ANNALS OF SURGERY
Vol. 217, No. 5, 518-524

Successful Transplantation of Marginally Acceptable Thoracic Organs

I. L. Kron, M.D.,* C. G. Tribble, M.D.,* J. A. Kern, M.D.,* T. M. Daniel, M.D.,* C. E. Rose, M.D.,† J. D. Truwit, M.D.,† L. H. Blackbourne, M.D.,* and J. D. Bergin, M.D.†

From the Departments of Surgery and Medicine,† University of Virginia, Charlottesville, Virginia*

Objective

This study evaluates the efficacy of personally inspecting marginal thoracic organ donors to expand the donor pool.

Summary Background Data

The present donor criteria for heart and lung transplantation are very strict and result in exclusion of many potential thoracic organ donors. Due to a limited donor pool, 20–30% of patients die waiting for transplantation.

Methods

The authors have performed a prospective study of personally inspecting marginal donor organs that previously would have been rejected by standard donor criteria.

Results

Fourteen marginal hearts and eleven marginal lungs were inspected. All 14 marginal hearts and 10 of the marginal lungs were transplanted. All cardiac transplant patients did well. The mean ejection fraction of the donor hearts preoperatively was 39 ± 11% (range 15–50%). Postoperatively, the ejection fraction of the donor hearts improved significantly to 55 ± 3% ($p < 0.002$). Nine of the ten lung transplant patients did well and were operative survivors. Our donor pool expanded by 36% over the study period.

Conclusions

The present donor criteria for heart and lung transplantation are too strict. Personal inspection of marginal thoracic donor organs will help to maximize donor utilization.

A proliferation of transplant programs and procedures has resulted in a well-publicized donor organ shortage.[1] At our own institution, a 20–30% mortality exists in patients waiting for heart or lung transplantation. We developed two hypotheses to be tested. The first was that young trauma victims should not have intrinsic cardiac dysfunction and any dysfunction that did exist was related to the neurologic insult. The second hypothesis was that mild pulmonary dysfunction was common in potential lung donors and should be treatable after transplantation. To test these hypotheses, we developed a policy of personally inspecting marginal thoracic organs.

Presented at the 104th Annual Session of The Southern Surgical Association.

Supported in part by funds from the American Heart Association grant 92009290 and the AHA Virginia affiliate grant VHA-VA90G16.

Address reprint requests to Irving L. Kron, M.D., University of Virginia, Health Sciences Center, Department of Surgery, Box 181, Charlottesville, VA 22908.

Accepted for publication January 12, 1993.

Our experience with this policy is the purpose of this study.

METHODS

This is a prospective study of all donors used on the University of Virginia Cardiothoracic Transplant Service between 1990 and 1992. Heart donors were considered marginal if there was evidence of cardiac dysfunction or segmental wall motion abnormalities before their recovery.[2] Cardiac dysfunction was defined by an ejection fraction ≤ 45% and/or a significant segmental wall motion abnormality using standard two-dimensional echocardiographic criteria. All donor echocardiograms were performed and interpreted by the cardiologist at the referring hospital. These donors were considered acceptable at the time of inspection if there was no obvious reason for this poor function such as the presence of coronary artery disease or cardiac trauma. Criteria for acceptance of these marginal organs under consideration included: 1) minimal requirement of inotropic support (<10μg/kg/min dopamine), 2) normal hemodynamic parameters, 3) viable appearance of the donor heart without evidence of severe cardiac contusion.

The standard criteria for lung donors have been well described by the Pittsburgh Group.[2] These criteria include a normal chest roentgenogram, normal gas exchange (PaO_2 > 400 mm of mercury [mm Hg] on inspired oxygen fraction [FiO_2] of 100%), normal gram stain of tracheal secretions, and a normal bronchoscopy. We considered a lung donor to be marginal with a PaO_2 of less than 350 mm Hg on 100% FiO_2, presence of infiltrates on chest x-ray, or purulent secretions on bronchoscopy. We found these marginal lungs acceptable at the time of donation if the patient had been on a ventilator less than 48 hours and the secretions could easily be cleared by suctioning even if purulent material was present. A gram stain revealing bacteria did not exclude a donor unless there was evidence of gross fungal contamination. If the gram stain revealed bacteria and the donor organ was used for lung transplantation appropriate antibiotics for the culture were used therapeutically in the lung recipient. Minor infiltrates not associated with severe contusion were not a criterion for exclusion.

Statistical Analysis

Paired data were compared by the Student's *t*-test. Statistical significance was achieved if the p value was less than 0.05.

RESULTS

Over the study period, 62 heart transplants, 26 lung transplants, and 2 heart-lung transplants were performed. Fourteen marginal hearts were examined (23% of the total number of heart transplants) and all 14 were found to be acceptable for transplantation. All marginal hearts had echocardiographically proven wall motion abnormalities or low ejection fractions (EF) noted before organ recovery (Table 1). The mean ejection fraction of the donor hearts was 39 ± 11% (range 15 to 50%) before organ recovery. All heart donors were on less than 10 μg/kg/min of dopamine and all hearts were believed to have adequate contractility and hemodynamics at the time of inspection during the recovery. All marginal heart transplant patients did extremely well, with only one patient requiring more than 3 days inotropic support postoperatively. The mean ejection fraction for the group transplanted with marginal hearts improved to 55 ± 3% by the seventh postoperative day ($p < 0.002$). There was no hospital or long-term mortality in any of these patients, and none showed any evidence of impairment in function at follow-up echocardiography (EF 55 ± 3% on postoperative day 30). At postoperative catheterization, hemodynamic measurements were within the normal range (Table 1).

Eleven marginal lungs blocks were inspected, and ten (35% of total lungs transplanted) were used for transplantation. The one lung excluded was related to severe pulmonary contusions noted at the time of inspection. The specific details related to the lungs are listed in Table 2. Nine of the ten patients who underwent transplantations did well and survived the operative procedure. One patient with pulmonary hypertension died of reperfusion injury and Pseudomonas pneumonia after a single lung transplantation. This organism was not cultured from the donor preoperatively. There was one late death in this group due to cytomegalovirus pneumonitis 4 months postoperatively in a heart-lung recipient. There were six preoperative infiltrates noted in the marginal lung donors. All infiltrates had cleared by the third post-transplantation day (Fig. 1).

DISCUSSION

The major aim of transplantation is to avoid using an inferior organ in a critically ill patient awaiting transplantation of their heart or lung. Donors by definition are unstable due to their previous trauma or due to the physiology related to severe head injury. DePasquale stated the concept well in an editorial, "Certainly it makes little sense to replace one diseased heart with another."[4] The difficulty is the limited number of donors available. It was hard for us to believe that young patients who had undergone serious head trauma would have abnormal cardiac function unless they were in shock and required extensive resuscitation.

Brain death leads eventually to cardiac death. Taniguchi reported that the average period from cerebral death

Table 1. MARGINAL HEART DONORS

Name	Donor Echo		Recipient Echo			Recipient PCWP		
	LVEF	Wall Motion Abnormality	Day 1	Day 7	Day 30	Day 7	Day 30	Status
PT	45	Anterior/IVS		55	60	6	12	Alive
JD	45	Anterior		55	55	16	15	Alive
JR	45	Global	55	52.5	50	21	20	Alive
JC	30	Anterior	50	55	52.5	22	22	Alive
HV	45	IVS		47.5	55	23	20	Alive
TJ	40	Anterior	45	55	55	6	6	Alive
JB	45	Anterior/IVS	65	60	55	18	14	Alive
CE	45	Global	42.5	57.5	55	9	15	Alive
JD	15	Anterior	35	50	50	24	16	Alive
LB	45	Anterior	50	55	60	13	10	Alive
JB	30	Global	50	55	52.5	20	19	Alive
KH	50	IVS	55	60	55	16	8	Alive
IB	20	Global	45	52.5	60	8	12	Alive
JH	45	IVS/inferior	47.5	55	55	18	18	Alive
Mean	39 ± 11		49 ± 8*	55 ± 3*	55 ± 3*	16 ± 6	15 ± 5	

* $p < .002$, compared with donor echocardiogram.
IVS = interventricular septum; PCWP = pulmonary capillary wedge pressure.

to cardiac arrest was 4.3 days in patients with no hormonal supplementation. However, when hormonal supplementation was used, one could prolong cardiac death to 11.5 days.[5] Histologic changes in the heart may occur after neurologic injury. And that possibly these changes may be mediated by alterations in the autonomic nervous system.[6] Novitzky has studied this concept extensively. He studied a baboon model of brain death and found major pathologic changes occur that affect the conduction tissue, smooth muscle of coronary arteries, and the myocardium itself. He suggested that these changes might be preventable with cardiac denervation.[7] Novitzky also noted that myocardial injury in this model could be prevented with verapamil hydrochloride or hormonal therapy with triiodothyronine in both laboratory and clinical investigations.[8–10] Cooper found that normal hearts from non-brain dead baboons were able to be better stored for long-term preservation than those from human brain dead donors.[11] Tixier noted that hearts in an experimental model of brain death were en-

Table 2. MARGINAL LUNG DONORS

Name	Donor Status				Recipient Status
	Aspiration	Bronchoscopy	O_2 Challenge	CXR	
—	No	Clear	457	Infiltrate	Not used*
VT	Yes	Secretions	429	Clear	Alive
VT	No	Secretions	445	Infiltrate	Alive
KK	No	Secretions	445	Infiltrate	Alive
VS	Yes	Foreign body	418	Clear	Expired – late*
BF	No	Not performed	325	Clear	Alive
JL	No	Clear	347	Clear	Alive
RP	No	Secretions	535	Infiltrate	Alive
RJ	No	Secretions	549	Infiltrate	Expired – early‡
JG	Yes	Secretions	370	Infiltrate	Alive
HL	Yes	Secretions	370	Infiltrate	Alive

* Large posterior contusion.
† Cytomegalovirus pneumonitis (day 121).
‡ Pseudomonas pneumonia (day 5).

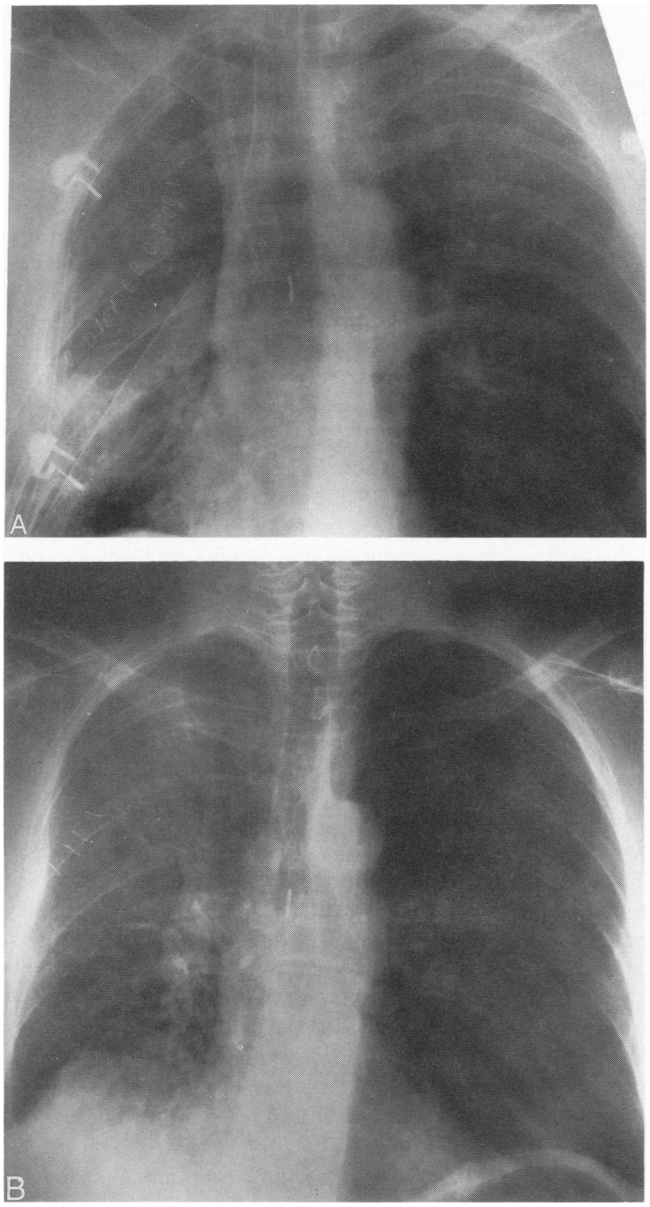

Figure 1. a: Chest X-ray of patient JG 1 day after right single lung transplant. The right middle lobe infiltrate is identical to the donor chest X-ray pre-operatively. b: Chest X-ray of patient JG 3 days after transplant with complete resolution of the right middle lobe infiltrate.

ergy depleted and could be resuscitated with substrate enhancement.[12] Clearly, these observations strongly suggest that brain death has a deleterious effect on the heart, and removing these previously normal hearts from this environment may result in good long-term function. That belief has been confirmed by our clinical experience and the experience of others using different criteria.[13]

The issue with lung donors is different in that there are no known deleterious effects of brain death on lung function other than neurogenic pulmonary edema. Poor lung function has been related to aspiration at the time of cerebral injury, as well as infection due to long-term endotracheal intubation. Heart-lung transplantation was initially carried out at Stanford University, and they developed the early criteria for lung donation. Their criteria were understandably strict and initially only on-site lung donors were used because of the logistics of long-range procurement.[14] Selection criteria for lung donors have continued to be strict, and only 10 to 20% of heart donors are also suitable lung donors.[15,16] The Pittsburgh Group as well as Cooper and colleagues from Toronto developed the modern criteria for acceptable lung donors.[3,17]

We found that we were unable to obtain an adequate supply of lung donors using these criteria. We speculated that as long as the donors' purulent secretions were bacterial they could be treated with antibiotics. Minor infiltrates due to atelectasis and secretions should be treatable postoperatively, and minor abnormalities of gas exchange could be corrected by appropriate fluid and ventilator management.

To date, these speculations have proven to be correct. We have been able to treat all of the bacterial colonization in our recipients with antibiotics matched to cultures obtained from the donor. All infiltrates have disappeared within a few days after transplantation. These lungs have been adequate and far better than the recipients' native diseased lungs. However, we do not know what the limitations are. At this point we would not use a lung colonized with fungal elements because a fungal infection would be a potentially lethal disorder in immunosuppressed patients. We do not know if wet lungs due to neurogenic pulmonary edema can be used and treated. We have not attempted to use lungs with a PaO_2 < 300 mm Hg on 100% FiO_2. However, one can increase the number of lungs used with these more flexible criteria.

In summary, one must be aggressive to gain adequate heart and lung donors. Personal inspection is helpful in determining both heart and lung viability. We have found this to be truly life-saving in that we have expanded our heart and lung donor pool by 36% by this aggressive approach.

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Discussion

DR. FREDERICK L. GROVER (San Antonio, Texas): I certainly enjoyed Dr. Kron's very pertinent and timely presentation and appreciate having been given the opportunity to review this manuscript well in advance of the meeting. Dr. Kron has called our attention to a very critical problem in the area of heart and lung transplantation, the short supply of organ donors. According to UNOS statistics 2,127 heart transplants, 402 lung transplants, and 51 heart/lung transplants were performed in the United States in 1991. As of September 30, 1992, 2,570 patients are on the UNOS waiting list for heart transplants, 937 for lung transplants and 160 for heart/lung transplants reflecting a very significant shortfall in organ availability. Potential solutions to this problem are liberalizing organ donor criteria, increasing donor consent by better education of the public and medical personnel, and by the use of xenografts. Dr. Kron has elected to improve his donor pool by the first option, which is entirely appropriate, by advocating personal inspection of marginal hearts and lungs to see if some of these marginal organs are indeed usable. Since moving to Denver, I've had the opportunity to work with Dr. Michael Bristow, head of our cardiology division, who has been a strong advocate of liberalizing the donor pool for heart donors. Our criteria are even somewhat more liberal in that we will only reject hearts outright which have an echocardiographic shortening fraction of less than 10% which is equivalent to an ejection fraction of 17%, those which show moderate-to-severe structural heart disease or tumor or have significant coronary disease on arteriography. We would also turn down those donors with carbon monoxide poisoning with carboxyhemoblogin levels of greater than 20% and would be concerned about accepting donors with prolonged hypotension of greater than 6 hours, or those requiring more than 20 μg/kg/min of dopamine. We are concerned but would accept hearts with moderate hypokinesis with a shortening fraction on echocardiography of 10 to 25% equivalent to an ejection fraction of 17 to 42%. Using these criteria we've had a 91% 1-year survival rate in our heart transplant program in Denver. For lung donors our criteria both in San Antonio, prior to my moving to Denver, and Denver have been a PO2 of no less than 300 on 100% oxygen, a clear chest x-ray and a patient on a ventilator for 72 hours or less. We have been willing to accept patients with some organisms on sputum stain, excluding fungus, if the secretions could easily be cleared with suctioning and there is no evidence of aspiration. We have accepted patients with evidence of x-ray densities on the contralateral lung if it was thought to be due to contusion. This relatively strict criteria is, in part, responsible for our success in our initial group of lung transplants in Denver. However, now what has happened to Dr. Kron in Charlottesville is happening in Denver — our recipient list is growing. In recent discussions with Dr. Joel Cooper of St. Louis regarding the question of whether we should liberalize our criteria for lung donation for the same reasons as Dr. Kron, Dr. Cooper's group would agree that infiltration on one side is acceptable if the bronchoscopy and x-rays show relatively good clearing of secretions on the side to be used. The presence of organisms on Gram stain is not a contraindication unless there is evidence of overt aspiration or fungus. In addition, Dr. Cooper will accept lungs with a PO2 of less than 300 on 100% O2 if it is thought that the primary cause is pulmonary edema. He has liberalized the age range to 55 years for donors with a maximum 20 pack years of smoking. Our group in Denver and San Antonio as well as the Washington University would agree that one has to be very cautious, however, using marginal lungs in the pulmonary hypertension patients and can probably be the least strict for those patients with chronic obstructive pulmonary disease. Ischemic times of 6 hours have been acceptable and perhaps could even be extended to 7 to 8 hours. Although we have not been willing to accept donors on a ventilator for greater than 3 days, Dr. Cooper's group has taken donors who have been on ventilators up to 7 days. In addition, COPD patients can probably be sized up to 30% under their current lung size and those with pulmonary fibrosis, 30 to 40% larger than their current lung vertical dimensions. I have several questions for Dr. Kron. First, have you liberalized your sizing criteria for both the hearts and the lungs? Second, have you been willing to accept lungs from a patient on a ventilator for longer than 2 days which is quite conservative? Have you considered decreasing your required PO2 to 300 mm/Hg? How