Does donor arterial partial pressure of oxygen affect outcomes after lung transplantation? A review of more than 12,000 lung transplants

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Introduction: In lung transplantation (LTx), the arterial partial pressure of oxygen (PaO_2) is traditionally regarded as critical information for assessment of donor lung function. Each center sets its own thresholds; by convention, a donor PaO_2 of less than 300 mm Hg has been considered disqualifying. Limited literature exists to support such a practice. We analyzed all LTxs performed in the United States over a 9-year period to assess the effect of donor PaO_2 on graft survival.

Methods: The United Network for Organ Sharing (UNOS) database was queried for LTx (January 2000–November 2009). Of 12,545 LTx performed, 12,045 (96%) had donor PaO_2 data on a fraction of inspired oxygen of 1.0, recorded at the time of procurement.

Results: Mean donor PaO_2 was 407 ± 140 mm Hg. The majority of LTxs had a donor PaO_2 greater than 300 mm Hg (9593 (80%]) whereas PaO_2 was 200 mm Hg or less in 1830 (15%) and 201 to 300 in 582 (5%) donors. Use of donors with a PaO_2 of less than 200 increased over time from 5% (45) in 2000 to 21% (295) in 2009 ($P = .002$). Kaplan-Meier survival analysis showed no difference in graft survival with differing donor PaO_2s, irrespective of whether patients had a single or double LTx. A Cox multivariable analysis of 21 donor characteristics demonstrated that donor PaO_2 had no association with graft survival.

Conclusions: Donor PaO_2 levels did not affect graft survival. The use of donors with lower PaO_2s could substantially increase the donor pool. We are not suggesting that donor PaO_2 is not important when assessing potential lung donors but its level of importance in regard to other criteria appears less than previously believed. (J Thorac Cardiovasc Surg 2012;143:919-25)

Lung transplantation (LTx), like all solid organ transplantation, is struggling with the demand of donor organs exceeding supply and increasing waitlist mortality. Therefore, attempts to improve the supply of donor lungs by aggressive donor management,[1-3] use of ex vivo perfusion, use of cardiac death donors, and liberalization of the donor selection criteria[4,5] are actively being practiced to minimize the widely documented mismatch of demand and supply.[6]

In current practice, arterial partial pressure of oxygen (PaO_2) is considered critical information for assessment of donor lung function. Standard LTx donor criteria in the literature recommend that the donor PaO_2 should be more than 300 mm Hg and that use of donor lungs with PaO_2s of less than 300 mm Hg could be associated with decreased posttransplant pulmonary function. However, no significant evidence is available to support such a practice.[7,8] As stated in the consensus report from The Pulmonary Council of the International Society of Heart and Lung Transplantation:

> The origin of the ''standard'' arterial blood gas criteria for evaluating the suitability of the potential pulmonary donor is shrouded in the mists of time. In 1987 Harjula et al[9] described a single case of perioperative graft failure in which the arterial partial pressure of oxygen (PaO_2) was <100 mm Hg, with a fraction of inspired oxygen (FiO_2) of 0.4 (ie, PaO_2/FiO_2 ratio <250), and it is likely the acceptability ratio of 300 (PaO_2 of 120 mm Hg on an FiO_2 of 0.4) was then arbitrarily chosen to provide a slight margin of safety. It is more puzzling as to why this standard has been so closely adhered to since that report. The literature provides no answers as no studies have addressed this issue specifically.*

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Abbreviations and Acronyms

DCD = donation after cardiac death
FiO_2 = fraction of inspired oxygen
ISHLT = International Society for Heart and Lung Transplantation
LTx = lung transplant (transplantation)
OPTN = Organ Procurement and Transplant Network
PaO_2 = arterial partial pressure of oxygen
UNOS = United Network for Organ Sharing

With no strong literature available to validate this common practice, the purpose of this study was to assess specifically the effect of donor PaO_2 on graft survival using a large all-inclusive national database.

METHODS

In November 2009, a retrospective analysis of Organ Procurement and Transplant Network (OPTN) data was performed. The OPTN is the unified transplant network established by the United States Congress under the National Organ Transplant Act of 1984. The United Network for Organ Sharing (UNOS) is a private, nonprofit organization that administers the OPTN under federal contract.

UNOS/OPTN Thoracic database was queried for LTx from January of 2000 through November of 2009. Of the 12,545 LTx operations performed, 12,045 (96%) had donor PaO_2 data *on a fraction of inspired oxygen (FiO_2) of 1.0 recorded at the time of procurement.* The italicized phrase is how this data point is exactly listed in the UNOS database.

Transplants were divided into groups A to D based on donor PaO_2 at the time of procurement (A, <200; B, 201-300; C, 301-400; and D, >400 mm Hg).

For baseline characteristics, continuous variables were compared using the *t* test and analysis of variance, with the Tukey method for controlling for multiple comparisons. Categorical variables were compared using the χ^2 test. Survival curves were estimated using the Kaplan-Meier method, and equality of survival curves was tested using a log–rank test. Multivariate analyses were performed using Cox proportional hazards regression simultaneous models, in which all 21 donor variables available in the UNOS database were used to test their association with graft survival.

RESULTS

A total of 12,045 LTXs were analyzed, of which 40.4% (4864) were performed in female patients. Mean donor age was 32 ± 15 years (median, 29 years; range, 0-75 years). Mean recipient age was 50.7 ± 14.7 years (median, 56 years; range, <1-81 years). Mean donor PaO_2 was 408 ± 140 mm Hg. The majority of the transplants had a donor PaO_2 greater than 400 (7756 [64.4%]) whereas donor PaO_2 was 200 or less in 1830 (15.2%), 201 to 300 in 582 (4.8%), and 301 to 400 in 1877 (15.6%). Use of donors with PaO_2 less than 200 increased over time from 5% (45/867) in 2000 to 21% (295/1388) in 2009 ($P = .002$).

Donor and recipient characteristics in the different donor PaO_2 subgroups are listed in Tables 1 and 2. There was no significant difference in length of hospital stay after transplantation ($PaO_2 \leq 200$ mm Hg, 24 ± 27 days; 201-300 mm Hg, 25 ± 33 days; 301-400 mm Hg, 24 ± 29 days, >400 mm Hg, 24 ± 30 days). Kaplan-Meier survival analysis showed no significant differences in graft survival for different donor PaO_2 levels (Figure 1, *A*). When single (n = 5019) and double (n = 7026) LTx recipients were evaluated separately, there remained no significant difference in graft survival for different donor PaO_2 levels (Figure 1, *B*). A Cox proportional multivariate analysis of 21 donor characteristics demonstrated that there was no association of donor PaO_2 as a continuous variable to graft survival (Table 3). However, steroid dependence and hypertension appeared to be risk factors associated with poor graft survival.

DISCUSSION

LTx is an acceptable therapy for patients with end-stage lung disease. However, LTx is limited by an inadequate number of donors, as is common to all other fields of solid organ transplantation. This mismatch results in increasing waitlist time and mortality for LTx with an average waitlist time of 539 days and more than 7000 deaths occurring each year in patients awaiting a lung donor.[10] Two novel approaches have recently been developed to address this issue and potentially increase the donor pool for LTx. The first approach is donation after cardiac death (DCD). The number of programs using DCD for LTx has increased substantially; the number of DCD lung donors has increased 24% from 2006 to 2008.[11] Moreover, many studies have demonstrated comparable if not better outcomes using DCD compared with donation after brain death.[12-14] A second novel approach is a newly developed protective normothermic ex vivo lung perfusion technique used to render suboptimal lungs from a DCD or brain death donor viable for transplantation. This system allows the lungs after procurement to be perfused with an acellular solution for approximately 4 hours so that the lungs can be optimized as well as continually reassessed. Thus injured donor lungs that were initially unsuitable for transplantation may be successfully transplanted.[15] The first prospective clinical ex vivo perfusion trial, the ''Help'' trial, was recently completed by the Toronto group. They demonstrated that 23 LTx recipients whose donor lungs underwent ex vivo perfusion had similar early outcomes when compared with conventionally selected and transplanted donor lungs.[16]

In the attempt to increase the donor lung pool, other centers have liberalized their donor criteria, (eg, donor age > 55 years, smoking > 20 pack-years, pathology on chest x-ray films, and purulent secretions at bronchoscopy) and have demonstrated that their outcomes did not change.[4,5] In 2003, the International Society for Heart and Lung Transplantation (ISHLT) consensus group on LTx reported the current accepted ''ideal'' donor criteria as outlined in Table 4.[8] Most of the criteria have been analyzed and questioned for significance.[17] However, 1 criterion that