CARDIAC AND PULMONARY REPLACEMENT

SUCCESSFUL OUTCOME OF LUNG TRANSPLANTATION IS NOT COMPROMISED BY THE USE OF MARGINAL DONOR LUNGS

Lung transplantation is limited by a shortage of suitable donors. To address this shortage, we have begun using donor lungs that do not meet all of our previous rigorous donor criteria. Of 133 consecutive lung transplants done between June 1991 and March 1994, 89 donors were considered ideal because they satisfied all of the following accepted donor criteria (group I): age younger than 55 years, smoking less than 20 pack-years, arterial oxygen tension greater than 300 mm Hg (using inspired oxygen fraction of 1.0 and positive end-expiratory pressure 5 cm H_2O), and chest radiograph negative for infiltrate or trauma (contusion or pneumothorax). Thirty-seven donors failed to satisfy one of these criteria and seven donors failed to satisfy two of them, yielding 51 criteria denoting marginal status in the 44 donors in the marginal group (group II) as follows: age older than 55 years, 2; smoking history 20 or more pack-years, 9; unsatisfactory chest radiograph, 34; and arterial oxygen tension less than 300 mm Hg, 6. Sixty-three single lung transplants were done (group I, 44 versus group II, 19) compared with 70 bilateral sequential transplants (group I, 45 versus group II, 25). In 24 cases in group II, at least one of the lungs actually being implanted contained contusion or infiltrate. Evaluation of recipients from the two groups showed no significant difference in median duration of postoperative mechanical ventilation (3 days in both group I and group II) nor in alveolar-arterial oxygen gradient immediately after transplantation (group I, 304 ± 14 mm Hg versus group II, 275 ± 22 mm Hg; $p = 0.266$) or at 24 hours (group I, 125 ± 12 mm Hg versus group II, 122 ± 18 mm Hg; $p = 0.933$) (all values represent mean plus or minus the standard error). However, cardiopulmonary bypass was required to facilitate second graft insertion in bilateral sequential transplants more often in the marginal group (5 of 25, 20%) than in group I (6 of 45, 13%). There were three deaths within 30 days in group I (operative mortality, 3.4%) and none in group II. Currently, 74 (83.2%) of 89 remain alive in group I compared with 38 (86.4%) of 44 in group II. On the basis of these data, we conclude that successful outcome of lung transplantation can be achieved with the use of marginal donor lungs. (J THORAC CARDIOVASC SURG 1995;109:1075-80)

S. Sundaresan, MD[a] (by invitation), J. Semenkovich, MD[b] (by invitation), L. Ochoa, RN[a] (by invitation), G. Richardson, RN[a] (by invitation), E. P. Trulock, MD[c] (by invitation), J. D. Cooper, MD,[a] and G. A. Patterson, MD,[a] *St. Louis, Mo.*

From the Division of Cardiothoracic Surgery, Department of Surgery,[a] Mallinckrodt Institute of Radiology,[b] and Respiratory and Critical Care Division, Department of Medicine,[c] Washington University School of Medicine, Barnes Hospital, St. Louis, Mo.

Read at the Seventy-fourth Annual Meeting of The American Association for Thoracic Surgery, New York, N.Y., April 24-27, 1994.

Address for reprints: Sudhir Sundaresan, MD, Division of Cardiothoracic Surgery, Suite 3107 Queeny Tower, One Barnes Hospital Plaza, St. Louis, MO 63110.

0022-5223/95 $3.00 + 0 **12/6/63007**

The exponential increase in the number of lung transplants being done[1] has not been accompanied by a corresponding increase in the number of donors. Currently still only about 15% to 20% of multiple organ donors have lungs suitable for transplantation.[2] This donor shortage remains the main limitation to more widespread use of lung transplantation. The scarcity of suitable donor lungs arose in part from rigid application of strict donor criteria.[3-5] These criteria have evolved somewhat with experience. However, the ever-increasing number of recipients has compelled us to consider the use of

Table I. *Standard criteria for assessment of donor lung suitability*[5]*

Preliminary assessment
Age <55 years
ABO compatibility
Chest roentgenogram
Clear
Allows estimate of size match
History
Smoking <20 pack-years
No significant trauma (blunt, penetrating)
No aspiration/sepsis
Gram stain and culture data if prolonged intubation
No prior cardiac/pulmonary operation
Oxygenation
Arterial oxygen tension ≥300 mm Hg on inspired oxygen fraction of 1.0, 5 cm H_2O positive end-expiratory pressure
Adequate size match
Final assessment
Chest roentgenogram shows no unfavorable changes
Oxygenation has not deteriorated
Bronchoscopy shows no aspiration or mass
Visual/manual assessment
Parenchyma satisfactory
No adhesions or masses
Further evaluation of trauma

*Preliminary criteria must be satisfied before the retrieval team is sent; final assessment is done by the retrieval surgeon at the donor hospital.

"marginal" donor lungs (i.e., donor lungs that fail to meet one or more of the previous rigorous criteria). We report here our satisfactory results with the use of marginal donor lungs during a 2½-year period and present guidelines that have evolved regarding this approach as a means of addressing the donor shortage.

Methods

A total of 133 consecutive lung transplants done at our institution between June 1991 and March 1994 were retrospectively analyzed and form the basis of this report. Donors used for these transplants were placed into one of two categories on the basis of several of our previously published donor assessment criteria listed in Table I[5]; donors satisfying all of the accepted criteria were placed in group I ("ideal" donor group), whereas those failing to meet at least one of the criteria were placed in group II ("marginal" donor group).

Designation of marginal status on the basis of chest radiograph was made when infiltrates or evidence of trauma (contusion or pneumothorax) were present in either lung (even in proposed single lung transplants [SLTs] in which the radiographic changes were confined to the contralateral lung). Radiographic assessment was initially made by personnel in the donor hospital and relayed to us (as part of the initial donor data) before a donor team was sent to retrieve the organ. This preliminary radiologic assessment was confirmed by our retrieval team on arrival at the donor hospital.

Table II. *Criteria used in this study to determine group I (ideal) and group II (marginal) donor groups*

	Age >55 yr	*Smoking ≥20 pack-years*	*Unsatisfactory chest radiograph*	*Pao_2 <300 mm Hg*
Group I (n = 89)	0	0	0	0
Group II (n = 44)	2	9	34*	6

*In 24 of these 34, lung or lungs actually being implanted contained contusion, infiltrates, or both.

Donor arterial oxygen tension (Pao_2) was determined during ventilation at an inspired oxygen fraction of 1.0 and positive end-expiratory pressure of 5 cm H_2O. Donor organs were judged of marginal quality when, at these settings, Pao_2 was less than 300 mm Hg.

Donors older than 55 years or having a confirmed smoking history greater than 20 pack-years were also judged marginal.

Parameters used to evaluate early recipient outcome included the alveolar-arterial oxygen difference ($A\text{-}aDo_2$) immediately on return to the intensive care unit after transplantation and also at 24 hours after operation, number of days of mechanical ventilation required, and death occurring within 30 days of the transplantation. The percentage of patients currently alive in each group was used as a parameter of late outcome. Statistical comparison of values between the groups was done with the unpaired t test or the Fisher exact test. Values were considered significantly different when p was less than 0.05.

Results

Comparison of group I (ideal donors) versus group II (marginal donors). There were 89 donors in group I and 44 in group II (see Table II). Thirty-seven of 44 group II donors were deemed marginal on the basis of failure to satisfy only one of the listed criteria, whereas 7 of 44 failed to satisfy two of these criteria. As previously stated, designation of marginal status on the basis of chest radiograph was made when unsatisfactory radiographic findings (infiltrate, contusion, pneumothorax, or a combination of these conditions) were present in either lung (even in proposed SLTs when the radiographic changes were confined to the contralateral lung). Among the 34 donors in group II deemed marginal on the basis of these unsatisfactory radiographic findings, the lung or lungs actually being implanted contained contusion or infiltrate in 24 of the 34 cases.

Table III compares several clinical variables between the donors of the two groups. Mean donor age and duration of donor mechanical ventilation

Table III. *Summary of clinical details of group I and group II donors*

	Group I (n = 89)	*Group II (n = 44)*
Age (yr)	24.9 ± 1.0	29.2 ± 2.0*
Duration of mechanical ventilation (days)	1.9 ± 0.2	2.5 ± 0.4†
Major causes of death		
Intracranial bleeding	20/89 (23%)	15/44 (34%)
Isolated head injury	36/89 (40%)	9/44 (21%)
Blunt trauma with associated closed head injury	29/89 (33%)	17/44 (39%)
Clinical evidence of chest trauma	2/89 (2%)	15/44 (34%)

*p = 0.057 versus group I.
†p = 0.180 versus group I.

did not differ between the groups. The major causes of death in the two groups varied somewhat, with a greater frequency of blunt trauma and associated closed head injury in group II. Of note, clinically evident chest trauma (in addition to the documented radiographic changes ensuing from trauma, used as a criterion of marginal status in Table II), such as chest wall abrasions, thoracic stab or gunshot wounds, and chest tubes inserted for other indications, were far more prevalent in the marginal group (see Table III).

Transplant procedures. There were 63 SLTs (44 in group I and 19 in group II) and 70 bilateral sequential lung transplants (BSLT; 45 in group I and 25 in group II). Cardiopulmonary bypass was used in an obligatory fashion for all transplants done because of pulmonary vascular disease (21 in group I and 5 in group II) but not for any other SLT in either group. Cardiopulmonary bypass was also occasionally required to facilitate second graft insertion in bilateral transplants (in 6 [13%] of 45 BSLT in group I versus 5 [20%] of 25 BSLT in group II; p = 0.506).

Early recipient outcome. Table IV shows that there was no significant difference in recipient outcome between the groups with respect to A-aDo_2 (either immediately or at 24 hours after operation), median duration of mechanical ventilation, or 30-day operative mortality.

Late recipient outcome. Table IV shows that 74 (83.2%) of 89 group I recipients are currently alive compared with 38 (86.4%) of 44 group II recipients (p = 0.802).

Influence of donor Pao_2 on subsequent outcome. We focused on the subgroup of marginal donors with Pao_2 values less than 300 mm Hg (comparing their recipient outcomes with those having marginal donors with Pao_2 values greater than 300 mm Hg and with those recipients of ideal donor lungs) to evaluate the impact of this particular transgression of the rigorous donor criteria on subsequent recipient outcome. Fig. 1, which shows the A-aDo_2 (immediately and at 24 hours after operation), shows no significant difference among these three subgroups at either time point.

Table IV. *Comparison of early and late outcomes of recipients in groups I and II*

	Group I (n = 89)	*p Value*	*Group II (n = 44)*
A-aDo_2, immediate (mm Hg)	304 ± 14	0.266	275 ± 22
A-aDo_2, 24 hours (mm Hg)	125 ± 12	0.933	122 ± 18
Median number of days of ventilator support	3		3
Death <30 days	3/89 (3.4%)	0.113	0/44
Current survival	74/89 (83.2%)	0.802	38/44 (86.4%)

Discussion

This retrospective study has demonstrated that satisfactory outcome of lung transplantation can be achieved with the use of lungs from marginal donors. None of the parameters used in this study to evaluate early and late recipient outcome showed any significant difference between the groups. There were, however, discernible differences between the two groups. First, cardiopulmonary bypass appeared to be necessary to facilitate second graft implantation in BSLT more often in the marginal donor group than in the ideal donor group, although the difference between groups did not achieve statistical significance. The need for bypass was invariably based on unsatisfactory oxygenation or hemodynamics, or both (i.e., unacceptably elevated pulmonary artery pressure) after pulmonary artery clamping during excision of the second native lung. Second, our subjective impression is that the early postoperative recipient chest radiographs in the marginal donor group often demonstrated worsening of any preexisting infiltrate or contusion before resolution of these changes, which was usually discernible within about 72 hours. These findings are all compatible with a tolerable degree of reversible donor lung dysfunction, manifested mainly as reperfusion-related pulmonary edema. Nonetheless, these phenomena observed in the marginal donor group did not have any effect on the objective parameters used in

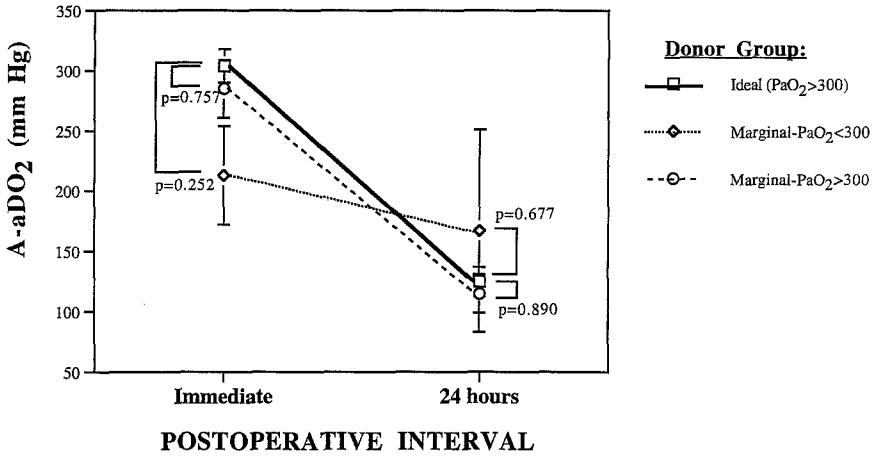

Fig. 1. Effect of donor Pao_2 on recipient oxygenation early after transplantation. A-aDo_2 values given for recipients in three subgroups: those with ideal donors (Pao_2 values greater than 300 mm Hg), those with marginal donors with Pao_2 values less than 300 mm Hg, and those with marginal donors with Pao_2 values greater than 300 mm Hg. No significant difference was noted between these subgroups at either time point.

this study and hence did not have an adverse impact on the early or late results for those recipients.

Puskas and associates[4] have previously reported on the utility of unilateral lung assessment in the evaluation of donors with unilateral infiltrates and unsatisfactory gas exchange. That report emphasized that assessment of the unilateral donor lung did not alter the strict criteria applied to potential lung grafts, but rather verified that the lung under scrutiny did satisfy these criteria even if the contralateral lung had been damaged by aspiration or trauma. It was demonstrated that successful SLT could be achieved under such circumstances and that this might be a useful strategy to increase the availability of single lung grafts from otherwise unsuitable donors.[4] In our study, six of the marginal donors had a Pao_2 value less than 300 mm Hg. We did not do unilateral lung assessments (as described by Puskas and associates[4]); thus we could not determine whether the reason for the poor donor oxygenation was due to a problem in the transplanted (ipsilateral) or contralateral lung. However, our study does represent an extension of that strategy for expanding the donor lung pool, in that greater clinical experience and careful judgment have permitted us, in selected circumstances, to relax the necessarily strict criteria normally applied to potential lung grafts and yet still achieve satisfactory results. Our data support this concept, in that there was no significant difference in recipient A-aDo_2 values for ideal donors, marginal donors with Pao_2 values less than 300 mm Hg, and marginal donors with Pao_2 values greater than 300 mm Hg, either immediately after transplantation or 24 hours later.

Clearly proper judgment is the critical factor in determining what degree of donor lung dysfunction is tolerable and in what circumstances this approach is acceptable. We continue to believe that the donor bronchoscopic examination is of paramount importance and that the findings of copious purulent secretions or evidence of aspiration (foreign matter, tracheobronchitis) represent strong contraindications to the use of that lung. As we have stated previously,[5] the presence of a chest tube (for treatment of iatrogenic pneumothorax as a result of central venous line insertion) or mild contusions or infiltrates are all of some concern, but such cases often yield quite acceptable grafts. Similarly, donor hypoxemia related to fluid overload or simple mucus plugging can usually be resolved by diuresis and bronchoscopy, respectively, again providing satisfactory lung grafts. We are increasingly in favor of implementing early antibiotic therapy (consisting of intravenous vancomycin and ceftazidime) in marginal donors with pulmonary infiltrates or contusions before commencement of the multiple-organ retrieval.

Ultimately, the use of a marginal donor lung is dictated by the recipient's underlying disease and anticipated procedure, as well as the aforementioned considerations. For bilateral lung transplants, a mild contusion or infiltrate in one lung may be acceptable. As long as the recipient does not have any profound inequalities in distribution of ventila-

tion or perfusion, then it may be preferable to implant the more "normal" lung first to minimize the requirement for cardiopulmonary bypass during implantation of the marginal graft. Similarly, some degree of reversible lung dysfunction is usually tolerable in SLT for emphysema, in which the native lung can oxygenate satisfactorily until the graft recovers. The duration of graft ischemia (generally confined to less than 8 hours) also has an impact on graft quality, and in the aforementioned situations we have occasionally extended the ischemic interval beyond 10 hours with satisfactory results. Under no circumstances, however, do we compromise donor lung quality in SLT for primary pulmonary hypertension, in which the graft will receive essentially all of the postoperative perfusion immediately. In these cases, the chest radiograph must be clear on the side of the proposed harvest; gas exchange, bronchoscopy, and size match must all meet the established criteria perfectly; and graft ischemic time is limited to 6 hours or less. With careful consideration of all these matters, it appears that the use of marginal donor lungs represents a safe method of enlarging the potential donor lung pool and does not compromise the subsequent early or late recipient outcome.

We gratefully acknowledge the help of Richard B. Schuessler, PhD, in performing the statistical analysis.

REFERENCES

1. Pohl MS, Cooper JD. St. Louis International Lung Transplant Registry results. In: Patterson GA, Couraud L, eds. Current topics in general thoracic surgery: lung transplantation. Amsterdam: Elsevier, 1995:455-65.
2. Trulock EP. Lung transplantation: recipient selection. Chest Surg Clin North Am 1993;3:1-18.
3. Todd TR, Goldberg M, Koshal A, et al. Separate extraction of cardiac and pulmonary grafts from a single organ donor. Ann Thorac Surg 1988;46:356-9.
4. Puskas JD, Winton TL, Miller JD, Scavuzzo M, Patterson GA. Unilateral donor lung dysfunction does not preclude successful contralateral single lung transplantation. J THORAC CARDIOVASC SURG 1992;103:1015-8.
5. Sundaresan S, Trachiotis GD, Aoe M, Patterson GA, Cooper JD. Donor lung procurement: assessment and operative technique. Ann Thorac Surg 1993;56:1409-13.

Discussion

Dr. Joseph LoCicero *(Boston, Mass.).* This is an important preliminary report that is necessitated by the fact that our record of recovering lungs from cadaver donors is abysmal. The 1992 statistics that were given show that about 20% of all donors have contributed lungs. In fact, the preliminary data for 1993 are considerably worse.

Donors have three opportunities to have lung injury: first is the initial trauma that they receive; second is the additional lung injury from the resuscitation period or the time during donor preparation; and third is the obligatory ischemia/reperfusion injury that all lungs must go through before transplantation. In addition, the authors have pointed out that there can also be underlying chronic preexisting lung damage, such as a heavy smoking history or possibly advanced age of the donor. Advanced age may lead to a statistically significant difference in outcome.

The measures of function used in this study both before and after operation are fairly crude but can supply some information about whether these lungs may have preexisting injuries. In addition to the $A\text{-}aDO_2$ and PaO_2 values, pulmonary mechanics can also be measured. Have you had any opportunity to measure pulmonary mechanics in donors before harvest? If so, has that provided any information about the eventual outcome? Second, do you know of any other objective measures besides these fairly crude measures of function? Have any biopsy samples been taken from these lungs? Is there any information on shed antigens in the donor plasma that we could use to begin to get some handle on whether these lungs have a significant injury? Finally, how bad can a donor organ be and still be acceptable for transplantation? What about multiple problems in the marginal donor? Would it be acceptable to use a 62-year-old heavy smoking donor with blunt trauma to the chest whose chest x-ray film shows bilateral infiltrates, with a PaO_2 of 200 mm Hg on 100% oxygen and white blood cells on bronchoscopy, but no bacteria?

Dr. Sundaresan. Concerning the first question related to evaluation of pulmonary mechanics before harvest of the donor, we can get a subjective impression about the pulmonary mechanics from airway pressures during mechanical ventilation. Other than that we have not pursued more sophisticated ways of evaluating that issue.

The second question had to do with other objective ways of measuring the possibility of underlying or perhaps unappreciated lung injury in the donor lungs, for example, the use of biopsies. Again, we have not used such methods on a regular basis. We have in the past done biopsy studies of donor lungs during a multiple organ retrieval when some clinical finding suggested that there might be a serious problem, such as diffuse granulomatous infection. In fact, we have managed to avoid using what we would consider unacceptable lungs through the use of frozen section when that was available. In terms of evaluating the grafts after transplantation, of course these recipients are subjected to regular follow-up bronchoscopic examination, but I do not think that exactly relates to your question.

The final question had to do with how bad a donor lung can be before it is turned down. There are two issues that have to do with when a marginal lung can be used. One issue concerns factors related to evaluation of the lungs, such as the x-ray films, the blood gas values, and bronchoscopic examination. The other issue concerns the recipient's disease and the procedure planned. The 62-year-old smoker in the example given, with blunt trauma and

bilateral contusions, might not be acceptable for any recipient except one who was moribund. Ultimately it is a judgment call related to the patient, the underlying disease, and whether the patient will receive a single or bilateral lung transplant.

Dr. Thomas M. Egan *(Chapel Hill, N.C.).* If I understand the data correctly, a large number of the marginal donors were marginal on the basis of an abnormal radiographic finding. The issue for those of us retrieving lungs is how to tell whether that abnormality is an abnormality caused by infection versus an abnormality caused by something else.

An interesting study was published 3 years ago that looked at the incidence of pneumonia in survivors of closed head injury who required intubation (Hsieh AH-H, Bishop MJ, Kublis PS, Newell DW, Pierson DJ. Pneumonia following closed head injury. Am Rev Respir Dis 1992;146:290-4). These authors determined that 40% of patients who required intubation because of a closed head injury ultimately had pneumonia at some time during the first week of hospitalization. Our problem is that we come on the scene on day 2 or day 3 after the injury and are trying to determine whether the lung from this head-injured patient will result in pneumonia 2 days later in our recipient.

Do you have any guidance for us in terms of how to tell whether the abnormality that we are seeing on chest x-ray films is infectious versus an area of contusion versus an area of interstitial pulmonary edema? Have you used lungs that had an infectious area that appeared to be localized to either one segment or one lobe that could then be resected?

Dr. Sundaresan. Your first question concerned the differentiation of infection versus contusion when there is an abnormality on the chest radiograph. I think that the limited history obtained on the donor and the knowledge of the clinical circumstances are probably the most useful things in determining whether there has been a traumatic contusion or an infectious or inflammatory problem in the lung. The bronchoscopic examination might also be useful, because purulent secretions on the side of the radiographic abnormality might correlate more closely with a septic problem.

Dr. Egan. Have you ever resected an area that you thought by palpation was infected?

Dr. Sundaresan. I am not aware that that has been done in this series of patients or, in fact, at all in our experience. We have encountered some lungs that had substantial injuries or inflammatory problems, but our subjective impression is that when left alone they tend to clear up quite rapidly.