

# Allogenic single-lung transplantation for chronic obstructive pulmonary disease in 4 cases★

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**Abstract:** Clinical data of 4 patients with chronic obstructive pulmonary disease who underwent allogenic single-lung transplantation were retrospectively analyzed. All cases received corpse donor lungs. One case with diffuse emphysema underwent right lung transplantation, and 3 received left lung transplantation, including one underwent right lung volume reduction during surgery and 2 cases underwent right lung volume reduction post-transplantation. The inductive treatment with daclizumab or antithymocyte globulin was done and the rejection was prevented with Tacrolimus, mycophenolate and prednisone. The surgery was successful in 4 cases. One case developed acute rejection on the fifth day post-transplantation, and controlled using methylprednisolone. Two cases discharged successfully, of whom one lived more than 2 years. Two cases died 74 days and 77 days after lung transplantation, respectively.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the most common chronic respiratory diseases all over the world. The morbidity rate and case mortality are high. Partial reversible airflow restriction and progressive development are features of COPD. Complete recovery could not be achieved by drug treatment. It is considered that allogenic lung transplantation is an effective method for final stage COPD, and single-lung transplantation is one of the main modes of lung transplantation. This paper retrospectively analyzed the effect of allogenic single-lung transplantation on COPD.

## SUBJECTS AND METHODS

### Design

Retrospective case analysis.

### Time and setting

The trial was performed at the Department of Thoracic Surgery, Guangzhou Respiratory Institute, First Hospital of Guangzhou Medical College between June 2003 and December 2005.

### Subjects

Four male COPD patients underwent allogenic single-lung transplantation, with an average age of (60±10) years (range 46–69 years). One primary disease was bilateral diffuse emphysema and the other 3 cases were severe diffuse emphysema complicated by partial bulla, accounted for 1/3 of the whole thoracic cavity, one of whom ever had a spontaneous pneumothorax. Preoperative forced expiratory volume in one second (FEV1) of three cases was 15%, 18% and 25% of predicted value, respectively. Pulmonary function test was not done for one case because of pulmonary encephalopathy on admission. One of the 4 cases received right lung transplantation, and the other 3 underwent left lung transplantation. All donor lungs were from male corpses aged 22–36 years. Written informed consent

was obtained from all patients and their families, and the protocol was approved by ethics committee of hospital. General condition and transplantation protocol for 4 COPD patients are listed in Table 1.

Table 1 General information and transplantation protocol for four cases of chronic obstructive pulmonary disease

Case	Sex	Age (yr)	Primary disease	Transplanted site	Operation protocol
1	Male	62	Bilateral diffuse emphysema	Right lung	Single-right lung transplantation
2	Male	63	Severe diffuse emphysema; bulla	Left lung	Single-left lung transplantation
3	Male	46	Severe diffuse emphysema; bulla	Left lung	Single-left lung transplantation and right-lung volume reduction
4	Male	69	Severe diffuse emphysema; bulla	Left lung	Single-left lung transplantation

## Methods

### Donor lung harvesting and transplantation

Entire bilateral lungs and heart were harvested by tracheal intubation at supine position, median sternotomy, and perfusion in both lungs<sup>[1]</sup> through the pulmonary artery. 4 °C Celsior fluids or dextran-40 (LPD) solution was used as perfusate.

Extracorporeal circulation was not adopted during transplantation. The transplantation started after identification of donor lungs. The patient lied in side, and was operated by a thoracoscope-assisted operation through a fifth intercostal small incision. The hilum of lung was anatomized, adhesion was separated, and left pulmonary artery was anatomized to block pulmonary artery. Thirty minutes after single-lung ventilation, oxygen saturation, oxygen partial pressure, heart rate and blood pressure showed no significant changes. Then dissociation and ligation of the first branch of pulmonary artery were performed. The pulmonary artery was blocked with Satinsky's clamp and disconnected. The upper and lower left-pulmonary vein were ligated and the

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pulmonary vein was disconnected between the ligatures. Left main bronchus was cut where two cartilage rings from the upper and lower lobe bronchus junction. The right main bronchus, about 1.5 cm from the right superior lobar branch gap, was cut, and the anatomic procedure of the remnant right lung was the same as the left one. The disease lung was removed, and ice was put into the thoracic cavity of affected side. The donor lung was put into the recipient thoracic cavity. End-to-end anastomosis was performed at trachea firstly, membrane was continuously sutured by prolene 420 4-0 thread, and the cartilaginous part was "8" intermittently sutured by PDS thread. The anterior and posterior walls of pulmonary artery were sutured continuously by prolene 420 4-0 thread. Donor pulmonary atrium was sutured continuously to patient's pulmonary vein by prolene 420 thread in sleeve type. After anastomosis, 1 000 mg methylprednisolone was used before discission of pulmonary artery. The auricle clamp was released at pulmonary atrium to restore pulmonary circulation. After all anastomosis were finished, thoracic cavity irrigation test was performed to determine no air leakage in the bronchial anastomotic stoma. Top and bottom thoracic closed drainage tubes were put and thoracic cavity was closed subsequently. After operation, the single-cavity endotracheal tube was replaced and the patients were sent to ICU.

### ***Treatment of recipient contralateral lung***

One case with diffuse emphysema received single-right lung transplantation. The other 3 cases with severe diffuse emphysema complicated by bulla received single-left lung transplantation because the pathological change in left lung was significant. In the three cases of bullae, one received contralateral lung volume reduction at 47 days after transplantation; one case underwent right-lung volume reduction at 28 days after transplantation, but pulmonary hemorrhage occurred at the right upper remnant lung 4 days after secondary operation and underwent lobectomy of right upper lung; the other case received single-left lung transplantation and right-lung volume reduction simultaneously. The bullae and some tissues of the right lower lung were resected.

### ***Prevention of rejection and infection post-surgery***

Tacrolimus (FK506), mycophenolate mofetil (MMF) and prednisone were used to prevent rejection. Dose of FK506 was determined by the blood drug level, maintaining in 10–15  $\mu$ g/L. The MMF dosage was 1 000 mg/d. In addition, daclizumab or anti-thymocyte globulin (ATG) should be used for inductive treatment. Daclizumab (50 mg) was used on the day and 2 weeks after surgery, respectively. The first day after operation, 100 mg ATG was used and then 50 mg was used everyday (total dose of 500 mg).

After surgery, cefepime, vancomycin, fluconazole and ganciclovir were used to prevent bacteria, fungi and viruses infection. Fiberoptic bronchoscopy was used to suck the endotracheal phlegm effectively. According to the amount of respiratory secretions, fiberoptic bronchoscopy was used for tracheal suctioning 1 or 2 times per day, and then was reduced to once every two days gradually until the patient could expectorate by oneself.

### **Main outcome measures**

Treatment effect of single-lung transplantation in 4 COPD

patients.

### **Design, enforcement and evaluation**

All authors participated in the design, enforcement and evaluation of the study.

## **RESULTS**

Case 1 developed acute rejection 5 days after single-right lung transplantation, and recovered after intensive intravenous treatment with 500 mg methylprednisolone for 3 days. Nasotracheal tube was removed at 11 days; oxygen was stopped at 23 days and discharged 64 days after operation. FEV1 was 46% before discharge and remained 46% 12 months later. The patient could go upstairs to the seventh floor without rest.

Case 2 with pulmonary encephalopathy on admission could maintain saturation of blood oxygen at the level of 98%–100% when transplantation was completed, but the level dropped by 92% out of the operating room. Urgent chest X-rays confirmed that the lung volume was compressed by 90% because of right pneumothorax. Closed drainage was performed to the right thoracic cavity. Intermittent breathing-machine-assisted ventilation was given 3 days after operation. Trachea cannula and drainage tube were removed 8 days and 18 days after operation respectively. Right pneumothorax, respiratory and cardiac arrest occurred 29 days after operation while the patient was going to toilet himself. Cardiopulmonary resuscitation and right thoracic close drainage were performed immediately and the patient's heart recovered subsequently. Because of persistent air leak in the right thoracic drainage tube after closed drainage, right lung volume reduction was performed 47 days after operation. After the secondary operation, infection occurred in the right lung and thoracic cavity which failed to be controlled. And the patient died 74 days after operation.

Case 3 received simultaneous single-left lung transplantation and lung volume reduction and recovered successfully in perioperative period. Intermittent machine-assisted ventilation was given after operation. Trachea cannula was removed at 6 days and oxygen was stopped 14 days after operation. FEV1 was 46% before rehabilitation discharge.

Case 4 received single-left lung transplantation and trachea cannula was removed 26 hours after operation. Right pneumothorax occurred 5 days after operation and the lung volume was compressed by 60% and closed drainage was performed. Because of persistent air leak, right lung volume reduction was done 28 days after operation. Four days later, patient felt unwell in the right chest. X-rays indicated there was a new dense oval shade at the remnant right upper lobe, susceptible hemorrhage. Thus exploratory thoracotomy was done. Hemorrhage was found at the incisal margin of lung which was cut by cutting stitching instrument (GIA nail). The remnant right upper lobe was resected. Respiratory and cardiac arrest occurred 9 days after lung volume reduction while the patient was going to toilet. Cardiopulmonary resuscitation was done immediately. Heart recovered subsequently but encephalic

resuscitation was failed. The patient died 77 days after operation.

## DISCUSSION

Although the success of lung transplantation is later compared with other human organ transplantation, it develops rapidly. Cooper's lung transplantation group had operated single-right lung transplantation successfully in 1983, which made lung transplantation move to a novel era. Nowadays, single-lung transplantation, double-lung transplantation and heart lung transplantation have gained clinical successes. Final stage COPD is the main indication of lung transplantation. Lung transplantation has been considered as an effective therapy for final and advanced stage of lung parenchyma diseases and pulmonary vascular disease. In 1988, Mal and Andtassian operated single-lung transplantation successfully for 2 cases of COPD in Beal Ion Hospital, Paris, France. Patients recovered well and the V/Q ratio did not become visible disturbance after transplantation. COPD has become the indication of single-lung transplantation from then on. To date, single-lung transplantation has been the majority in lung transplantation. Documents from 1995 to 2004 have shown that the final stage COPD accounts for 38% of all lung transplantation indications and single-lung transplantation is the most common surgery for COPD. But since 2003, cases of double-lungs transplantation is increasing<sup>[2]</sup>. Compared with single-lung transplantation, cases of double-lungs transplantation have a better long-term survival, less complications, and better pulmonary function<sup>[3]</sup>. But with the increase of age, recent death rate of double-lung transplantation cases is higher than single-lung transplantation. Nowadays, it is maintained that double-lung transplantation should be done for patients younger than 60 years. If patients are between 60 and 65 years old, single-lung transplantation is recommended<sup>[4-5]</sup>. In the present study, cases 1, 2 and 4 were over 60 years old, so single-lung transplantation was performed. Although case 3 was 46 years old, who suited for double-lung transplantation in theory, single-lung transplantation was still adopted due to restriction of technology and time of donor lung preservation. Todd *et al*<sup>[6]</sup> reported that the recipients undergoing simultaneous single-lung transplantation and contralateral lung volume reduction recovered well in perioperative period and pulmonary function was significantly improved. In the present study, although one of four cases had an obvious bilateral emphysema, but typical pulmonary bulla did not form. This case recovered well after operation and quality of life was good so far. The other 3 cases had obvious pulmonary bulla in contralateral lungs. One case, aged 46 years, received single-left lung transplantation and simultaneous right lung volume reduction and recovered successfully after operation. The other 2 cases developed pneumothorax after operation and died eventually despite of thoracic closed drainage and lung volume reduction. Some researchers consider that contralateral lung of COPD patients would develop temporary hyperdistention after single-lung transplantation. They think the hyperdistention is

brief and special treatment is not necessary if patients could unlink to breathing machine early, though surgical means is needed sometimes to balance ventilation-circulation<sup>[7]</sup>. The chest X-rays of these 4 cases show that because of unbalanced double-lung ventilation caused by COPD, mediastinum shifted to the transplanted side and the contralateral lung became more distended. Long-term mechanical ventilation could cause fused pulmonary bulla disrupting, leading to pneumothorax. Thus, for COPD patients who are not suitable for double-lung transplantation, sufficient preoperative preparation, accurate consideration of operation pattern, especially the effective combination of department of thoracic surgery, respiratory medicine, anesthesiology, ICU, and nursing would optimize therapeutic regimen, and benefit prognosis.

There is still no accepted ideal about operative therapy for COPD cases. Some studies demonstrate that for cases suitable for both lung transplantation and lung volume reduction, lung transplantation alone, lung volume reduction alone, or lung transplantation following lung volume reduction is feasible option<sup>[8]</sup>. In the cohort, main protopathy of the patients was bilateral diffuse emphysema complicated by bulla, less than 1/3 of the thoracic cavity. So the effect of lung volume reduction was not precise. In the case not suitable for double-lung transplantation, preoperative internal drainage to reduce tension in bullae, lung volume reduction in the definite emphysema area followed by contralateral lung transplantation, or simultaneous contralateral lung transplantation and lung volume reduction are all favorable methods. It is believed that with development of transplantation technique and improvement of controlling postoperative infection and organ rejection, lung transplantation shows a promising prospect for treating final stage COPD and improving quality of life.

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## 慢性阻塞性肺疾病 4 例单肺移植★

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**摘要:** 回顾性分析 4 例慢性阻塞性肺病单肺移植患者的临床资料, 均接受尸体供肺移植, 双肺弥漫性肺气肿 1 例接受右肺移植; 弥漫

性肺气肿并部分相互融合成肺大疱 3 例接受左肺移植, 此 3 例分别于移植术中 (1 例) 和移植后 (2 例) 接受右肺减容术。移植后采用他克莫司、霉酚酸酯及泼尼松预防排斥反应, 同时给予达利珠单抗或抗胸腺细胞球蛋白进行诱导治疗。4 例移植手术经过顺利, 1 例移植后第 5 天发生急性排斥反应, 经甲泼尼龙冲击治疗逆转。2 例受者顺利出院, 1 例存活已超过 2 年; 2 例分别于肺移植后第 74, 77 天死亡。

**关键词:** 肺移植; 肺疾病, 阻塞性; 器官移

植

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## CRTER 杂志对涉及中医药、针灸内容稿件提出的修稿要求

○ **实验主体为人的文章:** 应在“对象”中体现出纳入对象的中西医诊断标准, 并引入相应文献。“讨论”中结合上述诊断标准从中西医两个角度讨论中药的有效性。修稿时要注意中医病名一定要有对应西医病名的描述。

○ **“讨论”中应结合实验检测指标:** 从中西医角度, 即从传统医学理论和现代医学理论两个方面对等论述疾病发病机制, 药物作用也应与前面论述的疾病中西医发病机制相契合。

○ **描述“中药”作用的稿件:** 应在“材料和方法”中体现制剂类型、服药方法、效果 (水煎剂, 粉剂, 化学淬取, 含药血清, 灌胃, 腹腔注射, 局部外敷), 并在“讨论”中说明中药制剂类型、服药方法是否会影响本实验结果, 产生实验偏倚和不足, 并对这种偏倚和不足展开说明。

○ **中药里面含有多重生物碱:** 要对中药进行深入研究, 仅仅提取其有效物质是不够的, 应该采用标记的方法。

要告诉读者同行, 文章描述机体已经吸收了哪些物质, 或者是机体对于哪些物质有反应, 才可以找到服药和产生效应之间的关联。这个生物标记物可以是免疫的、内分泌的等等, 可以是具有显形和基因表型的标记物, 因为基因的表达不同, 个体之间是有差异的。

○ **实验如不能采用标记的方法确定是哪种有**

效成分产生的结果时: 要在“讨论”中应紧密围绕实验结果的指标, 说明“中药各有效成分”是如何起到结果作用的。

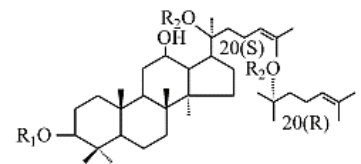
○ **中药组方中各个单味药的比例含量应明确:** 制备过程要描述至使实验具重复性, 如多少药材加多少水煎煮多少时间而成的等。

要对动物给药剂量的设定标准进行说明, 即是临床用药标准还是临床用药的多少倍。

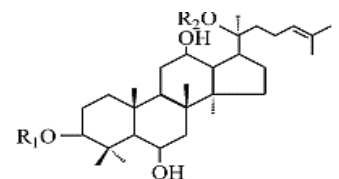
○ **当文章讨论单味中药作用时:** 应在“引言”或“讨论”合适的位置体现出该药有效成分, 该有效成分的化学结构式, 药物名称应以拉丁名、英文名或拼音名表述。同时要注意前述描述应来源于既定的“国家药品标准”, 如《中华人民共和国药典》。

范例: 文章所讨论的是“三七总皂苷”, 应在“引言”或“讨论”适当位置描述如下内容: 三七中的主要有效活性成分为三七总皂苷, 为五加科植物三七 [panaxnotoginseng (burk)f.h.chen] 的芦头按一定的工艺提取得的总皂苷。根据《中华人民共和国药典》记载三七的主要成分为三七总皂苷, 它主要含有人参皂苷Rb1、Re、Rg1和三七皂苷R1等20余种皂苷成分, 其中人参皂苷Rb1(Rb1)、人参皂苷Rg1(Rg1)是三七总皂苷中含量最高的两个成分。

人参皂苷Rb1的化学结构式为: R1=-Glc2→1Glc; R2=-Glc6→1Glc。



人参皂苷 Rg1 的化学结构式为:  
R1=-Glc; R2=-Glc。



○ **针灸类稿件应说明:** 针灸部位、针具、时间、深度、强度、频率。

○ **表述针刺取穴时:** 取穴依据不能单纯用中医理论来说明, 为使国际同行专家也能明白文章意图, 西医的理论解释是必要的, 同时应配合文献加以支持。

○ **动物实验中涉及针灸穴位时:** 应在穴位名后注明由世界卫生组织引进的由英文字母和数字相结合的穴位命名, 并用括号括起。例: 外关(SJ5), 翳风(SJ17)。

○ **涉及到人体针灸穴位时:** 应提供人体穴位图以直观明确针灸穴位位置。