Maximizing the Utilization of Donor Organs Offered for Lung Transplantation

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The number of patients awaiting lung transplantation (LT) and waiting time for surgery is increasing. In Australia, LT rates are 4.6/million population/yr, which despite low organ donation rates, are the highest published in the world. The Australian organ allocation system allows identification of marginal donors and therapeutic manipulation where appropriate. This study aims to assess the impact of utilization of marginal donors and aggressive donor management. A comparison between published donor criteria and local practice is made, allowing assessment of the effect of using marginal donors on outcome. Donor management included antibiotic therapy, strict fluid management, physiotherapy, bronchoscopy and bronchial toilet, and alteration of ventilatory settings including initiation of pressure support. Blood gases were repeated to assess the results of interventions. Between January 1, 1995 and May 31, 1998, we performed 140 transplants from 112 of 219 (51%) lung donor offers. Of these donors, 48 (43%) satisfied all published criteria for suitable donor organs (Group 1 = ideal donors) and 64 (57%) did not (Group 2 = marginal donors). Criteria breached by the marginal donors were: an initial ratio of arterial oxygen pressure to fraction of inspired oxygen ($Pa_{O_2}/F_{I_{O_2}}$) < 300 mm Hg (n = 20), abnormal radiology (n = 39), pulmonary infection (n = 24), 20 pack-years smoking (n = 5) and age > 55 yr (n = 4). Therapeutic manipulation resulted in improvement in the $Pa_{O_2}/F_{I_{O_2}}$ ratio in 20 donors (Group 3) who would not otherwise have been used. Immediate and 24 h postoperative gas exchange and length of intensive care unit (ICU) stay was not different for recipients from donors from all three groups. Overall survival was 94% at 30 d, 83% at 1 yr, 70% at 2 yr, and 62% at 3 yr and was not significantly different from the three groups. We conclude that organ utilization can be maximized by therapeutic manipulation and utilization of marginal donors without compromising results from transplantation. Gabbay E, Williams TJ, Griffiths AP, Macfarlane LM, Kotsimbos TC, Esmore DS, Snell GI. Maximizing the utilization of donor organs offered for lung transplantation.

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Lung transplantation (LT) is an established treatment for selected patients with end-stage lung and pulmonary vascular disease (1, 2). As LT has become increasingly accepted, the demand for donor lungs has increased and now far exceeds the number of organs available (3). Consequently the number of patients awaiting LT is increasing (3, 4). Once listed for transplantation, the median waiting time before surgery in the United States has nearly doubled in the last 6 yr (3, 4) and in some centers in Europe, up to 50% of patients awaiting transplantation will die on the waiting list (5).

Australia is a federation consisting of six states and two territories. It is a country of large area with a population of 18.6 million (Figure 1) (6). Until September 1996, LT was performed in only two states. As a result there are often large distances (up to 2,000 miles) between the donor and transplant center with often very long organ ischemic times (7). Despite this obvious impediment to transplantation and historically low organ donation rates, lung and heart–lung transplantation in Australia has been characterized by the highest published transplantation rates (7, 8).

The lung donor offer rate in Australia between January 1, 1995 and December 31, 1997 was 10.5/million population/yr (8) which compares poorly to the United States (13/million population/yr) (3) and parts of Europe (21/million population/yr) (9). On the other hand, over the same period, in Australia 241 people received a lung transplant (4.6/million/yr) (8) which compares favorably with lung transplantation rates in the United States (3.7/million/yr) (3) and Europe (3.1/million/yr) (9). The most likely explanation is that in Australia, there is a greater utilization of those donors offered for lung transplantation.

Donor organs have been judged suitable for transplantation on historically based, largely arbitrary criteria and not based upon strict scientific evidence (10). The current published criteria have been revised from those that were originally more rigid (11) and, given ongoing refinements in the

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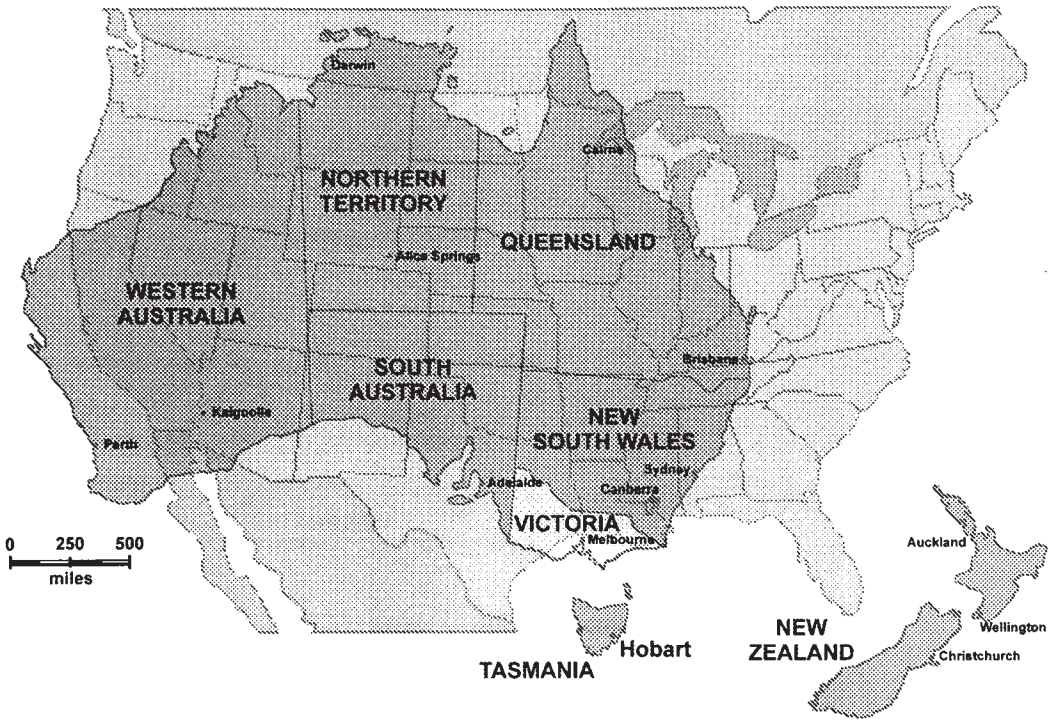

Figure 1. Scale map of Australia and New Zealand in comparison to the United States illustrating distances between the larger cities. Until September 1996, lung transplantation was performed only in Melbourne and Sydney.

management of lung transplant recipients, possibly remain conservatively biased (12). Additionally, both the etiology (e.g., trauma) and the consequence (e.g., aspiration) of brain death may result in deteriorating pulmonary function rendering lungs unsuitable for transplantation. As a result, lungs in many centers have been judged suitable for transplantation from only 10 to 20% of cadaveric donors (13). Overall in Australia, lungs are procured from 33% of cadaveric donors (8).

Our approach to maximizing organ utilization is outlined in Table 1 and includes encouragement to refer marginal donors; early discussion with the intensivists at the donor hospital; assessment in person by the transplant physician; and interventions including fluid management, fiberoptic bronchoscopic toilet of airways, antibiotics, alteration of ventilatory parameters, initiation or increase of positive end-expiratory pressure (PEEP), and physiotherapy. Further, on many occasions, we have applied liberal selection criteria for organ utilization.

This study reviews our experience with the use of marginal donors and aggressive donor management, giving particular emphasis to effects of this strategy on transplantation rates and results.

TABLE 1

APPROACH TO DONOR UTILIZATION AT THE ALFRED HOSPITAL

1. Encourage referral of marginal donors
2. Transplant respiratory physician contacts donor ICU and
   - Reviews clinical course, especially pulmonary secretions
   - Assesses reversibility of donor lung dysfunction
   - Discusses donor optimization
3. Assess donor in person
4. Therapeutic manipulation and reassessment of donor arterial blood gas
5. Select appropriate recipient(s) including backups
6. Marginal donors used if:
   - Ischemic time not extended
   - Recipient prognosis poor and unlikely to be transplanted otherwise
   - Bilateral recipient
   - Single lung recipient if clear unilateral lung dysfunction

METHODS

Australia has developed a system of donor organ procurement which is somewhat different from that used in North America (14). Initial identification of potential donors is most commonly made by intensive care unit (ICU) staff, interestingly with 30% of donors resulting from an initial direct approach by the donor's family. Once the family's consent is obtained, the ICU staff contact a "donor" coordinator who is responsible for confirming the documentation of brain death and detailing the status of the potential organ donor (14). If deemed potentially suitable, the entire donor heart–lung block is offered to the pulmonary "recipient" coordinator of the transplant unit in the same state, or for those states that do not have a transplant unit, to interstate units on a strict rotational basis. At the time of first contact, the pulmonary coordinator records details that include smoking and respiratory history, chest X-ray (CXR) findings, donor height and blood group, blood gas results, antibiotic therapy, and sputum volumes. The pulmonary coordinator liases immediately with a pulmonary transplant physician. The transplant center, rather than a central organization determines which recipients will receive the available organs.

For the purposes of analysis, an ideal donor (Group 1) is defined as one who meets all criteria in Table 2. A marginal donor (Group 2) is defined as one who did not meet one or more of the listed criteria. Group 3 is a subgroup of Group 2 where, at the time of referral, one of the exclusion criteria not met was a ratio of partial pressure of oxygen in arterial blood to fraction of inspired oxygen ($Pa_{O_2}/F_{I_{O_2}}$) < 300 mm Hg on 5 cm of PEEP.

An abnormal CXR is one in which there was a pulmonary opacity other than minor atelectasis, pneumothorax, or pleural effusion. Evi-

TABLE 2

STANDARD LUNG TRANSPLANT DONOR CRITERIA (10)

Age $<$ 55 yr
Clear chest X-ray
$Pa_{O_2}/F_{I_{O_2}}$ ratio $>$ 300 mm Hg on $F_{I_{O_2}}$ of 1.0, PEEP 5 cm H_2O
Absence of chest trauma
No evidence of aspiration, sepsis, or purulent secretions at bronchoscopy
Sputum or bronchoalveolar lavage Gram stain free of bacteria, fungus, and significant numbers of white cells
Smoking history of $\leqslant$ 20 pack-years

dence of infection is defined as the presence of purulent secretions and/or bacteria or fungi and white cells on the Gram stain of the bronchial washings or tracheal aspirate.

Our approach to donor utilization is summarized in Table 1. We regularly communicate with ICU staff and "donor" coordinators requesting to be notified of all donors who potentially may be suitable for lung transplantation, regardless of strict compliance with published criteria. As is our standard practice, the pulmonary transplant physician directly contacts the donor ICU medical (and/or nursing) staff to gain more detailed information regarding the donor including their clinical course, the amount, color and consistency of secretions and to assess potential reversibility of any lung dysfunction. This allows discussion of how best to optimize donor lung function. Ventilator settings, X-ray findings, antibiotic therapy, physiotherapy, suctioning protocols, and fluid management are discussed as appropriate. Personal explanation of the criteria for lung acceptability, particularly preparedness to assess and use nonideal pulmonary donors, commonly generates renewed enthusiasm to achieve organ donation among those who work in the critical care area. Clearly any discussions have to be handled in a sensitive manner, mindful of local issues and resources.

In the majority of cases, the donor is reviewed in person by the transplant pulmonary physician. A bronchoscopy is performed at the earliest opportunity to: assess the anatomy; assess the possibility of aspiration (evidence of a foreign body or presence of blood or other material entering the lower airways from above); assess the extent of secretions; perform airway toilet; and provide microbiological specimens. Blood gases are commonly repeated several times to assess the result of interventions and determine trends.

After the initial assessment and discussion with ICU staff, several potential recipients including backups are selected. Following reassessment, a final decision as to how to utilize the heart–lung block is made based upon a balance of recipient and donor factors. Marginal donors are usually used on the following provisos: the ischemic time is less than 6 h; a bilateral recipient is otherwise suitable and his or her prognosis is poor with a low likelihood of being transplanted otherwise. Occasionally, where there is marked unilateral donor lung dysfunction (e.g., due to trauma), a single lung transplant using the contralateral lung is performed.

Donor selection, donor/recipient matching, and surgical techniques are described elsewhere (15, 16). Donor organ procurement and preservation were standardized. For donor lungs, prostacyclin (Flolan; Wellcome, Sydney, Australia) was infused at 40 to 80 ng/kg/min for approximately 10 min intravenously and 4 to 6 L of cold modified Euro-Collins solution was administered at a pressure of 40 cm water through a cannula into the main pulmonary artery. The donor trachea was stapled after the lungs were inflated with 100% oxygen at a pressure of 5 cm water. Donor lungs were immersed into cold modified Euro-Collins solution for transport.

The immunosuppressive protocols used were similar to those reported by other centers (16). Maintenance therapy includes cyclosporine (initially to achieve a blood level of 300 to 450 μg/L via parent drug EMIT assay; Syva, CA), azathioprine (1.5 to 2 mg/kg/d), and prednisolone (maintenance 0.15 mg/kg/d). Surveillance bronchoscopies were performed at 0.5, 1, 2, 3, 6, 9, 12, 18, and 24 mo as well as yearly thereafter. Nonroutine bronchoscopies were performed for appropriate clinical indications. Acute rejection was defined and treated according to standard criteria (15, 16). Chronic rejection (= bronchiolitis obliterans syndrome) was treated with pulsed intravenous steroids and anti-thymocyte globulin (Atgam) (500 to 1,000 mg/d for 5 d aiming for an absolute CD3 count below 100 cell/μl) (17).

Infection prophylaxis was undertaken routinely. Intravenous antibiotics, covering known or suspected recipient and donor organisms, were initially given to all recipients post-transplant. All patients received long-term prophylaxis for *Pneumocystis carinii* with low-dose oral trimethoprim–sulfamethoxazole or its equivalent. Cytomegalovirus (CMV) prophylaxis was undertaken with intravenous ganciclovir 10 mg/kg/d for 2 wk followed by 5 mg/kg/d 3 times a week for 10 wk in CMV serologically positive donors and/or recipients. Recipient negative, donor positive serological mismatches additionally received 3.6 gm intravenous CMV hyperimmune globulin (Commonwealth Serum Laboratories, Parkville, Australia) on Days 0, 1, 2, 7, 14, and 28. Persistent colonization by *Aspergillus* species on routine bronchoalveolar lavage specimens was treated with oral itraconazole.

Statistical Analysis

Data are expressed as mean (± SEM) unless otherwise indicated. Comparisons between Group 1 and the other two groups (Groups 2 and 3) were made using Fisher exact test for categorical variables, the unpaired Student's *t* test for parametric continuous data, and the Mann-Whitney test for nonparametric continuous data. Correction for multiple testing (Tukey) was made. To determine factors that predicted a favorable outcome, regression analysis was performed with recipient $Pa_{O_2}/F_{I_{O_2}}$ ratio on return to ICU immediately after transplantation as the dependent variable. Survival differences were checked for significance by the rank log test. A significant difference was defined by $p < 0.05$.

TABLE 3

DONOR OFFERS STRATIFIED ACCORDING TO UTILIZATION (JANUARY 1, 1995–MAY 31, 1998)

Total number of donors offered to Alfred Hospital	219
Total number of donors utilized at Alfred Hospital	112 (51%)
Marginal donors used	64
Ideal donors used	48
Total number of donors offered to Alfred Hospital utilized at another transplant center	6
Total number of donors offered to Alfred Hospital that were used	118 (54%)
Total number of donors not used	101 (46%)

TABLE 4

REASONS DONOR LUNGS NOT USED FOR TRANSPLANTATION AT ALFRED HOSPITAL

Total	107*
Logistics	19 (18%)†
$Pa_{O_2}/F_{I_{O_2}}$ ratio $<$ 300 mm Hg on $F_{I_{O_2}}$ of 1.0	51 (48%)‡
Abnormal CXR	38 (36%)§
Collapse/consolidation	17
Hydropneumothorax	17
Pulmonary edema	8
Infection	20 (19%)
Pulmonary	14
Hepatitis B antigen–positive	3
HIV-positive	1
Hepatitis C antibody–positive	2
Smoking history $>$ 20 pack-years	7 (7%)
Age $>$ 55 yr old	4 (4%)
Probable renal malignancy	1 (1%)

* Combination of three reasons was present in five donors and combination of two reasons was present in 23 donors.

† Six of these donors were utilized for transplantation at another transplant center.

‡ Includes 12 donors whose gas exchange deteriorated despite resuscitative attempts.

§ Multiple CXR abnormalities were present in four patients.

TABLE 5

IDEAL CRITERIA NOT MET BY UTILIZED MARGINAL DONORS

Total number of marginal donors	64*
Pa_{O_2}/Fi_{O_2} ratio < 300 mm Hg on Fi_{O_2} of 1.0 on initial ABG	20 (31%)
Abnormal CXR	39 (61%)†
Collapse/consolidation ± pleural effusion	21
Hydropneumothorax	11
Pulmonary edema	9
Infection (pulmonary)	24 (38%)
Gram-negative aerobic bacteria	6
Gram-positive aerobic bacteria	16
Anaerobic species	6
Yeasts	4
Smoking history > 20 pack-years	5 (8%)
Age > 55 yr old	4 (6%)

* Combination of three reasons was present in four donors and combination of two reasons was present in 20 donors.

† Multiple CXR abnormalities were present in two patients.

RESULTS

Between January 1, 1995 and May 31, 1998, 219 donor offers were made available to the Alfred Hospital Heart and Lung Transplant Service in Melbourne (Table 3). Of these, lungs were transplanted at the Alfred Hospital from 112 (51%) of whom 64 (57%) were considered marginal in that they did not meet all published criteria for suitable donor organs (10) (Table 2). A greater proportion of donors from within the state of Victoria (local donors) were utilized. Of the total numbers of donors used for transplantation, 60 (out of 92 offered, 65%) were from local donors compared with 52 (out of 127, 42%) who were from another Australian state or New Zealand ($p < 0.05$).

On 107 (48%) occasions, the donor lungs were not used for transplantation at our institution (Table 4). On 19 occasions, the donors could not be used for logistic reasons. These included no blood group–compatible recipients (11 donors), positive lymphocytic cross match with the only suitable recipient (four donors), unavailability of ICU beds (three donors), and unavailability of procurement team because of another surgical emergency (one donor). These 19 donors were offered to, and on six occasions used by, another lung transplant center so that in total, lungs were transplanted from 118 (54%) of the 219 donor offers.

Other reasons donors were not used included poor gas exchange in 51 (48%) and abnormal CXR appearance including collapse/consolidation, neurogenic pulmonary edema (in association with normal cardiac function), and large hemopneumothoraces consequent upon trauma in 38 (36%). Evidence of severe pulmonary infection or potential transmissible disease in the donor negated the use of lungs in 20 (19%) donors. A combination of these factors was present in 27 (25%) donors not utilized. Donor age and smoking history were uncommonly given as reasons that a donor was not used; only on two occasions were they the only reason.

At the Alfred Hospital, transplantation was performed from lungs of 112 donors. Of these, 64 (57%) donors were considered marginal in that they did not satisfy the ideal donor criteria. The criteria breached by the marginal donors are listed in Table 5. In 20 cases, the Pa_{O_2}/FI_{O_2} ratio was < 300 mm Hg before any intervention by the procurement team. On all occasions the final Pa_{O_2} on arterial blood gas prior to procurement was ⩾ 300 mm Hg on FI_{O_2} of 1.0 and 5 cm PEEP. Abnormal radiology and presence of infection were the most common criteria not met and in 24 donors, at least two criteria were not satisfied.

We separately analyzed the changes that occurred in the gas exchange of donor lungs before procurement (Figure 2). An arterial blood gas (ABG) on 100% FI_{O_2} and 5 cm PEEP was neither available nor requested in 13 donors whose lungs

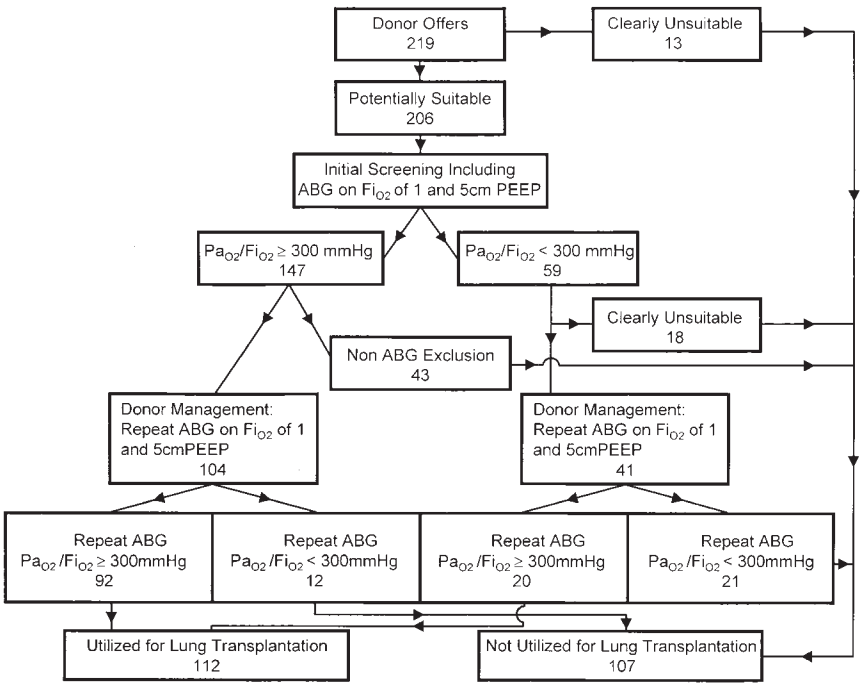

Figure 2. Results of serial arterial blood group analysis in the 219 donors who make up the study group. A final (preexcision) Pa_{O_2}/FI_{O_2} ratio ⩾ 300 mm Hg was a minimal requirement for transplantation.

when first discussed were clearly not usable because of widespread infection or grossly abnormal radiology. ABG was available in 206 donors, in whom the initial Pa_{O_2}/FI_{O_2} ratio was < 300 in 59 (29%). After intervention by the procurement team including physiotherapy, increasing tidal volume and PEEP where appropriate, and bronchial toilet, in 20 (of these 59; 34%), the gas exchange improved to an extent to allow transplantation of the organs (median improvement [range], 87 [37 to 246] mm Hg). Of the 147 donors in whom the initial Pa_{O_2}/FI_{O_2} ratio was ≥ 300, 43 were unsuitable for transplantation for logistic reasons (n = 13); or because of presence of infection (n = 12) and/or markedly abnormal radiology (n = 27). In these, no further blood gases were performed. Of the remaining 104, in 12 (11%), gas exchange deteriorated to an extent that transplantation of these organs was considered inappropriate. In each of these 12, the cause for deterioration in gas exchange (e.g., neurogenic edema, pulmonary sepsis) was evident.

The results from transplantation stratified according to the three donor groups are shown in Table 6 and Figures 3 and 4. Between January 1, 1995 and May 31, 1998, we performed 140 lung transplants. When compared with recipients transplanted from an "ideal" donor there were no differences in the length of ICU stay or 30-d mortality of recipients transplanted from marginal donors or the subgroup in whom donor gas exchange was initially suboptimal (Table 6). In total, 30-d mortality was 6%, which compares favorably with internationally published results (18). The only difference found was that lungs from the subgroup of donors who had an initial Pa_{O_2}/FI_{O_2} ratio of < 300 mm Hg (Group 3) were less likely to be used as single lung transplants when compared with lungs from ideal donors (Group 1; $p < 0.05$). On two occasions, where there was marked unilateral lung dysfunction we performed single lung transplantation of the less affected lung.

Recipient gas exchange from the three groups of donors is shown in Figure 3. The Pa_{O_2}/FI_{O_2} ratio in recipients of organs from ideal donors, marginal donors, and donors with suboptimal gas exchange were, respectively, 245 ± 19, 244 ± 14, and 264 ± 25 mm Hg immediately after transplantation and 245 ± 18, 251 ± 13, and 260 ± 22 mm Hg, 24 h after transplantation. There was no significant difference between Group 1 and the other two groups.

Univariate regression analysis performed with recipient Pa_{O_2}/FI_{O_2} ratio on return to ICU as the dependent variable, revealed that only graft ischemic time was predictive of a favorable outcome ($r = 0.26$, $p < 0.05$). Donor Pa_{O_2}/FI_{O_2} ratio at referral and immediately before explantation and donor age were not predictive of recipient Pa_{O_2}/FI_{O_2} ratio. Multivariate regression analysis was performed with these variables and in addition with the noncontinuous variables, donor smoking history, gender, and presence of radiologic abnormalities or clinical sepsis. Only graft ischemic time was predictive of recipient Pa_{O_2}/FI_{O_2} ratio.

TABLE 6

UTILIZATION OF ORGANS AND RESULTS FROM TRANSPLANTATION IN THE THREE DONOR GROUPS

Donor Group	Number of Transplants*	Number of Single Lung Transplants	Ischemic Time (*min*)‡	ICU Stay (*d*)‡§	30-d Mortality†
Total donors (n = 112)	140	58 (41%)	318 ± 17	8.6 ± 1.8	8 (6%)
Ideal donor (n = 48)	66 (47%)	34 (52%)	324 ± 16	7.8 ± 1.7	5 (8%)
Marginal donor (n = 64)	74 (53%)	24 (32%)	304 ± 22	9.2 ± 1.8	3 (4%)
Suboptimal gases donor (n = 20)‖	22 (16%)	4 (18%)¶	297 ± 13	6.1 ± 2.1	1 (5%)

* Number (% of total transplants).
† Number (% of total of that donor group).
‡ Mean ± SEM.
§ Total days spent in ICU during initial transplant admission.
‖ Donors with initial Pa_{O_2}/FI_{O_2} ratio < 300 mm Hg. This is a subgroup of marginal donor group.
¶ $p < 0.05$ compared with Group 1.

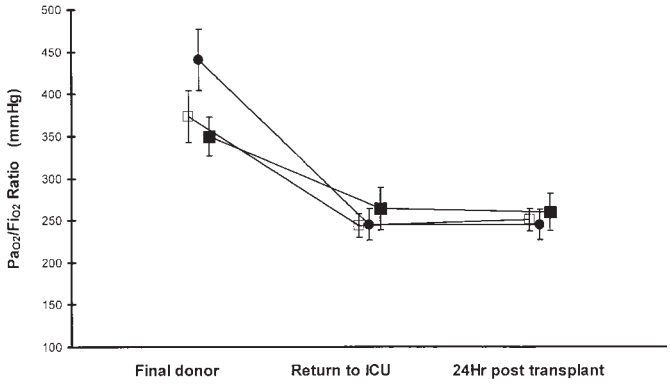

Figure 3. Recipient gas exchange from the three groups (mean, error bars = SEM). Final donor refers to final measured gas exchange before explantation. Return to ICU refers to first measured gas exchange on return to the ICU and 24 hr post-transplant refers to gas exchange 24 h after surgery. Group 1 (*closed circles*) refers to donors who meet all criteria in Table 2. Group 2 (*open squares*) refers to donors who did not meet at least one listed criteria. Group 3 (*closed squares*) is a subgroup of Group 2 where, at the time of referral, one of the exclusion criteria not met was a $Pa_{O_2}/FI_{O_2} < 300$ mm Hg on 5 cm of PEEP.

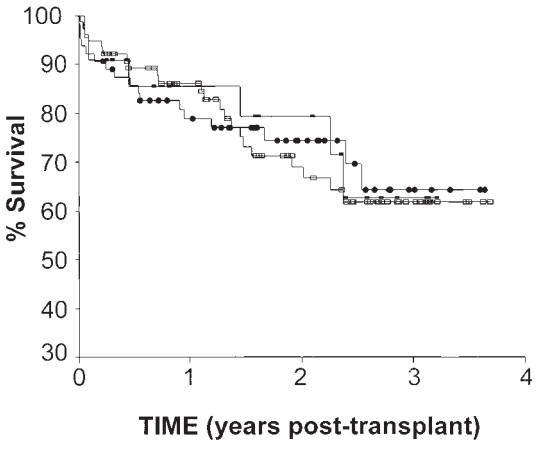

Figure 4. Actuarial percentage survival in the three groups. Group 1 (*closed circles*) refers to donors who meet all criteria in Table 2. Group 2 (*open squares*) refers to donors who did not meet at least one listed criteria. Group 3 (*closed rectangles*) is a subgroup of Group 2 where, at the time of referral, one of the exclusion criteria not met was a $Pa_{O_2}/FI_{O_2} < 300$ mm Hg on 5 cm of PEEP. Each mark represents the number of days post-transplant for each patient alive at time of writing. There was no significant difference in the survival curves between Group 1 and the other two groups (rank log test; $p > 0.8$).

The actuarial survival of the three groups is shown in Figure 4. Overall patient survival was 83% (number alive = 88), 70% (n = 42), and 62% (n = 15) at 1, 2, and 3 yr, respectively. Survival for Groups 1, 2, and 3 were, respectively, 78% (n = 36), 87% (n = 52), and 86% (n = 13) at 1 yr; 75% (n = 20), 67% (n = 22), and 78% (n = 7) at 2 yr; and 64% (n = 7), 61% (n = 8), and 62% (n = 3) at 3 yr. There was no significant difference in survival between Group 1 and the other two groups ($p > 0.8$ by rank log test).

DISCUSSION

Although there remains a greater demand than availability of donor organs and patients die awaiting lung transplantation, it is imperative to explore ways in which transplantation rates can be increased. Despite intense community education programs, cadaveric organ donation has not increased substantially (3, 8, 9). In Australia, cadaveric donor organ donation rates are particularly poor and we have lessons to learn from the rest of the world (19). Potential donor organ rates are low, in part because of low mortality from motor vehicle accidents and gun shot wounds and because of reducing frequency of hypertension-related cerebral events. However, failure to initiate ventilatory or hemodynamic support and refusal of permission by next of kin are important factors (20). In this setting, it is imperative to maximize opportunities presented to the recipient retrieval team.

By direct transplant physician contact with the ICU staff, followed by therapeutic manipulation and reassessment, and by applying liberal criteria for donor utilization, 51% of lung donor offers were ultimately used for transplantation at the Alfred Hospital. This compares favorably with the proportion of lung donors used in the United States and Europe (13, 21). We believe that these donor utilization rates reflect our overall approach to donor utilization (Table 1) rather than any one factor. Specifically, we performed 74 lung transplants from 64 donors who at initial assessment did not meet published criteria. This represented 53% of patients receiving transplantation at our institution. The use of these marginal donors did not adversely affect results from transplantation. There was no difference between recipients of lungs from ideal donors compared with marginal donors in terms of length of ICU stay, postoperative gas exchange (both immediately and 24 h after transplantation) nor short- and medium-term mortality. We chose these parameters to enable us to identify if the use of marginal lungs would be associated with deleterious results.

Superficially, it might appear that lungs were transplanted from some donors who did not meet certain criteria yet not from others who breached the same criteria. This is because in those donors not utilized, the severity of dysfunction was greater.

For all donors utilized, only graft ischemic time was found to be predictive of recipient Pa_{O_2}/FI_{O_2} ratio. The presence of pulmonary sepsis, radiologic abnormalities, and/or poor gas exchange in the donor was not predictive. However, some donors with these abnormal criteria were considered unsuitable for transplantation and therefore the presence of donor sepsis and/or lung collapse remains an important consideration in deciding if a transplant should go ahead. However, the implication from our findings is that provided the abnormalities are mild and the ischemic time is not prolonged, then such donors can be safely used for transplantation.

Donors are felt to be unsuitable if there is evidence of pulmonary sepsis because of the risk of transmissibility of infection. Zenati and colleagues (22) found that organisms cultured in the donor lung were generally different from those associated with early infections in the recipient. In our study, pulmonary infections were identified in 24 donors who would otherwise not have been used. Our approach to these donors was to treat the recipient with at least 10 d of appropriate antimicrobial agents based upon sensitivities of the organisms.

Our policy is that a final donor arterial oxygenation of 300 mm Hg on FI_{O_2} of 1.0 with 5 cm PEEP is a minimal requirement for transplantation. Although this figure is a refinement from earlier guidelines, it has nonetheless been arbitrarily chosen. We as well as others (23, 24) have found that the final donor oxygenation was not significantly related to immediate postoperative gas exchange which is more likely to be dependent upon type of transplant, ischemic time, or presence of acute lung injury. Although we did not specifically examine it, these results appear to strengthen the case for further liberalization of donor oxygenation requirements to include a final (before excision) Pa_{O_2}/FI_{O_2} ratio of < 300 mm Hg.

Other units have also found that liberalization of donor criteria did not compromise the successful outcome from lung transplantation. Sundaresan and colleagues (24) compared the results from transplantation of lungs from 44 donors who did not meet published criteria with transplantation from 89 donors who did and found no difference in overall mortality, postoperative gas exchange, and length of mechanical ventilation. The "marginal" donor group included six with $Pa_{O_2} <$ 300 mm Hg, whose use, when analyzed separately, was not associated with a worse outcome. In 1994, Shumway and colleagues reported the results of transplantation at the University of Minnesota from 1986 to 1994 (25). In June 1991, they liberalized their donor criteria, accepting donors of age > 50 yr (but less than 60), Pa_{O_2} of 100 mm Hg on FI_{O_2} of 0.4 and with small pulmonary infiltrates. This policy was not associated with any difference in actuarial survival in the 25 recipients of lungs fitting the liberalized criteria.

We adopted a policy of therapeutic manipulation of donors in an attempt to improve their gas exchange. Resuscitation involved antibiotic therapy in suspected sepsis and physiotherapy, close scrutiny and adaptation of fluid balance, increases in tidal volume and PEEP, and bronchial toilet to remove secretions and reduce atelectasis. Resuscitation was attempted in all donors who might otherwise not have been suitable for transplantation.

We examined changes in donor gas exchange to quantify the effects of this resuscitation approach. In 20 donors (out of 59 [34%] with an initial Pa_{O_2}/FI_{O_2} ratio of < 300 mm Hg) there was an improvement in gas exchange to a Pa_{O_2}/FI_{O_2} ratio of ≥ 300 mm Hg.

Our results are in agreement with other individual transplant centers (26) and organ procurement organizations (27) who report a 30 to 100% increase in transplantation rates on adopting a policy of aggressive resuscitation of the brain-dead lung donor. Further, Follette and colleagues (28) have reported that the administration of high-dose steroids after brain death improved oxygenation and increased lung donor utilization.

Our experience and that of others serves to illustrate that brain death is not a static process but is characterized by upregulation of proinflammatory cytokines which may contribute to progressive impairment of gas exchange and the development of multiorgan failure (29). Especially if managed by an ICU inexperienced in donor management, organs can deteriorate rapidly after brain death. Conversely, a large number can be "salvaged" by a rational approach to organ resuscitation.

We have tended to avoid performing single lung transplantation from lungs of donors with initially suboptimal gas exchange because of a perception that this might compromise

results from transplantation. This contrasts with Puskas and colleagues (30) who have reported the performance of successful single lung transplantation from four donors with unilateral lung dysfunction whose arterial oxygen tensions were between 213 and 300 mm Hg. They found that unilateral assessment of the less affected lung revealed $Pa_{O_2} > 300$ mm Hg enabling utilization of that lung. Our approach generally is that if a recipient is to receive slightly compromised lungs, then he or she would be better served by receiving two lungs than one. On two occasions however, where contralateral lung dysfunction was severe, we performed ipsilateral single lung transplantation without performing unilateral assessment of the ipsilateral lung as suggested by Puskas and colleagues (30).

In summary, between January 1995 and May 1998, by using liberal selection criteria and by a policy of therapeutic manipulation of donors, we were able to transplant 74 patients from 64 donors who on initial assessment did not meet published selection criteria. This policy did not adversely affect results from transplantation. Our experience illustrates what can be achieved by adopting mechanisms that maximize the use of available donor organs. Our approach is not prescriptive but relies on an individual application to each donor and recipient. We strongly agree with Sundaresan and colleagues (24) that clinical judgment is vital in determining the degree of acceptable donor lung dysfunction and in which circumstance the use of suboptimal donors is appropriate. We believe that any move away from a case-by-case approach to donor utilization toward prescriptive (recipe book) criteria will adversely affect transplantation rates and should be viewed with caution.

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