

# Lung autotransplantation technique for treating central lung cancer of upper lobe

ZHANG Guoliang (张国良), LIU Jun (刘军), JIANG Guanchao (姜冠潮), SHEN Chenyang (沈晨阳), LI Mengzan (李梦赞)

**Objective** To assess the feasibility of applying lung autotransplantation technique in the treatment of central lung cancer of the upper lobe.

**Methods** Two patients underwent double-sleeve right upper and middle bilobectomy. Because the length of resected bronchus or pulmonary artery involved by tumor was too long to perform tension-free anastomosis, we had to transplant the lower lobar vein into the proximal stump of the upper lobar vein. Another two patients underwent pneumonectomy firstly, because we could not perform sleeve lobectomy in suit as the tumor extended through the oblique fissure to the margin of the lower lobe. Subsequently, we resected the tumor parts at a separate table, and replanted the preservable part of the lung into the chest.

**Results** Being followed up to December 1999, the patient 1, 3 and 4 had been alive with tumor free for 31, 18 and 13 months. The patient 1 and 3 had a good living quality but the patient 4 had a very poor activity. The patient 4 received resection of the replanted lung for pulmonary artery bronchus pleural fistula on the 42nd day after operation. The second patient died of tension pneumothorax associated with bronchopleural fistula on the 19th day after operation.

**Conclusion** Lung autotransplantation is an alternative technique for pulmonary preservation in patients with stage III central lung cancer of the upper lobe whose cardiopulmonary function is too poor to undergo pneumonectomy.

**Key words** Carcinoma, bronchogenic; Extracorporeal resection; Lung autotransplantation

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Since we successfully used lung autotransplantation technique in the treatment of stage III lung cancer in May 1997,<sup>[1]</sup> another 3 patients with central lung cancer of the upper lobe had undergone this kind of procedure by the end of 1998. A retrospective study and follow-up survey are reported.

## PATIENTS

### Patient 1

A 45-year-old man with a 4-month history of cough, hemoptysis and short of breath was diagnosed as having central lung cancer of the right upper lobe associated with

obstructive pneumonia. Bronchoscopy demonstrated in the right upper lobe orifice a neoplasm extending to the middle segmental bronchus. Pathologically, the biopsy specimen of the neoplasm revealed abnormal cells and squamous metaplasia. CT scan on thorax revealed a 5 cm mass at the right lung that occluded the right upper lobe bronchus and made subsegmental atelectasis distal to the lesion. The tumor seemed to encase the pulmonary artery of the upper lobe and extended closely to the right main pulmonary artery. After bronchoscopy and enhanced CT examination, a sleeve upper and middle bilobectomy was considered technically possible. Pulmonary function test was made before and after operation (Table 1). After chemotherapy, the patient underwent a double sleeve right upper and middle bilobectomy including 6.8 cm of the bronchus and 2 cm of the pulmonary artery resected simultaneously. The tension in the site of bronchial anastomosis, however, can not be relieved although the pericardium around the inferior pulmonary vein was incised. In order to ensure the tension-free anastomoses of both bronchus and artery, the lower pulmonary vein was divided in the pericardium and the isolated lower lobe specimen was flushed with heparin solution (12 500 U/500 ml S. at 23 °C) and sheared at a separate table. Subsequently the lower pulmonary vein was anastomosed into the proximal stump of the upper lobar vein. The bronchus and pulmonary artery were anastomosed in turn. The time of operation and temperature of flushing solution were recorded (Table 2). During the operation, radical hilar and mediastinal lymphadenectomy was performed. The patient received mechanical ventilation for 6 hours at ICU and recovered rapidly 6 days after operation. Pathologic examination showed a well-differentiated squamous carcinoma, hilar lymphnode metastasis (3/3), no mediastinal lymphnode metastasis (0/17), and negative results in the specimens of the stump of the superior and inferior bronchus. pTNM was stage IIIa T<sub>3</sub>N<sub>1</sub>M<sub>0</sub>. Three weeks later on spiral CT the reconstruction of the vascular reflux and bronchus showed a good blood perfusion and ventila-

**Table 1** Pre and postoperative pulmonary function test

Patient	VC (L)	%	FEV1 (L)	%	MVV(L)	%	FEF <sub>25%-75%</sub> (L/s)	PaCO <sub>2</sub> (mm Hg)
1 Pre	2.26	58	1.72	56	67	48	1.37	21.0
Post	2.18	54	1.49	46	49	34	0.90	38.7
3 Pre	1.90	62	0.72	31	24	22	0.25	48.0
Post	2.04	67	0.75	32	29	27	0.32	39.8

VC: vital capacity; FEV1: forced expiratory volume in one second; MVV: maximum voluntary ventilation; FEF<sub>25%-75%</sub>: forced expiratory flow rate from 25% to 75%; %: percentage of the predicted.

**Table 2** Time of operation(min) and temperature of perfusion (°C)

Patient	Date	Lung in vitro	LPV suture	LPV anas	Bronchial an	IPA anas	PA occl	Total time	Room (°C)	Perfusion(°C)
1	05/12/1997	15	8	15	14	10	180	300	23	23
2	08/18/1997	20	10	25	80	80	177	415	19	8
3	07/02/1998	233	10	20	72	16	340	450	19	19
4	11/18/1998	125	10	50	48	56	312	480	30	8

LPV: lower pulmonary vein; PA: pulmonary artery; anas: anastomosis; occl: occlusion

18 weeks, recurrence occurred in the above edge of bronchial anastomosis. Local lesion disappeared after intracavity irradiation. The patient returned to work and had no evidence of recurrence until December 1999.

## Patient 2

A 63-year-old woman was found to have central lung cancer of the right upper lobe and coronary heart disease. Bronchoscope showed that the tumor blocked the bronchial orifice of the right upper lobe completely. She was given a new adjuvant chemotherapy. During thoracotomy, a double sleeve right upper and middle bilobectomy was performed. Four cm of the bronchial and pulmonary artery stem was removed respectively. It was difficult to appose the ends of the artery because of the amplitude of the sleeve and the inferior pulmonary vein. To reduce the tension, the lower pulmonary vein was incised and the detached lower lobe was perfused and immersed in heparin solution (12 500 U/500 ml NS at 8°C) for 20 minutes(at this time mediastinal lymphadenectomy was done). After it was sheared, the detached lobe was replanted into the thorax, reimplanting the inferior vein on the proximal stump of the superior one and anastomosing the bronchus and artery in turn. The patient died from bronchial anastomosis fissure and tension pneumothorax on the 19th day after operation. Pathologically, a poorly differentiated adenosquamous carcinoma protruding into the bronchus and infiltrating into the pulmonary artery muscular layer was noted. The hilar lymph node was found to be metastatic(4/4) and mediastinal lymphnode showed negative results (0/11). pTNM was stage IIIa T<sub>3</sub>N<sub>1</sub>M<sub>0</sub>.

## Patient 3

He had had bronchial asthma for 42 years. Bronchoscopy showed a neoplasm occluding completely the left upper lobe orifice, thickening and deformation in the left lower lobe orifice. Pre-and postoperative pulmonary function test was performed (Table 1). During the operation, the tumor was found to invade over the oblique fissure into the apex of the medial basal segment. After pneumonectomy, on a separate table the specimen was sheared by resecting the origin of the lower pulmonary vein and a partial pericardium rounding it and cutting off the vascular branch of the medial basal segment. After removing the tumor and lymphnode, the bronchial orifices of the dorsal, posterolateral, anteromedial segment of the lower lobe were exposed separately. The above three segmental bronchial orifices were sutured and got together for anastomosis later. The wounded surface of the lower pulmonary oblique fissure was sutured with figure-of-U. The vein, bronchus and artery were anastomosed in turn. The bronchial anastomosis site was encircled with coastal pedicle muscle flap. The patient recovered satisfactorily after mechanical ventilation for 18 hours. Pathologic examination revealed a well differentiated squamous cell carcinoma with lymphnode metastasis in the pulmonary hilum and bronchial crista (11/11). No mediastinal lymphnode metastasis was found (0/14). pTMN was stage IIIa T<sub>3</sub>N<sub>1</sub>M<sub>0</sub>. Followed up to December 1999, the patient was tumor-free alive for 18 months and got a satisfactory improvement in living quality. Asthma has scarcely recurred.

## Patient 4

A 52-year-old man was admitted to the hospital for the treatment of central lung cancer of the left upper lobe associated with obstructive pneumonia, mycotic infection,

orifice and that the lower lobe orifice was compressed. After thoracotomy, the left upper lobe was found to be atelectatic, consolidated and attached to the chest wall and the pericardium. The oblique fissure could not be dissected. After pneumonectomy was performed, the lower lobe was cut out from the specimen on a separate table. The orifice of the basal segmental artery trunk was exposed. The dorsal artery was ligated because it was too short to be anastomosed. The lower lobe bronchus was divided obliquely at 1 cm above the dorsal bronchus and its orifice was made elliptical including three segmental orifices. The wounded surface of the lower lobe was sutured interruptedly and the pulmonary artery, bronchus, and vein were exposed above the level of the suture. The pulmonary vein, bronchus and pulmonary artery were anastomosed in turn. The bronchial anastomosis site was encircled with pedicled pleural flap. On the second day after operation, the patient had more bloody mucoid sputum. Chest X-ray showed an ill-defined opacity in the replanted left lobe and the mediastinum shifting to the right. On the 9th day after operation the bloody mucoid sputum gradually disappeared and chest radiography showed an intermediate mediastinum. The patient was discharged from mechanical ventilation. Pathological examination showed a highly differentiated squamous cell carcinoma that blocked the bronchus and invaded the wall of the pulmonary artery as well as multiple tiny abscesses in the lung. Lymph node metastasis was evident in the hilar(8/8), subcarina(1/3) and mediastinum (0/30). pTNM was stage IIIa T<sub>3</sub>N<sub>2</sub>M<sub>0</sub>. On the 42nd day after operation, the patient had to receive the second thoracotomy for active bleeding in the thoracic cavity and hemoptysis. A fistula between the pulmonary artery and bronchus, central necrosis, and extensive collateral circulation of the replanted lobe was found during the thoracotomy. The residual lobe had to be removed and the main bronchial stump was closed with pedicled costal muscle flap. The patient was discharged from the hospital on foot. The second pathological examination showed there were degenerative necroses and stale bleeding in the residual lobe. No carcinoma cell was found. In December 1999 the patient had a poor activity, but X-ray showed no sign of tumorous recurrence.

## DISCUSSION

### Operative indications

Bronchovascular double sleeve lobectomy is a satisfactory technique in the treatment of central lung cancer of the upper lobe.<sup>[2-5]</sup> It has already been one of the routine procedures. But if the tumor involves the bronchus and/or

2), and also because of the tractive limit of the inferior pulmonary vein, it is necessary to appose the ends of the bronchus or the artery. To eliminate the tension of the anastomosis of the bronchus and artery, the inferior pulmonary vein is divided in the pericardium and reimplanted on the proximal stump of the superior one. It is a new procedure using lung autotransplantation technique in the treatment of central lung cancer. Under the above situation, the tumor was excised in vivo and the isolated lobe was replanted within a very short time. For example, the lobes of patient 1 and 2 were replanted in 20 minutes. Another situation is that the tumor extends through the major fissure and adheres to the margin of the lower lobe. According to our experience, the only choice of the later situation is to perform pneumonectomy, because the distal direction resecting line of the bronchus and pulmonary artery in the oblique fissure for double sleeve lobectomy can not be exposed. Nevertheless some of the operative candidates with poor cardiopulmonary function are unable to undergo pneumonectomy. This problem is solved by lung autotransplantation technique. In our patients, we removed the malignant mass from the specimen and sutured the surface of wound at the margin of the inferior lobe at a separate table after pneumonectomy. The preservable inferior lobe was replanted into the thorax by anastomosing the lower lobar vein on the proximal stump of the superior one, the lower bronchus and artery on the root of the main bronchus and pulmonary artery. In patient 3 the tumor invaded the pericardium abutting the inferior lobar vein. To thoroughly remove the tumor, we incised a part of the root of the inferior lobar vein and pericardium. We suggest that lung autotransplantation technique is indicated for the treatment of central lung cancer of the upper lobe in the patients with poor cardiopulmonary function that makes pneumonectomy impossible. The patients have the following characteristics: extended sleeve resection of the bronchus; extended sleeve resection of the pulmonary artery; tumor involved part of the pericardium, adjacent to the inferior lobar vein; tumor extended across the oblique fissure into the margin of the lower lobe, but the deep of the lower lobe was not involved. Lung autotransplantation technique is an alternative procedure for pulmonary preservation.

### Relative factors affecting the survival of replanted lobe Ischemic time of lung

In our patients, 2 were subjected to intracorporeal tumor resection, and the rest 2 extracorporeal tumor resection. In each group, one was successful. In the intracorporeal resection group, the time of the lung in vitro was

group the time for isolating lobe in vitro and blocking pulmonary artery was longer than that of the former (Table 2). The longest time was shown in patient 3 who has a good living quality up to now. This suggests that the replanted lobe can be survived with the isolated lobe in vitro for 223 minutes and the blocked pulmonary artery for 340 minutes.

### Flushing of isolated lobe

40 ml of heparin solution (12 500 U heparin/500 ml N.S.) at room temperature was used to flush the inferior lobar vein in patient 1 and 3 until the solution flowed out from the pulmonary artery was clear. The lower lobe was subsequently immersed in the heparin solution. Both of the replanted lobes survived. But in patient 2 and 4, the lobes were flushed and immersed using heparin solution at 8 °C, and the replanted lobes did not survive. Dr. Shen ZM reported<sup>[9]</sup> that low-temperature flush to the transplanted organs is not indispensable for a successful transplantation, on the contrary those transplanted organs without low-temperature flush may survive well. The best temperature to preserve the big parenchymatous organs was 15-25 °C. He didn't refer to any material about lung. Because of the complicated clinical factors, we do not know whether the failure of our 2 patients is related to the flush at 8 °C. However, 2 successful patients showed that the replanted lobe can survive by flushing with heparin solution at 19-23 °C (Table 2).

### Pulmonary vein embolism

The factors for pulmonary vein embolism include inadequate isolated lobar vessel perfusion, narrowing of vein anastomosis, twisting or compression of vessel, insufficient anticoagulant, and reperfusion injury of the isolated lobe and so on. We infused 12.5 mg heparin quickly 5 minutes before blocking the pulmonary artery, infused 25 mg heparin slowly, and washed anastomosis site with 12.5 mg heparin solution locally. Before the pulmonary artery was blocked and excised, it was transiently blocked for 5 minutes two times with 5-minute intemission, so as to increase the ability to combat ischemia reperfusion injury.<sup>[7]</sup> Heparin was infused continually with 50 mg/24 hours after operation for 5 days. In our patients, 3 showed no secondary bleeding and embolism. Pulmonary artery broncho-pleural fistula occurred in patient 4 because of necrosis of the replanted lobe which was caused by incomplete embolism of the pulmonary venous system. Venous drainage obstruction resulted from over-closely interrupted suture to the wounded surface of oblique fissure, and secondary

agulation treatment and decrease of the dose of heparin also contribute to pulmonary venous embolism.

### Bronchial anastomosis

No complications can be found after correct vascular anastomosis. Bronchial anastomosis remains a major problem. The failure of our two patients was related to bronchus pleural fistula. In patient 3, bronchial anastomosis was checked for air tightness and encircled by an intercostal pedicled muscle flap, which offers good vascularity to the distal bronchus and separates it from the pulmonary artery anastomosis. It is a good measure. On the 10th day after operation, patient 2 received bronchoscopy treatment to evacuate sputum and remove a blood clot at the anastomosis site with biopsy forceps. After that she was found to be hemoptysis. On the 17th day after operation in another ICU, his machinery assistant respiration mode was changed to pressure support and he was supported to 22 cm H<sub>2</sub>O. This caused bronchopleural fistula and tension pneumothorax. We suggest that the pressure supported on machinery ventilation can not be more than 7 cm H<sub>2</sub>O after bronchoplasty.<sup>[8]</sup>

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### 应用自体肺移植技术治疗上叶中心型肺癌

张国良, 刘军, 姜冠潮, 等.

北京医科大学人民医院胸外科, 100044 中国

【摘要】 目的 探讨应用自体肺移植技术治疗上叶中心型肺癌的可行性。 方法 2例作双袖状右上中叶联合肺叶切除, 因支气管切除过长或肺动脉切除过长, 吻合张力过大, 做下肺静脉切断, 肺短时间离体后作下叶重植, 将下肺静脉移

除, 下叶修剪后重植于胸腔内。 结果 随访至 1999 年 12 月, 第 1、3、4 例患者已分别无瘤存活 31、18 和 13 个月。第 1 和 3 例患者生活质量良好, 但第 4 例患者活动能力极差。第 4 例术后 42 d 因肺动脉、支气管胸膜瘘, 做移植肺切除。第 2 例术后 19 d 死于支气管胸膜瘘、张力性气胸。 结论 对心肺功能不能耐受全肺切除的 III 期上叶中心型肺癌患者, 自

体肺移植是一种可供选择的能保全肺组织的肺癌根治术式。

【关键词】 癌, 支气管原; 体外切除; 自体肺移植

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