

## ORIGINAL ARTICLE

# A retrospective database analysis to evaluate the potential of ex vivo lung perfusion to recruit declined lung donors

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## SUMMARY

Ex vivo lung perfusion (EVLP) is currently used for both standard and extended-criteria donor (ECD) lungs. To enlarge the donor pool, we might have to extend the threshold for ECD donation. The purpose of this study was to estimate how many additional ECD lungs could be recruited by EVLP. We reviewed all multi-organ donors (MODs) from our collaborative donor hospitals (January 2010–June 2015). All unused lung donors were categorized using registered donor data and evaluated by two independent investigators to identify which lungs could be transplanted after EVLP. 584 MODs were registered at our transplant center. 268 (45.9%) were declined as lung donor at the moment of registration, and 316 (54.1%) were considered as a donor for lung transplantation. In the latter, lungs from 220 (37.7%) donors were transplanted and 96 donors (16.4%) were not. We identified 78 of 364 declined donors (21.4%) whose lungs could potentially become transplantable after EVLP. With this retrospective database analysis of unused lung donors, we identified a large potential for EVLP to further increase the donor pool in transplant centers where the majority of donor lungs are already extended.

*Transplant International* 2017; 30: 1002–1010

## Key words

ex vivo lung perfusion, expanded donor pool, extended-criteria donor, unused donor lungs

Received: 12 January 2017; Revision requested: 15 March 2017; Accepted: 19 May 2017;

Published online: 13 July 2017

## Introduction

Lung transplantation has become a successful treatment strategy for an increasing amount of well-selected patients with end-stage pulmonary diseases, due to surgical improvements and the development and optimization of immunosuppressive therapy. Unfortunately, only a small proportion of multi-organ donors (MODs) are currently suitable to donate lungs for transplantation. Reported acceptance rates vary from 15% to 35% between centers [1,2]. Consequently, the patients on the

waiting list outnumber the amount of transplantable organs, resulting in a persistent waitlist mortality [3].

Therefore, many strategies have been explored to increase the availability of transplantable donor lungs to improve outcome for patients in need of a pulmonary allograft [4,5].

First, we are increasingly transplanting donor organs that do not fulfill the strict criteria of lung transplantation, the so-called extended-criteria donors (ECD) to enlarge the existing pool of standard-criteria donors (SCD) [6]. Secondly, ex vivo lung perfusion (EVLP)

was introduced in the lung transplant field by Stig Steen in 2001, as a tool to expand the current donor pool by re-evaluating donor lungs prior to transplantation [7]. EVLP is a normothermic perfusion technique that can be achieved by a pump-driven perfusion machine which circulates a preservation solution through the vasculature of the lung. Lungs are also ventilated *ex vivo* and can be continuously monitored and evaluated. Therefore, it has been proposed as the ideal method to recruit more donor organs as we can evaluate questionable donor organs and potentially even increase their quality. Recently, we became interested in not only re-assessing the donor organ on EVLP, but also preserving it in superior circumstances compared to static cold preservation [8].

Several research groups have already published their initial experience with perfusing high-risk or extended-criteria donor lungs with EVLP prior to transplantation to expand the donor pool [9,10]. However, although some groups classify these ECD donor lungs as “initially rejected donor lungs” [11,12], we believe that EVLP is not always mandatory to safely transplant ECD lungs. Both short-term outcome and long-term outcome after ECD lung transplantation without EVLP have been reported to be comparable with SCD donor lung transplantation provided that they are allocated to a suitable patient with an acceptable survival probability [13,14]. Also in our center, ECD lung transplantation results in comparable long-term outcome compared to SCD lung transplantation [6,15].

If we want to further implement EVLP in clinical practice, it is crucial to estimate the potential of EVLP to increase transplant activity and donor organ quality. Therefore, the aim of this study was to retrospectively review our database of MODs and to analyze the reasons of donor lung decline and the conditions where lungs could be salvaged by EVLP technology.

## Methods

### Data collection and categorization

We retrospectively reviewed our database of all MODs offered to our center from January 2010 until June 2015. Our transplant center is organized within a network of 33 collaborative donor hospitals, and we report all offers within this network to Eurotransplant.

First, we divided all MODs in two categories: “declined as lung donor” and “considered as lung donor”. The decision to consider a MOD as a potential lung donor was driven by the expert opinion of our

transplant physicians that is based on interpretation of both medical and technical information provided by the donor center. MODs considered to be good candidates to donate lungs for transplantation were allocated by Eurotransplant, based on international allocation rules [16]. The actual number of donors whose lungs were finally accepted for transplantation was recorded, and these lungs could be allocated by Eurotransplant first to other centers or were transplanted in our center based on our local allocation system. They are categorized as ECDs if on one or more of the following criteria were met: age >55, PaO<sub>2</sub>/FiO<sub>2</sub> < 300, abnormal chest X-ray, smoking history, presence of aspiration, presence of chest trauma, or donation after circulatory death (DCD). All other lungs were considered SCDs.

Secondly, we categorized all MODs whose lungs were not transplanted. This group included the lungs that were initially declined as lung donor (“declined as potential lung donor”), the grafts that were declined after receiving additional information from the donor center prior to leave for procurement (“declined without *in situ* evaluation”) and the grafts that were ultimately declined *in situ* after opening the chest with direct macroscopic assessment of the lungs (“declined after *in situ* evaluation”).

Next, data of donors whose lungs were not transplanted were re-assessed individually by two independent investigators to identify the reason for decline. This assessment was performed using the available donor data within the database and based on consensus between the investigators. With this information, all nontransplanted donor lungs were assigned to subcategories listed in Table 1. If more than one reason was identified, the most important factor (as assessed by the investigators) was listed.

### EVLP candidate selection

Finally, two investigators (A.M. & A.P.N) identified potential donor grafts among the nontransplanted organs that could be salvaged using EVLP technology. The manner of recovering these organs was based on reassessment (additional evaluation of the organ function), improved preservation (prolonged out-of-body time), and reconditioning (potential improvement of specific injuries during EVLP). The selection criteria for currently rejected donor lungs that potentially could be salvaged by EVLP were: neurogenic lung edema, pulmonary emboli, PaO<sub>2</sub>/FiO<sub>2</sub> below 300 without obvious explanation, minor pulmonary infections (consolidation

**Table 1.** Subcategories of lung donors declined for transplantation.

No consent	Logistical reason	Patient-related factors	Death-related organ injury	Unknown
Family refusal	No matched recipient	Advanced age	Abnormal arterial blood gases (low PaO <sub>2</sub> /FiO <sub>2</sub> )	No information available on why lungs were rejected
No consent medical examiner	Procurement team not present in time	Smoking	Abnormal chest X-ray/CT scan	No reason found based on donor data, technical investigations, or blood gases
	No operating room or surgical team available	Chronic obstructive pulmonary disease (COPD)	Aspiration	
		Malignancy	Hemodynamic unstable donor	
		Systemic disease	Pulmonary emboli	
		Pulmonary fibrosis	Lung edema	
		Pleural disease	Parenchymal haematoma/contusion/polytrauma	
			Pulmonary infection/systemic infection	
			Unknown warm-ischemic time (DCDII)	

PaO<sub>2</sub>/FiO<sub>2</sub> = Arterial partial oxygen pressure over fractional inspired oxygen concentration.

on chest X-ray or purulent sputa with PaO<sub>2</sub>/FiO<sub>2</sub> above 200), unknown warm ischemic time, and logistical reasons for donor lung decline (extended time for allocation or to schedule the transplant procedure).

## Results

### Categorization of MOD offers

584 MODs were recorded at our center between January 2010 and June 2015 (= “multi-organ donors”). Of those 584 MODs registered within our collaborative donor hospitals, 268 (45.9%) were declined as lung donor and lungs were not allocated (= “declined as potential lung donor”). 316 (54.1%) MODs were considered as a lung donor (= “considered as potential lung donor”) and were reported to Eurotransplant for allocation. However, 53 (9%) were declined based on additional information or second evaluation of donor data by the transplant center to which lungs were allocated (= “declined without in situ evaluation”). Another 43 (7.4%) were declined upon procurement in the donor hospital (= “declined after in situ evaluation”).

Lungs from 220 MODs were successfully transplanted (= “transplanted”). Of those, 72% could be categorized as ECDs based on previously published criteria [6], and only 28% were SCDs. Donor characteristics of the individual categories are listed in Table 2.

### Declined lung donors

In the “declined as potential lung donor” group, three MODs were declined as there was no consent for organ donation. Donor-related factors ( $n = 106$ ) included: old age ( $n = 58$ ), a history of smoking or COPD ( $n = 35$ ), or a significant medical history ( $n = 13$ ) such as pulmonary hypertension, cardiovascular disease, and malignancy. Death-related organ injury ( $n = 150$ ) included: abnormal chest X-ray/arterial blood gases/bronchoscopy results ( $n = 71$ ), pulmonary infection ( $n = 32$ ), aspiration ( $n = 19$ ), poly-trauma with lung contusion ( $n = 14$ ), DCD category II ( $n = 7$ ), a hemodynamic instable donor with unknown warm ischemic time ( $n = 4$ ), presence of pulmonary emboli ( $n = 2$ ), or neurogenic lung edema ( $n = 1$ ). In nine cases, no obvious reason could be identified why lungs were not transplanted based on the registered donor data and medical investigations.

In the “declined without in situ evaluation” group ( $n = 53$ ), no suitable recipient could be found in time within the Eurotransplant database in 22 cases. The lung procurement team did not arrive on time in four cases where the abdominal procurement team already started to avoid long warm ischemic times in a hemodynamically instable donor. Donor-related factors ( $n = 13$ ) included: a significant medical history that interfered with transplantability ( $n = 10$ ), a severe smoking history that was not previously reported ( $n = 2$ ), or high donor age ( $n = 1$ ). Death-related organ

**Table 2.** Descriptive analysis of all MODs and their subgroups.

MODs	Declined as potential lung donor		Considered as potential lung donor	Declined as lung donor without in situ evaluation	Declined as lung donor after in situ evaluation	Donors used for lung transplantation
	n = 268	n = 316				
n = 584	Not allocated		Allocated		n = 43	n = 220
Gender						
Male	327 (56%)	149 (55.6%)	178 (56.3%)	34 (64.2%)	30 (69.8%)	1114 (51.8%)
Female	247 (42.3%)	109 (40.7%)	138 (43.7%)	19 (35.8%)	13 (30.2%)	106 (48.2%)
Not registered	10 (1.7%)	10 (3.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Donor age (year)						
Median (25% IQR-75% IQR)	56 (45-66)	62.0 (49-76)	52 (43-62)	55 (41-65)	50 (44-61)	52 (43.5-61.0)
<45	143 (24.5%)	52 (19.4%)	91 (28.8%)	17 (32.1%)	12 (27.9%)	62 (28.2%)
45-54	125 (21.4%)	34 (12.7%)	91 (28.8%)	9 (17.0%)	12 (27.9%)	70 (31.8%)
55-59	65 (11.1%)	28 (10.5%)	37 (11.7%)	7 (13.2%)	4 (9.3%)	26 (11.8%)
>60	241 (41.3%)	144 (53.7%)	97 (30.7%)	20 (37.7%)	15 (34.9%)	62 (28.2%)
Not registered	10 (1.7%)	10 (3.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
PaO <sub>2</sub> /FiO <sub>2</sub>						
Median (25% IQR-75% IQR)	393 (298-478)	296.0 (188-402)	436 (371-503)	392 (331-469)	414 (366-489)	449 (383-508)
>450	170 (29.1%)	34 (12.7%)	136 (43.1%)	15 (28.3%)	14 (32.6%)	107 (48.6%)
351-450	172 (29.4%)	49 (18.3%)	123 (38.9%)	20 (37.7%)	21 (48.8%)	82 (37.3%)
301-350	50 (8.6%)	18 (6.7%)	32 (10.1%)	8 (15.1%)	5 (11.6%)	19 (8.6%)
≤300	122 (20.9%)	103 (38.4)	19 (6.0%)	10 (18.9%)	2 (4.7%)	7 (3.2%)
Not registered	70 (12.0%)	64 (23.9%)	6 (1.9%)	0 (0%)	1 (2.3%)	5 (2.3%)
Smoker						
Yes	196 (33.5%)	86 (32.1%)	110 (34.8%)	21 (39.6%)	21 (48.8%)	68 (30.9%)
No	309 (52.9%)	139 (51.9%)	170 (53.8%)	27 (51.0%)	18 (41.9%)	125 (56.8%)
Not registered	79 (13.5%)	43 (16.0%)	36 (11.4%)	5 (9.4%)	4 (9.3%)	27 (12.3%)
Donor category						
DBD	463 (79.3%)	209 (78.0%)	254 (80.4%)	39 (73.6%)	32 (74.4%)	183 (83.2%)
DCD	121 (20.7%)	59 (22.0%)	62 (19.6%)	14 (26.4%)	11 (25.6%)	37 (16.8%)
BMI						
Median (25% IQR-75% IQR)	24.7 (22.5-27.7)	25.3 (23.2-27.8)	24.6 (22.1-27.3)	26.2 (22.8-28.6)	25.3 (22.5-27.8)	24.3 (22.0-26.7)
<20	46 (7.9%)	21 (7.9%)	25 (7.9%)	7 (13.2%)	4 (9.3%)	14 (6.4%)
20-25	255 (43.6%)	100 (37.3%)	155 (49.1%)	15 (28.3%)	17 (39.5%)	123 (55.9%)
>25	272 (46.6%)	137 (51.1%)	136 (43.0%)	31 (58.5%)	22 (51.2%)	83 (37.7%)
Not registered	11 (1.9%)	10 (3.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

**Table 2. Continued.**

	MODs n = 584	Declined as potential lung donor n = 268		Considered as potential lung donor n = 316		Declined as lung donor without in situ evaluation n = 53		Declined as lung donor after in situ evaluation n = 43		Donors used for lung transplantation n = 220	
		Not allocated		Allocated							
Chest X-ray											
Clear	215 (36.8%)	53 (19.8%)	162 (51.3%)	21 (39.6%)	23 (53.5%)	118 (53.6%)					
Consolidation	168 (28.8%)	92 (34.3%)	76 (24.0%)	15 (28.3%)	10 (23.2%)	51 (23.2%)					
Atelectasis	48 (8.2%)	24 (8.9%)	24 (7.6%)	6 (11.3%)	3 (7.0%)	15 (6.8%)					
Pleural fluid	14 (2.4%)	9 (3.3%)	5 (1.6%)	1 (1.9%)	3 (7.0%)	1 (0.5%)					
Contusion/ pneumothorax	11 (1.9%)	4 (1.5%)	7 (2.2%)	3 (5.7%)	0 (0%)	4 (1.8%)					
Edema	14 (2.4%)	3 (1.2%)	11 (3.5%)	2 (3.8%)	1 (2.3%)	8 (3.6%)					
Not registered	114 (19.5%)	83 (31.0%)	31 (9.8%)	5 (9.4%)	3 (7.0%)	23 (10.5%)					
Bronchoscopy											
Clear	7 (1.2%)	0 (0%)	7 (2.2%)	1 (1.9%)	0 (0%)	6 (2.7%)					
Nonpurulent secretions	17 (2.9%)	2 (0.7%)	15 (4.8%)	3 (5.7%)	2 (4.7%)	10 (4.5%)					
Purulent secretions	19 (3.3%)	8 (3.0%)	11 (3.5%)	4 (7.5%)	2 (4.7%)	5 (2.3%)					
Inflammation	2 (0.3%)	0 (0%)	2 (0.6%)	0 (0%)	0 (0%)	2 (0.9%)					
Not registered	539 (92.3%)	258 (96.3%)	281 (88.9%)	45 (84.9%)	39 (90.6%)	197 (89.6%)					
Lung donor score (ET)											
Median	8 (7–9)	9 (8–10)	8 (7–8)	8 (7–10)	8 (7–9)	7 (7–8)					
(25% IQR–75 IQR)											
<7	175 (30.0%)	29 (10.8%)	146 (46.2%)	16 (30.2%)	17 (39.5%)	113 (51.4%)					
8	158 (27.0%)	54 (20.1%)	104 (32.9%)	14 (26.4%)	15 (34.9%)	75 (34.1%)					
9	119 (20.4%)	78 (29.1%)	41 (12.9%)	9 (17.0%)	9 (20.9%)	24 (10.9%)					
>10	132 (22.6%)	107 (40.0%)	25 (8.0%)	14 (26.4%)	2 (4.7%)	8 (3.6%)					

Lung donor score determined by Eurotransplant (ET) criteria [14].

injuries ( $n = 11$ ) referred to an abnormal chest X-ray in five cases, to pulmonary infection in three cases, or abnormal arterial blood gases in three cases. In another three cases, no obvious reason could be identified why lungs were not transplanted based on the registered donor data and medical investigations.

In the “lungs declined after in situ evaluation” group ( $n = 43$ ), donor-related factors ( $n = 16$ ) leading to decline of the lung donor for transplantation included: intrinsic lung diseases such as emphysema ( $n = 14$ ), fibrosis ( $n = 1$ ), and pleural disease ( $n = 1$ ). Death-related organ injuries ( $n = 21$ ) that led to inability to transplant the donor lungs were identified as: a significant pulmonary infection ( $n = 10$ ), abnormal arterial blood gases ( $n = 6$ ), pulmonary emboli ( $n = 2$ ), parenchymal hematoma ( $n = 2$ ), or severe lung edema ( $n = 1$ ). In six cases, no obvious reason could be identified why lungs were not transplanted based on the registered donor data and medical investigations.

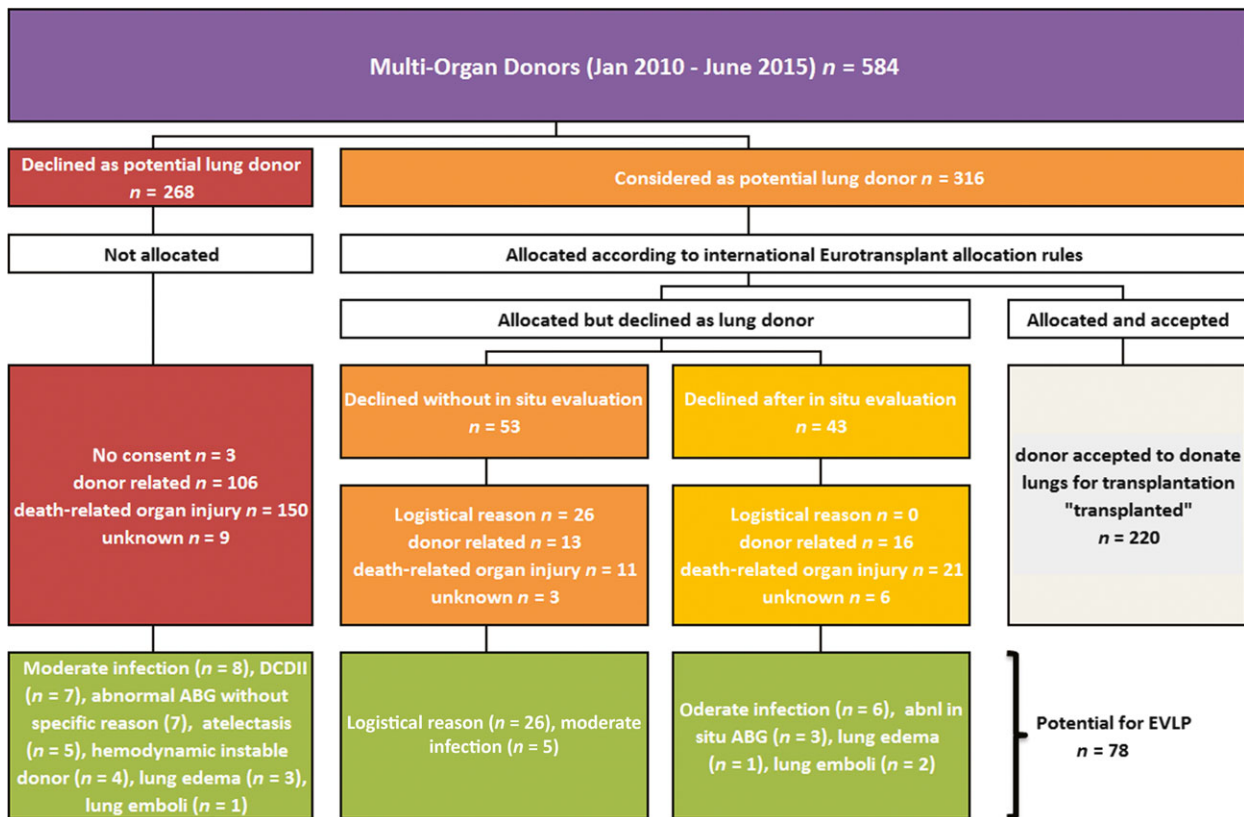
All categories and subcategories, including the lung donors that were selected as candidates for EVLP recovery, are summarized in Fig. 1.

### Candidates for EVLP

In total, lungs of 78 lung donors were identified as potential candidates to be recovered by EVLP evaluation, preservation, and reconditioning based on expert opinion. From the group “declined as potential lung donor”, these included: eight MODs with minor pulmonary infection, seven DCD II donors, seven MODs with low arterial blood gases without obvious reason, five with atelectasis, four hemodynamically unstable MODs with unknown warm ischemic time, three MODs with neurogenic lung edema, and one MOD with lung emboli.

In the “declined without in situ evaluation” group, cases in which a logistical reason led to refusal of the lung donor ( $n = 26$ ) and MODs with minor pulmonary infections ( $n = 5$ ) were considered as good candidates for EVLP evaluation–preservation–reconditioning.

In the “declined after in situ evaluation” group, lungs of potential lung donors could potentially be recovered if they would have been carefully evaluated or actively reconditioned on EVLP in six cases of minor infection, abnormal arterial blood gases ( $n = 3$ ), lung edema



**Figure 1** Overview of multi-organ donors (purple) that were further categorized as “declined as potential lung donor” (red) or as “considered as potential lung donor” (orange). Also in the latter, they could still be declined without in situ evaluation (blue) or after in situ evaluation (yellow). Lungs of 220 of 584 donors were actually transplanted. Lungs that were not transplanted, but could be candidates for ex vivo lung perfusion evaluation, superior preservation, or active rehabilitation are listed in the green boxes below.

( $n = 1$ ), or macroscopic appearance of lung emboli ( $n = 2$ ).

## Discussion

In our study, we retrospectively analyzed donor data registered in our center to provide insights in MODs that are declined as lung donor in current clinical practice. We hypothesized that EVLP could increase the donor pool when lungs would be more carefully evaluated, preserved in superior conditions or even be actively reconditioned.

In Belgium, deceased organ donation is based on presumed consent legislation (opting-out system) leading to a high rate of 29.1 deceased donations per million inhabitants [17]. In this opting-out system, every deceased individual is classified as a potential donor, in absence of an explicit opting-out for organ donation before death. In case family members object to organ donation of their relative, their wishes will be respected unless the patient is explicitly registered to be an organ donor (opting-in). In this database, organ donors that were not offered due to objection of the patient (opting-out) or family members were not registered because no consent was obtained (although legally this is not obligated because of the presumed consent legislation). In two cases, there was an unforeseen objection of the family during a second evaluation and the donor procedure was abandoned. In one particular case, the body was not released by the legal medical examiner after a suicide attempt, so we could not proceed to organ donation.

The acceptance rate of MODs for lung transplantation in our study population was 37.7%. 584 MODs were offered to our center by our own university hospital and a collaborative donor network of 33 local hospitals, over a period of 66 months (January 2010–June 2015), which corresponds to an annual number of MODs of 88 (this does not include organs offered by ET out of our local donor network). On average in Belgium (2010–2015), 330 MODs are reported annually for transplantation to ET, of which 168 are considered as lung donor and 107 are actually used. This leads to an acceptance rate of 32.5% of all MODs for lung transplantation. Overall in Eurotransplant, this percentage is even lower, between 2010 and 2015, the average acceptance rate of MODs for lung transplantation was 26.6% [3].

We believe that improved donor management is an important cornerstone that might explain this high acceptance rate of our MODs. Efforts to improve management strategies have been incorporated in ICU practice. These include protective ventilation strategies [18],

fluid restriction, steroid administration and early identification of potential donors [19,20]. Our high acceptance rate supports that optimal management strategies with preset goals should never be completely abandoned in favor of machine perfusion.

We defined a subset of criteria that could be used to select grafts that could be salvaged by EVLP. First, infection leads to a high number of rejected organs. Although it might not be feasible to completely heal a pulmonary infection during only a limited perfusion time on EVLP, a reduction in the microbial load [21] and endotoxin levels has already been demonstrated and could increase the quality of the infected donor lung [21,22]. Therefore, it seems feasible to transplant lungs that first seemed unfit because of pulmonary infections, as we can minimize the microbial load in those lungs with high dose antibiotic treatment. These lung grafts were also included as candidates for EVLP recovery. Secondly, EVLP could also provide a solution for many logistical issues as we can potentially prolong the preservation time of the donor organs before transplantation. This can be done by either placing the lungs on a portable EVLP device in the donor center [23], or alternatively, a stationary device after a longer cold ischemic time can be used [24]. Which technique is superior is still a subject of debate. Thirdly, atelectasis could be reversed on EVLP by meticulous recruitment maneuvers without derecruitment by abdominal compression. Also, lungs with a low PaO<sub>2</sub> without any obvious reason (such as infection) could be recruited and evaluated carefully. Fourth, lungs with neurogenic lung edema could be dried out by perfusing the lungs with a perfusate high on oncotic pressure or by activation of the alveolar fluid clearance during normothermic metabolism. Lastly, lungs with pulmonary emboli could also be salvaged by perfusion alone where small emboli can be washed out [25] or by the addition of fibrinolytics [25,26]. In many cases, lungs are re-evaluated *ex vivo* to guarantee a qualitatively good donor lung for transplantation. Unfortunately, not all lungs can be recovered by EVLP. For example, lungs that are injured by direct trauma are difficult to preserve on EVLP due to air leak and leakage of perfusate in the alveoli. Therefore, structural damage was considered as not salvageable.

Already in 2002, Ware *et al.* [27] estimated that 40% of lungs that were not suited for transplantation could be salvaged by more objective *ex vivo* evaluation. Due to technical improvement and refinement of the technique, including the ability of longer perfusion time on EVLP, this percentage of organ recovery by EVLP could be higher as initially reported. The conversion rate of

unused donor lungs to transplantable donor lungs with EVLP highly depends on the inclusion criteria for EVLP. Previous studies in experienced EVLP centers showed conversion rates of 55–95% with extended-criteria or high-risk donor lungs [9, 10, 21]. Selection of EVLP candidates in this cohort among the rejected lungs remains a subjective process and goes beyond selecting extended-donor lungs such has been previously proposed. However, all donor data were independently evaluated by two EVLP experts who performed over 300 EVLP cases in clinical and preclinical setting.

Early outcome after lung transplantation with EVLP seems promising; however, the long-term outcome is not well characterized yet. Tikkanen *et al.* [28] showed a similar 1-, 3-, and 5-year graft survival, chronic lung allograft dysfunction (CLAD)-free survival, and quality of life in their cohort of 63 EVLP grafts. Freedom from CLAD was even superior in brain-dead donors when EVLP was used. Up to now, data on outcome after EVLP are limited to ECD and SCD donor lungs that are often transplanted in other donor centers without perfusion on EVLP prior to transplantation. Therefore, further expansion of inclusion criteria for EVLP reconditioning should be validated in preclinical safety models by a thorough evaluation of these rejected donor lungs on EVLP. We are convinced that our analysis contributes to a better insight in selection of EVLP candidates and to the development of strategies to successfully implement this technology in daily transplant activity.

In this cohort, 72% of the used donors could be retrospectively categorized as ECD and were successfully transplanted. Our group has previously published similar long-term outcome for ECDs compared to SCDs in a cohort of 431 donors, from which 63% were ECDs [6].

The limitation of this study is its retrospective nature using registry data. Also, the categorization was performed using expert opinion as there is limited evidence reported to guide this analysis. However, this study did result in an improved donor database registration in our transplant center. Donor lungs that are not transplanted are now currently assigned to categories 1–4 based on the medical history of the donor, acute donor or organ injury, logistical reasons, or technical investigations that led to organ decline. Also, the timing of refusal of the donor lungs will be registered for each declined lung donor. In addition, lungs from donors declined as lung donor are currently brought to the laboratory for EVLP evaluation–preservation–reconditioning to validate our hypothesis in a preclinical safety study. These two

ongoing studies in our center are designed to validate our current hypothesis that EVLP could increase the acceptance rate by recruiting lungs to the transplantable donor pool that are currently not used for transplantation. Validation of the findings of our current retrospective study are of course of paramount importance, as there are no data available currently on which particular lungs could benefit from EVLP besides a limited series of case reports. We can therefore only speculate that our EVLP strategy in these lungs will increase the number of safe transplantations.

Although inclusion of EVLP in several clinical program has led to an increase in the donor pool and transplant activity, the use of these donor lungs without EVLP has also been implemented with good short-term outcome compared to SCD lung transplantation. Therefore, the question remains what the real impact of EVLP could be, if lung donors declined by experienced ECD lung transplant centers are selected for EVLP recovery. With this first retrospective data analysis of unused lung donors, we identified that there is a large potential for EVLP to increase the donor pool. Preclinical studies will have to validate this hypothesis and examine the safety of accepting these lungs for transplantation.

### Authorship

KD and BD: performed the donor database registry search. AM and AN: reviewed all registered donor data and evaluated the potential for EVLP. AM and DVR: wrote the manuscript. JS, RV, GV, SV and BV: helped with the study design, categorization of the donor data and critical appraisal of the manuscript.

### Funding

A.N. is supported by the Clinical Research Fund from the University Hospitals Leuven. S.V. and R.V. were sponsored by grants from the Research Foundation Flanders (FWO; 12G8715N, 1515816N, and 1803516N). R.V. was supported by a grant from the FWO (KAN2014 1.5.139.14), and the start fund of UZ Leuven. G.V. and B.V. were supported by research funding from KU Leuven (C24/15/030).

### Conflict of interest

The authors declare no conflict of interests



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