Allogeneic single lung transplantation in 7 cases☆

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Abstract: The present case report was designed to summarize the clinical experience of operative technique, lung preservation, lung perfusion, and perioperative management. Of 7 cases who underwent allogenic single lung transplantation (LT), 3 were idiopathic pulmonary fibrosis, 2 were chronic obstructive pulmonary disease, 1 was silicosis, emphysema, and bulla, and 1 was tuberculosis in both sides and presented with destroyed lung in one side. All donors were already brain death. Donor lungs were well preserved utilizing Euro-Colins liquid or low- potassium dextran solution. Donors and recipients were matched in blood type. Of 7 cases selected, 5 received single right lung transplantation, and 2 received single left LT. End-to-end anastomosis was performed for pulmonary branches and pulmonary arteries, while atrium-to-atrium anastomosis was performed for pulmonary vein. Antibiotics and immunosuppressants were routinely used prior to and subsequent to LT. Following LT, heart and lung function, usage of antibiotics, and adjustment of immunosuppressant were monitored. Stomal complications regarding bronchus and pulmonary artery and vein did not appear in any patient. Five cases survived for about 2 months, one for approximately 1 year, and one for nearly 2 years. Four cases died of multi-organ failure caused by pulmonary infection, and one of severe pulmonary hemorrhage caused by aspergillus sydowi infection. Rejection occurred in 6 cases. One case suffered from rejection three times. Selection of indication, selection and preservation of donor lung, LT operation and pre- and post-operative management of LT have acquired satisfactory achievements. High mortality occurred in patients with preoperative poor cardiac and pulmonary functions and postoperative severe infections accompany with application of immunosuppressant.

Key words: Lung transplantation; lung preservation; complication; organ graft

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INTRODUCTION

Since 1987, when Coopper[1] reported their first successful lung transplantation (LT), approximately 20 000 LTs have been performed all over the world. According to international literature, one-year mortality is less than 10%, and 5-year mortality is nearly 50%. In China, the LT starts in 1990s [2]. Here, we report 7 single-LTs, 3 of which was cooperated with other hospitals in 1990s [3], and the other 4 by ourselves between December 2004 and October 2007.

SUBJECTS AND METHODS

Design: Retrospective case analysis.

Time and setting: Performed at Departments of Thoracic Surgery, Tangshan Workers' Hospital, Daping Hospital, Third Military Medical University of Chinese PLA, the General Hospital of Lanzhou Military Area Command of Chinese PLA, China-Japan Friendship Hospital in 1990s and at the Department of Thoracic Surgery, China-Japan Friendship Hospital between December 2004 and October 2007.

Subjects: Seven patients comprising 6 males and 1 female, averaging 51 years of age (range 48–59 years) were enrolled in this study. All recipients received allogenic single lung transplantation. Pathological diagnosis results showed that of the 7 patients, idiopathic pulmonary fibrosis was found in 3 patients, chronic obstructive pulmonary disease(COPD) was found in 2 patients, tuberculosis in both sides, and destroyed lung in one side was found in patient, and silicosis, emphysema, and bulla was found in 1 patient. In this study, 5 patients underwent single right lung transplantation, while the other 2 patients underwent single left lung transplantation. Biocular intubation and high frequency ventilation were used in 4 cases, and only binocular intubation was used in the rest 3 cases. Femoral artery-femoral vein bypass was employed in 3 cases. All donors were already brain death. Donor lungs were well preserved utilizing Euro-Colins liquid or low- potassium dextran solution. The pulmonary functions of the 7 recipients are presented in Table 1.

Table 1 General data and lung function of the 7 recipients

Patient	Gender	Age(yr)	Etiological factor	MVV(L/s)
1	F	53	COPD	25.4
2	M	48	COPD	11.0
3	M	56	DL,RLC	70.4
4	M	52	COPD	24.8
5	M	54	IPF	39.4
6	M	59	IPF	69.7
7	M	33	Silicosis	16.4
Average	-	51	-	36.7

Patient	FVC(L)	FEV1(L)	FEV1 (%)	Donor	Operation
1	35.2	0.21	60.0	H	RLT
2	11.0	0.14	100.1	H	LLT
3	37.8	0.38	51.9	H	RLT
4	46.4	0.26	124.1	H	RLT
5	31.5	0.39	118.1	H	RLT
6	41.3	0.52	90.8	H	RLT
7	1.15	0.47	12.5	H	LLT
Average	33.4	0.39	79.6	–	–

F: female; M: male; COPD: chronic obstructive pulmonary disease; DL: destroyed lung; IPF: idiopathic pulmonary fibrosis; H: health; RLT: right lung transplantation. LLT: left lung transplantation; MVV: maximal voluntary ventilation; FVC: forced vital capacity; FEV1: forced expiratory volume in one second

The other basic data of the 7 recipients

Patient 1 exhibited continuous oxygenation, little activity, both lungs infected frequently, right ventricle enlarged, tricuspid valve regurgitation, and pulmonary artery pressure (PAP) = 66 mm Hg.
Patient 2 exhibited oxygenation > 10 hours per day, indoor activity, lung infected, right ventricle moderately enlarged, tricuspid valve moderate regurgitation, a little high PAP.
Patient 3 exhibited oxygenation 5−10 hours per day, indoor activity, lung infected, right ventricle enlarged, and tricuspid valve mild regurgitation.
Patient 4 exhibited indoor activity, lung infected slightly, tricuspid valve mild regurgitation, and PAP = 50 mm Hg.
Patient 5 exhibited intermittent oxygenation, indoor activity, cyanosis, lung infected, left ventricle enlarged, pericardial effusion, tricuspid valve severely insufficiency, and PAP = 75 mm Hg.
Patient 6 exhibited seldom oxygenation, indoor activity, right ventricle enlarged, tricuspid valve moderate regurgitation, a little pericardial effusion, and PAP = 75 mm Hg.
Patient 7 exhibited intermittent oxygenation, act indoor, and tricuspid valve moderate regurgitation.

The basic information of donors

All 7 donors were male and completely brain death, with 22−48 years of age. Donors and recipients were matched in blood type.

Methods

Usage and monitor of immunosuppressant

Cyclosporin A, azathiopurine, and glucocorticosteroid were used in the first 3 patients. For the 3rd to 6th cases, cellcept (500 mg, oral) and Tac antibody (50 mg, i.v.) were used on the morning of the operation day and the day before transplantation. For the 7th LT, cellcept (1 000 mg, oral) and Tac antibody (20 mg, i.v.)were used on the morning of the operation day. 500 mg methylprednisolone was i.v. injected before the pulmonary circulation was reopened during the operation. Postoperatively, FK506, Cellcept, and corticosteroid were used in combination. The dosage of FK506 was followed by its concentration in the circulation and reduced gradually: the concentration of FK506 should be 15−20 μg/L (4 degree) for the first postoperative 21 days, then 10−15 μg/L (3 degree) for the following 5 weeks, 8−10 μg/L (2 degree) for 1 month sequentially, and finally 4−7 μg/L (1 degree) for life long.

Application of antibiotics

The 3rd generation of cephalosporin was given just 30 minutes before (2 g) and subsequent to operation. If lung bacterial infection occurred preoperatively, such as patients 1, 4 and 6, cephalosporin was also given to control the infection and then proper antibiotics was selected according to bacterial culture and drug sensitivity. Aciclovir was routinely used for anti-virus. If the transplanted lung was infected by virus postoperatively, 2-week intravenous and subsequent 12-week oral administration of aciclovir was given. Aciclovir should be intravenously administered for 3 months in severe cases. Fluconazol was routinely used for anti-fungus.

Monitoring

Postoperatively, all 7 recipients were sent to ICU, and mechanical ventilation was performed. Parameters monitored included electrocardiogram, pulse oxygen saturation, partial pressure of carbon dioxide in artery, central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, biochemistry, sputum culture and blood drug concentration.

Main outcome measures

LT related indices and postoperative follow-up results.

RESULTS

Anastomotic stoma-related complications were not found in all patients, such as stomal leak and hemorrhage.
The 1st recipient survived for 9 days, and acute rejection, severe pulmonary infection and arrhythmia occurred on the 7th day.
The 2nd recipient survived for 48 days, and acute rejection, severe pulmonary infection, arrhythmia, and acute renal failure occurred on the 6th and 21th days.
The 3rd recipient survived for 56 days, acute rejection and pulmonary infection occurred on the 10th day.
Following lung transplantation, the medical ventilation was used for 3−7 days for the former 3 recipients. The 3 recipients could do indoor activity, and the 2nd and 3rd recipients could walk 500−700 meters.
The 4th recipient was ventilated for 72 hours postoperatively, and after that he could do indoor activity. While on the 7th day, slight rejection occurred, no special treatment was given. He was discharged on the 58th day. Now after 1 year and a half, his life was not influenced by the LT.
The 5th recipient received acute rejection on days 4, 7, and 14 after LT. Following 1 000 mg methylprednisolone administration, the recipient was awake and could do activities in bed. But he died of severe pulmonary infection and multi-organ failure caused by hormone usage on day 26.
The 6th recipient was extubated on the 4th day. From then on, he could enjoy his indoor life for about 2 weeks. On the 21st day, he got hemoptysis (approximately 50 mL). After that, aspergillus was found in his sputum, and two more hemoptysis occurred, the amount of which reached 400 mL. The hemorrhage from non-transplanted lung was confirmed by fibreoptic bronchoscopy. Following therapy with fluconazol and amphotericin for several days, the recipient died on the 28th day just before salvage operation.
The 7th recipient was ventilated for 20 hours postoperatively. Following 4-day in-bed recovery, he could do daily indoor activity. He was discharged on the 33th day. One month later, bronchial anastomosis stenosis occurred and FOB therapy was intervened. Thereafter, he got smooth recovery. Now, after approximately 5 months postoperatively, he acts as a healthy person.
Allogenic single lung transplantation-related indices and

postoperative follow-up results of 7 patients are shown in Table 2.

Table 2 Allogenic single lung transplantation-related indices and postoperative follow-up results

Patient	Warm-Ischemic time (min)	Cold-Ischemic time (min)	Total anastomotic time(min)	Complication	Follow up tim (mon)	Prognosis
1	5	278	89	AR; LI; ARR	< 1	Dead
2	2	150	77	AR; LI; ARR	< 2	Dead
3	7	230	85	AR; LI	< 2	Dead
4	14	317	95	MAR;	24	Living
5	10	312	107	AR; LI	< 1	Dead
6	7	260	110	LI; HE	< 1	Dead
7	7	270	110	AS	12	Living
Average	7.4	259.6	96.1	–	–	–

AR: acute rejection; LI: lung infection; ARR: arrthmia; MAR: minor acute rejection; HE: hemoptysis; AS: anastomosis stenosis

DISCUSSION

Indications

The best indication for single LT is idiopathic pulmonary fibrosis [4]. It should be noticed that proper functioning of the other organs are neccessary in the indication [5], sometimes only moderately cardiac disorder is permitted. In this study, the 5th recipient got right heart failure, pericardial effusion, pleural effusion, and seroperitoneum preoperatively. So the perioperative preparation for transplantation was complicated and not satisfied. Several acute rejections attacked postoperatively, and finally the recipient died of multi-organ function failure.

Lung preservation

The shorter the warm-ischemic time is, the better the preservation will be. In this study, all operations were performed through the 4th intercostal space incision. Through this incision, ischemic time can be maximally reduced, and the operation field can be exposed well. As we mentioned above, the average warm- ischemic time in this group was 7.4 minutes, ranging from 2 to 14 minutes. Keeping respiration and stable circulation is the basic rule for transplantation. All transplanted lungs survived well in our study after cold-ischemic time which ranged from 150 to 317 minutes (average 259.6 minutes), so it is accepted to keep cold-ischemic time in 6 hours [6].

Anastomotic technique

Though investigation all over the world, there has been no difference found for the technique of anostomosis [7-8]. After several animal experiments, the possible problems occurring during the LT can be solved. In the present study, the average anastomotic time was 96.1 minutes, and one case got moderate anastomotic complications [9].

Cooperation

Most recipients have multiple organ dysfunction (pulmonary dysfunction, cardiac dysfunction, and so on), which makes it a complicate procedure for graft-preparation. In the present study, we had 5 recipients with organic cardiac dysfunction, which complicate the perioperative period. Only with the cooperation of several departments, such as intensive care unit, department of anesthesiology, cardiac surgery, cardiac medical department, and respiratory medical department, can we successfully finish lung transplantation.

Therapy for anti-rejection and severe pulmonary infection

Till now, no apparent progression of anti-rejection therapy has been acquired. Though living lobar transplantation can be achieved, it can not become popular [10]. Shortage of donor and bronchiolitis is the primary problems that we must face to [7, 11-12]. Besides, infection is another important problem that leads to the failure of LT. The already existed infection which resists therapy, usage of hormone, and immunodepressant, which causes secondary infection or fungal infection, are difficult to cope with. For instance, aspergillus sydowi infection can cause severe hemorrhage, and the hemoptysis caused by aspergillus sydowi infection leads to the death of the 6th recipient in the present study.

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同种异体单肺移植 7 例报告☆

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摘要：总结 7 例同种异体单肺移植资料的移植方案、肺保存及移植后管理监测情况。7 例同种异体单肺移植患者中特发性肺纤维化 3 例，慢性阻塞性肺病 2 例，双侧矽肺、肺气肿 1 例，双肺结核右毁损肺 1 例。7 例供体均为脑死亡者，供肺均采用 Euro-Colins 液或低钾右旋糖酐液灌注并良好保存。受体与供体血型匹配，5 例患者行右侧单肺移植，2 例行左侧单肺移植。肺支气管、肺动脉为端端吻合，肺静脉为心房-心房吻合。移植前后均常规应用抗生素和免疫抑制剂。肺移植后进行全面指标监测，包括心肺功能、抗生素使用及免疫抑制药物的调整。7 例患者均未出现支气管、肺动静脉吻合口并发症。5 例移植后 2 个月内死亡，1 例存活近 1 年，另 1 例存活近 2 年。死亡者中 4 例死于肺感染导致多脏器功能衰竭，1 例死于多曲霉菌感染致严重肺出血。6 例移植后出现排斥反应，其中 1 例出现 3 次。肺移植手术适应证的选择、供肺的选择和保存、肺移植操作以及移植前后的管理已逐渐成熟，移植前心肺功能差者、移植后使用免疫抑制药物同时合并严重感染者病死率仍很高。

关键词：肺移植；器官保存；并发症；器官移植
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