Original Article

Effects of case volume on short- and long-term outcomes following cadaveric lung transplantation in Japan

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Background: Despite the low number of lung transplantations (LTs) in Japan, 10 LT facilities are accredited and good outcomes have been reported. A database review was conducted to clarify the impact of case volume at LT facilities in Japan on short- and long-term outcomes.

Methods: All cadaveric LT cases treated between 2000 and 2021 in Japan were analyzed using the database of the Japanese Society of Lung and Heart-Lung Transplantation (JSLHT). The nine institutions represented were categorized into the low-volume (LV; <80 cumulative LT cases, <8 LTs/year, n=5) and high-volume (HV; ≥80 cumulative LT cases, ≥8 LTs/year, n=4) centers. Ninety-day and 1-year mortality, as well as 5- and 10-year survival data were evaluated.

Results: A total of 658 cadaveric LTs were performed at the nine institutions. The 90-day rates of mortality at the HV and LV centers were 3.5% and 3.9%, respectively (P=0.801), while the 1-year mortality rates were 9.2% and 11.5%, respectively (P=0.199). Additionally, log-rank analysis of Kaplan-Meier curves showing case volume did not reveal a significant difference in long-term survival between the HV and LV centers (P=0.272), though the LV centers had wide differences for long-term outcomes (P=0.030).

Conclusions: Case volume did not have effects on short- or long-term outcomes following LT in Japan, while there were large variations in long-term outcomes among the LV centers compared to those of the HV centers.

Keywords: Lung transplantation (LT); case volume; mortality; long-term survival

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Introduction

Lung transplantation (LT) is the definitive treatment for end-stage lung disease. The International Society for Heart and Lung Transplantation (ISHLT) has reported that more than 4,000 LTs are performed annually worldwide (1), while the registry report of the Japanese Society of Lung and Heart-Lung Transplantation (JSLHT) noted that there were less than 100 LT procedures performed each year in Japan, with the maximum 93 in 2021 (2). Despite the low numbers, 10 facilities in Japan have been certified to perform LTs as of December 2021.

Relationships between case volume and surgical outcome have been reported for both liver transplantation (3,4) and LT (5-11) cases, though Yoon *et al.* found that the number of LTs performed at institutions in Korea had no relationship with outcomes (12). Despite the low number of LTs in Japan, good outcomes have been reported (2). The present study was conducted to evaluate the effect of case volume on mortality following cadaveric LT procedures performed at medical institutions throughout Japan. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-90/rc).

Methods

This was a retrospective analysis of anonymized case records in a database provided by JSLHT. This research was conducted in accordance with the Declaration of Helsinki (as revised in 2023). This study was approved by the Ethics Committee of Dokkyo Medical University of No. 2022-009 and individual consent for this retrospective analysis was waived.

Highlight box

Key findings

- Case volume did not have effects on short- or long-term outcomes following lung transplantation (LT) in Japan.

What is known and what is new?

- There were large variations in long-term outcomes among low-volume centers in Japan.

What is the implication, and what should change now?

- The present study found that case volume did not have an influence on short- or long-term outcomes, indicating that the accreditation system for LT in Japan functions well.

All patients who underwent a cadaveric LT procedure between March 2000 and December 2021 at nine of 10 accredited LT centers in Japan were analyzed, as one of the facilities had not yet performed that by the end of 2021. Institutional case volume was defined as cumulative number of cadaveric LTs performed as well as number per year in the last decade. For centers that had been performing such procedures for less than 10 years, the calculation was based on time since accreditation. Data regarding number of LTs per year at each center were collected from the registry report of JSLHT (2). According to case volume, the transplant centers were then categorized as high-volume (HV group; ≥80 cumulative LT cases, ≥8 LTs/year, n=4) and low-volume (LV group; <80 cumulative LT cases, <8 LTs/year, n=5).

Primary outcomes after 90 days and 1 year were used for short-term mortality, and calculated as follows: (number of patients died within period)/(number of patients died during period + number of patients survived beyond period). Additionally, long-term survival was stratified based on case volume.

Statistical analysis

Statistical analyses among groups were performed with a chi-square test to compare variables, using the Prism 6 software package (GraphPad Software, San Diego, CA, USA). Survival curves were obtained using the Kaplan-Meier method and comparisons within each group were performed with a log-rank test, using the SPSS statistics software program, version 25 (IBM Corp., Armonk, NY, USA). A P value less than 0.05 was considered to indicate a significant difference.

Results

A total of 658 cadaveric LT procedures were performed at the nine active LT centers in Japan between 2000 and 2021, with the total number at each ranging from 9 to 175. Relationships between cumulative and annual numbers of LTs performed are shown in *Figure 1*. The median cumulative number of LTs performed was 125.8 in the HV group and 31.0 in the LV group, while annual numbers ranged from 8.5 to 15.7 (median, 11.2) and 1.1 to 4.3 (median, 2.46), respectively. The cumulative number of LTs was correlated with number of LTs per year (r^2=0.743). Bilateral LTs were performed more often in the HV as

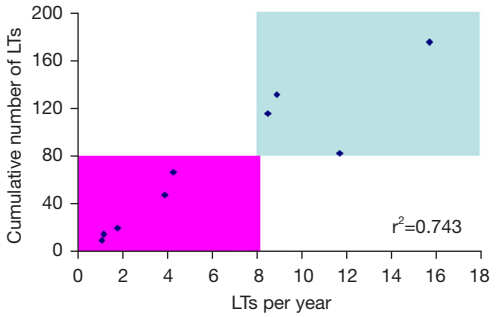

Figure 1 Associations among nine centers in Japan for cumulative and annual numbers of LT procedures. The blue rectangle indicates the HV group (n=4) and the red rectangle indicates the LV group (n=5). LT, lung transplantation; HV, high-volume; LV, low-volume.

Table 1 Characteristics of centers divided by volume

Characteristics	HV centers (n=503)	LV centers (n=155)	P value
Number of LTs	125.8±38.7	31.0±24.5	
Center A	175		
Center B	131		
Center C	115		
Center D	82		
Center E		66	
Center F		47	
Center G		19	
Center H		14	
Center I		9	
Disease			0.326
ILD	184 (36.6)	64 (41.3)	
PH	71 (14.1)	18 (11.6)	
LAM	68 (13.5)	28 (18.1)	
COPD	39 (7.8)	11 (7.1)	
Others	141 (28.0)	34 (21.9)	
Procedure			0.0003
Bilateral	255 (50.7)	53 (34.2)	
Unilateral	248 (49.3)	102 (65.8)	

Data are presented as mean ± SD, n, or n (%). HV, high-volume; LV, low-volume; LT, lung transplantation; ILD, interstitial lung disease; PH, pulmonary hypertension; LAM, lymphangioleiomyomatosis; COPD, chronic obstructive pulmonary disease; SD, standard deviation.

Table 2 Survival data for each group

Groups	90-day mortality (%)	1-year mortality (%)	5-year survival (%)
HV group	3.5	9.2	74.9
Center A	1.8	8.1	72.9
Center B	7.1	11.6	75.2
Center C	2.7	10.0	75.2
Center D	2.7	5.5	76.2
LV group	3.9	11.5	70.7
Center E	6.3	14.8	74.1
Center F	4.3	14.6	56.7
Center G	0.0	0.0	93.8
Center H	0.0	23.1	46.8
Center I	0.0	0.0	100.0

HV, high-volume; LV, low-volume.

compared to the LV group (P<0.001), though there were no differences in disease composition between the two groups. Related characteristics of the nine centers are summarized in *Table 1*.

Mortality and survival data in each group are summarized in *Table 2*. The total 90-day mortality rate after LT at all institutions was 3.6% (23/635), while that in the HV and LV groups was 3.5% (17/483) and 3.9% (6/152), respectively. There was no statistically significant difference regarding 90-day mortality between the groups (P=0.801) or among the nine centers (0–7.1%, P=0.312). The mortality rate at 1 year following LT at all institutions was 10.1% (59/585), with that for the HV and LV groups 9.2% (41/446) and 11.5% (18/157), respectively. Again, there was no statistically significant difference between the groups (P=0.199) or among the centers (0–23.1%, P=0.288).

The 5- and 10-year survival rates after LT at all centers were 73.7% and 61.4%, respectively. The 5-year survival rates for the HV and LV groups were 74.9% and 70.7%, respectively, while the 10-year rates were 63.9% and 55.0%, respectively (*Figure 2*), with no statistically significant differences between the groups noted (P=0.272). Survival rates for the individual centers in the HV and LV groups are shown in *Figure 3A,3B*. There were statistically significant differences among the five centers in the LV group (P=0.030), but not among the four in the HV group (P=0.888).

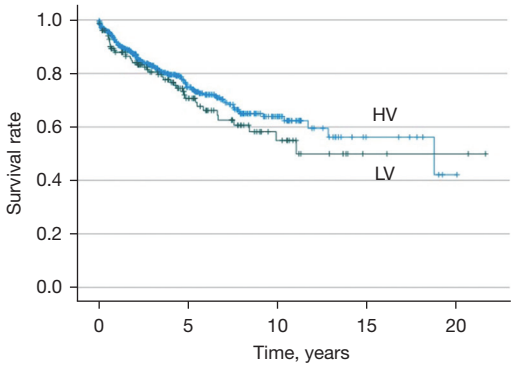

Figure 2 Overall survival curves for the HV and LV groups. HV, high-volume; LV, low-volume.

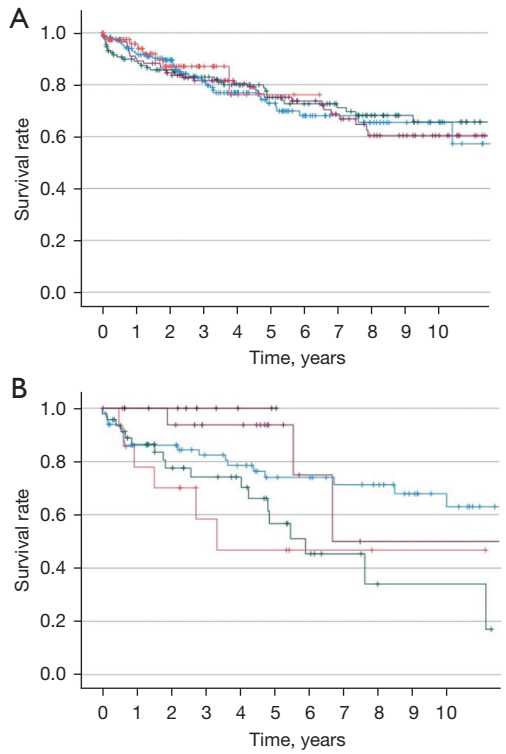

Figure 3 Overall survival curves for each center in the (A) HV group (n=4) [blue (center A); green (center B); purple (center C); red (center D)] and (B) LV group (n=5) [blue (center E); green (center F); purple (center G); red (center H); brown (center I)]. HV, high-volume; LV, low-volume.

Discussion

The present study found no significant differences between the HV and LV groups for 90-day and 1-year mortality, as well as long-term survival rates following LT. During the study period, the 90-day and 1-year mortality rates for affected patients in Japan were 3.6% and 10.1%, respectively, and the 5- and 10-year survival rates were 73.7% and 61.4%, respectively. While there was no significant difference in disease composition between the HV and LV groups, a bilateral LT procedure was more commonly performed in the HV group. Additionally, there was no significant difference for long-term survival between the groups, though large variations in survival rate were noted among the LV group institutions.

The nine institutions where LTs were performed were divided into HV and LV groups according to the cumulative and annual numbers of procedures. Although there were no significant differences in regard to short- and long-term outcomes between the groups, there were large variations regarding long-term survival of patients treated among LV group centers, whereas those in the HV group showed homogenous outcomes. Several other reports have noted a threshold dividing institutions into HV and LV groups based on case volume. An analysis of the United Network for Organ Sharing national thoracic organ transplantation database performed by Weiss and colleagues showed that HV centers (≥20 LTs per year) had lower rates of 30-day mortality (8), while Yang and colleagues found that 33 LTs per year was the threshold of case volume affecting 1-year survival (11). All of the centers in Japan performed fewer than 20 LTs per year, with the greatest mean number in any 1 year for those in the HV group found to be 15.7. Thus, the HV and LV groups in the present study were divided based on eight procedures per year, which is considered to be a practical threshold when examining such cases in Japan.

Although case volume among the present centers varied widely, 90-day and 1-year mortality rates were not significantly different between the HV and LV groups, or among all of the centers. Several reports have noted that case volume affects the short-term outcome of LT cases (5,8,9,11). One of those presented a review of more than 10,000 patients who underwent LT, which showed no difference between LV (<21.8 LTs per year) and HV (>34.2 LTs per year) centers in regard to postoperative complications, though the HV centers were better able to minimize the adverse effects of such complications, thus leading to improved short- and long-term survival rates (5). Others have also noted that the presence of multidisciplinary teams (13,14) and a standardized clinical pathway (15) may be important for perioperative care of LT patients (12,16). It has been found that the rates of 30-day mortalities following lung cancer surgery in Japan (17,18)

were lower as compared to other countries (19,20). In Japan, qualified medical personnel perform LTs in addition to routine lung cancer surgery and there is usually no special team designated for LT. It is thus considered that overall perioperative management of patients who underwent an LT procedure might have had a greater influence on the present results as compared to case volume. This study was conducted using a database that did not include data related to perioperative management, thus none were available to examine the effects of perioperative management for good outcomes. A higher rate of single LT procedures was observed in the LV group. It is considered that centers dealing with a limited number of patients might opt for single LT, which is expected to have shorter operation times and lower perioperative complications.

Some reports have indicated that HV centers show better long-term survival results as compared to LV centers (5,8,16). In the present study, there was no statistically significant difference for long-term survival found between the HV and LV groups, though the survival curve of the HV group was shown to be superior. Risk-adjusted analyses were not performed, due to a lack of related data available in the database. However, the higher rate of bilateral LT procedures in the HV group may be associated with the good long-term survival of cases treated at those centers, because the outcome of a bilateral LT is usually superior as compared to a unilateral LT (1,2).

In the present LV group, there were significant variations in regard to long-term outcomes, while that was not seen in the HV group. Yang *et al.* also reported that LV centers had large variations in outcomes as well as a higher risk of poor results (11). A similar tendency was seen for the centers in Japan, as those in the LV group (<8 cases per year) had large variations in long-term survival, though not all in that group had poor survival rates. As several papers have pointed out, inexperience in LV centers can lead to poor results, though a good team, when organized, seems able to achieve good results even with a small number of LTs. The average survival rate for the LV group was much better than that reported by the ISHLT (1) and the results obtained at the HV centers showed stability. It is expected that with an increased number of transplants performed at LV centers the results of those with poor performance will improve. Such an increase at those centers will likely lead to a decline in results at the better performing centers due to the appearance of death cases, and the results will eventually converge.

Japan has an accreditation system for transplantation facilities that intend to perform cadaveric organ transplantation, with 10 centers approved for performing LTs, even though the annual number of such procedures is low as compared with other countries. The present study found that case volume did not have an influence on short- or long-term outcomes, indicating that the accreditation system for LT in Japan functions well. The requirements for accreditation in Japan are diverse and include number of usual thoracic surgeries performed, experience with bronchoplasty and angioplasty in lung cancer cases, number of publications related to LT, and qualifications of the anesthesiologists and paramedical staff members, along with several others.

The present study has some limitations that should be noted. First, it was conducted as a retrospective database study and the anonymized data did not allow for examination of the outcome of patients who underwent re-transplantation. Second, the only variables noted in the database were age, gender, procedure, diagnosis, and outcomes, thus it was not possible to conduct analyses of a variety of factors possibly influencing outcome. It will be necessary to examine trends in the decade following this study, which summarizes results of all transplantations performed in Japan from 2000 to 2021, as the number of LTs is increasing following revision of the organ transplant law.

Conclusions

Short- and long-term outcomes of cadaveric LT procedures performed in Japan over the recent decade were found to be reasonable. Case volume did not have effects on short- or long-term mortality, though the number at each LT center was relatively low. On the other hand, centers in the LV group, each with less than eight cases per year, had large variations regarding long-term outcomes.

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