Should lungs from donors with severe acute pulmonary embolism be accepted for transplantation? The Hannover experience

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Lung transplantation has evolved to an accepted treatment modality for patients suffering from end-stage lung disease. The number of listed patients waiting for a lung transplant is dramatically higher than the number of available donor organs, which contributes to a 1-year mortality on the waiting list of approximately 20% and of 40% after 2 years of listing.¹ Many strategies aiming for an increase of donor organs have been discussed controversially and are partially under clinical examination, such as the utilization of lungs from non-heart-beating donors² or the concept of living-related lung transplantation.³ Other approaches to the problem are even more experimental, such as pulmonary xenotransplantation. During the 2003 annual meeting, The International Society for Heart and Lung Transplantation discussed the issue of redefining current lung donor criteria and the concept of using marginal donor organs for selected recipients in a main session. Many groups presented their outcomes following lung transplantation using lungs from donors who were heavy smokers,⁴ from donors with onset of fatal asthma,⁵ or from elderly donors up to 77 years of age.⁶ One major consensus of this intense discussion, however, was that some donors are still considered as inadequate for lung donation, such as patients who show signs of severe pneumonia or aspiration as well as those who died from fulminant pulmonary embolism.

Here, we report on 3 cases in which lung grafts from patients with fatal severe acute pulmonary embolism were successfully transplanted. We further describe a novel strategy of in situ retrograde lung flush perfusion that we are routinely using in our clinical program now, which is of special importance for lung graft retrieval from donors with acute pulmonary embolism.

Clinical Summary

Between January 2001 and March 2003 lung grafts from 3 multi-organ donors who died from hypoxia due to severe pulmonary embolism were allocated by EuroTransplant and offered to our program for transplantation.

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Received for publication May 6, 2003; accepted for publication May 28, 2003.

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J Thorac Cardiovasc Surg 2003;126:1641-3

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0022-5223/2003 \$30.00 + 0

doi:10.1016/S0022-5223(03)00952-8

The first donor was a 21-year-old female who developed sudden cardiac arrest immediately following 24 hours of air traveling from Australia to Europe. Following 30 minutes of cardiopulmonary resuscitation, she was admitted to an emergency hospital and initial screening using computed tomography scanning revealed the diagnosis of a large thrombus occluding approximately 90% of the main pulmonary trunk as well as the left and right main pulmonary artery with signs of right heart dilation. Hemodynamics were stable under catecholamine support. Interestingly, arterial blood gas analysis revealed adequate measures with a PaO_2 of 376 mm Hg and a PaCO_2 of 38.0 mm Hg at an FiO_2 of 1.0. Bronchoscopy showed normal findings with no signs of aspiration or mucus accumulation. No intravenous lysis therapy was initiated. First surgical inspection of the heart revealed severe right heart dilation. The pulmonary artery pressure was not measured.

Donor number 2 was a 17-year-old obese female who also died from hypoxia after cardiopulmonary resuscitation by an ambulance team for sudden cardiac arrest. With signs of right heart failure such as a prominent filling status of the jugular veins, in combination with the obese body constitution, the ambulance physician in charge suspected pulmonary embolism as the underlying initial event and administered intravenous lysis therapy before taking the patient to hospital. With mild catecholamine support at the time of arrival in the emergency hospital, cardiac function was satisfying. At an FiO_2 of 1.0 arterial blood gas analysis showed a PaO_2 of 544 mm Hg and a PaCO_2 of 22.3 mm Hg. First inspection of the right heart at the time of retrieval showed no right heart dilation. Invasively measured pulmonary artery pressure revealed normal parameters.

The third donor was a 26-year-old, also obese, female patient and a heavy smoker who was on a diet for 7 days. She developed sudden cardiac arrest while shopping. Following 20 minutes of cardiopulmonary resuscitation she was admitted to an emergency unit. Under mild catecholamine substitution she was hemodynamically stable. Echocardiography revealed severe dilation of the right atrium and ventricle, suggesting the diagnosis of acute pulmonary embolism. Immediately, intravenous thrombolysis was initiated. After 5 days in the intensive care unit, the patient was diagnosed as brain-dead and she was allocated for multiorgan donation. At the time of retrieval her arterial blood gas analysis showed a PaO_2 of 566 mm Hg at standard ventilation with an FiO_2 of 1.0 and a positive end-expiratory pressure of 5 mm Hg. At first surgical inspection her right ventricle and atrium showed normal contraction patterns. Her systolic pulmonary artery pressure was 28 mm Hg.

Brain death was diagnosed in all 3 donors by 2 independent neurologists following the general guidelines. All 3 recipients were transplanted without cardiopulmonary bypass support. Recipient data are depicted in Table 1. The first recipient's health status was dramatically deteriorated at the time of transplantation. She re-

TABLE 1. Recipient data

Donor no.	Recipient age (y)	Gender	Indication for LuTx	Post-LuTx ventilation time	Post-LuTx ICU stay	Cause of death
1	46	Female	Redo DLTx for chronic graft failure	5 days	6 days	Severe <i>Nocardia asteroides</i> Sepsis 6 months after Tx
2	58	Female	Right SLTx for emphysema	8 days	12 days	Alive, excellent graft function
3	46	Female	DLTx for alpha1-ATD-emphysema	10 hours	1 day	Alive, excellent graft function

LuTx, Lung transplant; ICU, intensive care unit; DLTx, bilateral LuTx; SLTx, single LuTx; ATD, antitrypsin deficiency.

ceived a redo bilateral lung transplant for advanced end-stage graft failure and required intensive care monitoring and treatment pre-transplant. Following redo transplantation her grafts functioned very well, with no signs of clinically relevant reperfusion injury. She recovered rapidly and uneventfully and lived a satisfying life at home until she developed *Nocardia asteroides* pneumonia followed by treatment-refractory fatal sepsis.

The second patient developed mild pulmonary hypertension in the early phase after transplantation and radiographically showed signs of severe reperfusion edema in her transplanted right graft. Therefore, she required extended nitric oxide-supplemented ventilation. During that phase the compliance of her grafted lung was very low compared with that of her native emphysema lung, which required separated ventilation of her lungs with 2 different ventilators. Consequently, weaning from mechanical ventilation was delayed. However, on postoperative day 8 she was taken off the ventilator and recovered without experiencing further complications.

The third patient was extubated 10 hours after transplantation and discharged from hospital on day 13 without any negative event. Both recipients 2 and 3 are alive at home with no need for oxygen administration.

Discussion

The imbalance between the number of patients listed for a lung transplantation and the number of available donor organs has led to extended waiting times after listing and, ultimately, to significant mortality on the waiting list.¹ Consequently, novel strategies to increase the number of donor organs have been discussed and partially introduced into the clinical setting. A first and very important step was the idea of extending the currently accepted criteria for donor selection. Many programs have begun to use marginal or extended donors after reports suggesting equivalent outcomes.

The Toronto group has previously published a first greater retrospective review on 128 consecutive lung and heart-lung transplants of which 51% were grafts retrieved from "extended donors."⁷ In that study by Pierre and coworkers,⁷ donors were considered extended if any one of the following criteria were met: age greater than 55 years, smoking history longer than 20 pack-years, presence of chest radiographic film infiltrate, Pao₂ of less than 300 mm Hg, or purulent secretions on bronchoscopy. From their study they have concluded that although many extended donor lungs will result in acceptable postoperative function, caution needs to be exercised in the use of certain extended donor lungs because there seems to be an increased early mortality rate in that group of recipients. This particular finding underlines the

need for further studies to clearly identify the new borderline for which donor lungs can be accepted for transplantation with a reasonable chance for successful outcome and below which, on the other hand, lungs should be rejected for transplantation. This study further suggests different donor variables such as donor age, bronchoscopic and radiograph findings, time of ventilation prior to organ retrieval, and smoking history, which each can identify a donor as an "extended" donor and which each could possibly be extended to increase the number of transplantable donor organs.

Multiorgan donors who died from hypoxemia due to severe pulmonary embolism, to our knowledge, have never been considered as lung donors in the literature, and further, they have not been mentioned in the whole discussion on the extension of donor criteria in lung transplantation. Since our successful transplantation of the lungs of donor number 1 (described above), who developed severe pulmonary embolism after a long-distance flight, into a patient who was listed for "high urgency" redo lung transplantation for very advanced and life-threatening end-stage chronic lung graft failure, we are now considering such donors as potential lung donors. Especially for the evaluation of these donors we have changed our strategy in that we routinely perform invasive pulmonary artery pressure assessment prior to organ retrieval, which we believe should not extend to a mild degree of pulmonary hypertension. We further would not accept lungs from those donors who show a Pao₂ of less than 250 mm Hg with an adequate ventilatory setup at an Fio₂ of 1.0 and a positive end-expiratory airway pressure of 5 mm Hg. Also, those donors should not extend on other variables such as mild smoking history, older than 55 years of age, or aspiration, to name some.

If no further contraindication for the transplantation of these organs exists, we routinely insert a left atrial pressure catheter into the left atrium through the right upper pulmonary vein to measure the preflush left atrial pressure. For lung flush preservation we use 8 L of a low-potassium dextran (Perfadex, Vitrolife, Göteborg, Sweden) solution that is flushed through the lungs via the retrograde route. For that the left atrial auricle is cannulated and the pulmonary artery is incised at the bifurcation of the left and right main stem. While flushing the lungs the left atrial pressure is continuously monitored and kept at the preflush level by adjusting the height of the solution bag. This prevents, first, the disruption of the smooth postcapillary pulmonary venous vessels by high flush pressures and, second, a volume overload of the left ventricle when the heart is also going to be transplanted. We are convinced that the retrograde lung flush is very essential in donors with pulmonary embolism, as in all 3 donors tremendous amounts of thromboembolic material were retrogradely flushed out of the vasculature through the incision in the pulmonary artery.

In conclusion, we are aware that lung donors who died from hypoxemia due to severe pulmonary embolism are high-risk donors and, thus, should be evaluated for transplantation very carefully. However, they should not be rejected as potential lung donors just by the diagnosis because extended evaluation strategies combined with the opportunity of retrograde flush perfusion might help to ultimately retrieve well-functioning lung grafts, especially for patients who have reached a disease state that may not allow them to wait for the next organ offer. Because there are no reports either on the use of lung grafts from donors with pulmonary embolism nor on evaluation strategies or technical aspects in the literature, we believe it was appropriate to report on our initial experience.

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Isolated persistent fifth aortic arch with systemic-to-pulmonary arterial connection

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Persistent fifth aortic arch (PFAA) is thought to be an extremely rare congenital heart disease (CHD). All previously reported cases were associated with major cardiac anomalies and diagnosed coincidentally.¹ Moreover, its presence was usually beneficial to the associated cardiac anomalies. We report here a unique case of isolated PFAA (without associated cardiac anomaly) with systemic-to-pulmonary arterial connection, which caused severe congestive heart failure (CHF) in a 2-month-old male infant.

Clinical Summary

A 2-month-old male infant weighing 3940 g was referred to our hospital for evaluation of a suspected atypical huge patent ductus arteriosus (PDA). He was the product of a 39-week gestation with

a birth weight of 3480 g. He presented with severe CHF and failure to thrive. Chest radiographs revealed marked cardiomegaly, increased pulmonary vascular markings, pulmonary edema, and a convex pulmonary artery segment. The electrocardiogram demonstrated biventricular hypertrophy. A repeat echocardiogram done at our institution showed the segmental combination of solitus normal heart {S,D,S} (S = viscerotransposition, D = D-ventricular loop, S = conotruncus solitus); dilated left atrium, left ventricle, and pulmonary arteries; normal left-sided aortic arch; and preserved ventricular performance. From the parasternal short-axis view, a continuous, turbulent flow was detected at the bifurcation of the pulmonary trunk, which was not typical for PDA flow. From the modified suprasternal long-axis view, we detected a huge vessel originating from the left anterior aspect of distal ascending aorta (AsAo) but proximal to the transverse aortic arch (Figure 1) and connecting to the superior margin of the bifurcation of the pulmonary trunk. Isolated persistent fifth aortic arch with systemic-to-pulmonary arterial connection was suspected. Contrast computed tomographic 3-dimensional reconstruction of the heart and great vessels and ascending aortogram confirmed the diagnosis. Hemodynamic data revealed large left-to-right shunt (pulmonary/systemic blood flow ratio > 4) and severe pulmonary hypertension (pulmonary/systemic systolic blood pressure ratio = 1). The patient then underwent successful surgical ligation of this abnormal vessel through median sternotomy.

Discussion

Persistent fifth aortic arch is thought to be an extremely rare CHD because the fifth aortic arch almost always involutes during normal

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Received for publication April 4, 2003; accepted for publication June 18, 2003.

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J Thorac Cardiovasc Surg 2003;126:1643-4

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0022-5223/2003 \$30.00 + 0

doi:10.1016/S0022-5223(03)00954-1