Marginal donor lungs: A reassessment

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Objective: Lung transplantation is limited by the shortage of suitable donors. To overcome this problem, many programs have begun to use *marginal* or *extended* donors after reports suggesting equivalent outcomes with no additional risk. As our use of extended donor lungs increased and our recipient selection criteria expanded, we believed it was appropriate to reevaluate outcomes with extended donor lungs compared with outcomes with standard donor lungs and recipients outside of the currently accepted guidelines.

Methods: We performed a retrospective review of 128 consecutive lung or heart-lung transplants from January 1, 1997, to June 30, 2000. The primary endpoint was 30-day mortality. Donors were considered extended if any one of the following criteria were met: age greater than 55 years, smoking longer than 20 pack-years, presence of chest radiographic film infiltrate, PO_2 of less than 300 mm Hg, or purulent secretions on bronchoscopy. Guideline and nonguideline recipients were defined on the basis of previously published criteria.

Results: Of a total of 123 donors, 63 (51%) were extended. Forty-eight donors failed 1 criterion, 10 failed 2 criteria, and 5 failed 3 criteria. One hundred twenty-eight transplants were performed. The 30-day mortality for the standard donor group was 4 (6.2%) of 65 versus 11 (17.5%) of 63 for the extended donor group ($P = .047$).

Conclusions: Although many extended donor lungs will result in acceptable post-operative function, caution needs to be exercised in the uses of certain extended donor lungs because there seems to be an increased early mortality rate in that group of recipients. Nonguideline recipients appear to have acceptable early mortality, except when they received extended donor lungs.

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Read at the Eighty-first Annual Meeting of The American Association for Thoracic Surgery, San Diego, Calif, May 6-9, 2001.

Received for publication May 14, 2001; revisions requested July 11, 2001; revisions received Sept 7, 2001; accepted for publication Sept 14, 2001.

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J Thorac Cardiovasc Surg 2002;123:421-8

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0022-5223/2002 \$35.00 + 0 12/6/120345

doi:10.1067/mtc.2002.120345

Donor organ availability continues to be a serious problem facing all solid-organ transplants and is particularly serious with regard to lung transplantation.¹ The demand for donor lungs clearly exceeds the supply, and patients continue to die while on waiting lists before a suitable organ becomes available. The donor lung may become injured by the mechanism of death, fluid resuscitation, neurogenic pulmonary edema, aspiration pneumonia, or nosocomial pneumonia. Only about 20% of multiorgan donors ultimately have lungs that are suitable for lung transplantation according to currently accepted criteria. These rigid criteria were instituted in the mid-1980s during the early development of clinical lung transplantation.²

A number of options are available to improve donor availability and to reduce mortality on the waiting list. Epoprostenol (prostacyclin) infusion may prolong survival in patients with primary pulmonary hypertension. Lung volume reduction may provide an alternative or bridge to lung transplantation for select patients with emphysema. A priority system for allocating organs will help the neediest recipients receive transplants before more stable patients on the waiting list. Such a priority system may improve overall survival on the waiting list for the entire group of

TABLE 1. Criteria used to define extended donors

	Age >55 y	Smoking >20 pack-years	CXR infiltrate	Po ₂ <300 mm Hg	Purulent bronchoscopic findings
Extended donor (n = 63)	9	26	41	0	8

CXR, Chest radiograph.

TABLE 2. Donor characteristics

	Standard donor (n = 60)	Extended donor (n = 63)
Donor age (y)	32 ± 14	44 ± 16*
Duration of mechanical ventilation (h)	44 ± 39	60 ± 46*
Ventilation >4 d	2/60	11/63*
Cause of death (n)		
ICH/SAH	32	40
Head injury	28	23
Total donor lung ischemic time (h)	5.3 ± 1.3	5.5 ± 1.7

ICH, Intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

**P* < .05.

patients. Live donors and non-heart-beating lung donors are other options. Social awareness and political or legislative changes have the potential to significantly improve the donor pool. Unfortunately, many of these and other options simply have not alleviated the current donor shortage.

To overcome this donor shortage, some programs have initiated the use of *marginal* or *extended* donors after reports suggesting equivalent outcomes with respect to early morbidity and mortality.³⁻⁵ Others have demonstrated equivalent 1-year pulmonary function and survival with extended donor lungs.⁶ As our own program's use of extended donor lungs increased and our recipient selection criteria expanded, we believed it was appropriate to evaluate our outcomes with these organs compared with outcomes with standard or ideal donor lungs and to compare guideline and nonguideline recipients.

Methods

Between January 1, 1997, and June 30, 2000, data were collected on 128 consecutive lung or heart-lung transplants at the Toronto General Hospital. A retrospective analysis was then performed. Donors were divided retrospectively into 1 of 2 groups: standard or extended. Donors were considered extended if any 1 of the following criteria were met: age greater than 55 years, smoking history greater than 20 pack-years, presence of chest radiographic infiltrate, Po₂ of less than 300 mm Hg on 100% oxygen with 5 cm H₂O positive end-expiratory pressure, or purulent secretions on bronchoscopy. Standard donors fulfilled all of the previously accepted criteria for lung retrieval (ie, age <55 years, smoking <20 pack-years, clear chest radiograph, Po₂ >300 mm Hg, and clear

bronchoscopy).² Donors were assessed by either the lung transplant fellow or the staff lung transplant surgeon from our program.

Donor arterial Po₂ was based on the final donor Po₂ measurement before flushing the lungs. Although some donors had initial Po₂ values of less than 300 mm Hg, after donor resuscitation and management, there were no final Po₂ values of less than 300 mm Hg. Four donors had initial Po₂ values of less than 300 mm Hg. Mucoid secretions on bronchoscopy that could be suctioned clear were considered normal, and those donors were placed into the standard donor group. Only donors with truly purulent secretions were placed into the extended donor group.

The multiorgan donor was managed to maintain euolemia and to avoid excessive fluid administration. We routinely give 2 g of intravenous methylprednisolone (Solu-Medrol; Upjohn, Don Mills, Ontario, Canada) after initial contact with the donor hospital. The lung procurement follows standard procedures, with an antegrade flush through the main pulmonary artery; however, we use a low potassium dextran solution (Perfadex; Vitrolife, Uppsala, Sweden).⁷

Guideline or nonguideline recipients were defined retrospectively by using the "International Guidelines for the Selection of Lung Transplant Candidates."⁸ A subgroup analysis was finally performed, looking at combinations of (1) standard donor plus guideline recipient, (2) standard donor plus nonguideline recipient, (3) extended donor plus guideline recipient, and (4) extended donor plus nonguideline recipient.

The primary end point was 30-day mortality. Secondary end points included 90-day mortality, the ratio of Po₂ to fraction of inspired oxygen (FiO₂) on arrival in the intensive care unit (ICU), and ICU length of stay.

Statistical analysis was performed with the SigmaStat software package (Jandel Scientific, San Rafael, Calif). Comparison between groups was done with the unpaired *t* test for continuous variables or the χ^2 test for categorical variables. Multiple table comparisons were performed with the Mantel-Haentzel test. Data are reported as means ± SD.

Results

For 128 lung or heart-lung transplants, we had 123 donors, of whom 63 (51%) were extended donors. Table 1 outlines the criteria and number for the extended group. There were no donors with a final Po₂ of less than 300 mm Hg. Four donors had an initial Po₂ of less than 300 mm Hg, but no deaths occurred in this group. Forty-eight of the 63 extended donors failed to satisfy only 1 criterion. Ten extended donors failed to satisfy 2 criteria, and 5 extended donors failed to satisfy 3 criteria.

TABLE 3. Recipient characteristics

	Standard donor	Extended donor
Age (y)	47	46
Age ≥65 y (n)	8	4
Sex (M/F)	41/24	23/40*
Underlying diagnosis (n)		
COPD	16	22
CF		
<i>B cepacia</i> negative	9	6
<i>B cepacia</i> positive	5	9
IPF	17	12
Pulmonary hypertension	10	6
Other	8	8
Type of transplant (BLT/SLT/HLT)	50/12/3	57/6/0

COPD, Chronic obstructive pulmonary disease; CF, cystic fibrosis; IPF, idiopathic pulmonary fibrosis; BLT, bilateral lung transplant; SLT, single lung transplant; HLT, heart-lung transplant.

* $P < .05$.

Table 2 compares several clinical variables between the 2 groups of donors. The mean donor age was older in the extended donor group (44 vs 32 years, $P = .0001$). The duration of mechanical ventilation before retrieval was also significantly longer in the extended donor group (60 vs 44 hours, $P = .025$). In addition, the proportion of donors ventilated for greater than 4 days was higher in the extended donor group ($P = .024$). Cause of death was similar between groups ($P = .337$). The total ischemic time of the donor lung or lungs was not different between groups ($P = .399$).

There were 18 single lung transplants, 107 bilateral lung transplants, and 3 heart-lung transplants. Table 3 shows the recipient characteristics. All 3 heart-lung recipients received standard donor lungs. One of the bilateral lung transplants was a split left donor lung lobar transplant in a small patient with pulmonary fibrosis (extended donor). One bilateral lung transplant was combined with a liver transplant for cystic fibrosis (standard donor), and 1 single lung donor also received a coronary artery bypass (standard donor). One bilateral lung transplant was a retransplant for chronic rejection in a patient with cystic fibrosis (standard donor). One bilateral lung transplant was a left upper lobe transplant with a complete right lung transplant (extended donor).

Cardiopulmonary bypass was used in 16 (25%) of 65 recipients from standard donors and 24 (38%) of 63 recipients from extended donors ($P = .172$). Our policy is to use bypass electively for patients with primary pulmonary hypertension or Eisenmenger syndrome. We also used cardiopulmonary bypass for patients with prior pneumonectomies and for heart-lung transplantation. Collectively, these were considered planned pump cases. All other situations were considered unplanned pump cases. Cardiopulmonary bypass was used selectively for all other indications, depending on intraopera-

TABLE 4. Nonguideline recipients (37/128 [29%])

Criteria	No.
Age	19
<i>B cepacia</i>	14
CABG + transplant	1
Retransplant	1
Malignancy (BAC)	1
Liver-lung transplant	1

BAC, Bronchoalveolar carcinoma; CABG, coronary artery bypass graft.

TABLE 5. Recipient outcome: Standard versus extended donors

	Standard donor	Extended donor
30-Day mortality	6.2% (4/65)	17.5% (11/63)*
90-Day mortality	7.7% (5/65)	22.2% (14/63)*
First PO_2/FiO_2 ratio (mm Hg)	374 ± 143	358 ± 131
ICU length of stay (d)	10.5 ± 16.0	8.4 ± 12.5

* $P < .05$.

TABLE 6. Recipient outcome: Subgroups 30-day mortality

	30-Day mortality
Standard donor + guideline recipient	6.5% (3/46)
Standard donor + nonguideline recipient	5.3% (1/19)
Extended donor + guideline recipient	15.6% (7/45)
Extended donor + nonguideline recipient	22.2% (4/18)

tive factors. There were 7 (11%) of 65 unplanned pump cases in the standard donor group and 13 (21%) of 63 unplanned pump cases in the extended donor group ($P = .196$).

The only recipient factor that was significantly different between the 2 groups was the sex distribution. There were more male patients (63%) in the standard donor group and more female patients (63%) in the extended donor group ($P = .005$). Recipient age and diagnosis was not different between groups.

Table 4 shows the number of nonguideline recipients. Twenty-nine percent were nonguideline recipients, mostly because of older age or colonization with *Burkholderia cepacia*.

Table 5 shows the results of 30-day mortality, 90-day mortality, first PO_2/FiO_2 ratio on arrival in the ICU, and ICU length of stay. The 30-day mortality rate for the extended donor group was significantly higher than that for the standard donor group (17.5% vs 6.2%, $P = .047$). The 90-day mortality was 5 (7.7%) of 65 in the standard group and 14 (22.2%) of 63 in the extended group ($P = .0391$). There was no significant difference between groups with respect to

TABLE 7. Standard donor deaths within 30 days (n = 4)

Patient No.	Age (y)	Sex	Diagnosis	Cause of death	Date of death (d)	Extended criteria	Donor-related death?
1	54	M	α_1	CAD/CHF	1	Standard	No
2	52	F	IPF	Intraoperative arrest/CAD	0	Standard	No
3	55	F	IPF	PE	4	Standard	No
4	65	M	α_1	Cardiac arrest	12	Standard	No

α_1 , α_1 -Antitrypsin deficiency; CAD, coronary artery disease; CHF, congestive heart failure; IPF, idiopathic pulmonary fibrosis.

TABLE 8. Extended donor deaths within 30 days (n = 11)

Patient No.	Age	Sex	Diagnosis	Cause of death	Date of death (d)	Extended criteria	Donor-related death?
5	38	M	PPH	Sepsis, <i>Serratia</i> species	14	CXR	No
6	33	M	CF, <i>B cepacia</i>	Sepsis	9	Age	No
7	42	F	CF, <i>B cepacia</i>	Sepsis	18	CXR	No
8	27	M	CF, <i>B cepacia</i>	Intraoperative arrest	10	CXR, PB	Yes
9	55	F	Sjogren syndrome	Sepsis, <i>Pseudomonas</i> species	2	Smoke	No
10	45	M	IPF	Reperfusion injury (right SLTx)	7	CXR	Yes
11	23	F	CF	Intraoperative arrest, brain death	11	PB	Yes
12	45	F	IPF	Reperfusion injury	1	CXR	No
13	64	M	IPF	Cardiogenic shock	9	CXR	Yes
14	43	F	PPH	Reperfusion injury	1	CXR, smoke	Yes
15	29	F	COPD	Reperfusion injury	2	CXR, PB	Yes

PPH, Primary pulmonary hypertension; CXR, chest radiographic infiltrate; CF, cystic fibrosis; PB, purulent secretion on bronchoscopy; IPF, idiopathic pulmonary fibrosis; smoke, >20 pack-years smoking history; age, donor age >55 years.

first PO_2/FiO_2 ratio on arrival in the ICU ($P = .4223$) and ICU length of stay ($P = .496$).

There was no apparent difference in the 30-day mortality between guideline (11%) and nonguideline (13.5%) recipients ($P = .208$). Table 6 shows the 30-day mortality for the combination of donors and recipients. None of the subgroup comparisons was statistically significantly different, but the relative risk of death for standard donor plus nonguideline recipient versus marginal donor plus nonguideline recipient was 1.92 ($P = .18$).

A detailed retrospective analysis was carried out on each of the 15 deaths. Although admittedly subjective, we believed that our personal involvement in each case allowed assignment of cause of death to be either definitely donor related, definitely donor unrelated, or possibly donor related. Four deaths occurred in the standard donor group, and 11 deaths occurred in the marginal donor group (Tables 7 and 8). Our consensus opinion was that none of the 4 deaths in the standard donor group was likely related to the donor. Patient 1 died of a perioperative myocardial infarction with unrecognized coronary disease. Patient 2 had a

myocardial infarction on the operating table and could not be weaned from cardiopulmonary bypass. This patient also had unrecognized coronary disease. These 2 deaths resulted in our current policy of performing routine heart catheterization in all patients over the age of 50 years. Patient 3 was doing well postoperatively and died of a sudden massive pulmonary embolism. Patient 4 was doing extremely well and was about to be discharged home when he had an unexpected cardiac arrest, presumably caused by an arrhythmia, on postoperative day 12, resulting in death.

Our joint assessment was that 5 of the 11 deaths in the marginal donor group were explained by factors other than the quality of the donor lung (Table 8). Patient 5 died with nosocomial *Serratia* species-induced pneumonia (non-donor source). Patients 6 and 7 had cystic fibrosis and died of *B cepacia*-induced sepsis, and patient 9 died of a nosocomial *Pseudomonas* species-induced pneumonia (non-donor source). Patient 12 had a split left lung-lobar transplant and died of reperfusion injury. We believe that this was due to hyperperfusion through too small a vascular bed, as has been seen after living-donor lobar transplanta-

tion. The right lung from the same donor was simultaneously implanted into another recipient without complication. The donor radiograph only had mild basal atelectasis that was cleared by the time of procurement. Therefore, we have not assigned this death to the quality of the donor lung. The remaining 6 of 11 extended donor group deaths were believed to be at least partially related to the quality of the donor lung. Thus, 0 of 65 standard donor-related deaths and 6 of 63 extended donor-related deaths remain statistically significant ($P = .033$).

The cause of death in the 6 extended donor lung recipients whose death was believed to be possibly related to the quality of the donor lungs are as follows (Table 8). Patient 8 had an intraoperative cardiac arrest preceded by hemodynamic instability after the left lung graft had been implanted. Emergency cardiopulmonary bypass was instituted, but a combination of cardiac and pulmonary problems ultimately resulted in death on postoperative day 10. Patient 10 had a right single lung transplant for idiopathic pulmonary fibrosis. The donor had an infiltrate-contusion in the left upper lobe related to a motor vehicle accident, and we elected to transplant just the right lung. There was hemodynamic instability while the native right lung was being mobilized; cardiopulmonary bypass was instituted, and the case was completed. The patient had severe reperfusion injury and died on postoperative day 7. Patient 11 had sudden cardiac arrest intraoperatively shortly after reperfusion of the first implanted lung. Open cardiac massage and cardiopulmonary bypass were instituted, but the patient ultimately had profound neurologic injury and died on postoperative day 11. Patient 13 underwent transplantation with the aid of cardiopulmonary bypass. Gas exchange was impaired after weaning from bypass; the patient had ventricular fibrillation and was placed back on bypass. He was weaned a second time, and the chest was closed when hypotension and ventricular fibrillation again developed. Once again, he was placed back on bypass. Ultimately, he was weaned with the aid of an intra-aortic balloon pump. He died on postoperative day 9 of cardiogenic shock and acute lung injury. Patient 14 had severe reperfusion injury immediately and died on postoperative day 1. Patient 15's donor had a motor vehicle accident and had received a massive blood transfusion for a retroperitoneal hematoma. The recipient had severe reperfusion injury and died on postoperative day 2.

There were 3 deaths among 9 patients with cystic fibrosis and positive results for *B cepacia* in the extended donor group and no deaths in 5 patients with *B cepacia* in the standard group. Because *B cepacia* is an independent risk factor for posttransplant mortality, we compared the proportion of patients with *B cepacia* in each group to confirm that they were evenly distributed and found that to be the case. There were 5 of 65 patients with *B cepacia* in the standard group and 9 of 63 in the extended group ($P = .346$).

Discussion

We converted to using low-potassium dextran solution as our lung preservation solution in 1997 after observing superior results compared with those obtained with modified Euro-Collins solution.⁷ At the same time, our use of extended donor lungs significantly increased compared with in previous years, while reports were emerging in the literature suggesting equivalent outcomes with extended donor lungs compared with outcomes with standard donor lungs.^{3,4} It was our impression that we had room to extend both our donor and recipient criteria. Before analyzing these data, our clinical impression was that extended donors did not increase early mortality.

Kron and colleagues³ reported the first series of lung transplants using marginal or extended donor lungs in 1993. They evaluated 11 extended donors and used 10, which amounted to 35% of the total lungs transplanted. One of their 10 extended donor transplant recipients died, for an early mortality rate of 10% in that group. All of their extended donors had been on a ventilator for less than 2 days, and all secretions on bronchoscopy could be easily cleared by suctioning. The mean duration of ventilation in our extended donor group was 60 hours, and 17% of those donors were ventilated for greater than 4 days before retrieval. This prolonged period in the ICU puts the donor at greater risk of nosocomial pneumonia and fluid overload and may partly contribute to the increased early mortality in the extended donor group in our study.

The 1995 report from the Washington University group⁹ is the largest and most detailed series looking at the use of extended donor lungs. They had a total of 133 transplants, 33% of which were performed with extended donors. The majority of their extended donors were defined as such because of the presence of chest radiographic infiltrates. The 30-day mortality was 3.4% in the standard donor group and 0% in the extended donor group, and postoperative ventilation and gas exchange were not significantly different either. They concluded that successful outcomes can be achieved with the use of extended donor lungs. Unfortunately, they did not report the distribution of recipient diagnosis in their article but do suggest that extended donor lungs should be used primarily in recipients with emphysema.

In this study we have applied the same criteria to identify marginal donor lungs as were used by the Washington University group. Obviously, it is difficult or impossible to quantify chest radiographic infiltrates or purulent secretions. That is unfortunate because we believe that these 2 criteria are very important in determining whether a marginal donor will provide a good graft. It is our impression that the most difficult judgment decisions pertain to the chest radiograph, the bronchoscopic findings, and the intraoperative assessment of the donor lung by means of direct inspection and palpation. The experience of the retrieval surgeon is critical

TABLE 9. Deaths with extended criteria per extended criteria

Criteria	Proportion
Smoking >20 pack-years	2/26 (8%)
Age >55 y	1/9 (11%)
Abnormal chest radiograph	8/41 (20%)
Purulent bronchoscopic findings	3/8 (38%)

to a good outcome when using extended donor lungs. During the span of this study period, we began to use lungs with bilateral interstitial edema on radiographs and localized areas of purulent secretions. On one occasion, a left lower lobe pneumonia was excised by means of lobectomy, and only the left upper lobe was transplanted on that side into the recipient, who subsequently did well. On the contrary, patient 15, who died, received lungs from a donor with bilateral infiltrates, purulent secretions, and a significant blood transfusion caused by trauma. This situation clearly represents an extension beyond the limits of *extended*.

Bhorade and colleagues⁶ from Loyola University Medical Center reported their experience with extended donor lungs in 2000. Their criteria for extended donors were slightly different from ours and were as follows: age greater than 55 years, smoking greater than 20 pack-years, presence of chest radiographic infiltrate, donor ventilator time of greater than 5 days, or donor use of inhaled drugs (cocaine or marijuana). There were no purulent bronchoscopic secretions, and all donors had PO₂ values of greater than 350 mm Hg. Most of their extended donors were defined as such because of a smoking history or the use of cocaine or marijuana. Only 7 donors were ventilated for more than 5 days, and only 5 donors had radiographic infiltrates, most of which were believed to be atelectasis. They reported on a total of 113 lung transplants, 52 of which were from extended donors, for an extended donor rate of 46%. The hospital mortality for standard donors was 20%, and that for extended donors was 12%, which was not significantly different. They concluded that liberalization of donor criteria does not affect outcome after lung transplantation. In their study the factor that seems to have the greatest effect on mortality is a donor ventilation time of greater than 5 days, but only 13% of their extended donors were in this subgroup.

Since our program began in 1983, we have performed more than 400 lung transplants, with an overall 30-day mortality of 9%, and 12% of those patients were over the age of 60 years. As our program evolved, we began extending the indications for lung transplantation and accepting patients that did not meet the guidelines proposed by the International Society for Heart and Lung Transplantation

(ISHLT) in 1998.⁸ Our 30-day mortality compares favorably with that of other large and experienced lung transplant programs. Harringer and colleagues¹⁰ from Hannover, Germany, reported their 10-year experience, with a 90-day mortality of 14%, and Meyers and coworkers⁹ reported the St Louis 10-year experience, with an early hospital mortality of 8%. In fact, in their 10-year overall review, the St Louis extended donor use rate dropped to 26% compared with 33% in their study cohort from 1995.

From the cohort (n = 128) included in this study, 29% are nonguideline recipients, as defined by the ISHLT⁸; that is, they are older (n = 19 [15%]) than the guidelines would recommend or are colonized with *B cepacia* (n = 14 [11%]). Our other nonguideline recipients had transplants that required concurrent aorta-coronary bypass, combined liver-lung transplant, or single lung transplantation for bronchoalveolar carcinoma after previous pneumonectomy and wedge resections. One case involved a retransplant for chronic rejection in a patient with cystic fibrosis. Early mortality with these nonguideline recipients did not seem to be increased, at least when standard donors were used (Table 6). There seems to be room to further extend recipient selection criteria, but care needs to be taken not to place organs from truly extended donors into high-risk recipients. Late outcomes with nonguideline recipients need to be evaluated in the future as our experience with this group increases.

Currently, our program performs primarily bilateral lung transplantations. Eighty-four percent of the transplants in the study cohort were bilateral lung transplants, and the conclusions should probably be restricted to this group of recipients. Moreover, only 1 patient with a single lung transplant died early, and there were only 3 heart-lung transplants, all of which were in the standard donor group.

In this study we found that the use of extended donor lungs at a rate of 51% was associated with a significant increase in early mortality at both 30 and 90 days after lung transplant. Most of the deaths occurred within 30 days. Early 30-day mortality was 6.2% in the standard donor group and increased to 17.5% in the extended donor group. We do believe that extending the criteria for lung donation is justified and safe; however, the limits are difficult to define, particularly with respect to subjective indexes such as the chest radiographic and the bronchoscopic findings. It may be that a marginal donor rate of 51% is too high, especially with certain higher risk recipients.

Theoretically, an aggressive policy of donor assessment and use should result in a decrease in waiting time on the list and decreased deaths on the waiting list. It may also allow for expansion of recipient criteria. However, it does not seem ethically justified to use an extended donor if the waiting list is short or if the patients are not rapidly deteriorating on the list. If a transplant program has a fairly large donor pool, then this may be the case; however, for most

programs, the waiting list is long and the donor pool is small, limited, or both. In this situation it seems justified to use an extended donor lung in certain circumstances.

What defines *extended* is a weakness of the currently accepted criteria. Most extended donor lungs will function well. Unilateral infiltrates, basal or dependent atelectasis, and mucoid secretions suctioned out completely almost always result in good graft function. Identification of these particular situations depends on the clinical experience of the retrieval surgeon and hands-on inspection in the donor operating room. Donor age by itself has also not been a problem in our experience and, in our opinion, is a less important criterion.

Most worrisome are the bilateral infiltrates or truly purulent secretions. Although the majority of extended donor lungs will function adequately, it is this subgroup that seems to have the highest risk of death (Table 8). We examined the number of deaths with an extended criteria per extended criteria to get some numeric sense of the risk contained in each criteria (Table 9). Admittedly, a multivariate regression with each donor criteria as an independent variable would be the most powerful analysis. Unfortunately, because of the small number of deaths, which is more important than the total number of patients, we were unable to examine this rigorously. However, purulent secretions on bronchoscopy and an abnormal chest radiograph seem to predict mortality.

Currently, we continue to use extended donor lungs but not those with bilateral infiltrates or truly purulent secretions. We strongly favor standard donors for single lung transplantation, heart-lung transplantation, and other complex or redo cases. We also favor standard donors for recipients with pulmonary hypertension, pulmonary fibrosis with secondary pulmonary hypertension, and cystic fibrosis with *B cepacia* colonization. The increased mortality with *B cepacia* is well recognized,¹¹ but whether early extubation and movement out of the ICU will reduce this is not known.

Our recipients seem relatively evenly matched in the 2 groups with respect to age and underlying diagnosis; however, there were significantly more female subjects in the extended donor group. It is unclear why this is the case. Perhaps because of smaller absolute lung size in female subjects, we were more likely to use an extended donor for fear that another donor of appropriate size would not come along soon enough, especially in rapidly deteriorating patients. Ultimately, the balance of male to female subjects is even when looking at the mortality in each group (Table 7 and 8).

In summary, many extended donor lungs will result in a good outcome after transplantation; however, extended donor use can result in increased early mortality compared with that with standard or ideal donors. Extended donors should be assessed by an experienced lung transplant surgeon, particularly if plans exist to use that lung in a higher

risk recipient. Donors with bilateral infiltrates not related to atelectasis, frankly purulent secretions, or both, should be used with extreme caution. Extended donor age and smoking history do not seem to affect early outcome but may play a role in late functional results. Further work is needed to define the limits for extended donors, and these limits may change as lung preservation techniques are improved.

References

1. Trulock E. Lung transplantation. *Am J Respir Crit Care Med*. 1997; 155:789-818.
2. Sundaresan S, Trachiotis G, Aoe M, Patterson G, Cooper J. Donor lung procurement: assessment and operative technique. *Ann Thorac Surg*. 1993;56:1409-13.
3. Kron I, Tribble C, Kern J, Daniel T, Rose C, Truweit J, et al. Successful transplantation of marginally acceptable thoracic organs. *Ann Surg*. 1993;217:518-24.
4. Sundaresan S, Semenkovich J, Ochoa L, Richardson G, Trulock E, Cooper J, et al. Successful outcome of lung transplantation is not compromised by the use of marginal donor lungs. *J Thorac Cardiovasc Surg*. 1995;109:1075-80.
5. Shumway S, Hertz M, Petty M, Bolman R. Liberalization of donor criteria in lung and heart-lung transplantation. *Ann Thorac Surg*. 1994;57:92-5.
6. Bhorade S, Vigneswaran W, McCabe M, Garrity E. Liberalization of donor criteria may expand the donor pool without adverse consequence in lung transplantation. *J Heart Lung Transplant*. 2000;19: 1200-4.
7. Fischer S, Matte-Martyn A, DePerrot M, Waddell T, Sekine Y, Hutcheon M, et al. Low-potassium dextran preservation solution improves lung function after human lung transplantation. *J Thorac Cardiovasc Surg*. 2001;121:594-6.
8. Maurer J, Frost A, Estenne M, Higenbottam T, Glanville A. International guidelines for the selection of lung transplant candidates. *J Heart Lung Transplant*. 1998;17:703-9.
9. Meyers B, Lynch J, Trulock E, Guthrie T, Cooper J, Patterson G. Lung transplantation: a decade of experience. *Ann Surg*. 1999;230:362-71.
10. Harringer W, Wiebe K, Struber M, Franke U, Niedermeyer J, Fabel H, et al. Lung transplantation—10 year experience. *Eur J Cardiothorac Surg*. 1999;16:546-54.
11. Chaparro C, Maurer J, Gutierrez C, Krajden M, Chan C, Winton T, et al. Infection with *Burkholderia cepacia* in cystic fibrosis—outcome following lung transplantation. *Am J Respir Crit Care Med*. 2001; 163:43-8.

Discussion

Dr Michael S. Mulligan (Seattle, Wash). Toronto has long been a source of innovative and significant contributions. It is a privilege to comment on this article. Your very credible skepticism is both timely and important.

I have several questions. First, as you stated, several reports have suggested equivalent outcomes when standard and marginal donors are used. As background for the audience, these series include the 1993 University of Virginia report (although their definition of marginal was more conservative, with a PO_2 of up to 350 mm Hg and ventilator time of less than 2 days), the 1995 Washington University report (perhaps the largest series, which was later commented on by Dr Patterson at the 1999 meeting of the American Surgical Association), the 1999 Australian series (which used the same criteria as you did but also included patients who had yeast on their Gram stain), and finally, the 2000 Loyola series, which defined a marginal PO_2 as less than 350 mm Hg.

Obviously, differences in chest radiographic and bronchoscopic findings are difficult to standardize among series. Lessons learned from one series cannot necessarily be applied to another. Furthermore, no consistent use of marginal donors in recipients with a particular diagnosis could be defined, but most avoided marginal donors for single lung transplants in primary pulmonary hypertension and strongly recommended the use of these donors in emphysematous recipients. Do you think your use in recipients with primary pulmonary hypertension, patients with cystic fibrosis with *B Cepacia* colonization, and even in reduced lung transplants explained your increased mortality in the extended or marginal group?

Second, given that reperfusion injury and acute dysfunction increase major histocompatibility complex II antigen expression and thereby possibly increase susceptibility to acute rejection and obliterative bronchiolitis, do you think that 30-day or even 1-year follow-up is adequate?

Third, in your series only one lung recipient died. Your policy favors double lung transplants. Some argue that with one marginal lung, a double lung is preferred. Others believe that with a single transplant, at least one lung is not vulnerable to reperfusion injury. Can you comment on the use of marginal donors with specific regard to single and double lung transplants?

Finally, in your report and in the series from Barnes Hospital, donor treatment with high-dose methylprednisolone (Solu-Medrol) is recommended. Are you aware of any data that demonstrate a beneficial effect of this practice?

Dr Bryan F. Meyers (*St Louis, Mo*). We have just recently reviewed 550 transplants at Washington University in St Louis and cannot demonstrate that using a marginal donor is an increased risk factor on the basis of survival or the development of acute rejection or bronchiolitis obliterans. I know that the University of Toronto has prior experience with marginal donors that was favorable, and I wonder if you looked at the possibility that this is just a bad run and a statistical aberration in a small number of patients. I noticed that you had an increased number of female donors. Female recipients and certain underlying recipient diagnoses are independent risk factors for early mortality on the basis of the ISHLT database. Do you think it might just be a fluke?

Dr Pierre. I will first address the issue about the female recipients. Female recipients in the ISHLT database are protec-

tive. They have a lower 1-year mortality than male recipients. Why we have more female recipients in our extended recipient group and why that group should have a higher mortality is hard to explain. I tried to address that somewhat, but I do not have a good explanation.

Dr Mulligan, you outlined a number of the previous studies that looked at marginal donor lungs, and I think an explanation as to how our donors and recipients differ would take some time, but your specific questions about the use of extended or marginal donor lungs in higher risk recipients is, I think, very important. My own belief is that I do not think we should be using these lungs in patients with *B cepacia*. I do not know that I can prove that getting the patients extubated and out of the ICU earlier will reduce the incidence of *B cepacia* infection or mortality from *B cepacia*, but patients with *B cepacia* do seem to represent a fair number of the deaths in this series. Therefore, I do think that patients with pulmonary hypertension, redo patients, and other difficult or complicated cases in which high risk might be expected in the perioperative period should probably also receive standard donor lungs or donor lungs that do not have marginal or extended criteria, such as bilateral infiltrates, or any question about the bronchoscopy.

In terms of long-term follow-up, I agree that this is a short-term study looking at 30-day or 90-day mortality. Long-term data will be very important to look at the outcome with respect to extended or marginal donor lungs, particularly when it comes to the other extended criteria, such as advanced donor age or smoking history, and the risk of malignancy will also become an issue.

As far as single lungs go, we do favor using marginal donor lungs in bilateral lung transplantation and avoid them in the use of single lungs. The one patient who died did receive a marginal donor lung for a single lung transplant; the donor lung was marginal because of an infiltrate and a contusion on the left side, and it was the right side that was transplanted. However, that patient obviously did not do well.

Regarding the use of methoprednisolone, there are not a lot of data supporting that. There is one report from Sacramento looking at the retrieval of organs after the administration of methoprednisolone, suggesting that the overall yield in retrieval was increased by the use of preoperative methoprednisolone to the donor.