

# Suicidal hanging donors for lung transplantation

## Is this chapter still closed? Midterm experience from a single center in United Kingdom

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### Abstract

In the context of limited donor pool in cardiothoracic transplantation, utilization of organs from high risk donors, such as suicidal hanging donors, while ensuring safety, is under consideration. We sought to evaluate the outcomes of lung transplantations (LTx) that use organs from this group.

Between January 2011 and December 2015, 265 LTx were performed at our center. Twenty-two recipients received lungs from donors after suicidal hanging (group 1). The remaining 243 transplantations were used as a control (group 2). Analysis of recipient and donor characteristics as well as outcomes was performed.

No statistically significant difference was found in the donor characteristics between analyzed groups, except for higher incidence of cardiac arrest, younger age and smoking history of hanging donors ( $P < .001$ ,  $P = .022$  and  $P = .0042$ , respectively). Recipient preoperative and perioperative characteristics were comparable. Postoperatively in group 1 there was a higher incidence of extracorporeal life support (27.3 vs 9.1%,  $P = .019$ ). There were no significant differences in chronic lung allograft dysfunction-free survival between group 1 and 2: 92.3 vs 94% at 1 year and 65.9 vs 75.5% at 3 years ( $P = .99$ ). The estimated cumulative survival rate was also similar between groups: 68.2 vs 83.2% at 1 year and 68.2% versus 72% at 3 years ( $P = .3758$ ).

Hanging as a donor cause of death is not associated with poor mid-term survival or chronic lung allograft dysfunction following transplantation. These results encourage assessment of lungs from hanging donors, and their consideration for transplantation.

**Abbreviation:** LTx = lung transplantation.

**Keywords:** hanging donors, lung transplantation, outcomes

### 1. Introduction

The number of patients with end stage pulmonary disease registered for a lung transplant (LTx) in UK has increased by

13% since 2007. A shortage of thoracic organs though, remains a significant barrier for patients awaiting transplantation. Forty percent of this population are transplanted while 8% die on the list within 6 months of listing, whereas 69% are transplanted and 17% die on the list within 3 years, respectively.<sup>[1]</sup> Trends in deceased donation over the last 10 years reveal that despite the fact that there is an increase in donor numbers, it is only donation after cardiac death and older donors that have increased, resulting actually in fewer transplantable organs. A large number of donors though, do not fulfill standard criteria for lung donation and a large number of organs are declined on retrieval findings. National Health Service Blood & Transplant (NHSBT) data analysis show that only 24% of actual donors after brain death (DBD) and 4% of donors after cardiac death (DCD) result in lung transplants.<sup>[2]</sup>

In context of limited potential donor pool, there is imperative need to examine whether opportunities for donation are missed. One practice to help mitigate the current organ shortage is extending donor criteria and optimizing the utilization of organs from high risk donors while ensuring safety. Organs from such donors are considered at greater risk for the recipient because of the lifestyle of the donor or the mode of death.<sup>[3]</sup> Suicidal hanging death in particular, is caused by asphyxia following the compressive narrowing of airway, venous congestion, and cerebral anemia by compression of the neck blood vessels. Hypoxic brain injury secondary to cerebral anoxia in addition to airway obstruction affect particularly the lungs due to pulmonary edema and barotrauma.<sup>[4]</sup> Surgeons therefore, need to balance the use of offered organs from this donor group against the risk of

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death while waiting for another offer. There is limited yet data on the relationship between donor cause of death and lung transplant outcomes. NHSBT recently has evaluated the outcome of use of organs from higher risk donors over a 10-year period and it seems that these organs can be used to the benefit of carefully selected recipients.<sup>[5]</sup>

There is still little evidence on the association of donor cause of death by suicidal hanging and lung transplant outcomes and literature is limited to few case reports and small case series.<sup>[4–7]</sup> We have reported in the past the outcomes of 8 lung transplant patients with suicidal hanging as donor cause of death which were compared with 279 lung transplant recipients, concluding that there was no statistical difference in 1- and 3-year survival between 2 groups.<sup>[4]</sup> Based on that results, we utilized more hanging donors in our lung transplant program and in that study we retrospectively analyzed recipient and donor characteristics as well as outcomes of hanging donor transplants performed at our center over a 4-year period.

## 2. Methods

The Institutional Review Board at our center approved this study and waived the need for individual patient consent. The study design was a prospective observations study on lung transplants from hanging donors over a 4-year period. We evaluated all the adult LTx recipients of hanging and nonhanging donor lungs whose transplantation procedures were performed in our department between 2011 and 2015. Of note, the utilization of hanging donor lungs was undertaken by our lung transplant program since 2011. Patients undergoing repeated transplantation had their survival censored at the time of repeated transplantation. Recipients were divided into 2 groups according to the donor cause of death: group 1 consisted of recipients with hypoxic brain injury secondary to suicidal hanging as the donor cause of death (n=22) and group 2 with donors having other than hanging causes of death (n=243).

### 2.1. Organ assessment/procurement and transplantation protocol

The lungs were matched to the recipients according to blood group, height, total lung capacity, time already spent on the LTx waiting list, and the clinical status of the recipient at the time of the transplantation. Donor lungs were procured in standard fashion using antegrade and retrograde Perfadex flush. Transplantation was performed using standard accepted techniques. Postoperatively, all patients were managed according to our institution's standard practices.

Detailed donor data, such as demographic parameters, cause of death, clinical status, laboratory investigations, and past social and medical history, were analyzed. Demographics and perioperative recipient data as well as mid-term outcomes were collected. Data also collected postoperatively included PaO<sub>2</sub>/FiO<sub>2</sub>, chest roentgenographic findings, primary graft dysfunction (PGD) scores, time to extubation, as well as significant adverse events. PGD scores were calculated using standard criteria based on PaO<sub>2</sub>/FiO<sub>2</sub> values and chest roentgenographic findings of pulmonary edema. "Chronic lung allograft dysfunction" (CLAD) was defined by a persistent (at least 3 weeks) decline in pulmonary function (FEV1 with/without FVC) >10% from baseline (baseline defined as the average of the 2 best post-transplant values for FEV1 and FVC obtained at least 3 weeks apart).<sup>[9]</sup>

### 2.2. End points of the study

Primary end points of the study were overall survival after LTx and CLAD-free survival. Secondary end points included postoperative recipient characteristics: PaO<sub>2</sub>/FiO<sub>2</sub> ratio at the end of the transplant and at 24, 48, and 72 hours after transplant, duration of mechanical ventilation, ICU and total hospital stays, and the need for postoperative use of extracorporeal membrane oxygenation (ECMO).

### 2.3. Statistical analysis

All data were analyzed with the use of IBM SPSS Statistics for Windows, Version 23 (IBM Corp, Armonk, New York) and are presented as continuous or categorical variables. Continuous data were evaluated for normality by use of one sample Kolmogorov–Smirnov test and confirmed by histograms. Continuous variables were expressed as the mean ± standard deviation in cases of normally distributed variables or median (interquartile range) in cases of non-normally distributed variables. Categorical variables are presented as total numbers of patients and percentages. Continuous data were analyzed by use of the unpaired *t* test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Pearson's  $\chi^2$  or Fisher exact tests were used for categorical data, dependent on the minimum expected count in each cross-tab. Laboratory test changes over the perioperative course were analyzed with the use of a paired *t* test for normally distributed variables. Kaplan–Meier survival estimation was applied for survival analysis of the entire patient cohort. A log-rank test was applied for comparison of overall survival and freedom from CLAD estimates of patients from the hanging and control groups. Values of *P* < .05 were considered statistically significant.

## 3. Results

Over the 4-year period 211 lung offers to our department had hypoxic brain injury secondary to suicidal hanging as a donor cause of death. Of these, 149 (70.6%) organs were declined due to hanging as a primary cause (5.7%), function (23.2%), past medical history (13.7%), no suitable recipient (14.2%), logistics (10.4%), virology (2.4%), and not meeting criteria (0.9%). Sixty-two (29.4%) organs were assessed by the retrieval team and only 22 (10.4% of all offers) were retrieved and transplanted. In 8 cases lungs were retrieved from donation after circulatory death (DCD) donors.

During that period 265 LTx were performed at our center. Twenty-two recipients received lungs from donors after suicidal hanging (Group 1) and the remaining 243 transplantations were used as a control (Group 2). The donors' baseline and organ procurement data are presented in Table 1. No statistically significant difference was found in the donor characteristics between analyzed groups, except for the incidence and the duration of cardiac arrest, which was, as expected, significantly higher in hanging donors (*P* < .001 and *P* = .008, respectively), the younger age and the smoking history of them (*P* = .022 and *P* = .0042, respectively).

The recipients from the hanging and control group had comparable preoperative demographics and distribution of diagnoses. Postoperatively in hanging group there was a higher incidence of ECMO support (27.3 versus 9.1%, *P* = .019). The recipients' baseline characteristics and intra/postoperative data are presented in Tables 2 and 3, respectively. There were no significant differences in CLAD-free survival between group 1

**Table 1**  
Donors' baseline characteristics and organ procurement data.

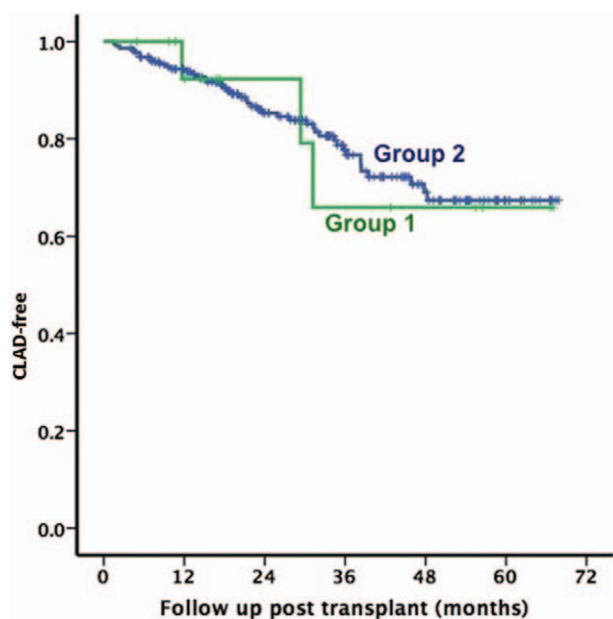
	Hanging (n=22)	Control (n=243)	P value
Age, years	34 ± 15	43 ± 13	.001*
Female	9 (40.9%)	133 (55%)	.107
Height, cm	169 ± 10	170 ± 10	.743
Weight, kg	69 ± 13	74 ± 14	.083
Cardiac arrest	22 (100%)	55 (22%)	.0001*
Cardiac arrest time, minutes	36 ± 22	25.7 ± 20	.008*
Mechanical ventilation duration, days	2.8 ± 1.6	2.8 ± 2.5	.16
Abnormal chest x-ray	12 (55%)	174 (71.6%)	.76
Abnormal bronchoscopy	11 (50%)	85 (36%)	.421
PO <sub>2</sub> on FiO <sub>2</sub> 100% preretrieval, kPa	58 ± 11	56 ± 12	.579
Smoking	15 (68%)	98 (40%)	.012*
Heavy smoking	3 (14%)	33 (14%)	.956
Cannabis smoking	3 (14%)	18 (7%)	.302
DCD	7 (32%)	54 (22%)	.102
EVLP/OCS use	3 (13%)	20 (8%)	.075

DCD=donation after circulatory death, EVLP=ex-vivo lung perfusion, OCS=organ care system.  
\*Indicates P values of the variables that are significantly different.

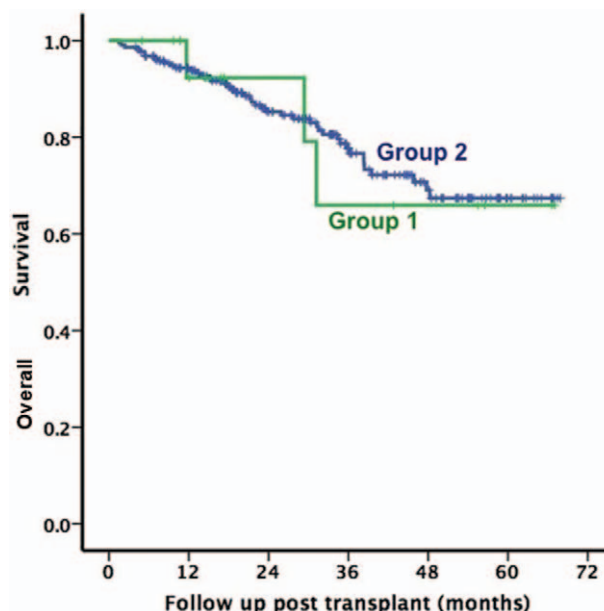
and 2: 92.3 versus 94% at 1 year, 65.9 versus 75.5% at 3 years and 65.9 versus 67.4% at 5 years (log-rank *P* = .99) (Fig. 1). The estimated cumulative survival rate (Fig. 2) was not significant between groups: 68.2 versus 83.2% at 1 year (log-rank *P* = .127), 68.2% versus 72% at 3 years (log-rank *P* = .102) and 68.2% versus 61.3% at 5 years (log-rank *P* = .3758).

#### 4. Discussion

The availability of suitable donors is the major limitation to increasing the lung transplants performed. Organ utilization indicates donor selection and although extended criteria donors have recently been considered by many programs, the lung utilization rate remains <30% in most countries.<sup>[10-12]</sup> On the



**Figure 1.** Freedom from chronic lung allograft dysfunction for patients after bilateral sequential lung transplantation with organs from hanging donors (Group 1) and other donors (Group 2).



**Figure 2.** Kaplan-Meier survival estimate for patients after bilateral sequential lung transplantation with organs from hanging donors (Group 1) and other donors (Group 2).

other side, most lung transplant programs do not use certain high-risk donors, such as suicidal hanging donors, since the relationship between donor cause of death and lung transplantation outcomes remains unclear. One can argue that none of the more controversial areas has been rigorously analyzed. Hanging is one of the most commonly used methods for suicide worldwide. In England and a number of developing and developed countries, its incidence has increased over the last 30 years.<sup>[13]</sup> Epidemiological studies have revealed that mean age of that cases is less than 40 years, with predominance of male gender, depression and history of smoking and drug or alcohol addiction.<sup>[14]</sup> In suicidal hanging, injury is secondary to the compression of the large blood vessels in the neck as well as the occlusion of the airway; slow cerebral ischemia and respiratory

**Table 2**  
Recipients' baseline characteristics.

	Hanging (n=22)	Control (n=243)	P value
Age, years	42.6 ± 14.2	43.12 ± 12.8	.33
Female	11 (50%)	133 (54%)	.945
Height, cm	167.1 ± 9.4	169.8 ± 10.5	.723
Weight, kg	63.8 ± 14.6	74.08 ± 14.3	.646
Redo transplant	2 (9.1%)	6 (25%)	.318
Ventilation preop	3 (13.6%)	4.1 (10%)	.939
ECMO preop	4 (18.2%)	19 (7.8%)	.099
Primary diagnosis			
CF	9 (40.7%)	99 (41%)	.988
Emphysema	5 (22.7%)	71 (29%)	.521
A1 antitrypsin deficiency	4 (18.2%)	25 (10%)	.258
PF	1 (4.5%)	19 (8%)	.579
PH	1 (4.5%)	9 (4%)	.843
Sarcoidosis	1 (4.5%)	3 (1%)	.224
Bronchiectasis	1 (4.5%)	10 (4%)	.923

CF=cystic fibrosis, ECMO=extracorporeal membrane oxygenation, PF=pulmonary fibrosis, PH=pulmonary hypertension, preop=preoperative.

\*Indicates P values of the variables that are significantly different.

**Table 3****Intraoperative data and postoperative outcome.**

	Hanging (n=22)	Control (n=243)	P value
Intraoperative data			
CPB used	12 (54.5%)	133 (55%)	.97
CPB time, minutes	214 (21–247)	153 (53–555)	.38
Total ischemic time, minutes	461.3±120	420.5±144.3	.174
Postoperative data			
PaO <sub>2</sub> /FiO <sub>2</sub> on arrival	311±153	314.4±113	.530
PaO <sub>2</sub> /FiO <sub>2</sub> on 24 hours	344±123	355.5±121	.795
PaO <sub>2</sub> /FiO <sub>2</sub> on 48 hours	341±133	355.4±124	.638
PaO <sub>2</sub> /FiO <sub>2</sub> on 72 hours	320±95	365.2±110	.115
Postop ECMO	7 (31.8%)	22 (9%)	.008*
Ventilation, hours	33 (23–285.5)	204 (0–3360)	.885
ICU stay, days	8.5 (5–20.7)	14.4 (1–140)	.94
Hospital stay, days	35 (20–53)	38.12 (0–190)	.845

CPB = cardio-pulmonary bypass, ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit, postop = postoperative.

\* Indicates P values of the variables that are significantly different.

symptoms—respiratory distress, hypoxia, and pulmonary edema. The pulmonary edema may be from a neurogenic origin or secondary to negative intra-thoracic pressures generated as victim attempts inspiration through an obstructed airway. The pathophysiology responsible for this negative pressure or postobstructive pulmonary edema is likely multifold. Based on Starling's law, the oncotic and hydrostatic pressure of the capillary bed must balance the oncotic and hydrostatic pressure of the interstitium to prevent a net egress of fluid. Attempted inspiration against an obstructed upper airway causes a drop in the intrathoracic pressure, resulting in increased venous return and increased pulmonary capillary pressure, with a concomitant decrease in pulmonary interstitial pressure resulting in pulmonary edema. Furthermore, it is demonstrated that decreasing intrathoracic pressure with an obstructed airway results in an increase in alveolar interstitial fluid accumulation. In addition to the increased venous return, left ventricular compliance decreases and afterload increases because of the decrease in negative pressure. The resultant increased overall pulmonary blood volume raises the pulmonary capillary hydrostatic pressure, further exacerbating the pulmonary edema.<sup>[15–18]</sup> Hypoxia associated with hanging increases also pulmonary capillary vascular resistance, increasing the hydrostatic pressure. The hypoxia-induced hyperadrenergic state causes translocation of blood from systemic to pulmonary circulation and an increase in both pulmonary vascular resistance and pulmonary capillary permeability. Elevated inflammatory cytokines have been associated with strangulation which could contribute to loss of capillary integrity.<sup>[18,19]</sup> Cardiorespiratory arrest time is also varying and in many cases duration is uncertain and at best surmised on the basis of factors such as body temperature and on when the patient was last seen.

Lungs are infrequently recovered from hanging donor patients and typically declined for transplantation because of the sensitivity of the lungs to injury and the unpredictable function of the donor lung in the recipient. With sudden occlusion of the upper airway during hanging, air may get trapped in the lungs, possibly causing barotrauma to the small airways and parenchyma. As suggested by Mohite et al,<sup>[4]</sup> careful inspection of the lung surface for bullae and spontaneous hemorrhage may rule out the possibility of barotrauma. Other concerns about lungs from hanging donors, such as the possibility of aspiration of gastric contents and injury to the airways, can be ruled out by donor

bronchoscopy.<sup>[20]</sup> Changes that occur after that mode of death and prolonged intensive care unit (ICU) management can also significantly injure the lung, leading to severe deterioration of the gas exchange capacity. Pulmonary edema though, is reversible in most cases, with careful fluid management focusing on drying the lungs, positive end-expiratory pressure ventilation. Inotropic support to reduce the left atrial pressure, and corticosteroids to counter the effect of inflammatory mediators are also highly recommended in donor management.<sup>[4,21]</sup>

In a retrospective analysis of 18,250 lung transplant recipients using the UNOS Standard Transplant Analysis and Research Registry for lung transplantation from 1987 to 2010, it was found that recipients with asphyxiation or drowning as donor cause of death (1.9% of all causes of death) did not have worse outcomes or survival compared with recipients whose donors died of other causes. Also, this donor cause of death was not associated with incidence of acute rejection in first year post transplantation.<sup>[22]</sup> Mohite et al published the outcomes of 302 LTx that were performed in our center over a 7-year period to November 2013, grouped on the basis of the cause of death. No statistically significant difference was found in the donor characteristics between hanging group and all other causes of death group, except for the incidence of cardiac arrest, which was significantly higher in hanging donors. Preoperative characteristics, intra-operative, and post-LTx variables including PaO<sub>2</sub>/FiO<sub>2</sub> ratios, duration of mechanical ventilation, and intensive care unit and hospital stays were comparable. The prevalence of bronchiolitis obliterans syndrome did not differ between the 2 groups. One-year and 3-year survival rates were also comparable in both groups. Two out of eight recipients in the hanging group required extracorporeal life support after LTx and could not survive.<sup>[4]</sup> Similarly, Renard et al presented their single European center experience utilizing hanging donor lungs over a 4.5-year period to July 2015. Outcomes of twenty lung transplant patients with suicidal hanging as donor cause of death were compared with 279 lung transplant recipients, concluding that there was no statistical difference in 1- and 2-year survival between 2 groups. Donor demographics, recipient diagnosis, primary graft dysfunction at 72 hours and postoperative lung function were comparable in both groups.<sup>[8]</sup>

In order to solve these conundrums, a great deal can be learned from the cumulative experience of all UK centers and specifically some of the answers were provided recently by the NHS Blood



and Transplant (NHSBT) data analysis. NHSBT reviewed the utilization of organs from high risk donors, including hanging, over a 10-year period to March 2013. Quite predictably, it was found that referral, family approach, and organ utilization in these groups were less than for standard risk donors. In regards to hanging donors, 218 utilized offers resulted in only 29 single and double lung transplants during that period. Twenty lung transplants were from brain death donors and 9 from cardiac death. One year results in this group included graft failure in 4 recipients and 9 patient deaths.<sup>[5]</sup>

Even though these high-risk donors had a higher rate of cardiac arrest and incidence of smoking, we assume that they may have characteristics associated with good outcomes, such as younger age. However, there is no evidence of inferior outcomes after lung transplant from donors who have had a period of cardiac arrest provided that good lung function is preserved.<sup>[23,24]</sup> Chronic rejection is a major cause of death after the first year following lung transplantation. BOS is the most common pathologic finding on biopsy and clinically, in the absence of tissue for pathology, it refers to a progressive irreversible drop in FEV1. Recently though, a broader definition of chronic rejection, termed “chronic lung allograft dysfunction” or CLAD, has been used to encompass a more inclusive definition of post-transplant dysfunction.<sup>[9]</sup> In our study, we measured CLAD instead of BOS and CLAD-free survival results were comparable in hanging group in 1, 3, and 5 years after lung transplant.

It is well known that different insults to the donor lung before and after declaration of brain death or cardiac death, preservation, transplantation process, and reperfusion in the recipient, play an important role in the development of ischemia-reperfusion injury, properly defined as primary graft dysfunction. It appears that cardiac death donor lungs were equally distributed between groups and perioperative data, like transplant on cardiopulmonary bypass and total ischemic duration, were comparable. Postoperatively though, the need of ECMO support was higher in the hanging donor group, with 3 recipients requiring venovenous (VV) and 4 venoarterial (VA) support. All 3 postoperatively supported VV ECMO recipients were young cystic fibrosis patients—one was redo lung transplant—bridged to transplant on support. Two of them were weaned successfully within 10 days and the other one was weaned within 11 days but died following bowel ischemia and multiorgan failure. Further analysis of mortality in hanging donor group revealed that bleeding and multiorgan failure were the main causes of death in the early postoperative phase (<30 days) in all 4 recipients who required postoperatively VA support. One recipient with pulmonary hypertension and a large ASD with anomalous pulmonary vein drainage was bridged to transplant on VA support and had multiple surgical re-explorations. Two recipients, one with background of pulmonary fibrosis and the other with sarcoidosis and both with severe secondary pulmonary hypertension, had severe coagulopathy and bleeding after lung transplant, requiring VA support. The fourth patient was a young CF recipient with massive adhesions and uncontrolled bleeding post transplant that required multiple blood and blood product transfusions. Bleeding and massive blood transfusion may have presented as primary graft dysfunction in these patients and it can be argued whether lung failure and mortality is associated solely with donor cause of death. Two deaths in the hanging donor group were in the late postoperative phase (>30 days). One recipient with A1 antitrypsin deficiency had a smooth early postoperative period but died 42 days after transplant following perforated gastric ulcer, peritonitis, and multiorgan

failure. The other recipient was a young CF patient who was readmitted 4 months post-transplant with viral pneumonitis and grade 3 acute rejection.

#### 4.1. Limitations of the study

Donor lungs acquired from patients who are asphyxiated by hanging are undoubtedly marginal grafts and typically are not used because of the lung injury. In this study, we report a single medical center outcomes of 22 lung transplantations utilizing suicidal hanging donors with similar perioperative and mid-term outcomes compared with those from all other causes of death, over a 4 year period. This study might be encouraging for lung transplant surgeons to consider these organs and helpful for expanding the donor pool, but we cannot exclude bias and confounding in terms of patient selection and their treatment. With only 22 patients in the study arm, this is underpowered for demonstrating noninferiority. The possibility of selection bias cannot be denied as only 29.4% of the lungs from hanging donors were assessed and 10.4% were eventually utilized. The highly selected lungs from hanging donors still had 31.8% postoperative ECMO support compared with only 9% in the control group. The study power was limited and despite utilizing more hanging donors in our program, the study cohort was reasonable but still small with several variables and outcomes not reaching statistical significance.

## 5. Conclusion

Optimal utilization of hanging donor lungs should be performed in a safe and ethical manner. Our data suggests that use of suicidal hanging donor lungs has not necessarily jeopardized postoperative clinical course or mid-term survival of recipients. Although these donors contribute only a small proportion of donor pool, there is a potential for expanding the donor pool if they are considered. These results encourage assessment of lungs from hanging donors and their consideration for transplantation. Further larger studies are required to confirm the findings of the present study.

### Author contributions

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**Visualization:** A. Popov.

**Writing – original draft:** O. Ananiadou.

**Writing – review & editing:** O. Ananiadou, P. Mohite.

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