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ORIGINAL ARTICLE

Outcomes and pulmonary function in living lobar lung transplant donors

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Summary

Successful living-donor lobar lung transplantation (LDLLT) largely depends on donor outcome; however, there are few studies that have assessed outcomes of LDLLT donors, particularly pulmonary function. We investigated the outcomes and pulmonary function after donor lobectomy in LDLLT donors. Retrospective evaluation of consecutive 33 LDLLT donors was performed. Preoperative characteristics and perioperative and postoperative variables were investigated. Evaluation of pulmonary function 3, 6 and 12 months after donor lobectomy was performed prospectively. All donors were well alive after donor lobectomies. Morbidity was found in five donors (15%). Postoperative complications consisted of re-accumulation of pleural effusion requiring readmission in three donors and prolonged air leakage in two donors. Sacrifice of pulmonary arteries was performed in 20 donors (61%) with 1.4 ± 0.6 branches. Forced vital capacity was 77.8 ± 6.1%, 84.8 ± 6.0% and 89.4 ± 6.6% of the preoperative value 3, 6 and 12 months after donor lobectomy, respectively. Forced expiratory volume in 1 s was 80.5 ± 7.8%, 85.6 ± 8.9% and 89.3 ± 8.7% of the preoperative value 3, 6, and 12 months postoperatively. Living-donor lobectomy was performed with low morbidity. Pulmonary function even after lobectomy was better preserved than expected.

Introduction

To save the life of a rapidly deteriorating critically ill patient, living-donor lobar lung transplantation (LDLLT) has been performed successfully [1–3]. In LDLLT, two separate donors are required for each individual recipient. That is, typically, the recipients undergo bilateral pneumonectomy, followed by implantation of a right lower lobe from one donor and a left lower lobe from the second donor during the same procedure. In this way, the success of LDLLT is largely dependent upon donor outcome. Although a few studies have assessed outcomes of the living lobar lung donors [1,2,4–7], there were not enough data on outcomes after donor lobectomy, particularly pulmonary function [6,7]. All donors should be informed of not only the potential morbidity and mortality associated with donor lobectomy, but also the potential outcomes with regard to pulmonary function and its chronological recovery. The primary purpose of this study was to evaluate pulmonary function after donor lobectomy prospectively in LDLLT donors. Furthermore, we also assessed surgical procedures and postoperative outcomes in LDLLT donors retrospectively in our institution.

Patients and methods

Between June 2008 and May 2011, a total of 33 donor lobectomies were performed at Kyoto University Hospital for use in the consecutive 19 LDLLT (14 bilateral and 5 single LDLLT). All donors had previously completed a clinical evaluation that included blood studies, pulmonary function test and chest computed tomography scans. Three-dimensional (3D) multidetector computed tomography (CT) angiography was performed to display the complex pulmonary arterial and venous anatomy (Fig. 1).

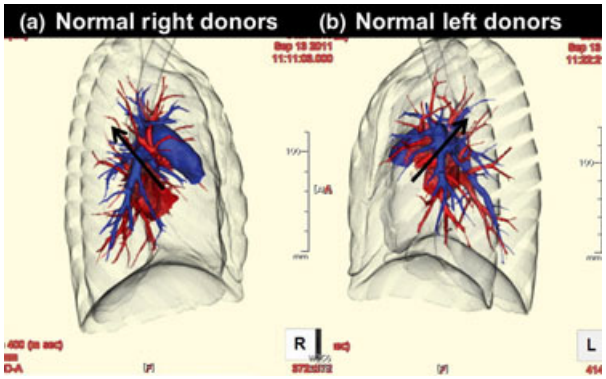

Figure 1 Three-dimensional multidetector computed tomography angiography for the confirmation of the pulmonary arterial and venous anatomy. Right donor lung (a) and left donor lung (b). The arrow shows the planned cutting line of the pulmonary artery.

Table 1. Donor selection criteria for living-donor lobar lung transplantation.

Relatives within the third degree or a spouse
20 ≤ age ≤ 60 years
ABO identical or compatible
No significant medical history or active medical problems
No recent viral infection
No abnormalities on the electrocardiograph and echocardiogram
No significant pulmonary pathology on computed tomography on donor side
Arterial oxygen tension ≥ 80 Torr
Forced vital capacity, forced expiratory volume in 1 s ≥ 85% of predicted
No previous thoracic operation on the side to be donated
Nonsmokers (If current smokers, requirement of cessation of smoking at the time of offering donation and continuous cessation after donor lobectomy)
Absence of coercion
Satisfactory psychosocial evaluation

Donor selection criteria were outlined in Table 1. For size accommodation in LDLLT, we previously proposed a method using calculated FVC by the number of segments [2,8], which is called Date's formula [9]. Given that the right lower lobe consists of 5 segments, the left lower lobe of 4, and the whole lung of 19, we estimated the graft FVC using the following equation: The graft FVC = measured FVC of the right donor × 5/19 + measured FVC of the left donor × 4/19. When graft FVC was larger than 45% of predicted FVC of the recipient (calculated according to height, age and sex), we accepted the size disparity regardless of recipient's diagnosis. The 33 patients constitute the cohort of patients for this outcome analysis. This study was approved by the Institutional Review Board of Kyoto University.

Donor management at the surgery was described in elsewhere [2]. Briefly, epidural catheters for postoperative analgesia were placed routinely the day before the surgery to avoid complications related to heparinization during the donor lobectomy. After induction of general anaesthesia, donors were intubated with a left-sided double lumen endotracheal tube. Fibreoptic bronchoscopy was performed to determine if lower lobectomy was feasible. Then the donors were placed in the lateral decubitus position, and a posterolateral thoracotomy was performed through the fifth intercostals space. Fissures were developed using linear stapling devices. The pericardium surrounding the inferior pulmonary vein was opened circumferentially. Dissection in the fissure was carried out to isolate the pulmonary artery to the lower lobe and to define the anatomy of the pulmonary arteries to the middle lobe and to the lingular segment in the right and left side of the donor. If the branches of the middle lobe artery and lingular artery were small, they were sacrificed by ligation and division. After intravenous prostaglandin, E1 was administered, heparin (100 IU/kg) and 500 mg of methylprednisolone were administered intravenously. After placing vascular clamps in appropriate positions, the division of the pulmonary vein, pulmonary artery and bronchus were carried out in this order. Vascular stumps were oversewn with a 5-0 Prolene continuous suture (Ethicon, Tokyo, Japan). Auto pericardial patch was used if necessary. The bronchial stump was closed with 4-0 Prolene interrupted sutures. Then, each bronchial closure was covered with a pedicled pericardial fat tissue. Heparinization was reversed by administering protamine. The thoracotomy was closed in a standard manner after placement of one or two chest tubes. The patient was extubated in the operating room. Chest tube was removed when the chest tube drainage became less than 200 ml/day. After the discharge, the donors basically visited the outpatient clinic 1, 3, 6 and 12 months after surgery. At each clinic, a clinical evaluation that included blood studies, pulmonary function test and chest rentogenography was performed.

For all donors, the inpatient and outpatient medical records, pulmonary function test results and chest X-ray and CT films were reviewed.

Statistical analysis

Statistical analysis was performed using the StatView (version 4.5) software package (Abacus Concepts, Berkeley, CA, USA). All values are expressed as the means ± standard deviation. The data were evaluated by Student's *t*-test and Fisher's exact test for 2-group analysis. A value of $P \leq 0.05$ was considered to be statistically significant.

Results

The study included 24 female and 9 male healthy donors who fulfilled the donor inclusion criteria (Tables 1 and 2). Their ages were 40.7 ± 12.0 years. Ten donors (30%) were ex-smokers or current smokers. All donors stopped smoking at least at the time of their offers to become donors. Eleven donors (33%) had comorbidities, such as asthma in three, depression in three and diabetes mellitus, hyperthyroidism, elevated liver enzyme, iron-deficiency anaemia, paraoxysmal atrial fibrillation and cerebral spinal fluid deficiency syndrome in one. However, all these comorbidities were well controlled or treated before donor lobectomy. According to preoperative evaluation, FVC was 114.7 ± 13.5% of a predicted value and FEV1 was 105.7 ± 11.4% of a predicted value. In addition, all donors did not show any significant findings in chest CT. Preoperative 3D multidetector CT angiography presumed possible requirement of pulmonary arterial plasty after donor lobectomy in four left donors, and in effect pulmonary arterial plasty was performed with auto pericardial patch in three of those four donors.

Right lower lobectomy was performed in 19, whereas left lower lobectomy in 14 (Table 2). In 20 donors, small branches of pulmonary artery were sacrificed to obtain an adequate arterial cuff for safe implantation. In details, small pulmonary arterial branches were sacrificed in 9 of 19 right lobectomies, whereas it was 11 of 14 in left lobectomies ($P = 0.09$). No challenging procedures were required for pulmonary veins and bronchus. Bleeding was 139 ± 73 ml and no blood transfusion was required. The graft ischemic time was 155 ± 42 min for the first lung and 128 ± 31 min for the second lung, in each LDLLT.

Table 2. Donor characteristics pre- and intra-donor lobectomy.

Preoperative variables	
Age	40.7 ± 12.0 years
Gender	
Male:Female	9:24
%FVC	114.7 ± 13.5
%FEV1	105.7 ± 11.4
Arterial oxygen tension	94.7 ± 6.3 Torr
Comorbidity	
Yes:No	11:22
Intraoperative Variables	
Surgical procedures	
RLL:LLL	19:14
Sacrifice of PA branches	20 donors (27 branches)
Operation time	245 ± 45 min
Bleeding	139 ± 73 ml

FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; LLL, left lower lobectomy; PA, pulmonary artery; RLL, right lower lobectomy.

After the operation, one chest drain was placed in 32 donors, and two chest tubes in one donor. The drainage period was 3.6 ± 1.9 days after lobectomy (Table 3). Only two patients required a chest tube placement more than a week for a prolonged air leakage (8 and 10 days). There was no mortality related to donor lobectomy. Postoperative complication was accumulation of pleural effusion requiring readmission in three donors and prolonged air leakage requiring more than 7 days of chest drainage in two donors.

In terms of pulmonary function, FVC was 77.8 ± 6.1% of the preoperative value 3 months after lobectomy, but increased to 84.8 ± 6.0% and 89.4 ± 6.6% of the preoperative value 6 months and 1 year after surgery (Fig. 2a).

Table 3. Postoperative data in donors.

Postoperative variables	
Duration of chest tube placement	3.6 ± 1.9 days
Complications	
Prolonged air leakage	2
Re-accumulation of pleural effusion(requiring readmission)	3

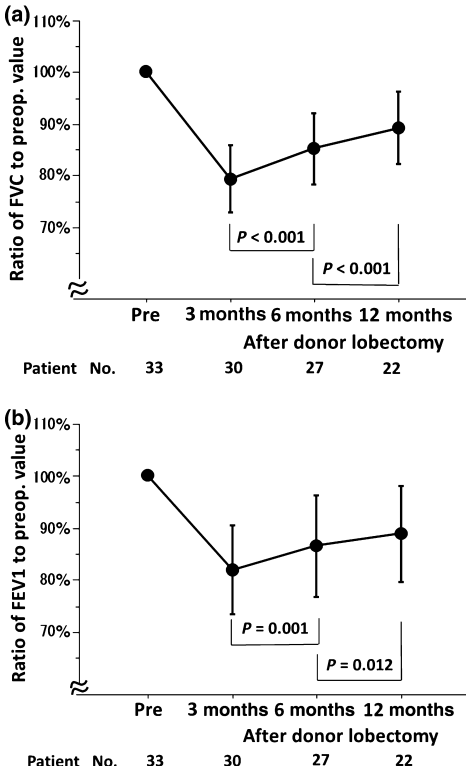

Figure 2 Trend of pulmonary function test. (a) Ratio of FVC (forced vital capacity) to the preoperative value. (b) Ratio of FEV1 (forced expiratory volume in 1 s) to the preoperative value. Pre, before donor lobectomy; preop, preoperative.

FVC increased significantly 6 months after lobectomy in comparison with 3 months postoperatively ($P < 0.001$) and 1 year after lobectomy in comparison with 6 months postoperatively ($P < 0.001$). There was no significant difference between the right and left lobectomy in each time point. Likewise, FEV1 was 80.5 ± 7.8% of the preoperative value 3 months after lobectomy, but increased to 85.6 ± 8.9% and 89.3 ± 8.7% of the preoperative value 6 months and 1 year after surgery (Fig. 2b). FEV1 increased significantly 6 months after lobectomy in comparison with 3 months postoperatively ($P = 0.001$), and 1 year after lobectomy in comparison with 6 months postoperatively ($P = 0.012$). There was also no significant difference in FEV1 between the right and left lobectomy in each time point. In terms of recipients' outcome, 17 of 19 recipients (90%) were discharged home without oxygen support after LDLLT and survived more than 6 months after lung transplantation. On the other hand, one recipient, who required prolonged extracorporeal membrane oxygenation support after LDLLT, died of sepsis on day 14. In addition, the other patient, who had been on rehabilitation without oxygen support after LDLLT, died of massive aspiration on day 98.

Discussion

The use of living-donor lung lobes for a transplantation in two children with terminal pulmonary disease was first described in 1992 [10]. Since then, LDLLT was developed by Dr Starnes and his colleagues with satisfactory intermediate survival and functional results [1]. Because of the severe donor shortage particularly in Japan, LDLLT has been one of the last options to save the critically ill patients with a wide range of pathophysiology [2]. Usually, two healthy donors are needed in LDLLT and the safety of donors should always be a primary concern. Each of these individuals undergoes lobe resection in one of the lungs, resulting in some degree of permanent loss of lung function. However, there are few studies in the literature regarding the complications and the trend of lung function after donor lobectomy. Thus, we decided to evaluate pulmonary function after donor lobectomy prospectively in living lobar lung transplant donors in this study. Furthermore, we also assessed surgical procedures and postoperative outcomes retrospectively in living lobar lung transplant donors in our institution.

In terms of lung function, we confirmed that both FVC and FEV1 recovered constantly up to more than 90% of the preoperative value 1 year after donor lobectomy. These values were more than the predicted values after lower lobectomies. Although several studies also investigated postoperative pulmonary function and stated that postoperative pulmonary function was well conserved, there were no descriptions about the timing of the pulmonary function tests taken postoperatively [6,7]. To the best of our knowledge, our study is the first report showing the trend of pulmonary function after donor lobectomy. In our study, there was a significant increase in both FVC and FEV1 12 months postoperatively in comparison with 6 months after donor lobectomy. As we collected the data only within 1 year after donor lobectomy, we have no idea as to the maximal FVC value which can be reached after donor lobectomy. However, our results provided the important information that pulmonary function improves continuously at least 1 year after surgery, which should be informed to all the prospective donors preoperatively from now on.

Relatively high morbidity has been described in the previous studies [1,2,4–7], but there have been no reports of deaths in living lung transplant donors. Morbidity rates varied from 20% to 60% in the previous reports [1,2,4–7], probably because the definition of complications differed from study to study and each report included a combination of various minor and major complications. According to a report from the international forum on the care of the live organ donor in 2005 [11], the data on approximately 550 live lung donors showed that 4% of live lung donors experienced an intraoperative complication and 5% of donors experienced complications requiring surgical or bronchoscopic intervention. Furthermore, 3% of live donors were readmitted to the hospital because of postoperative morbidities. In our study, there were no intraoperative complications, whereas 5 of 33 (15%) demonstrated postoperative complications. Two donors required prolonged chest tube drainage for air leakage. In lobectomies for the use of the lobe to transplantation, the proximal dissection of the structures can often be the cause of the prolonged air leakage [4,7]. The rest of the three donors required readmission for the accumulation of pleural effusion around 1 week after discharge. All patients were successfully treated with thoracentesis and/or chest tube placement for about a week and preemptive antibiotic therapy. Pleural effusion did not look contaminated and no microbiological evidence was determined in all cases.

Three-dimensional multidetector CT angiography was reportedly useful for preoperative evaluation for the anatomy of pulmonary arteries and veins [12]. We also used 3D multidetector CT angiography for better understanding of the anatomy of pulmonary vessels of the donors. To date, we have not encountered unacceptable unusual anatomy of the donor vessels. In fact, we have sacrificed at most only small branches to lingular segment or right middle lobe. This information preoperatively obtained by 3D-CT angiography not only leads to safely explant lower lobes from living donors but also relieve surgeons from

stress to perform surgery on living donors to some extent. According to our results, more pulmonary arterial branches tended to be sacrificed in the left lower lobe donors than in the right lower lobe donors, but there was no significant difference.

There are several limitations in this study. The sample size was relatively small and follow-up time was relatively short. The retrospective study is the most practical way of addressing our question because of the incidence of LDLLT in a single surgical centre, but the results should be interpreted carefully. In our study, although surgical procedures and postoperative outcomes were assessed retrospectively, pulmonary function after donor lobectomy was evaluated prospectively. Furthermore, actual change in quality of mental health as well as physical health after donor lobectomy might be evaluated as Prager *et al.* commented in their study [6].

In conclusion, living-donor lobectomy was performed with low morbidity in our institution. Pulmonary function even after lobectomy was better preserved than expected.

Authorship

FC, TF, TS and TB: participated in study design. FC and HD: participated in the writing of the article. FC, TF, TS, MS, TS and HS: participated in the performance of the study. FC and HD: participated in data collection and analysis.

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