reduces injury in rat lungs transplanted from non-heart-beating donors. *J Thorac Cardiovasc Surg.* 2013;146(2):429e1–436e1.
 16. • Sanchez PG, Davis RD, D'ovidio F, et al. Normothermic Ex vivo lung perfusion as an assessment of marginal donor lungs—the novel lung trial. *J Heart Lung Transpl* 2013; 32(4, Suppl):S16–S17. *First multicenter and prospective clinical trial to study the safety of using EVLP to screen the suboptimal donor pool.*
 17. • Sanchez PG, Bittle GJ, Burdorf L, et al. State of art: clinical ex vivo lung perfusion: rationale, current status, and future directions. *J Heart Lung Transpl* 2012; 31(4):339–48. *Comprehensive review of the physiological and technical aspects regarding ex vivo lung perfusion.*
 18. • Warnecke G, Moradiellos J, Tudorache I, et al. Normothermic perfusion of donor lungs for preservation and assessment with the Organ Care System Lung before bilateral transplantation: a pilot study of 12 patients. *Lancet*; 380(9856):1851–58. *First report of transportable normothermic ex vivo lung perfusion.*
 19. Pierre AF, DeCampos KN, Liu M, et al. Rapid reperfusion causes stress failure in ischemic rat lungs. *J Thorac Cardiovasc Surg.* 1998;116(6):932–42.
 20. Lunde PK, Waaler BA. Transvascular fluid balance in the lung. *J Physiol.* 1969;205(1):1–18.
 21. West JB. Distribution of pulmonary blood flow and ventilation measured with radioactive gases. *Scand J Respir Dis Suppl.* 1966;62:9–13.
 22. Hauge A, Nicolaysen G. Transvascular fluid balance and capillary permeability in the lung. *Int Anesthesiol Clin.* 1983; 21(2):1–26.
 23. Warnecke G, Weigmann B, Van Raemdonck D, et al. The INSPIRE international lung trial with the Organ Care System technology (OCS™). *J Heart Lung Transpl.* 2013;32(4, Suppl):S16.
 24. Steen S, Sjoberg T, Pierre L, et al. Transplantation of lungs from a non-heart-beating donor. *Lancet.* 2001;357(9259):825–9.
 25. Wierup P, Haraldsson A, Nilsson F, et al. Ex vivo evaluation of nonacceptable donor lungs. *Ann Thorac Surg.* 2006;81(2):460–6.
 26. • Cypel M, Yeung JC, Liu M, et al. Normothermic ex vivo lung perfusion in clinical lung transplantation. *N Engl J Med* 2011;364(15):1431–40. *First prospective clinical trial studying the use of ex vivo lung perfusion to screen the suboptimal donor pool.*
 27. Wallinder A, Ricksten SE, Silverborn M, et al. Early results in transplantation of initially rejected donor lungs after ex vivo lung perfusion: a case-control study. *Eur J Cardiothorac Surg.* 2014;45(1):40–5.
 28. Moradiellos FJ, Naranjo JM, Córdoba M, et al. 90 Clinical lung transplantation after ex vivo evaluation of uncontrolled non heart-beating donors lungs: initial experience. *J Heart Lung Transpl.* 2011;30(4, Suppl):S38.
 29. Dark JH, Karamanou D, Clark S, et al. 323 successful transplantation of unusable donor lungs using ex-vivo lung perfusion: the newcastle experience. *J Heart Lung Transpl.* 2012;31(4, Suppl):S115.
 30. Sage E, Mussot S, Trebbia G, et al. O-097 lung transplantation of initially rejected donors after ex-vivo lung reconditioning: the French experience. *Interact Cardiovas Thorac Surg.* 2013;17 (suppl 1):S1–62.
 31. Valenza F, Rosso L, Gatti S, et al. Extracorporeal lung perfusion and ventilation to improve donor lung function and increase the number of organs available for transplantation. *Transpl Proc.* 2012;44(7):1826–9.
 32. Boffini M, Ricci D, Barbero C, et al. Ex vivo lung perfusion increases the pool of lung grafts: analysis of its potential and real impact on a lung transplant program. *Transpl Proc.* 2013;45(7): 2624–6.
 33. Cypel M, Aigner C, Sage E, et al. Three center experience with clinical normothermic ex vivo lung perfusion. *J Heart Lung Transpl.* 2013;32(4, Suppl):S16.
 34. Hopkins PM, Chambers DC, Naidoo R, et al. Australia's experience with ex-vivo lung perfusion of highly marginal donors. *J Heart Lung Transpl.* 2013;32(4, Suppl):S154.