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ORIGINAL ARTICLE

Efficacy of three-dimensional computed tomography volumetry for recipients in downsizing oversized grafts in brain-dead donor lung transplantation

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Abstract

Objective Brain-dead donor lung transplantation frequently requires reduction in the size of oversized lung grafts for patients with a small chest cavity. We focused on the role of three-dimensional computed tomography (3D-CT) volumetry for recipients on downsizing oversized lung grafts.

Methods We performed 53 brain-dead donor bilateral lung transplantations, including 15 lobar lung transplants (Lobar group) and 38 standard lung transplants with full-sized grafts (Full group), between December 2010 and December 2018. Recipient chest volume before transplantation was measured using 3D-CT volumetry, and donor lung volume was evaluated by predicted total lung capacity. Post-transplant outcomes and pulmonary function were retrospectively compared between the groups.

Results The ratio of the recipient chest volume to the donor lung volume was significantly lower in the Lobar group (0.42 ± 0.15) than in the Full group (0.77 ± 0.30, $P < 0.01$). The calculated size matching between the donor and recipient after downsizing the grafts was significantly correlated to the ratio of the recipient chest volume to the donor lung volume (Spearman $r = 0.69$; $P < 0.01$). Early post-transplant outcomes did not significantly differ between the groups. Although the Full group showed slightly better pulmonary function after transplantation, the 1-, 3-, and 5-year overall survival rates were similar to the Lobar group (100%, 93%, and 81% in the Lobar group vs. 92%, 78%, and 70% in the Full group; $P = 0.50$).

Conclusions Brain-dead donor lobar lung transplantation showed favorable post-transplant outcomes. The assessment of recipient chest cavity volume using 3D-CT volumetry may help surgeons precisely downsize oversized lung grafts prior to transplantation.

Keywords Lobar lung transplantation · Three-dimensional computed tomography volumetry · Brain dead donor · Oversized graft

Introduction

Lung transplantation is well established as a standard therapy for end-stage lung failure. In Japan, brain-dead donor lungs are allocated to recipients by the Japan Organ Transplant Network according to the waitlist order, ABO blood-type compatibility, and matching of the predicted vital capacity or body height.

In lung transplant candidates with restrictive lung diseases, thoracic cavity size is decreased due to chest wall shrinkage and contraction of intercostal spaces, resulting in a size mismatch between the recipient small chest cavity and the donor lung graft volumes [1]. Therefore, patients with a small chest cavity frequently require downsizing of the allocated full-sized lung grafts in brain-dead donor lung transplantation [2–7]. However, there is currently no optimal indication and strategy to reduce the oversized lung volume [6].

Clinical use of three-dimensional computed tomography (3D-CT) has been introduced to the field of living-donor

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lobar lung transplantation and used for evaluating recipient chest cavities and living-donor lung graft volumes. This technology could potentially be applied for size matching in brain-dead donor lung transplantation by comparing the transplant recipient's chest cavity volume measured by 3D-CT volumetry with a brain-dead donor's predicted lung volume.

The purpose of this study was to elucidate the role of 3D-CT volumetry for recipients in downsizing oversized lung grafts recovered from brain-dead donors, and to compare the post-transplant outcomes between brain-dead-donor lobar lung transplantation and standard full-sized lung transplantation.

Subjects

Between December 2010 and December 2018, we performed 53 brain-dead donor bilateral lung transplantations, including 15 lobar lung transplants (Lobar group) and 38 standard lung transplants with full-sized grafts (Full group). Each transplant case was carefully reviewed and approved by the Lung Transplant Evaluation Committee at Kyoto University Hospital. The study protocol was approved by the institutional review board of Kyoto University Hospital, and written informed consent was obtained from each participant.

Methods

Brain-dead donor lungs were allocated to the recipients by the Japan Organ Transplant Network according to the wait-list order, ABO blood-type compatibility, and matching of the predicted pulmonary function value or body height [8]. When both the donor and recipient are ≥ 18 years old, the donor's predicted vital capacity (VC) should be $100 \pm 30\%$ of the recipient's predicted VC. Predicted VC was calculated by Japanese way (VC-J). When the donor and/or recipient are < 18 years old, the donor's height should be $100 \pm 12\%$ of the recipient's height for bilateral transplantation [9]. Graft size matching after the pulmonary lobar resection was calculated based on the number of resected pulmonary segments.

Recipient chest volume just prior to transplantation was retrospectively measured using 3D-CT volumetry. A newly developed high-speed and high-quality 3D image analysis system (Synapse Vincent, Fuji Film Co., Ltd., Tokyo, Japan) was used to obtain 3D images of the total lung volume [10]. Since precise data of donor CT were not available, donor lung volume was retrospectively evaluated by the predicted total lung capacity (pTLC) that was calculated using the regression equations of the European Respiratory Society [6].

The transplant procedure was basically the same between lobar transplantation and standard transplantation with full-sized grafts. Lobar-to-lobar bronchial anastomoses were applied for lobar lung transplantation to avoid leaving donor bronchial stumps closed. The final decision to reduce the volume of oversized lung grafts by lobectomy was made in the operating room based on visual assessment of the size discrepancy between the large lung graft and the small chest cavity. Flushing of the graft was completed, and lobar pulmonary resection was performed usually on a back table before implantation.

Postoperative management and follow-up were the same between the Lobar group and Full group. Early post-transplant outcomes, including PaO_2/FiO_2 at intensive care unit (ICU) admission, the use and rate of extracorporeal membrane oxygenation (ECMO), incidence of bronchial complications, 30-day mortality, and in-hospital mortality, were compared between the groups. Pulmonary function and 6-min walking distance were examined at 1, 3, 6, and 12 months and every year after transplantation. Long-term post-transplant outcomes, such as survival rates and incidence of chronic lung allograft dysfunction (CLAD), were assessed in both the groups.

Statistical analysis

Continuous variables were given as median (ranges) or mean ± standard deviation (SD). Student's t test or Mann–Whitney U test were used for analysis of continuous variables. Comparisons of categorical variables were made by χ^2 test or Fisher's exact test, as appropriate. The survival rates were determined by a Kaplan–Meier survival analysis. All P values were two-sided, and P values of < 0.05 were considered significant. Statistical analyses were performed using Graphpad Prism 5 (Graphpad Software Inc., La Jolla, CA). Spearman rank correlation was used to determine the relationship between the donor-to-recipient size matching and the ratio of recipient chest volume/donor lung volume.

Results

Pre-transplant patient variables

Patient characteristics are shown in Table 1. Although the patient height was similar between the groups, the Lobar group included significantly more underweight (BMI < 18.5) patients (13/15, 86.7%) than the Full group (17/38, 44.7%). Chest volume measured by the 3D-CT volumetry was significantly lower in the Lobar group (2.67 ± 0.86 L), compared to the Full group (4.04 ± 1.46 L, $P < 0.01$).

Regarding the indications for bilateral lung transplantation, the Lobar group had significantly more patients with

Table 1 Recipient characteristics

	Lobar ($n=15$)	Full ($n=38$)	P value
Gender (female)	5	19	0.36
Age (years)	32 ± 11	40 ± 13	0.05
BMI < 18.5	13	17	< 0.01
Height, cm	161 ± 7	162 ± 11	0.70
Chest volume, L	2.67 ± 0.86	4.04 ± 1.46	< 0.01
Ventilator dependent	4	4	0.20
Hospitalized	6	8	0.18
Indication for Tx			< 0.01
Interstitial lung disease	6	6	
Lung injury post-HSCT	0	7	
PAH	5	7	
Bronchiectasis, CF	3	8	
COPD	0	3	
LAM	0	5	
Others	1	2	

BMI body mass index; *Tx* transplantation; HSCT, hematopoietic stem cell transplantation; *PAH* pulmonary arterial hypertension; *CF* cystic fibrosis; *COPD* chronic obstructive pulmonary disease; *LAM* lymphagioleiomyomatosis

interstitial lung disease (6/15, 40%), including idiopathic pulmonary fibrosis (IPF) ($n=1$), pleuroparenchymal fibroelastosis ($n=2$), interstitial lung disease associated with collagen disease ($n=2$), and chronic hypersensitivity pneumonitis ($n=1$).

Lung grafts were properly downsized

The reasons for lobar resection were oversized grafts ($n=12$), infection in the right lower lobe ($n=2$), and both ($n=1$). The resected lobes were right middle lobe (RML, $n=3$), right lower lobe (RLL, $n=3$), left upper lobe (LUL, $n=1$), or left lower lobe (LLL, $n=1$). Two lobes were retrieved in 7 cases: RUL + LUL ($n=2$), RML + LUL ($n=2$), RML + LLL ($n=1$), RLL + LUL ($n=1$), and RUL + LLL ($n=1$).

In the Lobar group, donor-to-recipient size matching was significantly decreased after downsizing (pre-downsizing: 117.9 ± 8.5% vs. post-downsizing: 82.6 ± 14.6%, $P<0.01$; Fig. 1). Compared to the Full group (100.5 ± 13.0%), donor-to-recipient size matching was significantly higher before downsizing and lower after downsizing in the Lobar group ($P<0.01$).

The ratio of the recipient chest volume measured by 3D-CT volumetry to the donor full lung volume assessed by the predicted TLC (recipient chest volume/donor lung volume) was significantly lower in the Lobar group (0.42 ± 0.15) than in the Full group (0.77 ± 0.30, $P=0.03$). There was a significant correlation between the donor-to-recipient size matching in the y-axis and the ratio of

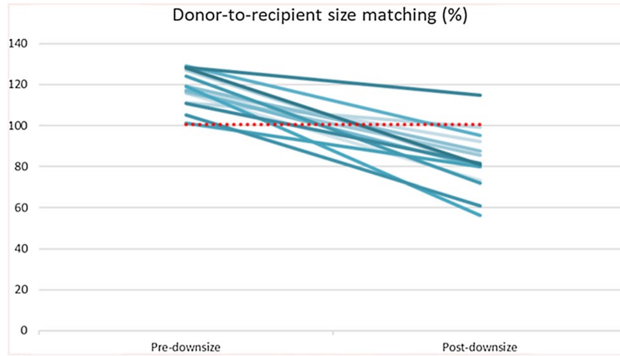

Fig. 1 Donor to recipient size matching was performed using predicted vital capacity. Donor-to-recipient size matching was significantly decreased after downsizing (pre-downsizing: 117.9 ± 8.5% vs. post-downsizing: 82.6 ± 14.6%, $P<0.01$) in brain-dead lobar lung transplant patients. The size matching between donor and recipient was significantly higher before downsizing and lower after downsizing in the Lobar group than in the Full group ($P<0.01$). The data of the Full group (100.5 ± 13.0%) were indicated by red color dotted line

recipient chest volume/donor lung volume in the x-axis, not before (Spearman $r=0.34$, $P=0.21$) but after downsizing the donor lung grafts (Spearman $r=0.69$, $P<0.01$; Fig. 2). A following approximate equation was derived from this strong correlation: $y=66.058x+54.575$.

Operative variables

Most patients required cardiopulmonary support during bilateral lung transplantation (the Lobar group: 15/15, 100%; the Full group: 28/38, 73.7%). Total graft ischemic time did not significantly differ between the groups (Lobar: 411 ± 89 min; Full: 422 ± 76 min, $P=0.66$).

Postoperative outcomes

Postoperative outcomes are shown in Table 2. Short-term outcomes were similar between the groups: PaO_2/FiO_2 at intensive care unit admission was 321 ± 141 mmHg in the Lobar group vs. 329 ± 170 mmHg in the Full group ($P=0.88$). Extracorporeal membrane oxygenation was required after transplantation in 3 patients (20%) in the Lobar group and in 5 patients (13%) in the Full group ($P=0.67$). The in-hospital mortality rate was 0% in the Lobar group vs. 5% in the Full group ($P=1.00$).

Long-term post-transplant outcomes were comparable between the groups: CLAD incidence was 13% in the Lobar group vs. 16% in the Full group ($P=1.00$). Bronchial complications were observed in 2 patients (13.3%) in the Lobar group and in 4 patients (10.5%) in the Full group ($P=1.00$). Post-transplant pulmonary function was slightly better in the Full group: %VC of predicted value was significantly higher in the Full group at 3 months after transplant,

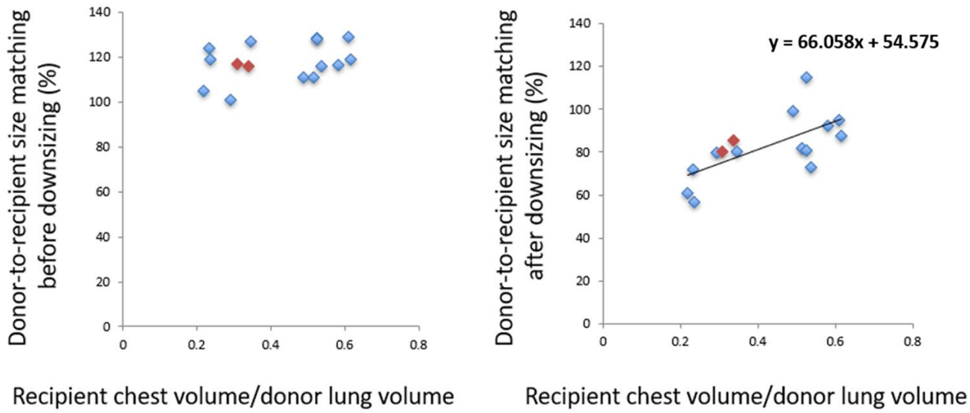

Fig. 2 Significant correlation was observed not before (Spearman $r = 0.34$, $P = 0.21$) but after downsizing the donor lung grafts (Spearman $r = 0.69$, $P < 0.01$) between the donor-to-recipient size matching and the ratio of recipient chest volume to donor lung volume. Recipient chest volume was evaluated by three-dimensional computed tomography volumetry, while donor lung volume was assessed by the predicted vital capacity. Two patients who underwent lobar lung transplantation due to infection were indicated by red color plots

Table 2 Post-transplant outcomes

	Lobar ($n = 15$)	Full ($n = 38$)	P value
ECMO	3 (20%)	5 (13%)	0.67
PaO_2/FiO_2 at ICU admission, mmHg	321 ± 141	329 ± 170	0.88
30-day mortality (%)	0 (0%)	0 (0%)	1.00
In-hospital death (%)	0 (0%)	2 (5%)	1.00
Bronchial complication	2 (13.3%)	4 (10.5%)	1.00
CLAD	2 (13%)	6 (16%)	1.00

ECMO extracorporeal membrane oxygen; *PaO_2* partial pressure of arterial oxygen; *FiO_2* fraction of inspired oxygen; *ICU* intensive care unit; *CLAD* chronic lung allograft dysfunction

and %FEV1 of predicted value was significantly higher in the Full group at 6 months and 1 year after transplantation (Fig. 3a). Although the 6-min walking distance was significantly higher in the full group at 3 months after transplant, after 6 months it increased to the same level (around 500 m) between the groups (Fig. 3b). The 1-, 3-, and 5-year overall survival rates were similar in both groups: 100%, 93%, and 81% in the Lobar group vs. 92%, 78%, and 70% in the Full group ($P = 0.50$; Fig. 4).

Discussion

One of major problems in lung transplantation is size mismatch between donor lung grafts and recipient chest cavities. In this study, most patients who underwent lobar lung transplantation suffered from malnutrition and interstitial lung disease, and the chest cavities were significantly smaller in the Lobar group than in the Full group. In patients with restrictive lung disease, such as interstitial lung disease, thoracic cavity size is reduced due to chest wall shrinkage and contraction of the intercostal space [1]. For those patients, optimal size adjusting of the lung graft is important because of the potential problems that may occur following the use of oversized grafts within a small chest. Previous experimental studies have shown that oversized grafts could cause atelectasis of the implanted lung and increase pulmonary vascular resistance [3].

Three surgical procedures have been employed to increase the utilization of available brain-dead donors for patients with small chest cavities, including lobar lung transplantation, split lung transplantation, and peripheral atypical resection. Since brain-dead donor lobar lung transplantation was first reported by Bisson et al. in 1994, several studies have shown favorable short- and long-term outcomes comparable with standard bilateral lung transplantation [2–6]. In the current study, brain-dead donor lobar lung transplantation demonstrated excellent early and late post-transplant outcomes in comparison with standard lung transplantation using full-sized grafts. However, life-threatening bronchial complications such as bronchial fistula have been reported in lobar lung transplantation [11, 12]. We performed lobar-to-lobar bronchial anastomoses to avoid leaving donor bronchial stumps closed, and thus there were no bronchopleural fistulae after brain-dead donor lobar lung transplantation (since initiating these types of transplantations, we have not had a patient experience bronchopleural fistulae). Furthermore, the incidence of bronchial complications was similar between lobar and standard transplantations [13].

The reduction in the graft size by lung resection is currently based on direct visual inspection of the size difference between the donor lung graft and the recipient chest cavity in the operating room [6]. Optimal strategies and thresholds to perform lobar lung transplantation,

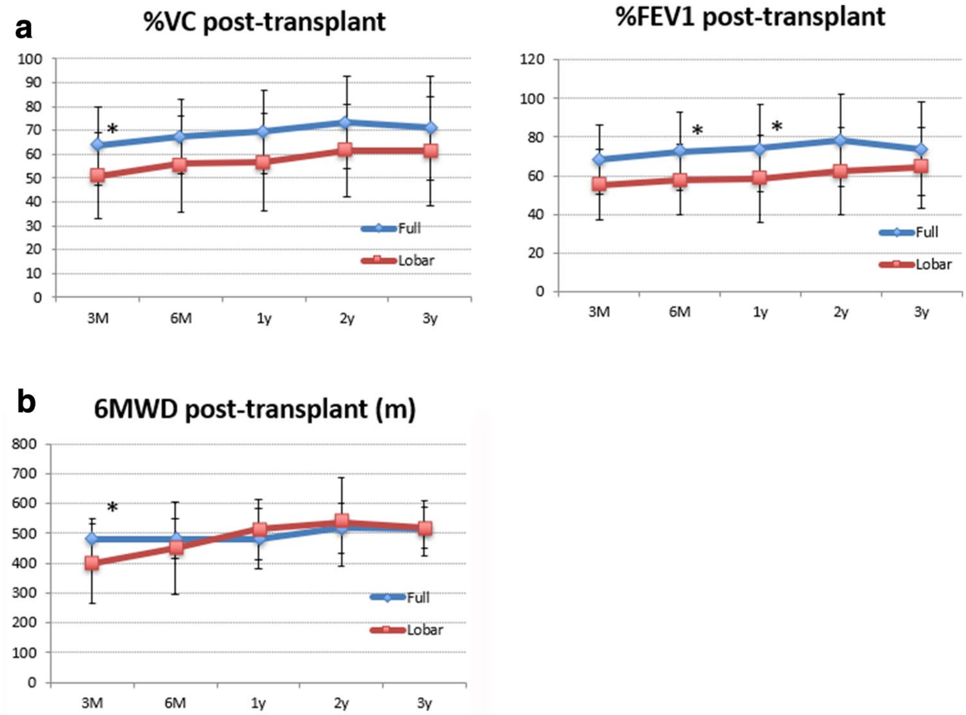

Fig. 3 Post-transplant pulmonary function, %vital capacity (%VC) and %forced expiratory volume in 1 s (%FEV1) of predicted values, was slightly better in the Full group (**a**). The 6-min walking distance (6MWD) did not differ between the groups except at 3 months after transplantation (**b**). $^*P<0.05$

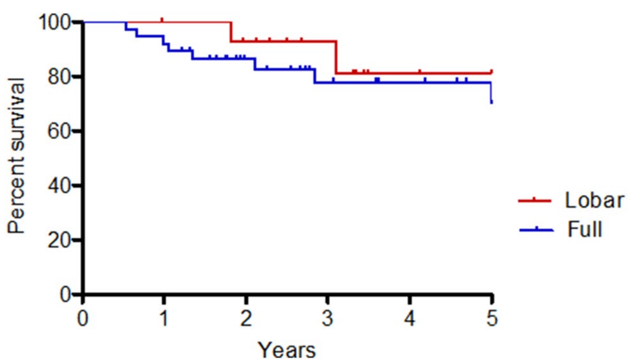

Fig. 4 The 1-, 3-, and 5-year overall survival rates were 100%, 93%, and 81% in the lobar transplant group and 92%, 78%, and 70% in the full lung transplant group ($P=0.50$)

especially for recipients with a small chest cavity, remain to be defined. Radiologic estimation of lung volume can provide information about both anatomical and functional lung volume. With recent advances in CT technology, volumetric CT data obtained from multidetector row CT can provide accurate lung volume measurements and can show better correlation with total lung capacity (TLC) [14, 15]. Therefore, in this study, we measured recipient chest cavity volume by 3D-CT volumetry, and donor lung volume was assessed by the predicted TLC. The ratio of the recipient chest volume to the donor lung volume was significantly lower in the Lobar group (0.42 ± 0.15) than in the Full group (0.77 ± 0.30), indicating that the recipient chest cavity was significantly smaller than the donor lung graft in the patients who underwent lobar lung transplantation. Importantly, the donor-to-recipient size matching after downsizing the grafts in the *y*-axis was strongly correlated with the ratio of recipient chest volume/donor lung volume in the *x*-axis, which suggests that the donor lungs were properly downsized by lobectomy and fitted into the recipient small chest cavities. An approximate equation ($y=66.058x+54.575$) derived from this strong correlation may help calculate the appropriate volume to be reduced in oversized lung grafts recovered from brain-dead donors. Further prospective study with large numbers of patients will be needed to clarify whether the approximate equation derived from this strong correlation can help calculate the appropriate volume to be reduced in oversized lung grafts.

The primary limitations of this study are the non-randomized retrospective nature and the small sample size. Despite the small sample size, our study has value in that this is the first report of brain-dead donor lobar lung transplantation in Japan to describe the utility of 3D-CT volumetry as a measurement of recipient chest volume to help preoperatively identify the size discrepancy between the allocated donor lung and recipient chest cavity volumes. Furthermore, although the ratio of recipient chest volume to donor lung volume calculated by pTLC may help accurately calculate the volume to be downsized before surgery, we still have to make a final decision intraoperatively on which lobe should be removed.

Conclusions

Brain-dead donor lobar lung transplantation was a useful strategy for patients with a small chest cavity, showing favorable post-transplant outcomes. The measurement of recipient chest volume by 3D-CT volumetry may help surgeons downsize lung grafts accurately and calculate the appropriate volume of reduction prior to transplantation.

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Compliance with ethical standards

Conflict of interest All the authors have declared no competing interest.

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