Utilization of the organ care system for bilateral lung transplantation: preliminary results of a comparative study†

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Abstract

OBJECTIVES: Lung transplantation (LTx) remains the gold standard for patients with end-stage lung disease. However, due to donor organ shortage and brain stem death-related lung injury, only a small proportion of lungs are used increasing the mortality rate on the waiting list. A portable normothermic continuous ex vivo perfusion using the organ care system (OCS) represents one of the tools to increase the pool of donor organs and to improve the function of marginal lungs. We sought to assess mid-term outcomes after LTx using OCS and to compare outcomes including overall survival and freedom from bronchiolitis obliterans syndrome (BOS) with those after conventional preservation.

METHODS: Included were 322 consecutive LTx performed at Harefield Hospital between January 2007 and December 2014. Recipients were divided into two groups depending on the organ storage strategy: the majority of patients (n = 308) were transplanted using lungs after cold storage (cold storage group), whereas 14 organs were preserved using OCS (OCS group). The primary end-points were overall survival and freedom from BOS after LTx. The secondary end-points were perioperative clinical characteristics and adverse events.

RESULTS: There were no statistically significant differences in terms of most baseline donor and recipient characteristics. The percentage of heavy smokers among donors [8 (2.9%) vs 6 (42.9%), P < 0.001] and the median number of pack-years smoked by donors [14 (7.24) vs 25 (24.30), P = 0.026] were statistically higher in the OCS group. Patients from the OCS group had significantly better postoperative FEV1 at 3 [69 (54;86) vs 93 (87;89), P < 0.001] and 6 [77 (60;90) vs 94 (84;100), P = 0.006] months. There were no statistically significant differences in terms of cumulative survival and freedom from BOS between the two groups.

CONCLUSIONS: Results after LTx using OCS are acceptable with excellent survival, and superior early outcome in terms of postoperative lung function despite higher risk in the OCS group. Further larger prospective trials are warranted to confirm our preliminary results and to elaborate long-term outcomes.

Keywords: Lung transplantation • Ex vivo perfusion • Overall survival outcomes • Freedom from bronchiolitis obliterans syndrome

INTRODUCTION

The existing shortage of donors remains one of the main limitations for lung transplantation (LTx) resulting in high mortality among patients on the waiting list [1–4]. In addressing the problem of discrepancy between the number of patients awaiting LTx and the number of transplantable donor organs, several strategies with the view to expand the donor pool have been established. For example, using lungs from donation after circulatory death (DCD) donors showed promising results [5–8]. However, social opinions and ethical considerations have limited this type of donation to a small number of countries, whereas in the rest of the world, only brain stem death is considered for organ donation. Other aggressive strategy to expand the donor pool is the use of organs from extended criteria donors, so-called marginal lungs that have increasingly been transplanted in recent years with controversial results [9, 10]. This strategy must always be associated with careful donor assessment and organ optimization before procurement and transplantation. In the recent decade, such assessment and organ function optimization became possible even after organ procurement using ex vivo lung perfusion (EVLP), increasing...
recipient’s safety when using marginal lungs [3, 11–14]. Moreover, first data have recently become available on a portable system, the organ care system (OCS) that has successfully been applied in several centres [3, 14–16]. The OCS represents a novel preservation strategy that made possible to assess, treat and transport donor lungs in normothermic condition while the lung is ventilated and enriched with oxygen at normal body temperature of 37°C.

In this study, we present early and mid-term outcomes after LTx using OCS and compare outcomes including overall survival and freedom from bronchiolitis obliterans syndrome (BOS) with those after conventional preservation.

METHODS

We included data of 322 consecutive LTx performed in our institution between January 2007 and December 2014. This article reports short-term results of the study, whereas long-term outcome measures will be reported later. All patients recruited is finished and all patients recruited are reported in this article. Inclusion criteria for using the OCS were donor lungs with abnormal parameters, such as donor smoking history of more than 20 pack-years, history of cannabis smoking, prolonged mechanical ventilation, pre-retrieval pO2/FiO2 ratio <300 mmHg, abnormal bronchoscopy, abnormal chest X-ray, history of cardiac arrest, donors age higher than 55-year old or DCD donors on the condition that at least one trained retrieval surgeon and one trained perfusionist signed off for OCS were on call at the time of organ offer and an OCS kit was available. Usually, a combination of parameters mentioned above led to the indication to use OCS. However, the last decision was made by each transplanting surgeon depending on the overall appearance of the organ offered. The only absolute exclusion criterion for normothermic preservation was mechanical lung damage (tears), i.e. after severe chest trauma. No donor lungs assessed using static EVLP were included in the control arm. All included patients were eligible for LTx and were on our institutional transplant waiting list. In fact, patients were assigned for a transplant independent from the type of preservation as follows: according to the blood group, duration on the waiting list and size matching. The decision in terms of using OCS was almost solely depending on the donor lung status and not on the recipient category. The primary end-points were overall survival after LTx and freedom from BOS. The secondary end-points were perioperative clinical characteristics as well as adverse events which occurred over the follow-up.

Definitions

The grade of PGD was defined based on ISHLT Working Group on Primary Graft Dysfunction Report: the pO2/FiO2 ratio <200 was considered as PGD Grade 3 independent of findings on the chest X-ray. The reason why the PGD was defined independent of the findings on the chest X-ray was the fact that in a substantial number of cases, X-ray assessment was not objective in terms of differentiation of infiltrates from other findings. On the other hand, numeric values, such as pO2/FiO2 ratio, are always objective. Lung function tests were performed on each hospital admission and transplant outpatient visit and BOS was diagnosed when post-transplant fraction of expired volume in 1 s (FEV1) measured on the regularly basis after LTx permanently dropped >20% of the best FEV1 achieved after LTx according to ISHLT recommendations [17]. Smoking history was defined as a temporary or permanent smoking habit at the time of organ donation or in the past. One pack-year was defined as 20 cigarettes (one pack) smoked per day for 1 year. Heavy smoking was defined as smoking habit with more than 20 pack-years, whereas smoking was defined as a smoking habit independent of the number of pack-years [18]. Abnormal chest X-ray was defined as atypically white or hazy shadow on the lung fields, diffuse haziness on the lung fields, fluid collection between the lung and the chest wall, flattening of the diaphragm or enlarged size of the chest. Abnormal bronchoscopic findings may involve abnormalities of the bronchial wall such as inflammation, secretion of pus, ulceration or swelling. FiO2 was considered 0.21 when patients were breathing spontaneously.

Follow-up

Follow-up was ensured by direct patient contact in the outpatient clinic or contact via the phone. The results of regular lung function tests performed in our hospital were used for diagnosis of BOS. The follow-up database was regularly updated by three designated physicians who had regular contact with patients. No patients were lost from follow-up. Patients were censored at the cut-off of the study. Follow-up time was reported in days from the date of the transplant till the date of death or diagnosis of BOS alternatively till the cut-off of the study.

Organ assessment and organ procurement protocol

Donor organ assessment performed at donor hospitals included radiological assessment, fibroptic bronchoscopy, gross organ inspection and palpation, assessment of compliance using deflation test and selective blood-gas analysis from each pulmonary vein. To improve donor gas exchange, an aggressive therapeutic manipulation was performed prior to lung procurement including antibiotic therapy, adaptation of fluid balance, increase in tidal volume and bronchial toilet. The standard preservation solution used in our centre is low potassium dextran (Perfadex, Medisan, Uppsala, Sweden) solution augmented with CaCl2, 3.6% tromethamine (THAM, Hospira Inc., Lake Forest, IL, USA) and epoprostenol sodium 2.5 ml/l. For donation after brain death, 4 l of the solution was administered antegrade and retrogradely through a Medtronic 15 Fr single-stage venous cannula and 1 l retrogradely through a Medtronic 15 Fr retrograde cannula with self-inflating balloon. For DCD, 3 l of pneumoplegia was administered antegrade and 2 l retrogradely.

Once the organs were removed from the chest, they were inspected and packed for storage on ice and transported half inflated in cases of road transport or inflated to 30% in cases of transport on the plane with FiO2 0.5.

When using OCS, the lungs were also carefully inspected, palpated and recruited before final acceptance. Particularly trauma-related findings, such as moderate or severe air leak leading to an insufficient lung recruitment or perfusate leak from injury site into the airways and potential oedema formation, represent relative contraindications for the use of OCS. The OCS lung (TransMedics Inc., Boston, MA, USA) is composed of an organ-specific perfusion module with disposable and non-disposable parts and a compact wireless monitor. The monitor displays real-time system and organ measurements, such as pulmonary pressure and resistance, pulmonary flow, blood temperature and respiratory rate (Fig. 1).
Set-up and transport on OCS Lung

The system was set up using the standardized protocol and primed with 1.5–2.1 buffered OCS solution (with 1 mmol of THAM/l) and 3 units of leucocyte reduced packed red blood cells. Additional drug additives include 500 mg of methylprednisolone, 1 unit of vial multivitamins, 20 units of insulin, 4 mg of milrinone, 40 mEq of NaHCO3, 10,000 units of heparin, 1 g of cefuroxime, 200 mg of ciprofloxacin and 200 mg of voriconazole. The perfusate was warmed up to 32°C. Once the target temperature was reached, a baseline blood-gas test was performed. The lungs were instrumented into the OCS via the connection of the pulmonary artery and trachea. Alternatively, in some cases of heart and lung procurement or anatomically short main pulmonary trunk, an additional piece of thoracic descending aorta was anastomosed to the main pulmonary trunk to achieve appropriate length sufficient for connection. The perfusate flow was gradually increased and maintained between 1.5 and 2 l/min, whereas the pulmonary artery pressure did not exceed 20 mmHg. The temperature was set to 37°C; once it reached 34°C, lung ventilation was initiated. The preservation mode’s ventilator settings were usually set to maintain a positive end expiratory pressure of 5 cm H2O and a tidal volume of 6 ml/kg of donor ideal body weight at a respiratory rate of 12 breaths per minute. After 10 min of stabilization at 37°C, baseline monitoring was initiated. During the monitoring phase, the pulmonary flow was set to 2–3 l/min to de-air and warm up the perfusate, the ventilator settings were adjusted to achieve a positive end expiratory pressure of 7 cm H2O and a tidal volume of 6 ml/kg of donor ideal body weight at an respiratory rate of 12 breathes per minute. Sequential re-oxygenation time was measured and the pO2/FiO2 ratio calculated. Sequential re-oxygenation test is an additional tool for the assessment of lung performance and measures the time required to increase the blood saturation from 73 to 93% with ambient air ventilation of donor lungs. The OCS system was then set back to preservation mode and the monitoring assessment was then repeated during the final assessment before deciding whether the lungs are suitable for transplantation, and before transferring the recipient to theatre. The pO2/FiO2 calculation and re-oxygenation time were again repeated 30 min prior to dissection. A bronchoscopy was performed during transportation of lungs on OCS to recruit any atelectatic area and optimize lung ventilation.

Statistical analysis

All data were analysed using IBM SPSS Statistics for Mac, Version 22 (IBM Corp., Released 2013, Armonk, NY, USA) and were presented as continuous or categorical variables. Continuous data were evaluated for normality using one sample Kolmogorov–Smirnov test and confirmed by histograms. Continuous variables were expressed as the mean ± standard deviation in cases of normal distributed variables or median (interquartile range) in cases of non-normal distributed variables. Categorical variables are presented as total numbers of patients and percentages. Continuous data were analysed with unpaired t-test for normally distributed variables and Mann–Whitney U-test was used for non-normally distributed variables. Pearson’s χ2 or Fisher’s exact tests were used for categorical data depending on the minimum expected count in each cross tab (≥5 or <5). P-values <0.05 were considered statistically significant. Kaplan–Meier survival estimation was applied for survival analysis and freedom from BOS of the entire patient cohort. Patients who survived (cumulative survival curve) or did not develop BOS (freedom from BOS curve) at the cut-off of the study were censored. Log-rank (Mantel–Cox) test was applied for the comparison of cumulative survival estimates and estimated freedom from BOS between patients from the two groups analysed.

RESULTS

Of 322 LTx performed on patients with end-stage lung disease between 2007 and 2014, recipients were divided into two groups depending on the organ storage strategy: the majority of patients (n = 308) were transplanted using lungs after cold storage (cold storage group), whereas 14 organs were preserved using the OCS (OCS group). A total of seven organs were initially accepted for normothermic preservation and were declined after assessment on the OCS due to poor function. Because the use of the OCS lung at our institution was commenced at later stages, there was a significant difference in terms of the median length of follow-up between the OCS group and the cold storage group: 175 (89;321) vs 653 (191;1297) days (P = 0.001). The last mean pO2/FiO2 ratio measured with the OCS lung before transplantation accounted for 463 ± 135 mmHg and the median re-oxygenation time was 90 (55;115) s. The mean perfusion time on the OCS was 342 ± 149 min. Table 1 represents donor procurement data of the institutional patient cohort using conventional cold storage preservation against the OCS group. There were no statistically significant differences between the two groups in terms of most baseline donor and recipient characteristics. However, there was a trend towards...
better oxygenation of the implanted lungs in the OCS group with higher postoperative pO2/FiO2 ratio at 0 h (P = 0.081) and 48 h (P = 0.072). Also, patients from the OCS group had significantly better lung function with higher postoperative FEV1 at 3 (P < 0.001) and 6 (P = 0.006) months postoperatively. There were no statistically significant differences in terms of median duration of ICU (P = 0.709) and total hospital stay (P = 0.357). In terms of development of Grade A0–A3 acute rejections over the follow-up, both the groups also appeared to be statistically comparable (Table 3).

There were no statistically significant differences in terms of overall cumulative survival (log-rank P = 0.267) and freedom from BOS (log-rank P = 0.449) between the two groups. The overall 30-day, 6-month and 1-year survival after LTx were 96.1 vs 85.7%, 88.0 vs 78.6% and 85.6 vs 78.6% in the cold storage and OCS groups, respectively (Fig. 2). One-year freedom from BOS accounted for 89.7% in the cold storage group and 100% in the OCS group (Fig. 3).

Table 1: Donor's baseline and organ procurement data

<table>
<thead>
<tr>
<th></th>
<th>LTx cold storage (n = 308)</th>
<th>LTx with OCS (n = 14)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44 (34.52)</td>
<td>49 (40.57)</td>
<td>0.128</td>
</tr>
<tr>
<td>Female</td>
<td>187 (60.7%)</td>
<td>5 (35.7%)</td>
<td>0.062</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169 (163,175)</td>
<td>173 (166,178)</td>
<td>0.223</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70 (65,80)</td>
<td>80 (67,90)</td>
<td>0.147</td>
</tr>
<tr>
<td>Blood group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O</td>
<td>134 (43.5%)</td>
<td>6 (42.9%)</td>
<td>0.512</td>
</tr>
<tr>
<td>A</td>
<td>145 (47.1%)</td>
<td>7 (50%)</td>
<td>0.083</td>
</tr>
<tr>
<td>B</td>
<td>22 (7.1%)</td>
<td>1 (7.1%)</td>
<td>0.741</td>
</tr>
<tr>
<td>AB</td>
<td>7 (2.3%)</td>
<td>1 (7.1%)</td>
<td></td>
</tr>
<tr>
<td>pO2/FiO2 ratio*</td>
<td>435 (360,502)</td>
<td>428 (263,480)</td>
<td>0.277</td>
</tr>
<tr>
<td>Ventilation duration (days)</td>
<td>2 (1.3)</td>
<td>3 (2.9)</td>
<td>0.757</td>
</tr>
<tr>
<td>DCD</td>
<td>60 (19.5%)</td>
<td>3 (21.4%)</td>
<td>0.741</td>
</tr>
<tr>
<td>History of cardiac arrestb</td>
<td>69 (22.4%)</td>
<td>5 (35.7%)</td>
<td>0.326</td>
</tr>
<tr>
<td>Cadiar arrest duration (min)</td>
<td>20 (8.35)</td>
<td>20 (3.33)</td>
<td>0.519</td>
</tr>
<tr>
<td>History of cardiac arrest</td>
<td>69 (22.4%)</td>
<td>5 (35.7%)</td>
<td>0.198</td>
</tr>
<tr>
<td>Abnormal chest X-ray</td>
<td>75 (24.8%)</td>
<td>4 (28.6%)</td>
<td>0.755</td>
</tr>
<tr>
<td>Abnormal bronchoscopy</td>
<td>101 (32.8%)</td>
<td>7 (50%)</td>
<td>0.246</td>
</tr>
<tr>
<td>Smoking history</td>
<td>143 (46.4%)</td>
<td>7 (50%)</td>
<td>0.793</td>
</tr>
<tr>
<td>Heavy smokers</td>
<td>8 (2.9%)</td>
<td>6 (42.9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pack-year</td>
<td>14 (7.24)</td>
<td>25 (24.30)</td>
<td>0.026</td>
</tr>
<tr>
<td>Cannabis smokers</td>
<td>18 (5.8%)</td>
<td>1 (7.1%)</td>
<td>0.581</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICH</td>
<td>202 (65.6%)</td>
<td>12 (85.7%)</td>
<td>0.689</td>
</tr>
<tr>
<td>HBI</td>
<td>35 (11.4%)</td>
<td>1 (7.1%)</td>
<td>0.709</td>
</tr>
<tr>
<td>Trauma</td>
<td>31 (10.1%)</td>
<td>1 (7.1%)</td>
<td>0.357</td>
</tr>
<tr>
<td>CVA</td>
<td>23 (7.5%)</td>
<td>0 (0%)</td>
<td>0.449</td>
</tr>
<tr>
<td>Meningitis</td>
<td>13 (4.2%)</td>
<td>0 (0%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Other</td>
<td>7 (2.3%)</td>
<td>0 (0%)</td>
<td>0.741</td>
</tr>
</tbody>
</table>

DCD: donors after cardiac death; ICH: intracranial haemorrhage; HBI: hypoxic brain injury; CVA: cerebrovascular accident.

aLast pre-retrieval pO2/FiO2 ratio measured after opening the chest and recruitment manoeuvres.

bHistory of cardiac arrest and the need cardiopulmonary resuscitation prior to donation.

longer duration of mechanical ventilation in donors from the OCS group (P = 0.083). A significant proportion of donor organs that did not meet standard acceptability criteria were also included in this study, whereas there were some differences between the two groups: the percentage of heavy smokers among donors (P < 0.001) and the median number of pack-years smoked by donors (P = 0.026) were statistically higher in the OCS group. The proportion of donors with the history of cardiac arrest and abnormal bronchoscopy was similarly distributed between the two groups (P = 0.326 and 0.246, respectively). Table 2 shows pre-operative recipient demographics, baseline clinical characteristics and distribution of recipient's diagnoses. The mean recipient's age was 46 (30.55) vs 48 (29.57), P = 0.762, with 154 (50%) vs 8 (57.1%) female patients, P = 0.601. Various diagnoses leading to the indication for LTx were similarly distributed between the two groups (P = 0.142). However, the proportion of patients with bronchiectasis appeared to be higher in the OCS group in a separate comparison (P = 0.042). The proportion of patients receiving long-term continuous oxygen therapy was significantly higher in the OCS group (P = 0.020).

Intraoperative variables and parameters of early postoperative outcome are presented in Table 3. Although there were no statistically significant differences in terms of the incidence of PGD, Grade 3 0 h (P = 1.000), 24 h (P = 0.630), 48 h (P = 0.319) and 72 h (P = 0.633) postoperatively, there was a trend towards

Reasons for discarding organs

An analysis of the reasons for organ discards is inevitable in the process of learning potential benefits of the OCS. The most common reason for declining the lungs in our series was poor gas exchange. There were no lungs that were declined due to high pulmonary artery pressure of poor compliance solely. Poor compliance was seen only in accompaniment with poor gas exchange.

Interestingly, the lungs that were declined on the OCS were consuming perfusion solution especially in the lower lobes. This became evident because the level of the perfusate in the reservoir at the end of 2–3 h of perfusion decreased by up to 400 ml. We also observed another common scenario for lungs declined on the OCS: lobes that were suboptimal at the time of procurement in terms of poor recruitment, oedema or consolidation also became worse after 2–3 h of perfusion.

DISCUSSION

The main purpose of this study is to critically examine outcomes after LTx using OCS lung and to compare the results with those of the conventional cold storage preservation. To our knowledge, this is the first study to present comparison to a control group and the study with the largest number of cases using OCS lung published so far.

There might be several reasons why lungs from the OCS group appeared to be not considerably different from the lungs transplanted in ice. First, a significant proportion of organs that were initially accepted for transplantation and were placed on OCS due to their marginal function appeared to be not salvageable and had to be declined on OCS. This proportion was relatively large considering the small OCS group (7 lungs declined after OCS assessment vs 14 transplanted) and consisted of very poor lungs that were excluded from the analysis. Second, as our centre is in general very aggressive in accepting marginal lungs, many extended criteria organs that should have been included in the OCS group were in fact precluded using OCS when only few surgeons and perfusionists reached the small OCS group (7 lungs declined after OCS assessment vs 14 transplanted).
Early and later results in the OCS group appeared to be encouraging and were comparable to or better than in the cold storage group. However, the overall incidence of Grade 3 PGD, the leading cause of early morbidity and mortality after LTx [19, 20], did not significantly differ between the OCS and the cold storage group, and postoperative oxygenation capacity of implanted lungs measured...
as pO2/FiO2 ratio was higher in the treatment group. Also, an analysis of freedom from BOS, the major cause of late mortality [19, 21], was performed for the available follow-up. Although both groups did not statistically differ, it was notable that all patients from the OCS group were free from BOS over the entire follow-up.

The only and first-in-man experience of the portable OCS lung device for preservation, assessment and transport of donor lungs as a patients’ series was published by Warnecke et al. [15]. In this pilot study, the authors investigated a series of 12 patients transplanted using lungs preserved with the OCS lung at two European LTx centres and presented promising early results. However, in the study by Warnecke donors older than 65 years, pO2 < 300 mmHg at the time of acceptance of lung was excluded from the study. Also, it was a descriptive study without a control group. Apart from this study, only few anecdotal reports have been published so far [8, 16, 22, 23].

As organ shortage triggers the use of extended criteria organs [9], organs from DCD donors [6–8] and further marginal clinical criteria, such as abnormal bronchoscopy or chest X-ray, history of cannabis smoking and hanging donors, the OCS represents a very valuable tool for the assessment of the function of such organs and gives clinicians the opportunity to optimize the function of potentially transplantable organs. OCS lung allows for a ‘safe check-up’ of each organ, whereas lung can be rejected any time when certain concerns regarding transplantability occur. Thus, the opportunity to detect graft dysfunction ‘in the box’ prior to transplantation represents one of the most important benefits of this system. More liberal and even aggressive approach for assessment of lungs using OCS is warranted and can potentially lead to a significant increase in donor organ pool.

Limitations

This study has several limitations. First, we present preliminary results from a single-centre analysis with retrospective design using prospectively collected registry data. Second, despite a relatively large patient cohort, overall there was a disproportion in the size of the patient cohorts of the OCS group compared with the cold storage group, leading to considerable limitations in statistical power and difference in follow-up. For that reason, no long-term follow-up is available for the OCS group requiring a further analysis in the future. Also, multiplicity was not corrected for explanatory endpoints. Third, despite extensive theoretical and practical training in OCS lung for the entire transplant team including retrieval surgeons, perfusionists and implanting surgeons, our initial results presented might have been biased by a natural learning curve as only a relatively small number of organs were transplanted using OCS. Also, selection bias could not be completely avoided as several patients refused being considered for LTx using OCS (in the UK potential recipients may decide in terms of exclusion of particular lung categories). For all these reasons, the results of this study should be interpreted with caution before larger studies with randomized assignment and longer follow-up confirm our preliminary results.

CONCLUSION

Implementation of the OCS lung for normothermic preservation, assessment and optimization of donor lungs before transplantation is safe and feasible. Despite the fact that only limited follow-up is available at the current stage, the outcomes have been associated with promising results so far. The results of this study should be enhanced by further research with larger patient cohorts and longer follow-up.

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Conflict of interest: Diana García-Sáez and André R. Simon are consultants for TransMedics, Inc. Other authors declare no conflict of interest.

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APPENDIX. CONFERENCE DISCUSSION

Dr A. Bertani (Palermo, Italy): I think you are showing, in this series, which is, as you stated, the largest available so far, some nice results with the use of the OCS system. You are showing possible better early outcome in terms of the oxygenation profile, pretty much the same results in terms of survival and development of BOS, and you strike the possibility also that you might have used worse donors in the OCS group because of the smoking history and the bronchoconspiry appearance.

My first comment, and, again, you stated this already as a limitation of the study, is the size of the sample. Comparing 14 patients to a bunch of patients is kind of difficult. So I think in viewing all the statistical significance, you should be very careful.

There are some points that I would like to ask you to comment on, which is mainly the donor characteristics. Did you try to perform a donor score? Isolated items could not be representative of a bad donor per se. For example, the history of smoking in a young and otherwise healthy donor could not mean that we are looking at a marginal lung and I would do the same for the recipient.

In your OCS cohort, you have no idiopathic pulmonary fibrosis patients, no pulmonary hypertension patients, and no extracorporeal membrane oxygenation patients. I would probably give a word of caution in terms of the sample size and type. This is the first question.

The second question, I wanted to ask you about your outcome. Your survival figures in the OCS group are, if I remember, 78% at 30 days and 1 year compared to about 90% at 30 days in the standard group. Do you have an explanation for that? Did you have any specific cause of death in the OCS group?

Dr Zeriouh: These are three different questions. I would like to begin with the last question, using different techniques. We were using ex vivo lung perfusion before, but in this last year we have not used ex vivo lung perfusion so far. In terms of the conversion rate from OCS, we did 23 patients with OCS, whereas 4 were declined after 12 hour assessment on OCS. The other thing is, we are going to establish a protocol for using the OCS for every DCD patient. The OCS has also the advantage that you can transport the system.

The first question about if we are using scores or not, no, we are not using any scores for donor assessment. The score, for example, from Otó and colleagues (a Melbourne colleague), is a very good tool, especially to predict any outcome of transplantation, and also the correlation of the outcome and performance of lung transplantation correlates with the score very well. However, as we know, with the score system, we need to give scores and points, and some scores are sometimes very subjective. For example, if you are giving 2 points for moderate secretion, what is moderate and what is major secretion?

So it might have some observer to observe variation in giving scores. The other thing, we are using the extended criteria which are defined by the International Society for Heart and Lung Transplantation. That means smoking has to be more than 20 pack years and age more than 55 years.

The third question, we have the survival figures; however, the survival figures for the OCS group only cover 1 year of follow-up. It’s not a nice curve to compare 6 year, 7 year outcome with 1-year follow-up.

For the second question, 3 patients died. These 3 patients, I remember them. All of them were mechanically ventilated before and had a high FiO2, more than 80%. 2 of them were cystic fibrosis patients who were septic. All 3 of them died in the first 6 months, 2 of them with severe septic shock and 1 of pulmonary graft dysfunction.

Dr G. Dellgren (Gothenburg, Sweden): Maybe it would be more appropriate to just have a contemporary control group. All the others you have done during the same sort of time interval as you have used OCS. When did you start to use OCS?

Dr Zeriouh: We started to use it in 2014.

Dr T. Egan (Chapel Hill, North Carolina): What was the perfusion solution in the OCS?

Dr Zeriouh: The perfusion solution is 1:5 Perfadex with a lot of medications. It is the protocol from TransMedics. I can give you the protocol. It is voriconazole, antibiotic therapy, THAM/bicarbonate solution, and three packed red blood cells, which is also a part of the priming solution.