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The Changes in Main Pulmonary Artery Pressure after Bilateral Lung Autotransplantation in Dogs

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In the Respiratory Center, Yongdong Severance Hospital, Yonsei University, we performed 10 cases of bilateral lung autotransplantation in mongrel dogs from July 1994 to June 1996, and we have analyzed the hemodynamic changes. Autotransplantation was performed in order to avoid postoperative rejection. The lung was flushed with an Euro-Collins(E-C) solution containing PGE1 which passed through a 10 French catheter inserted into an incision on the anterior half of the pulmonary artery to pulmonary parenchyme, and the vertical incision was made on the anterior half of the left atrium near the proximal part of the pulmonary vein. However, the bronchus was totally divided after clamping both sides. The lung was kept cold (4°C) in the thoracic cavity for an hour by using slushed ice made from an E-C solution. After an hour of cold ischemia, the pulmonary artery was sutured with Prolene 5-0. The pulmonary vein was sutured with Prolene 6-0 by using the continuous everting mattress method. The main bronchus was anastomosed using the telescope method. The arterial oxygen concentration and the pressures in the femoral and pulmonary arteries were measured both preoperatively and postoperatively. There were no significant hemodynamic differences between the preoperative and postoperative mean pulmonary artery pressure (MPAP) (paired t-test, P=0.05). Lung preservation using a cold (4°C) E-C solution containing PGE1 may be an acceptable method for short-term storage of a lung (for about an hour) in bilateral lung autotransplantation in dogs.

Key Words: Lung, autotransplantation, dog, pulmonary artery pressure

In animal experiments with single lung transplantation, the postoperative physiologic outcome of unilateral lung transplantation appears to be good, even though the transplanted lung does not function because the contralateral lung functions very well (Allgood *et al.* 1968). However, there have been reports that, after some period of lung storage using a cold preservation solution, severe hemodynamic change was seen in cases involving unilateral lung transplantation and contralateral pulmonary artery ligation where the recipient did not survive (Veith and Richards, 1969; Veith *et al.* 1969; Hong *et al.* 1990; Lee *et al.* 1994). Therefore, the first lung that is transplanted must be functioning well before proceeding to transplant the contralateral lung in bilateral transplantations (Ebert and Hundson, 1977). The survival of the recipient depends on how well the lung parenchyme has been preserved by using a cold preservation solution during the ischemic period (Jurmann *et al.* 1986).

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Bilateral lung transplantation in small animals is hindered by acute rejection and also by a high incidence of kinking or stenosis at the anastomotic sites of the pulmonary arteries and veins. These problems are similar to the hemodynamic problems occurring in ischemic injury to the transplanted lung. We also found that we were able to get rid of the acute rejection and the surgical technical faults including stenosis and kinking at the anastomotic sites by this experiment.

We analyzed the true hemodynamic changes in the systemic and pulmonary arterial pressure, which depend on parenchymal injury due to hypoxic ischemia during cold storage, following autotransplantation.

MATERIALS AND METHODS

Operative technique

From July 1994 to June 1996, at the Respiratory Center, Yongdong Severance Hospital, we performed bilateral lung autotransplantations in adult mongrel dogs weighing 15 to 25 kg (n=10). They were anesthetized intravenously with entobar (20 mg/kg), intubated with a double lumen endotracheal tube, and mechanically ventilated with a Bennett MA-1 volume-cycled ventilator (Puritan Bennett Corp., Overland Park KS. U.S.A.). With intravenous access obtained by a 17G needle in the jugular vein and electrocardiograms continuously monitored by limb leads, an 18G catheter was placed in the left femoral artery for continuous monitoring of the pressure and for gas analysis. After changing position to the left lateral decubitus position, the right lateral thoracotomy was performed through the 5th intercostal space, dissecting the pulmonary artery, the pulmonary vein, and the right main bronchus. After clamping both ends of the main bronchus and dividing it between the clamps, the pulmonary artery was clamped at both ends and an incision was made on the anterior half of the vessel between the clamps. A vertical incision was made on the anterior half of the left atrium proximal to the pulmonary vein between the clamps. After releasing the distal clamps on the pulmonary artery, a 10 French catheter was inserted into the distal portion of the pulmonary artery for infusion of a cold (4°C) Euro-Collins(E-C) solution (70 cc/kg) containing PGE1 (25 μg/1L E-C) at a pressure of 60 cmH_2O into the lung, and the lung was wrapped with cold gauze and kept cold with slushed ice made from an E-C solution in order to prevent warming of the lung during the 60 minutes of ischemia. The effusate was drained through the incised pulmonary vein for decompression of the flushed E-C solution in the pulmonary artery and lung parenchyme. During the flush, the lung was cooled topically by flooding the thoracic cavity with a cold (4°C) E-C solution and ice slush(Fig. 1). After an hour of cold ischemia, the left atrium was sutured with prolene 5-0 by the continuous everting mattress method, and the pulmonary artery was sutured using a prolene 6-0 continuous suture. The divided bronchus was approximated with prolene 4-0 by the telescope method. After de-clamping the pulmonary artery, the lung was ventilated to remove all the air in the pulmonary vasculature. After complete de-airing of the lungs, the suture in the left atrium was tied after the left atrial clamp was released and bleeding was controlled(Benfield and Coor, 1971). A 28 French thoracic catheter was inserted into the thoracic cavity and the chest was closed in layers by the usual method. The position was changed to the right lateral decubitus position for left lung autotransplantation using an identical method.

Statistical analysis of the data was performed by using the SAS (statistical analysis system) and the paired t-test.

The differences were regarded as significant when the p value was less than 0.05. All data are presented as mean ± standard error (SEM). All animals

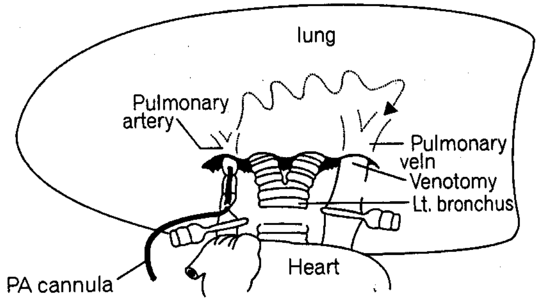

Fig. 1. Technique of isolated lung perfusion

received humane care in compliance with the "Principles of Laboratory Animal Care formulated by the National Society for Medical Research, the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Science and published by the National Institute of Health (NIH publication 80-23 revised, 1978), and the "Guide to the care and Use of Experimental Animals" formulated by the Canadian Council on Animal Care.

RESULTS

After the right lateral thoracotomy, the partial pressures of the systemic and the pulmonary arterial blood gases and the pressures of the femoral and the pulmonary arteries were measured before clamping the right main bronchus, the right pulmonary artery, and the right pulmonary vein. The cold (4°C) E-C preservation solution(70 cc/kg) & PGE1(25 μg/1L E-C) was perfused through a 10 French catheter into the pulmonary artery with pressure of 60 cmH_2O

Table 1. The changes in mean systemic arterial blood pressure (mmHg)

Body Wt.(kg)	Sex	SMAP	RPAC	RLR	LPAC	LLR
15	F	55.00	80.00	47.00	93.00	35.00
24	F	76.00	106.00	66.00	120.00	103.00
20	M	110.00	92.00	87.00	68.00	130.00
20	M	100.00	103.00	96.00	68.00	126.00
20	M	73.00	100.00	116.00	110.00	120.00
20	M	83.00	123.00	116.00	110.00	120.00
25	F	83.00	118.00	66.00	120.00	103.00
25	F	73.00	80.00	123.00	103.00	106.00
20	F	105.00		115.00	122.00	115.00
20	F	105.00		46.00	33.00	24.00
Average		86.3	100.25	87.8	94.7	98.2

SMAP: preoperative mean systemic artery pressure, RPAC: after right pulmonary artery clamp, RLR: after right lung reimplantation, LPAC: after left pulmonary artery clamp, LLR: after left lung reimplantation

Table 2. The changes in mean main pulmonary artery blood pressure (mmHg)

Body Wt.(kg)	Sex	MPA	RPAC	RLR	LPAC	LLR
15	F	18.00	16.00	28.00	33.00	23.00
24	F	39.00	35.00	30.00	26.00	24.00
20	M	6.00	5.00	28.00	19.00	17.00
20	M	11.00	13.00	37.00	32.00	29.00
20	M	16.00	33.00	20.00	12.00	22.00
20	M	17.00	32.00	20.00	12.00	22.00
25	F	35.00	20.00	43.00	26.00	23.00
25	F	12.00	14.00	10.00	17.00	71.00
20	F	12.00	11.00	10.00	15.00	73.00
20	F	18.00	16.00	27.00	36.00	27.00
Average		18.4	19.5	25.3	22.8	33.1

MPA: preoperative main pulmonary artery pressure, RPAC: after right pulmonary artery clamp, RLR: after right lung reimplantation, LPAC: after left pulmonary artery clamp, LLR: after left lung reimplantation and the flushed solution was drained through the incised site in the left atrium. Then the partial pressures of the systemic and pulmonary arterial blood gases and the pressures of the femoral and pulmonary arteries were measured at this physiologic right pneumonectomy after clamping the right main bronchus, pulmonary artery, and pulmonary vein.

Before this physiologic right pneumonectomy, the mean femoral artery pressure ranged from 55 to 110 mmHg, and the pulmonary artery pressure ranged from 6 to 35 mmHg. After clamping the right pulmonary artery and vein, and the division of the bronchus, the mean femoral artery pressure ranged from 80 to 123 mmHg and the mean pulmonary artery pressure ranged from 5 to 35 mmHg (Tables

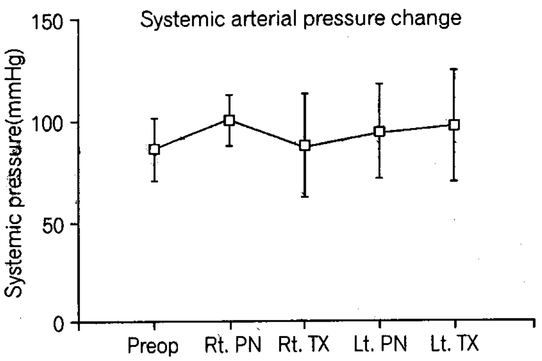

Fig. 2. The changes in the mean systemic arterial blood pressure. Preop: preoperative, Rt. PN: right pneumonectomy, Rt. TX: right lung transplantation, Lt. PN: left pneumonectomy, Lt. TX: left lung transplantation

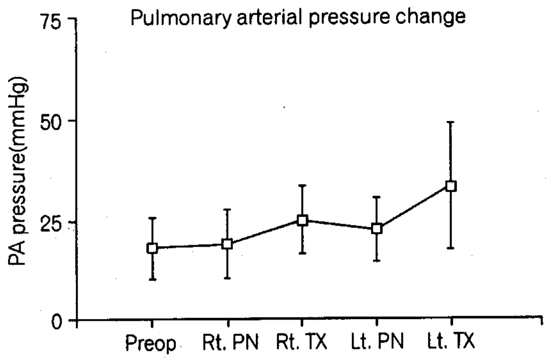

Fig. 3. The changes in the mean main pulmonary artery blood pressure. Preop: preoperative, Rt. PN: right pneumonectomy, Rt. TX: right lung transplantation, Lt. PN: left pneumonectomy, Lt. TX: left lung transplantation

Table 3. Differences between the sequential values of the mean systemic arterial blood pressure and the preoperative value

Difference	N	Mean±SD	T	p-value
SMAP/RPA	10	−18.6± 6.9	−2.7	0.03
SMAP/RLR	10	−1.5±10.5	−0.1	0.89
SMAP/LPAL	10	−8.4±13.0	−0.6	0.53
SMAP/LLR	10	−11.9±11.8	−1.0	0.34

SD: standard deviation, SMAP: preoperative main pulmonary artery pressure, RPA: after right pulmonary artery, RLR: after right lung reimplantation, LPAL: left pulmonary artery ligation, LLR: after left lung reimplantation

Table 4. Differences between the sequential values of mean main pulmonary artery blood pressure and the preoperative value

Difference	N	Mean±SD	T	p-value
SMAP/RPAL	10	−1.1±2.9	−0.4	0.71
SMAP/RLR	10	−6.9±3.4	−2.0	0.08
SMAP/LPAL	10	−4.4±3.8	−1.2	0.28
SMAP/LLR	10	−14.7±8.2	−1.8	0.10

SD: standard deviation, SMAP: preoperative main pulmonary artery pressure, RPA: after right pulmonary artery, RLR: after right lung reimplantation, LPAL: left pulmonary artery ligation, LLR: after left lung reimplantation

1, 2; Figs. 2, 3). An hour after right lung autotransplantation, the mean femoral and pulmonary arterial pressures ranged from 46 to 123 mmHg and from 10 to 43 mmHg, respectively(Tables 1, 2; Figs. 2, 3). The left lung autotransplantation was performed by an identical method to that of the right-side operation. We were able to obtain all the data by measuring the changes of the partial pressures of the femoral and pulmonary arterial blood gases, as well as the pressures of the femoral and pulmonary arteries in 10 dogs for more than 2 hours after the left lung autotransplantation.

The pressures of the femoral and pulmonary arteries ranged from 33 to 122 mmHg and from 12 to 36 mmHg, respectively, after clamping of the left bronchus, pulmonary artery, and pulmonary vein. Then, after left lung autotransplantation, the pressures of the femoral and pulmonary arteries ranged from 24 to 130 mmHg and from 17 to 73 mmHg (Tables 1, 2; Figs. 2, 3). We used the paired t-test and the SAS to evaluate the differences between the preoperative pressures and each sequential pressure listed in Tables 1 and 2, concluding that there were no statistical significant differences between each sequential pressure of the femoral and pulmonary arteries (paired t-test $p=0.05$) (Tables 3, 4).

Without the presence of stenosis or kinking of pulmonary vessels, preservation of the lung with a cold E-C solution containing PGE1 for less than 2 hours does not cause fatal changes in the systemic and pulmonary artery pressures or in the oxygen saturations of the systemic and pulmonary arteries in postoperative courses. Therefore, the preservation of the excised lung in the cold E-C solution may be applicable for bilateral lung transplantation.

DISCUSSION

Single lung transplantation has been successfully performed in patients with respiratory failures. However, bilateral lung transplantation has been the choice of treatment for patients with severe pulmonary emphysema, pulmonary hypertension, and bilateral bronchiectasis. Evaluating hemodynamic changes from ischemic injuries after bilateral lung transplantation has been a difficult task because of disorders of the cardiopulmonary system due to technical problems such as kinking or stenosis of the pulmonary artery and pulmonary vein, as well as acute rejection in small animals.

Lung transplantation has become the only method of treatment in patients with respiratory failure even though there may be such severe complications as disorders at the anastomotic sites, bacterial or viral infection, and acute rejection. The poor outcomes can be due to multiple factors such as cutting of nerve conduction, bronchial arteries or lymphatics, ischemic injury to the donor lung, kinking of the pulmonary artery, or obstruction of the pulmonary vein, which may cause a drastic elevation of pulmonary arterial pressure leading to pulmonary edema, cardiopulmonary disorders, and death (Yeh *et al.* 1962; Waldhausen *et al.* 1967; Daicoff *et al.* 1970; Lee *et al.* 1997). Particularly when using smaller animals, there is a high incidence of surgical technical error which leads to complications and death. Technical problems in the anastomosis of the pulmonary artery and vein can cause postoperative cardiopulmonary disorders. Therefore, avoiding stenosis or kinking of the vessels during anastomosis are said to be essential to preventing cardiopulmonary disorders (Waldhausen *et al.* 1967; Veith and Richards, 1969; Veith *et al.* 1969; Daicoff *et al.* 1970; Benfield and Coor, 1971).

In order to avoid acute rejection, we used an autotransplantation method in this experiment. In order to avoid surgical technical problems such as kinking or stenosis of the pulmonary arteries and veins, we made incisions only on the anterior part of the pulmonary artery after clamping both ends and on the anterior part of the left atrium proximal to the pulmonary vein after clamping both sides (Lee *et al.* 1997).

This experiment avoided acute rejection by using autotransplantation. By making a 50% partial incision on the anterior part of the pulmonary artery and vein, we could avoid stenosis or kinking of the pulmonary artery during re-suture. Thrombi can occur at the left atrial anastomotic site, causing obstruction of the pulmonary vein ostium. Yeh *et al.* and Garzon *et al.* reported thrombus at the left atrial anastomosis site and Lee *et al.* also experienced several left atrial thrombi after lung transplantation in dogs (Yeh *et al.* 1962; Garzon *et al.* 1968; Lee *et al.* 1989). In order to avoid left atrial thrombi, we incised the anterior half of the pulmonary vein and sutured this anterior half by the continuous everting mattress method.

Adding PGE1 to the E-C flush solution helped vasodilate pulmonary capillaries and cause the E-C solution to perfuse rapidly throughout the capillaries to eventually cool the lung parenchyme. This also kept the temperature of the lung parenchyme above 4°C and below 10°C, the optimal condition to minimize ischemic and cold injuries.

So, without the presence of stenosis or kinking of pulmonary vessels, preservation of the extracted lung with cold E-C solution containing PGE1 does not cause fatal changes in the systemic and pulmonary artery pressures or oxygen saturations of the systemic and pulmonary arteries in postoperative courses. Therefore, this method may be applicable for bilateral lung transplantation.

REFERENCES

Allgood RJ, Ebert PA, Sabiston DC: Immediate changes in pulmonary hemodynamics following lung autotransplanation. *Ann Surg 167: 352-358, 1968*

Benfield JR, Coor R: The role of the left atrial anastomosis in pulmonary replantation. *J Thorac Cardiovasc Surg 61: 847-856, 1971*

Daicoff GR, Allen PD, Streck CJ: Pulmonary vascular resistance following lung reimplantation and transplantation. *Ann Thorac Surg 9: 569-579, 1970*

Ebert PA, Hundson BH: Pulmonary hemodynamics following lung autotransplantation. *J Thorac Cardiovasc Surg 62: 188-192, 1977*

Garzon AA, Cheng C, Pangan J, Karlson KE: Hypothermic hyperbaric lung preservation for twenty-four hours with replantation. *J Thorac Cardiovasc Surg 55: 546-554, 1968*

Hong SN, Lee DY, Chung KY, Kim DK: Hemodynamic study after left lung reimplantation and right pulmonary artery ligation. *Korean J Thorac Cardiovasc 23: 640-645, 1990*

Jurmann MJ, Dammenhayn L, Schafers HJ, Wahlers T, Fieguth HG, Haverch A: Prostacyclin as an additive to single crystalloid flush: Improved pulmonary preservation in heart-lung transplantation (Abstract). *Heart Transplant 5: 385-389, 1986*

Lee DY, Bae KM, Paik HC, Park MS, Lee WY: The change of pulmonary arterial pressures after left lung transplantation and ligation of right pulmonary artery in dogs. *Korean J Thorac Cardiovasc 27: 345-352, 1994*

Lee DY, Kim DK, Kim KD, Kang MS, Cho BK, Hong SN, Park WK: Surgical techniques of right lung transplantation in dogs. *Korean J Thorac Cardiovasc 22: 416-424, 1989*

Lee DY, Kim HK, Moon DS, Hong YJ, Bae KM: Animal model for sequential bilateral reimplantation of the lung in dog. *Korean J Thorac Cardiovasc 30: 733-737, 1997*

Veith FJ, Richards K: Lung transplantation with simultaneous contralateral pulmonary artery ligation. *Surg Gynecol Obstet 129: 768-774, 1969*

Veith FJ, Richards K, Lalezar P: Protracted survival after homotransplantation of the lung and simultaneous contralateral pulmonary artery ligation. *J Thorac Cardiovasc Surg 58: 829-836, 1969*

Waldhausen JA, Daly WJ, Baez M, Giammona ST: Physiologic changes associated with autotransplantation of the lung. *Ann Surg 165: 580-589, 1967*

Yeh TJ, Ellison LT, Ellison RG: Functional evaluation of the autotransplanted lung in the dog. *Am Rev Respir Dis 86: 791-797, 1962*