ORIGINAL ARTICLE

Extended criteria donor lung reconditioning with the organ care system lung: a single institution experience

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SUMMARY

Lung transplantation is a life-saving procedure limited by donor's availability. Lung reconditioning by *ex vivo* lung perfusion represents a tool to expand the donor pool. In this study, we describe our experience with the OCS™ Lung to assess and recondition extended criteria lungs. From January 2014 to October 2016, of 86 on-site donors evaluated, eight lungs have been identified as potentially treatable with OCS™ Lung. We analyzed data from these donors and the recipient outcomes after transplantation. All donor lungs improved during OCS perfusion in particular regarding the PaO_2/FiO_2 ratio (from 340 mmHg in donor to 537 mmHg in OCS) leading to lung transplantation in all cases. Concerning postoperative results, primary graft dysfunction score 3 at 72 h was observed in one patient, while median mechanical ventilation time, ICU, and hospital stay were 60 h, 14 and 36 days respectively. One in-hospital death was recorded (12.5%), while other two patients died during follow-up leading to 1-year survival of 62.5%. The remaining five patients are alive and in good conditions. This case series demonstrates the feasibility and value of lung reconditioning with the OCS™ Lung; a prospective trial is underway to validate its role to safely increase the number of donor lungs.

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Key words
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Introduction

Lung transplantation is a lifesaving procedure for patients with end-stage lung disease. Despite all recent improvements in donor management and organ preservation, only about 15–20% of lungs offered from multiorgan donors are used for transplantation [1]. The others are considered unsuitable, seldom immediately upon the offer, for different reasons, including lungs injuries or logistical issues.

Therefore, donor pool expansion is mandatory and may be achieved through improvement in lung reconditioning or in lung preservation. Furthermore, the negative impact on the outcome of other clinical criteria (e.g., age >55 years) can be mitigated by reducing the cold ischemia time [2].

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On the other hand, some recruitment maneuvers (manual ventilation, use of diuretics) may not be effective or feasible because of limited time available or donor instability. It follows that often the difficulty of using nonideal donors is mainly because of inability to perform a prolonged assessment to distinguish reversible from irreversible injury. Recently, several studies demonstrated *ex vivo* lung perfusion (EVLP) as part of clinical practice to assess extended criteria lungs [3–5]. All EVLP systems to date are nonportable, except OCS™ Lung, used only after standard cold transport, thus not reducing the cold ischemic time, possibly limiting the benefits of the procedure.

The Organ Care System (OCS™) Lung (Transmedics, Andover, MA, USA) is the first portable *ex-vivo* ventilation and perfusion system available for lung grafts [6]. This device has been extensively investigated as preservation purpose in the ideal donors with the INSPIRE study (NCT01630434), with optimal results [2]. Only limited experiences with extended criteria donors treated with this technology have been published so far [7–9] and the only trial to evaluate its reconditioning effect was recently concluded with satisfactory results [10].

Therefore, in this paper we report the data of a single center case series, aimed at exploring safety and efficacy of the OCS™ Lung in extended criteria lung assessment and reconditioning.

Materials and methods

Study population

An *ex vivo* program for extended criteria donor lungs using the OCS™ Lung started at the Thoracic Surgery Unit of Padua in January 2014. Inclusion and exclusion criteria were developed to reflect nonideal donor lungs and were as follows:

Inclusion criteria:

1. Donor PaO_2/FiO_2 ≤300 mmHg at time of acceptance of lung despite active recruitment or proper sampling from left atrium or
2. Expected ischemic time>6 h or
3. Donor after Cardiac Death (DCD donor) or
4. Donor age ≥55 years old
5. Pulmonary edema, defined as bilateral interstitial infiltrates without evidence of infection, detected on the last chest radiography by the surgeon assessing the donor, or a major discrepancy between the patient clinical characteristics (e.g., young age, no smoking history) and lung function (low PaO_2/FiO_2 ratio).

Exclusion criteria:

1. Presence of moderate to severe traumatic lung injury with air and or blood leak.
2. Presence of active confirmed pneumonia or persistent purulent secretions on repeated evaluation bronchoscopy.
3. Previous history of pulmonary disease.
4. Multiple transfusions of >10 units packed red blood cells (pRBCs).
5. ABO incompatibility.
6. Recipient <18 years old.

For all included donors, we evaluated demographics and clinical characteristics, calculating Oto score [11].

A complete lung functional assessment during the OCS™ Lung preservation was recorded. This included pulmonary vascular resistance (dyn s/cm^5), peak airway pressure (cmH_2O) and mean pulmonary artery pressure (mmHg) trends throughout the perfusion session. In additions, arterial blood gas analysis to assess the oxygenation capacity of donor lungs was measured at the beginning and at end of each perfusion session on the system (PaO_2/FiO_2). For all transplanted patients, we recorded demographic data, use of extracorporeal membrane oxygenation (ECMO) in pre-, intra-, or postoperative period and cold ischemic times (considering time from aortic cross-clamp in the donor to lung reperfusion and excluding OCS™ Lung running time). Postoperative data collected for all recipients included primary graft dysfunction (PGD) scores at time 0, 24, 48, and 72 h, time on mechanical ventilation (MV) after surgery, length of intensive-care unit (ICU) stay and in-hospital stay, in hospital mortality and morbidity. All transplanted patients were followed up for incidence of acute rejection at 1, 6, and 12 months with trans-bronchial biopsy, for pulmonary function with measurement of best FEV1% and for survival at 1-year post-transplantation.

All transplants were performed according to the ISHLT ethics guidelines and the study was approved by the Institutional Review Board. All patients signed written informed consent for lung transplantation and for data publication.

OCS™ Lung preservation

The technique of OCS™ Lung perfusion was already described in our previous publication [12]. Donor lungs were perfused on the system using a perfusate composed of 1500 ml of OCS™ Lung Solution and three units of leukocyte reduced pRBCs typed to the corresponding recipient. Only in the first case, according to

Transplant International 2019; 32: 131–140

our policy at that time, 4°C Perfadex solution (XVIVO Perfusion, Göteborg, Sweden) instead of OCS™ Lung Solution was used.

In our policy, in addition to main functional analysis, a lung X-ray on the device [13] was routinely performed. Lungs were considered suitable for transplantation according to visual and bronchoscopy inspection, PaO_2/FiO_2 ratio >300 mmHg as well as stable perfusion and ventilation parameters trends for PAP, PVR, and PAWP (with no more than 20% rise in these trends throughout preservation).

After lungs were accepted for transplantation, the preservation session was terminated by cooling the donor lungs and termination of warm perfusion on the OCS™ Lung. During the implantation of the first lung, the second one was ice stored in all but the last case, in which *ex-vivo* perfusion was continued until the end of second pneumonectomy.

Transplantation technique

Postero-lateral thoracotomy was used for single lung transplantation while bilateral sequential transplantation was performed through bilateral anterolateral thoracotomies or clamshell incision.

In cases of respiratory or hemodynamic failure or in patients with secondary pulmonary hypertension, an ECMO device was implanted, and maintained in the postoperative period when needed, otherwise removed at the end of surgical procedure.

Statistical analysis

Continuous variables are expressed as median, with interquartile range as a measure of variability. Categorical variables are presented as percentages (number of counts).

Temporal trends of considered variables were studied using a Generalized Additive Model (GAM) approach [14], using LOESS [15] to allow for nonlinear trends estimation. Goodness of fit was assessed using bootstrap-based (repetitions 10 000) and by residual visual inspection.

The statistical significance was set at $P < 0.05$. The R-System with the gam and Harrell's rms libraries were used for analysis.

Results

From January 2014 to October 2016, of 86 on site donors evaluated, 47 lung grafts were considered suitable for transplantation after standard cold storage, four ideal donors were included in the INSPIRE trial and preserved with OCS™ Lung and 27 were directly rejected for nonreconditionable causes (emphysema, pneumonia, severe lung trauma). Finally, eight lung donors (9.6%) fulfilled the lung criteria specified above and were identified as potentially treatable using normothermic perfusion on the OCS™ Lung. In seven cases the donor was procured in another hospital and only one subject was present in our center.

Donors

Donors' characteristics are summarized in Table 1.

Donors' median age was 54 years (IQR 41–56 years), three males and five females. All of them were brain dead donors, because of cerebral bleeding in four patients (50%), head trauma in three patients (37.5%), and cerebral ischemia in 1 (12.5%).

Median donor ICU time was 3 days (IQR 2–4 days) whereas four patients (50%) had a positive smoking history with a median consumption of 24 pack-years (IQR 13–42 pack-years). Mean Oto score was 5 (IQR 4–8).

The main causes of lung marginality were: poor gas exchange (PaO_2/FiO_2 <300 mmHg) in three cases, lung edema and expected time of cold ischemia >6 h in two cases, respectively, and age >55 years with a lobar consolidation identified during retrieval in one. In three donors two or more additional criteria were present.

After surgical exploration, the final median PaO_2/FiO_2 ratio in the donor was 340 mmHg (IQR 266–472 mmHg). There were six cases of pulmonary artery reconstruction. According to this, the median instrumentation time for OCS™ Lung was 64 min (IQR 55–70 min). Median running time on the OCS™ Lung was 392 min (IQR 331–517 min).

Median pulmonary vascular resistance decreased overtime (Fig. 1) from 486 dyn s/cm^5 (IQR 385–572 dyn s/cm^5) to 325 dyn s/cm^5 (IQR 277–560 dyn s/cm^5, $P = 0.014$) while we observed a stability of median peak airway pressure (12 cmH_2O, IQR 11–12 cmH_2O; Fig. 2) and median arterial pulmonary pressure (7 mmHg, IQR 5–8 mmHg; Fig. 3). Median PaO_2/FiO_2 ratio significantly improved during OCS™ Lung perfusion, to 474 mmHg (IQR 401–482 mmHg, $P = 0.05$) as first assessment and finally to 537 mmHg (IQR 505–576 mmHg, $P = 0.005$; Fig. 4). No main bronchoscopic alterations were observed during perfusions.

Finally, in all cases except the first, the use of a lung radiography performed directly in the device was

Table 1. Main donors characteristics.

Donor ID	Age	Gender	Cause of death	ICU time (days)	Smoking history (P.Y.)	OTO score	Last PaO_2/FiO_2 ratio	Pulmonary artery reconstruction	Inclusion criteria	Pre-instrument time	OCS lung time (min)
1	18	F	Head trauma	2	0	5	319	No	Lung edema	56	456
2	61	F	Cerebral hemorragia	3	32	5	467	Yes	Age, lobar consolidation	73	395
3 [25]	54	M	Cerebral hemorragia in L-VAD positioning	3	50	4	511	No	L-VAD donor, lung edema and ischemic time >6 h	53	342
4	54	F	Cerebral hemorragia	4	0	7	171	Yes	Poor gas exchange	69	425
5	44	F	Cerebral hemorragia	2	0	3	361	Yes	Lung edema	49	364
6	61	M	Cerebral hemorragia	1	0	9	237	Yes	Age, poor gas exchange, and ischemic time >6 h	67	836
7	33	F	Head trauma	10	5	1	487	Yes	Ischemic time >6 h	76	304
8	54	M	Head trauma	5	15	9	276	Yes	Poor gas exchange	62	700
Median value	54	N.A.	N.A.	3	3	5	340	N.A.	N.A.	65	410

FiO_2, fraction of inspired oxygen; ICU, intensive-care unit; L-VAD, left ventricular assistance device; OCS Lung, organ care system; PaO_2, partial pressure of arterial oxygen.

included in the evaluation setting. No main alterations were observed in the lungs, except in the second case where a right lower lobe congestion discovered at the retrieval time was confirmed after reconditioning with pneumonia suspicion, leading to shift from a bilateral to a single left lung transplant recipient. Concerning the cases of lung edema, in one graft a reduction in the bilateral infiltrates was observed at the lung radiography compared with the previous radiographic donor assessment. In the other case a comparison was not feasible since this was the first patient included in the program, when the procedure for lung X-ray in the device was not still available.

Recipients

Table 2 shows recipient characteristics.

We reported four males and four females with a median age of 55 years (IQR 40–60 years) and a BMI of 20 (IQR 19–28). Four patients had idiopathic pulmonary fibrosis (IPF), two cystic fibrosis and one COPD and extrinsic allergic alveolitis, respectively. No patient presented secondary pulmonary hypertension and the mean pulmonary arterial pressure was 18 mmHg (IQR 13–20 mmHg). None of the patients required preoperative mechanical ventilation or ECMO. Median LAS score was 40.55 (IQR 37.30–43.52).

We report seven bilateral lung transplantations and one left single lung transplant; all but one were performed without intra-operative ECMO support. In the last patient, a central veno-arterial ECMO was necessary for hemodynamic instability before first lung implantation. At the end of the procedure, ECMO was switched to peripheral veno-venous and successfully removed after 4 days. Median cold ischemic time was 172 (IQR 159–192) for the first lung and 291 (IQR 269–313) min for the second lung. Two patients needed graft volume reduction for dimension discrepancy: this consisted of middle lobectomy and wedge resection of the lingula in one case and a middle lobectomy associated to a left upper lobectomy in the other.

Table 3 reports the main postoperative results. Median PGD scores at time 0, 24, 48, and 72 h were 2, 1, 1, and 0 respectively. At 72 h only one PGD score 3 was observed. Mechanical ventilation time was 60 h (IQR 25–132 h), while ICU and hospital stay were 14 (IQR 8–28 days) and 36 (IQR 30–52 days) days respectively. Two patients needed a surgical tracheostomy for prolonged ventilation.

The in-hospital mortality was 12.5%, consisting in one patient death 25 days after lung transplantation not

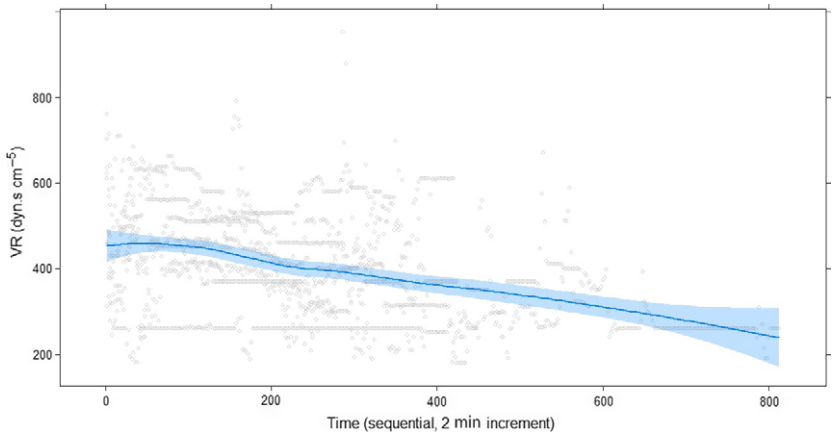

Figure 1 Pulmonary vascular resistance over time during OCS™ Lung perfusion showing a significant reduction in VR values, sign of donor lungs improving.

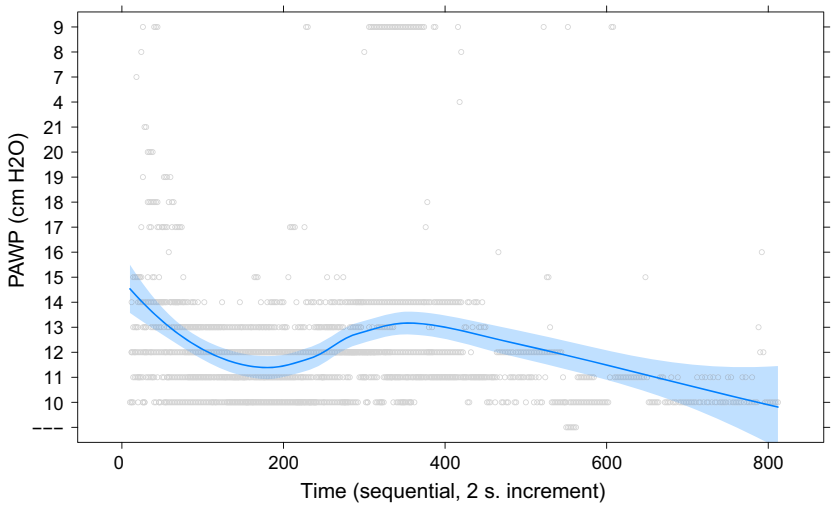

Figure 2 Pulmonary artery pressure over time during OCS™ Lung perfusion.

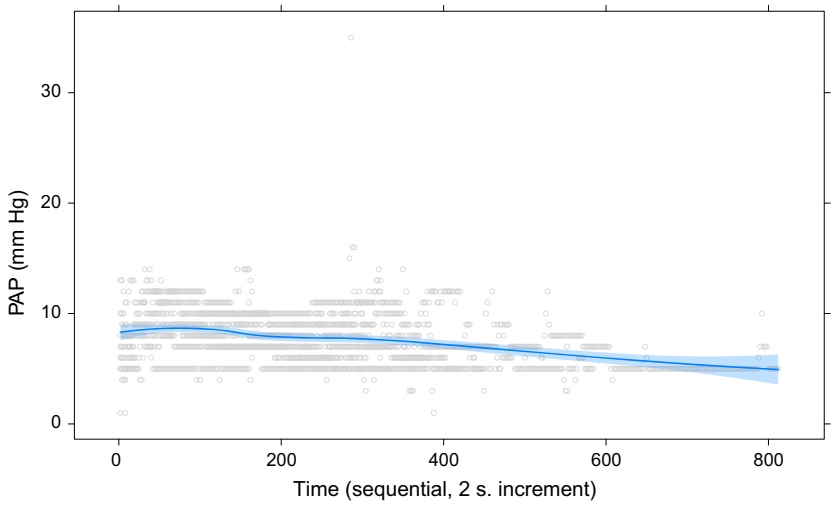

Figure 3 Peak airway pressure over time during OCS™ Lung perfusion.

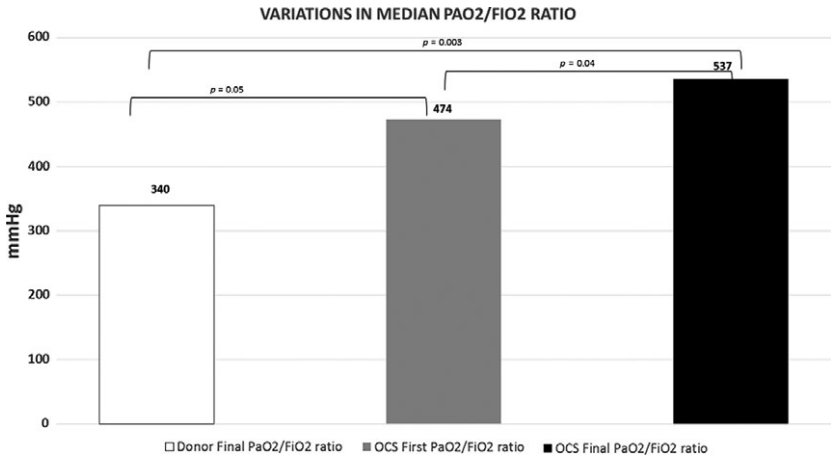

Figure 4 Lung oxygenation capacity (PaO_2/FiO_2 ratio) over time. A significant improvement between donor time assessment and first and final OCS™ Lung evaluation was observed.

related to graft issues (pancreatitis and myocardial infarction). Four patients developed one or more perioperative complications: renal failure requiring continuous veno-venous hemofiltration in two cases, atrial fibrillation in three cases, pulmonary embolism and clamshell surgical revision for parietal hematoma one case each. No anastomotic complications were observed during hospitalization.

At 1-month, among the seven patients who underwent transbronchial biopsy, four patients experienced acute rejection (one A3B0, two A2B0, one A1B0), successfully treated with high-dose steroids.

The follow-up period in the study population was 927 days (IQR 872–1062 days). One and two-year survival were both 62.5%, since two patients died after hospital discharge, for hemodialysis complications and for pulmonary infections.

The other five patients are alive in good condition with absence of acute rejection at 12 months and a best FEV1% of 74% (IQR 69–77). Finally, no anastomotic complications were observed during the follow-up period.

Discussion

Despite several improvements in the lung transplantation technique, the shortage and difficult management of lung donors preclude a wider application of this surgical procedure.

The introduction of EVLP in the mid-2000s [16] has dramatically revolutionized the approach to lung donors in terms of organ evaluation (e.g., nonheart beating donor) and extended criteria organs reconditioning. In fact, through both *ex vivo* perfusion and ventilation, lung grafts can be carefully assessed and eventual transient impairment corrected, thus allowing donor pool expansion [17].

Two approaches are currently available for *ex vivo* normothermic perfusion. These are represented by a static platform exclusively used at the recipient hospital, and by a portable device that encompasses organ perfusion at the donor hospital. The former entails a hypothermic phase, from retrieval until organ arrival at the recipient hospital that may cause significant time-dependent lung damage with unpredictable impact on the outcome of transplantation [18]. In addition, during transport no assessment of lung function is feasible.

On the contrary, the portable OCS™ lung significantly reduces the transport-related ischemic period, ensuring at the same time continuous monitoring of vascular and respiratory functions. Following a 12 cases pilot study by Warnecke *et al.* [6], a prospective, randomized, multicenter trial (INSPIRE) comparing OCS™ lung preservation with standard cold storage in ideal donors, started in 2011 and was recently concluded showing a noninferiority of normothermic perfusion (intention-to-treat protocol) for many study endpoints, reporting also that PGD grades at T0–T72 were significantly lower after normothermic perfusion [2].

A subsequent application of this system to extended criteria organs has been carried out through the initiation of a multi-center trial (EXPAND [10], NCT01963780), still underway, with objective inclusion/exclusion criteria. The strict adherence to well-defined criteria eliminates some major limitations of published EVLP studies on extended criteria organs, where several subjective inclusion criteria (such as poor lung deflation or inflation during donor evaluation) have been often

Transplant International 2019; 32: 131–140

Table 2. Main recipients characteristics.

Recipient ID	Age	Gender	BMI	Diagnosis	LAS	mPAP	Type of transplant	Intraoperative ECMO	Size reduction	Cold ischemic time first lung	Cold ischemic time second lung
1	17	M	12.9	CF	38.28	20	Bilateral	No	–	161	291
2	56	F	29.3	IPF	40.96	12	Left	No	–	193	–
3	61	M	27.1	IPF	47.82	20	Bilateral	No	–	183	292
4	26	F	18.8	CF	34.05	20	Bilateral	No	ML + Ling. Wedge resection	204	334
5	55	M	32.4	IPF	42.08	13	Bilateral	No	–	192	409
6	59	M	21.8	IPF	56.79	15	Bilateral	No	–	142	267
7	45	F	18.7	COPD	34.35	23	Bilateral	No	–	161	271
8	61	F	18.4	EAA	40.13	10	Bilateral	VA	LUL + ML	153	142
Median value	55	N.A.	22	N.A.		18	N.A.	N.A.	N.A.	172	291

BMI, body mass index; CF, cystic fibrosis; EAA, extrinsic allergic alveolitis; ECMO, extra-corporeal membrane oxygenation; IPF, idiopathic pulmonary fibrosis; LAS, lung allocation score; LUL, left upper lobe; ML, medium lobe; mPAP, median pulmonary artery pressure; VA, veno-arterial.

Table 3. Postoperative results.

Recipient ID	PGD (0 h)	PGD (24 h)	PGD (48 h)	PGD (72 h)	Complications	Tracheostomy	MV (h)	ICU LOS (day)	Hospital LOS (day)	In-hospital rejection	In-hospital mortality	FEV1 12 months (%)	Acute rej. 12 months	Follow-up duration (day)	Exitus
1	0	0	0	0	None	No	48	6	29	A2B0	–	58	A0B0	1551	–
2	3	1	2	0	CVVH	Yes	27	43	63	A0B0	–	–	–	169	Yes
3	2	2	2	1	None	No	72	11	33	A2B0	–	51	A0B0	1062	–
4	2	0	0	0	None	No	20	9	30	A3B0	–	75	A0B0	927	–
5	3	2	0	0	AF, PE	No	120	17	48	A0B0	–	55	A0B0	872	–
6	3	2	0	0	AF	No	168	26	26	–	Yes	–	–	26	Yes
7	0	0	0	0	None	No	14	6	38	A1B0	–	128	A0B0	664	–
8	3	3	3	3	CVVH, AF, surgical revision	Yes	192	35	99	–	–	–	–	109	Yes
Median value	2	1	1	0	N.A.	N.A.	60	14	36	N.A.	12.5%	58	N.A.	927	37.5%

AF, atrial fibrillation; CVVH, continuous veno-venous hemofiltration; FEV1, 1-second forced expiratory volume; ICU, intensive-care unit; LOS, length of stay; MV, mechanical ventilation; PE, pulmonary embolism; PGD, primary graft dysfunction.

adopted, ultimately resulting in considerable selection bias.

In this light, in the current study we applied similar inclusion/exclusion criteria as in the EXPAND trial. Differently, however, in this series we also included cases with significant pulmonary edema, as defined in the methods.

Although in clinical practice some of the criteria we selected are not necessarily an indication for the use of *ex vivo* methods (e.g., long cold ischemia or advanced age), these criteria are in all cases compatible with those conventionally used with the international literature definition of an extended donor. In particular for ischemia time longer than 6 h, it is well known that lungs are relatively stable to cold ischemia and could tolerate longer periods of time. However, the presence of other associated nonideal criteria can reasonably influence the ischemia tolerance of these organs [2], altering their functionality even after a short time. In our experience, of the two grafts reported with an ischemia time longer than 6 h, one presented additional inclusion criteria (age, gas exchanges) while in the other case there were important logistical issues (unavailability of the operating room because of contemporary urgency) that would have prolonged the cold ischemia far beyond the 6 h.

In our experience, the rate of organs needing OCS™ Lung reconditioning after on site assessment was 9.6%, comparable with the EVLP experience of Toronto (7.5%) [3] and Vienna (10.2%) [4] and higher than that reported by the Lund group (5%) [5]. A wider application of EVLP system, however, was recently published by the groups of Paris (21%) [19], a finding that is most likely related to the widening of the eligibility criteria. Almost 40% of our cases had multiple inclusion criteria, highlighting the complexity of donors that we managed.

In two cases, pulmonary edema was only found on the preoperative radiography and on the surgical exploration, despite a PaO_2/FiO_2 ratio slightly higher than 300 mmHg after intraoperative recruitment maneuvers. Indeed, PaO_2/FiO_2 ratio was lower than expected, since these two patients were young (18 and 44 years), and with no pathological cause in the clinical history nor at the bronchoscopy evaluation. Conversely, we did not enroll any DCD case, a donor category which certainly represents one of the most appropriate indications for EVLP [20], as this type of donor has only recently been introduced in Italy [21].

At our institution, the OCS™ Lung has been available since 2011 and the considerable experience gained with standard criteria donors allowed us to easily overcome the hurdles associated with the use of extended criteria lungs. Considering all EVLP procedures, the parameters monitored showed a considerable improvement of the organ function, in particular a significant increase in gas exchange at the end of preservation.

As early at the time of the first functional evaluation in the device, an important improvement in the oxygenation capacity of the graft was observed. This could be because of the possibility to the better recruitment of the lungs in the system (bronchoscopy, ventilation), that are not subjected to the influence of other organs nor to the chest external constriction. The further increase in the PaO_2/FiO_2 ratio verified at the end of the perfusion may also testify the reconditioning capacity of the OCS™ Lung. In our hands, the decline in vascular resistance during perfusion was the other most reliable parameter to predict future *in vivo* lung function. It is our belief that the addition of a radiographic assessment on the OCS™ Lung represents a helpful adjunct to timely detect the presence of any unrecognized inflammatory/infectious process that may impair the postoperative outcome, ultimately allowing the exclusion of organ unsuitable for transplantation. This radiographic evaluation is usually compared with the last donor chest-X ray performed before retrieval, because at this moment the procedure is applicable only at our hospital. In the future, sequential lung X-ray throughout OCS™ Lung running time will probably be implemented to carefully monitor the organ quality.

At our center, the acceptance rate after OCS™ Lung perfusion reached 100% of donors included and 94% of lungs evaluated (one right lung rejected), a percentage that is considerably higher compared with other EVLP series [3–5] reported in the literature and similar to those of Gothenburg [22] and Paris [19] groups. It is possible that this very encouraging result may also be because of a conservative case selection, where donors with extreme marginality and with *a priori* very little chance of a positive reconditioning were declined.

Compared with the static EVLP perfusion time, about 4 h, the OCS™ Lung reconditioning procedure was unsurprisingly longer, with a median value of 7 h. The use of this system has also allowed a considerable reduction in ischemia time, possibly contributing to the occurrence of only one case of PGD 3 at 72 h. In addition, in the last case performed we separated the lungs while being perfused and ventilated on the OCS™ Lung. Indeed, we left the second lung perfused and ventilated until the time of implantation, thus considerably reducing the cold ischemic time. Such an approach will

probably contribute to improve organ performance, above all in the most extended criteria cases.

Overall, our postoperative results are encouraging, with a single case of postoperative ECMO assistance for respiratory causes in a patient undergoing a major graft reduction (lobar transplantation) for size discrepancy. In all cases, an early extubation of patients was achieved while the only in-hospital death occurred for reasons unrelated to the graft function. Finally, during follow-up, no bronchial, or immunological complications were observed, with no rejection at 12 months. Such results (PGD 3 at 72 h, in-hospital mortality and duration of ventilation) are similar to those reported by the majority of the groups using the static EVLP systems [3–5]. In addition, the recent presentation of the EXPAND results [10] further corroborates our experience with comparable PGD rate 3 both at 72 h and within the first 3 days, although the short- and medium-term survivals of the multicenter trial is better (99% vs. 87.5% at 30 days and 91% vs. 62.5% at 1 year) than ours. Finally, it is noteworthy the higher (100% vs. 87%) lung utilization rate after OCS perfusion in our experience compared with the Expand trial.

On the other hand, the Toronto group reported shorter ICU stay and lower 1-year mortality for patients transplanted with grafts preserved for longer than 12 h with static EVLP, but the authors did not specify which type of extended criteria graft was involved in this study [23]. Two main reasons may have affected our 1-year mortality: the use of extended criteria graft itself and the small number of patients involved (with three deaths in the first year, but only one related to graft complications). Our data are consistent with those reported in the meta-analysis from Krutsinger *et al.* [24] (1-year survival between 68% and 94%), who have analyzed six different studies regarding extended criteria (DCD) donors. Despite the previous premises, a real comparison between the different methods (portable versus nonportable) is difficult given the different systems and protocols used (cellular or acellular solution, open or closed atrium). In any case, as previously mentioned, the use of portable systems surely allows to significantly reduce the cold ischemic transport before normothermic perfusion, and this aspect could be particularly advantageous in the presence of donors with multiple extended criteria. So, despite no clear advantage of one of the two systems over the other in terms of organ preservation or reconditioning has been reported to date with regard to both perioperative and long-term outcomes, the current need to avoid long cold ischemia time (because of logistic reasons or the presence of other extended criteria) appears to be the only clear indications favoring the use of OCS Lung.

Our study presents several limitations primarily related to the restricted population enrolled. In addition, the exclusion of extremely extended criteria donors may have affected our acceptance rate and precluded any conclusions on the capacity of the OCS™ Lung to recondition such severely injured extended criteria organs.

In conclusion, this study reports one of the first case series of extended criteria organs perfused and evaluated with the OCS™ Lung, whereas in the literature only limited experience on such cases has been reported. Normothermic *ex vivo* perfusion with the portable device allowed us to improve the characteristics of the lungs during perfusion ensuring at the same time the use of extended criteria organs in an extremely high percentage of cases with promising postoperative results. Further large-scale studies, however, are eagerly awaited to fully comprehend the OCS™ Lung reconditioning potential capacity.

Authorship

MS: developed the study and wrote the paper. GF: contributed to write the paper. AR: contributed to develop the study. FL: contributed to histological evaluation. GC: contributed to develop the study and revised the paper. GG: contributed to revise the paper. PF: contributed to revise the paper. DG: contributed to statistical analysis. FC: contributed to histological evaluation. GM: contributed to develop the study and revised the paper. EC: revised the paper. FR: contributed to develop the study and revised the paper.

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Conflicts of interest

The authors have declared no conflicts of interest.

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