Unilateral Lung Transplantation Using Right and Left Upper Lobes: An Experimental Study

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Abstract

Introduction: The shortage of organ donors is a serious problem in Japan. The right and left upper lobes of rejected extended-criteria lungs have the potential to be used for downsized lung transplantation; however, 2 upper lobes are too small for a size-matched recipient. This study aimed to investigate the feasibility of unilateral transplant using the right and left upper lobes.

Methods: After harvesting the heart-lung block from donor swine, a left lung graft was created using the right and left upper lobes and transplanted into the left thoracic space of the recipient swine (group A: n = 5). We then evaluated graft function for 6 hours and compared these results with those of a control group (group B: n = 5), in which orthotopic left lung transplantation had been performed.

Result: Mean partial pressure of oxygen in arterial blood gas after reperfusion was 507 torr in group A and 463 torr in group B ($p = 0.2$). Mean pulmonary arterial pressure was 30.3 mmHg in group A and 27.5 mmHg in group B ($p = 0.4$). Mean airway pressure was 6.4 mmHg in group A and 6.2 mmHg in group B ($p = 0.7$).

Conclusion: Our results suggest that unilateral left lung transplantation using the right and left upper lobes is technically and functionally feasible for size-matched recipients. In addition, this technique enables the use of rejected lungs if the upper lobes are still intact.

Ultramini Abstract

This study aimed to investigate the feasibility of unilateral lung transplant using the right and left donor upper lobes. Our results suggest that it is technically and functionally feasible and enables the use of rejected lungs if the upper lobes are still intact.

Donor shortage is a significant limiting factor for lung transplantation in Japan. Of 601 lung transplant candidates between 1998 and 2012, only 169 underwent lung transplantation; 242 died while on the waiting list. Utilization of extended-criteria lungs is quite important; therefore, 63% of donor offers have been accepted for lung transplantation in Japan[1].

Both lower lobes of extended-criteria lungs are often collapsed or infected. However, both the upper lobes of these lungs may still be usable for transplantation[2]. Aigner et al. reported successful utilization of the cut-down lobes of marginal donors for downsized lung transplantation[3],[4]. The 2 upper lobes are usually too small for size-matched recipients, but if unilateral lung transplantation using right and left donor upper lobes becomes feasible, it may be used for size-matched recipients. The aim of this study was to investigate the feasibility of utilizing right and left donor upper lobes for unilateral lung transplantation in a recipient.

Methods

The scheme of this experiment is shown in Figure 1. The orifice of the right upper bronchus (Fig. 2-A) and right upper pulmonary vein (PV) (Fig. 2-B) were reconstructed by suturing the right and left stumps side to side in accordance with the method described by Oto et al.[5] As a result, the stump of the right upper pulmonary artery (PA) came close to the stump of the left basal PA, which made in-series connection possible (Fig. 2-C).

Donor operation

Details of monitoring and anesthesia of the animals are described elsewhere[6]. In brief, ketamine chloride and atropine sulfate were injected intramuscularly as pre-medication. Ventilation was carried out through an endotracheal tube, and fraction of inspired oxygen was established at 1.0. Desensitization and optimal paralysis were fully maintained using halothane and vecuronium bromide. Airway pressure (AWP), blood pressure, pulmonary arterial pressure (PAP), central venous pressure (CVP), arterial blood gas, PA blood gas, and cardiac output (CO) were measured.

After a median sternotomy, 200 U/kg of heparin was injected intravenously. Ligation of the main PA marked the onset of graft ischemic time. Flushing of both lungs was carried out using 1,000 mL of low-potassium-dextrin-glucose solution[7], and the heart-lung block was extracted.

Study group

In group A, the animals receiving unilateral lung transplantation using right and left donor upper lobes (n = 5), both upper lobes were separated from the heart-lung block, and a wide anastomosing orifice of the right and left bronchi and PVs was created by side-to-side running suture (Figs. 2-A and 2-B). An end-to-end anastomosis of the right upper PA to the left basal PA (Fig. 2-C) was also created. In this manner, a double upper lobe graft was created (Fig. 3).

In group B, the control group of animals receiving orthotopic left lung transplantation (n = 5), the heart-lung block was extracted and a left PV cuff was created from the left atrium; the left PA and the left bronchus were cut at each bifurcation.

Recipient operation

The animal was placed in the right lateral position, and a fifth intercostal thoracotomy was performed. The left PV, left main PA, and left main bronchus were separated, and the left lung was extracted. Heparin (200 U/kg) was administered intravenously. The pulmonary structures were anastomosed in the following order: bronchus (Fig. 2-A), PA (Fig. 2-C), and PV (Fig. 2-B). The bronchus was anastomosed using a running suture of 4-0 Prolene, and the PA and PV were anastomosed using running sutures of 6-0 Prolene.

The clamps were released from the PV, PA, and bronchus. The animal was returned to the supine position. Arterial blood gas, PA blood gas, CO, AWP, PAP, CVP, and LA pressure were measured at 0, 30, 60, 120 and 180 minutes after reperfusion. After the measurement at 180 minutes, the graft was pushed into the thorax and the chest was closed; subsequently, measurements at 240 minutes through 360 minutes were obtained. Right main PA was intermittently clamped by tourniquet for 5 minutes before each measurement. Pulmonary arteriography was performed to check for stenosis or occlusion of the anastomoses (Fig. 4). The following 3 measured parameters were assigned to evaluate graft function: PaO_2 for oxygenation or gas exchange; PAP for problems in vessel anastomosis and influence of the small pulmonary vascular beds; and AWP for decreased lung compliance due to congestion of the graft, problems with bronchial anastomosis, or secretions.

The details of preoperative characteristics are described in Table 1. There were no significant differences between the 2 groups ($p > 0.1$).

Analysis and statistics

All results are expressed as mean ± standard error of the mean (SEM). The Mann-Whitney test was used to verify the differences in values for preoperative characteristics. Two-way repeated measurement analysis of variance was used for comparison of serial values. Differences were accepted as significant if the *p* value was less than 0.05.

Animal care

All pigs received humane care in compliance with the European Convention on Animal Care and the Principles of Laboratory Animal Care, formulated by the National Society for Medical Research, as well as the Guide for the Care and Use of Laboratory Animals, prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health, Bethesda, MD, USA (NIH Publication No. 86-23, revised 1996).

Results

Six hours after reperfusion, mean values for groups A and B, respectively, were as follows: PaO_2, 507 torr and 463 torr (p = 0.2) (Fig. 5-A); PAP, 30.3 mmHg and 27.5 mmHg (p = 0.4) (Fig. 5-B); and AWP, 6.4 mmHg and 6.2 mmHg (p = 0.7) (Fig. 5-B). The noninferiority of this technique was confirmed.

Discussion

Because of donor shortage, mortality is high among wait-listed lung transplant candidates. Extended-criteria lungs have been used to overcome this problem. Although both lower lobes of extended-criteria lungs are often collapsed or infected, the upper lobes may still be usable for lung transplantation. Many transplant teams would still prefer to perform a bilateral, full lung transplantation in a low risk recipient with the hope that the damaged lower lobes will recover during the first days after the transplant. However, when the damage of bilateral lower lobes was judged to be irreversible, all lobes including healthy upper lobes would be rejected at not negligible frequency. The aim of this study was efficient utility of such upper lobes.

When 2 upper lobes are used for bilateral lung transplant, the lung volume may be enough for undersized recipient; on the other hand, it may be too small for size-matched recipients. However, the volume of the 2 upper lobes may be sufficient for a size-matched recipient if these lobes are transplanted unilaterally into the thoracic cavity. For adults, unilateral lung transplantation is less invasive than bilateral transplantation, and the residual contralateral lung is still functional. Therefore, unilateral lung transplantation using right and left donor upper lobes may be feasible and could be used for size-matched recipients.

It should be noted that unilateral lung transplantation using right and left donor upper lobes has potential disadvantages. One limitation of this study was that swine lungs were used instead of human lungs. There are some anatomical differences between swine and human lungs, such as the shape of the rib cage, the orifice portion of the right superior bronchus, and the existence of the mediastinal lobe in pigs. Another limitation is that this is an acute-phase experiment. It might carry a higher risk for bronchial anastomotic complications, infection and ventilation-perfusion mismatch on the long-term. The bilobar grafts unexpectedly fitted into the good position of the left thoracic space without torsion or kinking in our experiment, however, the lobes are placed in a non-physiological manner; therefore, atelectasis and bronchial or vascular distortion could occur. Dead space may lead to persistent pneumothorax or thoracic empyema[8]. Further examination investigating shape, size and geometry of the lobes using human rejected lungs is required to clarify these points.

Conclusion

Our results suggest the feasibility of unilateral lung transplantation using right and left donor upper lobes in animals. This technique may enable utilization of the intact upper lobes of otherwise rejected lungs for transplantation.

Acknowledgement

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Figure Legends

Figure 1. Experimental design, group A. RUL: right upper lobe, LUL: left upper lobe

Figure 2. Method of anastomosis. A: bronchus, B: pulmonary vein (PV), C: pulmonary artery (PA)

Figure 3. Bilobar graft.

Figure 4. Pulmonary arteriography of the bilobar graft after reperfusion. Anastomotic portions of the left main pulmonary artery (PA) to the left upper PA (black arrow) and the left basal PA to the right upper PA (white arrow) show good patency.

Figure 5. A; Sequential value of oxygen partial pressure in arterial blood gas (PaO_2). No significant difference was seen in values of blood gas analysis between groups A and B. B; Sequential value of pulmonary arterial pressure (PAP) and airway pressure (AWP). No significant differences were seen in PAP or AWP between groups A and B.

Table 1. Pre-operative characteristic of recipients. Differences are not statistically significant.

	Group A (bilobar) (n = 5)	Group B (control) (n = 5)
Donor weight (kg)	26.6 ± 0.87	28.6 ± 0.86
PaO_2 of donor (torr)	535 ± 34	493 ± 36
Recipient weight (kg)	26.8 ± 0.73	27.7 ± 0.81
Ischemic time (min)	326 ± 10	259 ± 28
CO (L/min)	4.32 ± 0.37	4.4 ± 0.55
PAP (mmHg)	24 ± 2.92	31.2 ± 1.16
PaO_2 (torr)	529 ± 29	550 ± 18

CO: cardiac output, PAP: pulmonary arterial pressure, PaO_2: oxygen partial pressure in the arterial blood gas.

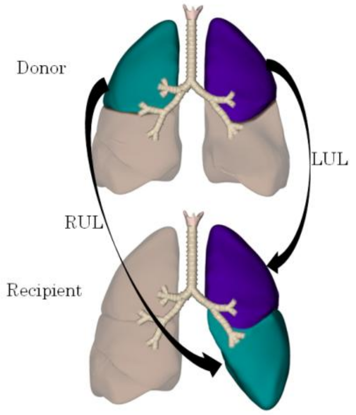


Fig.1

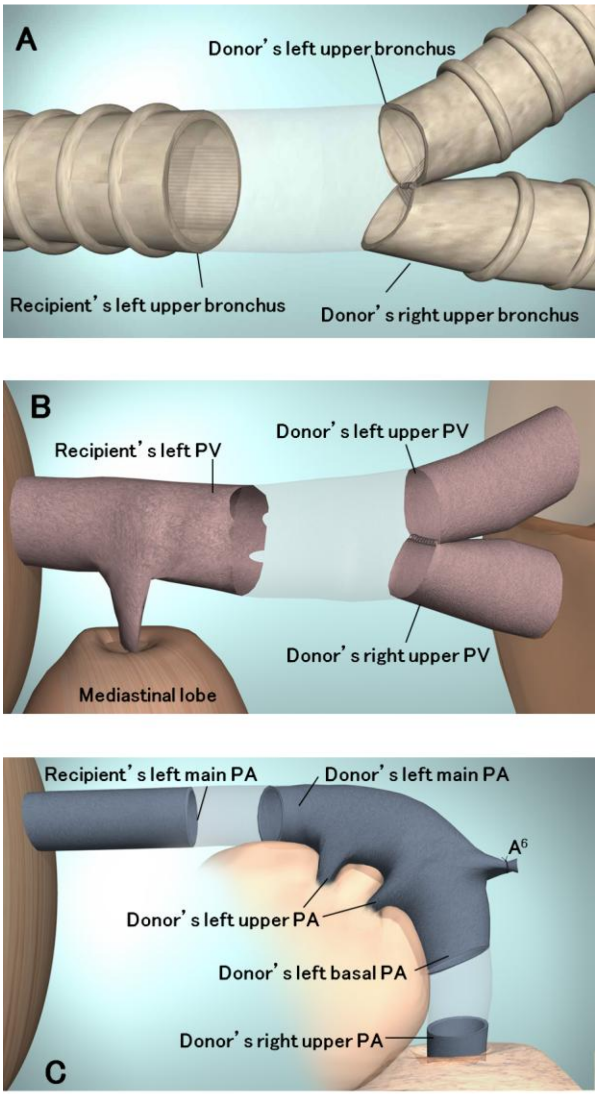

A
Donor' s left upper bronchus
Recipient' s left upper bronchus
Donor' s right upper bronchus
B
Recipient' s left PV
Donor' s left upper PV
Donor' s right upper PV
Mediastinal lobe
Recipient' s left main PA
Donor' s left main PA
A6
Donor' s left upper PA
Donor' s left basal PA
Donor' s right upper PA
C

Fig.2

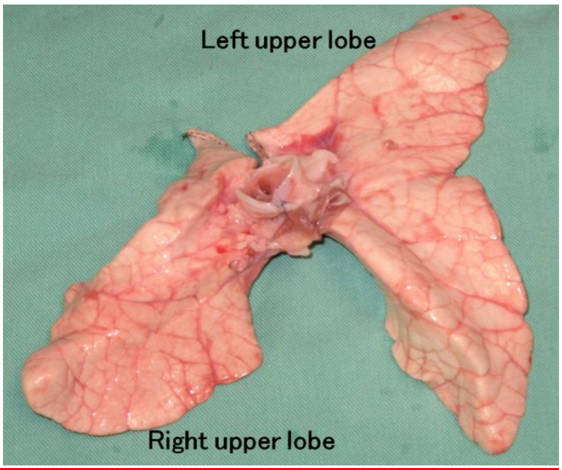


Fig.3

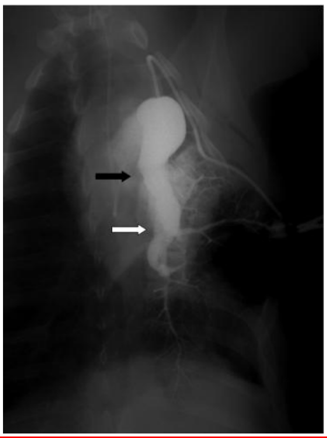
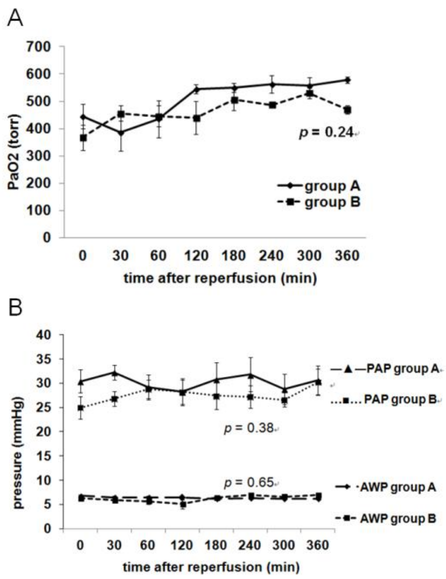


Fig.4



A
700
600
500
400
300
200
100
0
PaO2 (torr)
p = 0.24
group A
group B
0 30 60 120 180 240 300 360
time after reperfusion (min)
B
40
35
30
25
20
15
10
5
0
pressure (mmHg)
PAP group A
PAP group B
p = 0.38
p = 0.65
AWP group A
AWP group B
0 30 60 120 180 240 300 360
time after reperfusion (min)

Fig.5