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An Experimental Study of Canine Isolated Double Lung Transplantation

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ABSTRACT : The isolated double lung transplantation was performed in 8 adult mongrel dogs using transverse sternotomy in 6 and bilateral thoracotomy in 2 dogs. The first four dogs recieved donor lungs flushed with 4°C UW solution. Isolated double lung transplantation was completed in 5 dogs ; in the other 3, procedure was not completed because of intraoperative cardiac arrest or massive bleeding. Two dogs with the double lung graft were sacrificed because of severe pulmonary edema, and 3 dogs died of cardiac failure 1 to 6 hours after the operation.

We conclude that isolated double lung transplantation can be performed in dogs. However, survival time is limited because of progressive lung edema or cardiac failure.

INTRODUCTION

According to the report of the International Society of Heart Transplantation (ISHT), 157 single lung transplantations (SLT), 48 double lung transplantations (DLT), and 785 heart-lung transplantations (HLT) were performed worldwide from January 1981 to December 1989[1]. One-year survival was about 60% in patients with SLT and HLT, and about 40% in those with DLT. These rates were not satisfactory. Initially DLT was performed with cardiopulmonary bypass circulation, and anastomoses at the trachea, left atrium, and common pulmonary artery[2]. However, massive uncontrolled bleeding in the perioperative period or later tracheal anastomotic dehiscence occurred frequently. Recently, sequential single lung transplantation has been performed without using cardiopulmonary bypass[3]. We evaluated the technical problems of sequential single lung transplantation in dogs.

METHODS

A. Harvesting of the donor lung

Adult mongrel dogs weighing 10-15 kg were anesthetized with intravenous administration of nembutal at a dose of 20 mg/kg, intubated and ventilated with a Harbored ventilator. Tidal volume was 20 ml/kg. Midsternotomy was performed, and the pericardium was divided. Bilateral carotid arteries, superior and inferior venae cavae, and the aorta were taped. The common pulmonary artery was cannulated and 5,000 units of heparin was administered intravenously. Superior and inferior cavae, branchiocephalic truncus, and left subclavian artery were divided between ligatures. The left atrial appendage was opened, and the donor lung was flushed with 4°C UW solution, 30 ml/kg, at a gradient of 25 cm, from the pulmonary arterial cannula. The aorta was divided between liga-

tures at the level of the left subclavian artery, and the trachea was divided several rings above the carina. The heart-lung block was extracted, and immersed in cold saline at 4°C. The accessory lobe was removed, and the right and left main bronchi was divided just distal to the carina. The main pulmonary arteries were divided at the bifurcation of the common pulmonary artery. The aorta were divided at the atrio-ventricular septum and the right atrium was removed, then the left atrium was separated to the right and left cuff.

B. Operative procedure

1. Transverse sternotomy

The six recipient dogs were anesthetized and placed in the supine position. The femoral artery was cannulated, and systemic arterial pressure was monitored. Thoracotomy by transverse stenotomy was performed in the 5th intercostal space. The pulmonary veins were isolated intrapericardially and the pulmonary artery as far proximal as possible. On the right side, exposure was facilitated by division of the azygos vein and intrapericardial dissection of the right pulmonary artery posterior to the superior vena cava. The pulmonary veins were divided outside the pericardium. The first branch of the pulmonary artery and its descending branch were separately divided to maximize the remaining length of the pulmonary artery. The main bronchus was clamped and divided just proximal to the upper lobe take-off point. The pericardium was opened entirely around the pulmonary veins, and a clamp was placed on the atrial cuff proximal to the veins. The ties on the venous stumps were then removed and an incision was made to the cranial and caudal pulmonary veins, creating a generous atrial cuff (**Fig. 1**)

2. Lung implantation

The donor arterial cuff and pulmonary artery were suitably trimmed to match the recipient pulmonary artery and atrial cuff. The donor bronchus was divided 5 mm proximal to the lobe. The donor lung was placed in the pleural cavity and the bronchial anastomosis was initially performed with running 4-0 Prolene sutures. Without repositioning of the lung, the pulmonary artery anastomosis was performed with running 6-0 Prolene sutures. Then the atrial anastomsis was performed: the back wall was sutured from the inside with running 5-0 Prolene sutures; the front wall of the anastomosis was then sutured in a similar manners (**Fig. 2**). When the front wall anastomosis of the right atrium was performed, the free pericardial pledget was used, because the front wall of the right atrium was thin and brittle (**Fig. 3**). Before the sutures of the atrial anastomosis were tied, the atrial clamp was

Table 1. Canine isolated bilateral lung transplantation

Dog	Weight (kg) Donor	Recipient	Flushing of donor lung	WIT (min) of graft lung		Survival time (hour)	outcome
Transverse sternotomy							
DL1	12	13	UW-solution	Left	30	0	Arrest
				Right	/		
DL2	12	13	UW-solution	Left	/	0	Arrest
				Right	40		
DL3	11	15	UW-solution	Left	35	4	Pulmonary
				Right	90		edema
DL4	11	14	UW-solution	Left	30	6	Pulmonary
				Right	80		edema
DL5	10	11	(−)	Left	110	1	Cardiac
				Right	40		failure
DL6	11	12	(−)	Left	35	0	Bleeding
				Right	/		
Bilateral thoracotomies							
DL7	10	11	(−)	Left	45	5	Cardiac
				Right	120		failure
DL8	9	11	(−)	Left	180	4	Cardiac
				Right	45		failure

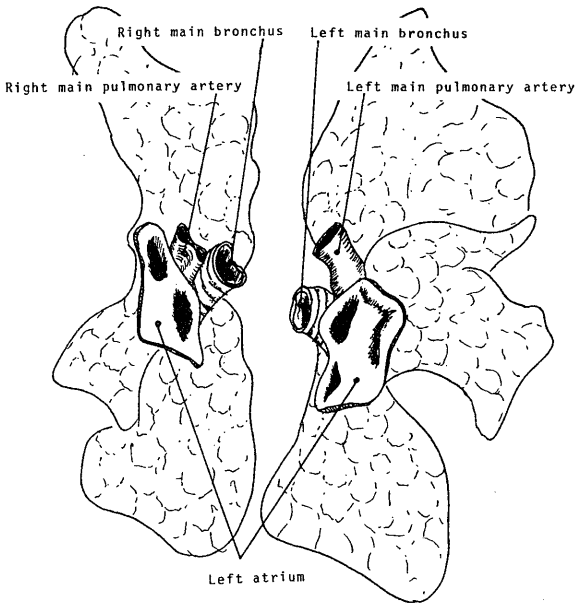

Fig. 1. Harvesting of donor lungs.

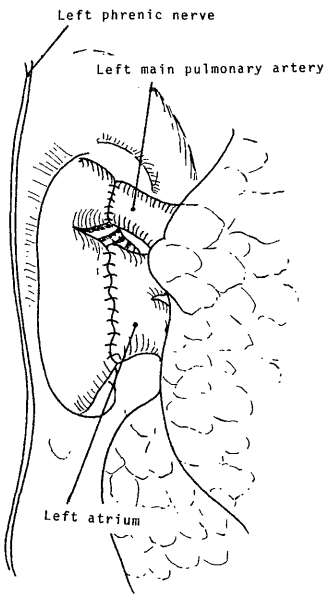

Fig. 2. Left pulmonary artery and atrial anastomoses

gradually released. The pulmonary artery clamp was then momentarily opened to flush the pulmonary artery, and the bronchial clamp was removed. After the grafted lung was ventilated and perfused, contralateral lung implantation

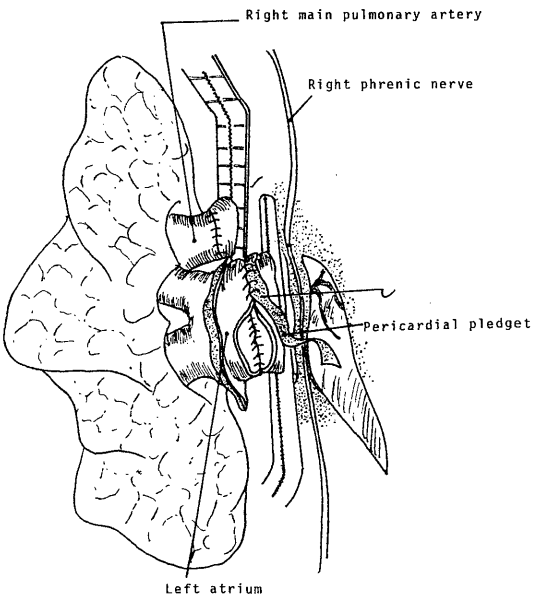

Fig. 3. Right atrial anastomosis supported by using a pericardial pledget.

was performed in the same manner. The left lung was grafted initially in 2 recipients, and the right lung was done first in 4 dogs. In the first 4 dogs, the donor lung was flushed with the preservative solution.

3. Isolated double lung transplantation using lateral thoracotomy

In two dogs the left lung was transplanted first, using left lateral thoracotomy in the 5th intercostal space. Then the animal was turned over, and right lung transplantation was performed using the right lateral thoracotomy. The donor lungs were not flushed with the UW solution. The warm ischemic time (WIT) was from 30 to 45 minutes in the early procedures, and 80 to 180 minutes in the later operations. The WIT in the recipients with transverse sternotomy tended to be longer than that with lateral thoracotomy. The donor lungs were flushed with the UW solution in the first two recipients.

RESULT

Bilateral lung transplantation was in completion in 2 dogs which recieved donor lungs flushed with the UW solution, because cardiac

arrest occurred after the initial lung graft was reperfused. One dog died of intraoperative bleeding without contralateral lung transplantation. Two dogs were sacrificed 4 and 6 hours, respectively, after the operation because of progressive pulmonary edema. Although cardiac arrest occurred in one of the two dogs which received a non-flushed lung, resuscitation was successful and bilateral lung transplantation was accomplished, the dog died one hour after surgery due to cardiac failure. Two dogs with lateral thoracotomy died of cardiac failure 5 and 4 hours, respectively, after the operation. In one dog, intraoperative cardiac arrest occurred due to trouble with the thoracic drainage tube, but resuscitation was successful.

DISCUSSION

The technique of single lung transplantation was developed by Vieth *et al*[4], using dogs as experimental models. In humans, a similar technique has been used, although Cooper *et al.*[5] made some revisions which involved an omentopexy at the bronchial anastomotic line. In contrast, there are some unsolved problems in double lung transplantation. This technique was first developed by Patterson and Cooper[2] in 1986. Both lungs of a donor were removed together. Under cardiopulmonary bypass conditions, each donor lung was juxtraposed the respective pleural cavity of the recipient, through each pleural-pericardial window. Anastomoses were performed at the trachea immediately above the carina, the left atrium, and the common pulmonary artery in succession. Because of cardiopulmonary bypass, hemorrhaging was significant during and after the operation in some cases, giving rise to graft failure in the early postoperative period. Another serious complication was tracheal anastomotic dehiscence due to ischemia at the tracheal anastomosis on the donor side. With the bronchial artery system blocked near the carina, perfusion to the main bronchus was apparently compensated by collateral circulation from the pulmonary artery[6]. However, blood supply at the carina and proximal main bronchus was not sufficient. Especially in cases of hypotension after the operation, ischemia could not be avoided even with omentopexy. On the other hand, collateral circulation between the coronary and bronchial artery system was confirmed. This channel was preserved in heart-lung transplantation, whereas it was blocked in double lung transplantation. Ischemia of the donor's carina may have increased in the latter procedure. Recently, Cooper[3] separated the donor lungs, which had been removed together, and transplanted them sequentially to avoid hemorrhage associated with cardiopulmonary bypass and anastomotic dehiscence due to ischemia. The recipient was placed in the supine position and the thorax was opened bilaterally with a transverse sternotomy. The right lung was transplanted first, then the left. Neither serious hemorrhage nor bronchial anastomotic dehiscence occured. Our procedure was developed to perform double lung transplantation without the use of cardiopulmonary bypass in dogs. In the initial stage, we tried to transplant each separate lung with a midsternotomy. This required forcefull displacement of the heart to the opposite side when the left lung was transplanted. Because of the narrow mediastinum of the dog, the superior and inferior venae cavae were twisted and blood return to the heart was reduced, cardiac arrest was leaded. Then we tried using bilateral thoracotomy by transverse sternotomy. With the animal in a right oblique position at 30 degrees, anastomosis of the left atrium during left lung transplantation was possible without forceful displacement of the heart to the opposite side. However, the heart was still slightly displaced, and bradycardia as well as hypotension occurred if the surgeon was not careful. Cooper *et al.* chose to transplant the right lung first, because anastomosis of the left atrium was relatively easy without forceful displacement of the heart to the left. Moreover, since the right lung has greater ventilation capacity and blood perfusion than the left lung, this sequence placed a smaller load on the right lung during single lung ventilation and perfusion. In right lung transplantation, ventilation rate and blood perfusion are not significantly different in the 2 lungs. Accessory lobe resection was performed because the pulmonary vein runs independently into the

caudal side of the left atrium while the bronchus and the pulmonary artery of the accessory lobe originate from the right side. Without sacrificing the accessory lobe, clamping of the left atrium is not feasible in right lung transplantation. We performed left lung transplantation first because it is technically easier and we are more experienced with it. The right intra-atrial groove is narrow and the thin wall of the left atrium is prone to intraoperative lesions, in addition the margin for suturing the atrium is insufficient. To cope with these problems, the clamp for the atrium should be as thin as possible and the pericardial pledget shoud be utilized in the anastomosis of the anterior wall of the left atrium. Using this procedure, anastomosis of the left atrium may be performed without intraoperative lesion.

The first 2 dogs that recieved transplantation of the lungs flushed with UW solution, died of irreversible cardiac arrest. This occurred when the pulmonary artery, bronchus, and left atrium were clamped in the opposite lung following the first lung transplantation. In the these 2 dogs, the UW solution was not washed out with Ringer-Lactate solution immediately before the transplantation. It is probable that a high concentration of potassium from the first transplanted lung entered into the blood circulation. If the lungs had been preserved for several hours, the extracellular potassium of the lung would have been absorbed into the cells and irreversible cardiac arrest would not have occured.

In the present experimental model, pulmonary edema developed when bilateral transplantation was completed. Typical alveolar edema was particularly evident in the lungs which were flushed with UW solution at 4°C, on the assumption that cooling preservation was necessary. The lung transplanted first was under volume-overload for 30-40 minutes, and the second lung had to be preserved until the first transplantation was completed. Therefore, the present procrdure is more prone to pulmonary edema than is conventional single lung transplantation. The lungs can be transplanted up to 6 hours after removal from the donor under cold preservation without the flushing solution, with no obvious change in pulmonary function[8]. If transplantation is feasible within at least 4 hours after lung removal, it is not necessary to flush the lung with preservation solution. In dogs it seems that either flushing the lung with preservative solution or washing out this solution with Ringer-Lactate injures the pulmonary capillary bed, producing pulmonary edema. In bilateral lung transplantation, the subject is placed in alternate lateral positions, and ventilation of the contralateral lung is essential. When single lung ventilation is impossible, extracorporeal circulation is difficult to perform, and preservation time is prolonged during chest closure. If cardiopulmonary bypass is unnecessary and preservation time is within an acceptable range, this technique may provide good results.

CONCLUSION

The separated and simultaneous transplantation of double lungs in dogs was technically feasible. However pulmonaly edema or cardiac failure tended to develop in the early postoperative period. Longer survival was difficult to achieve with double lung transplantation.

REFERENCES

1) Kriett JM, Kaye MP.: The registry of the International Society for Heart Transplantation: Seventh official report-1990, *J Heart Transplant* 1990; **9(4)**: 314
2) Patterson GA, Cooper JD, Dark JH, *et al:* Experimental and clinical double lung transplantation. *J Thorac Cardiovasc Surg* 1988; **95**: 70
3) Cooper JD.: The evolution of technique and indications for lung transplantation. *Ann. Sung.* 1990; **212(3)**: 249
4) Veith FJ. Richard K.: Improved technique for canine lung transplantation. *Ann Surg* 1970; **171**:553
5) Coopper JD, Pearson FG, Todd TRJ, Ginsberg RJ, Goldberg M, DeMajo WAP.: Technique of successful lung transplantation in humans. *J Thorac Cardiovasc Surg* 1987; **93**: 173
6) Labowski JS, Hardesty RL, Griffith BP: Pulmonary artery blood supply to the supracarinal trachea. *Heart Transplant* 1984; **4**: 40
7) Lajos TZ: Noncoronary collateral blood flow. *Ann Thorac Surg.* 1985; **40(1)**: 99

8) Kawahara K., Ishii N., Shirakusa T.: Functional evaluation of the lung with six hours cooling. *J Japan Assoc Thorac Surg.* 1986; **34(7)**: 977