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REGISTRY REPORT

Registry of the Japanese Society of Lung and Heart-Lung Transplantation: the official Japanese lung transplantation report 2008

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Abstract The year 2008 marked the 10th anniversary of the Japanese lung transplantation program started in accordance with the Japanese Organ Transplant Law, which took effect in 1997. A total of 105 lung transplantations, including 39 deceased-donor transplants and 66 living-related transplants, had been performed as of the end of 2007. This article is the 2008 official report of the Japanese Society of Lung and Heart-Lung Transplantation. It summarizes the data for clinical lung transplantation during the period 1998–2007 and discusses the current status of Japanese lung transplantation. The overall 5-year survival rate was 67.0%: including 53.4% and 74.6% for deceased-donor lung transplantation and living-donor lobar lung transplantation groups, respectively. The total operation-related and 1-month mortality rates after surgery were 3.8% and 10.4%, respectively. These data are better, or at least acceptable, in comparison with the international registry data.

Key words Lung transplantation · Brain-dead donor · Living-related donor · Registry report

Introduction

More than a decade has passed since the Japanese Organ Transplant Law took effect in October 1997. The law legalized organ transplantation from brain-dead donors. At the beginning, when the Japanese lung transplantation program started, it was authorized at only four centers: Tohoku (THK), Kyoto (KYT), Osaka (OSK), and Okayama (OKY) universities. After early success in these institutions, an additional four centers—Dokkyo (DKY), Chiba (CHB), Fukuoka (FUK), and Nagasaki (NGS) universities—were authorized to join the lung transplantation program in May 2005.

During the past decade, the Japanese organ transplantation program has progressed steadily although slowly. One of the specific reasons that the number of lung transplantations did not increase rapidly in Japanese society was an extreme shortage of deceased donors, resulting in a long waiting time for transplantation. That situation has led the lung transplant teams to consider an alternate protocol to save critical candidates who become too ill to wait for cadaveric donors, and that is living-related transplantation. Living-related transplantation is a potential, realistic transplant option in the Japanese lung transplant system to supplement deceased-donor transplantation.

The clinical data for all patients who underwent either deceased-donor lung transplantation (DDLT) or living-donor lobar lung transplantation (LDLLT) at the eight authorized institutions for lung transplantation have been registered and accumulated systematically by the

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Note: The Chiba University transplant team closed their lung transplant program as of September 2008.

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Japanese Society of Lung and Heart-Lung Transplantation; and the data have been reported at annual meetings of the Society. The first annual report based on the data up to the end of 2006 was presented in 2007 and published in 2008 by the Society.[1] This section of the 2008 official report thus summarizes the current status of DDLT and LDLLT in Japan from 1997 to 2007.

Centers and activity

At the beginning, in 1998, when the Japanese lung transplantation program started, only four institutions (THK, KYT, OSK, OKY) were approved for DDLT. Initially, there was a geographical imbalance of the institutional distribution; thus, in 2005 an additional four institutions (DKY, CHB, FUK, NGS) were approved and joined the program. As of the end of 2007, eight lung transplant centers were actively participating in the DDLT program and were accepting candidates for registration on the Japan Organ Transplant Network (JOTNW) lung waiting list. Among those institutions, Osaka University was the only one that has been approved for both heart-lung transplantation and lung transplantation. Heart-lung transplantation, however, had not yet been performed in Japan as of the end of 2007.

The annual number of newly registered candidates for lung transplantation is shown in Fig. 1. A total of 326 patients had been registered as candidates waiting for cadaveric lung transplantation between 1997 and 2007. Among those registered candidates, 130 (39.8%) died during the wait, 62 (19%) underwent a transplant by DDLT or LDLLT, and 134 were waiting for a transplant as of the end of 2007. The cumulative numbers of lung transplant candidates registered on the JOTNW waiting list in each of the institutions and their geographical distribution are shown in Fig. 2.

The numbers of deceased donors and DDLTs performed annually from 1998 to 2007 are shown in Fig. 3. A total of 63 brain-dead donations were offered to the Society, and 36 (57%) were accepted as unilateral or bilateral lung donors. The cumulative number of DDLTs during the period was 39, including 19 bilateral sequential transplantations and 20 either right or left single-lung transplantations. The average waiting time for DDLT was 2 years 9 months (1016.2 days; range 22–2381 days). The wait for a double lung (average 1126.6 days) is a little longer than that for a single lung (911.2 days), the difference being without statistical significance. Among those 326 registered candidates, 21 underwent LDLLT while waiting for DDLT because they were considered too ill to wait for a cadaveric donor within their limited time frame. The average waiting time of those 21 candidates from their registration on the JOTNW lung waiting list until LDLLT was 381.9 days.

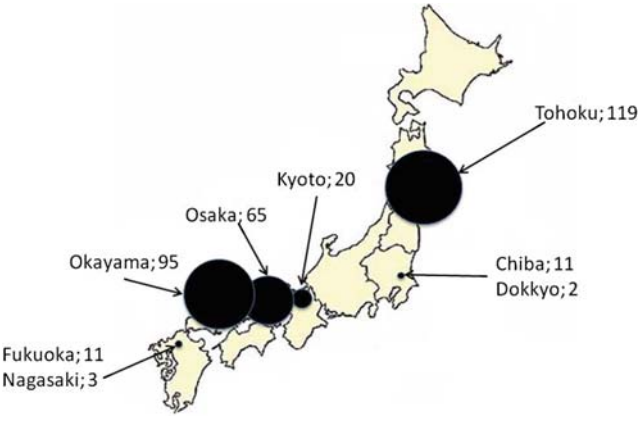

Fig. 2 Cumulative number of lung transplant candidates registered on the JOTNW lung waiting list 1998–2007, by geographic distribution

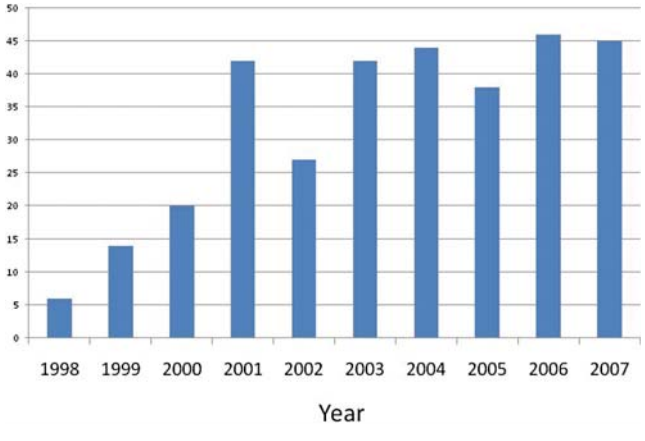

Fig. 1 Annual numbers of registered candidates for lung transplantation in the Japan Organ Transplantation Network (JOTN)

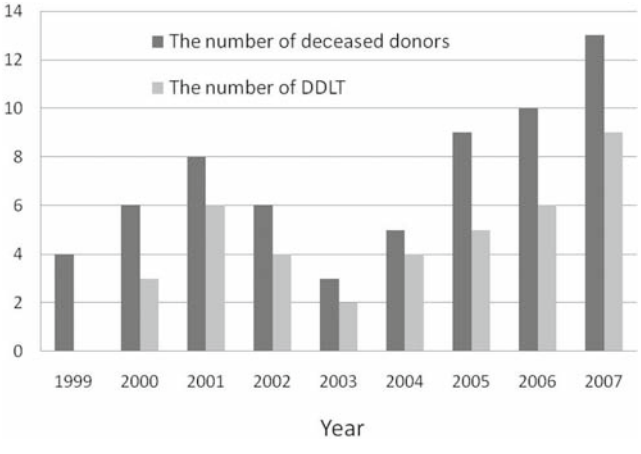

Fig. 3 Annual numbers of deceased donor offers and deceased donor transplantations (*DDLT*)

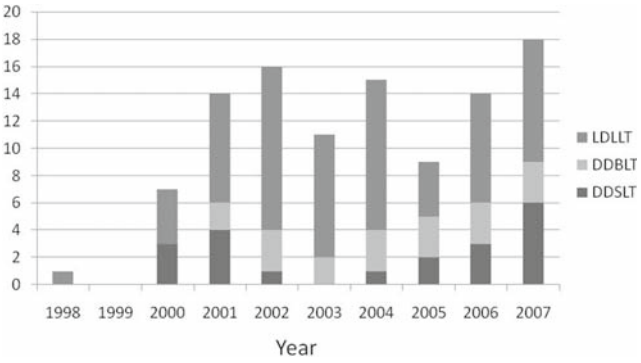

Fig. 4 Annual numbers of lung transplantations in Japan. *LDLLT*, living-donor lobar lung transplantation; *DDBLT*, deceased-donor bilateral lung transplantation; *DDSLT*, deceased-donor single lung transplantation

Table 1 Distribution of the deceased-donor and living-donor lobar lung transplants by transplant center

Transplant center	Lobar lung transplants (no.)		Total no.
	Deceased-donor	Living-donor	
Tohoku	12	5	17
Kyoto	5	3	8
Osaka	9	8	17
Okayama	12	48	60
Fukuoka	1	2	3
Total	39	66	105

The annual numbers of the DDLTs and LDLLTs are shown in Fig. 4. The distribution of the DDLTs and LDLLTs by transplant center is shown in Table 1.

Recipient profile and indications

The 39 DDLT and 66 LDLLT recipients included 16 males and 23 females in the DDLT group and 18 males and 48 females in the LDLLT group. The mean ages of the DDLT and LDLLT recipients were 38.7 years (19–58 years) and 30.4 years (4–55 years), respectively. The primary indications for DDLT were the following: lymphangioleiomyomatosis (LAM), 14 (35.8%); idiopathic pulmonary arterial hypertension (IPAH or PPH), 11 (28.2%); and idiopathic interstitial pneumonias (IIPs), 4 (10.3%). The primary indications for LDLLT were IPAH/PPH, 23 (34.9%); IPF, 16 (41.0%); and bronchiolitis obliterans (BO), 9 (23.1%) (Figs. 5, 6). Pediatric (age <18 years) lung transplantations were performed in 15 recipients; they were LDLLTs in all cases, including 11 bilateral lobar transplants and 4 single lobar transplants.

The discriminating feature of transplantation indications in Japan compared with those in international registry reports is that, generally, LAM, IPAH/PPH, and IIP are the major indications for lung transplantation.[2–4] Because obstructive lung disease, including α_1-antitrypsin deficiency emphysema, is the major indication for lung transplantation in adults and cystic fibrosis is the indication for particularly young age candidates in the international registry, the Japanese indications for transplantation seem to be unique. Transplantation for LAM is rare (almost 1%) in the international registry, whereas 35.8% of Japanese DDLTs were performed for this rare disease. Lung transplantation for cystic fibrosis,

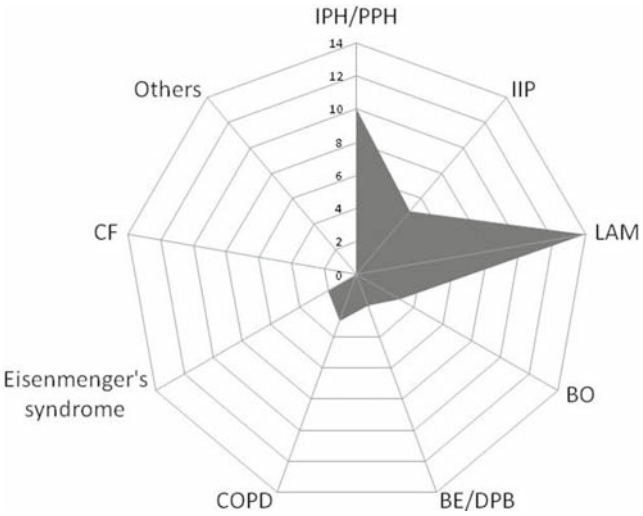

Fig. 5 Indications for DDLT lung transplantation (n = 39). *IPH/PPH*, idiopathic pulmonary arterial hypertension/primary pulmonary hypertension; *IIP*, idiopathic interstitial pneumonia; *LAM*, lymphangioleiomyomatosis; *BO*, bronchiolitis obliterans; *BE/DPB*, bronchiectasis/diffuse panbronchiolitis; *COPD*, chronic obstructive pulmonary disease; *CF*, cystic fibrosis

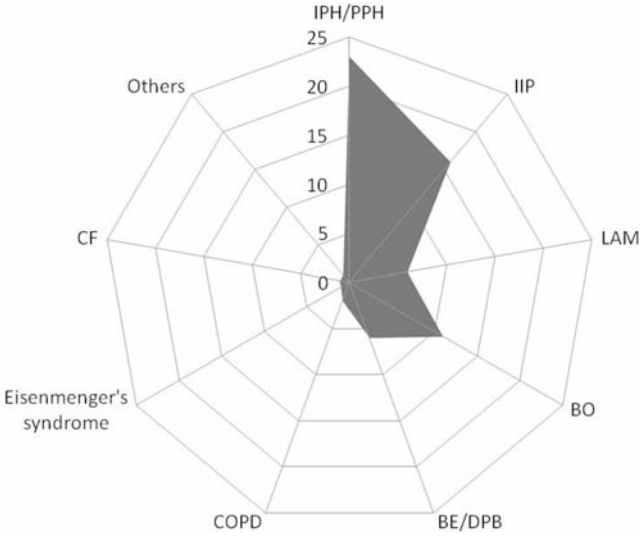

Fig. 6 Indications for LDLLT lung transplantation (n = 66)

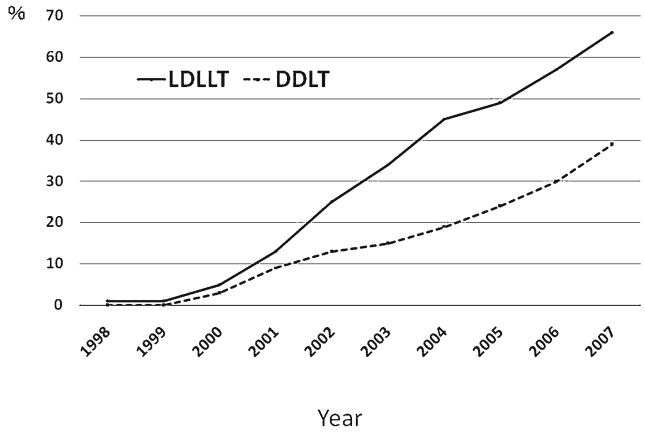

Fig. 7 Cumulative number of LDLLTs and DDLTs during 1998–2007 (total numbers: 66 LDLLTs, 39 DDLTs)

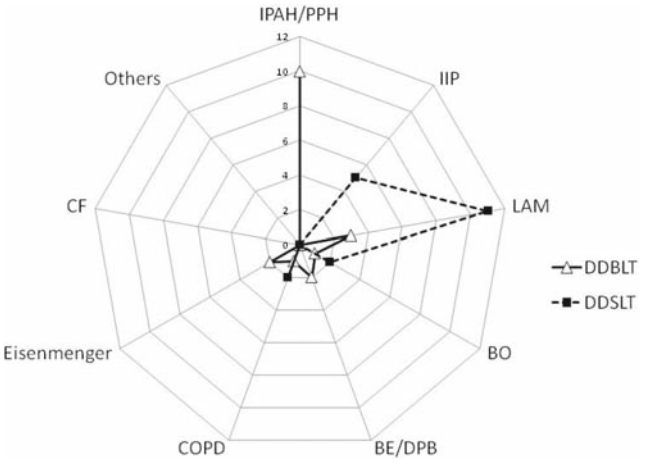

Fig. 8 Distribution of diagnoses and procedures for single and bilateral lung transplantations among the 39 deceased donor lung transplantation. *DDSLT*, deceased donor single-lung transplantation; *DDBLT*, deceased donor bilateral lung transplantation

which is a major indication for pediatric lung transplantation in the international registry, is rarely performed in Japan. The most common indication for transplantation in Japan is IPAH/PPH: 28.2% of DDLTs and 34.9% of LDLLTs were performed for this pulmonary vascular disease.

Transplantation procedures

Because of the extreme shortage of cadaveric donors for lung transplantation in the Japanese society, a substantial number of the lung transplants have been performed as LDLLTs. The cumulative numbers of DDLTs and LDLLTs are shown in Fig. 7. During the period 1998–2007, there were 39 DDLTs performed, whereas there were 66 LDLLTs. The distributions of diagnoses and procedures for single- and double-lung transplantation among 39 DDLTs are shown in Fig. 8. Among the 66 LDLLT recipients, 21 (31.8%) had been registered candidates on the JOTNW waiting list for DDLT; in contrast, 45 (68.2%) recipients underwent LDLLT without registration on the waiting list. The former patients were thought to be too sick to take the time for the registration process and wait for a deceased donor or were too young (small stature) to receive a volume-matched lung graft from the deceased donor pool as Japanese transplant law prohibits organ donation from pediatric donors under 15 years of age.

Survival

The overall survival for lung transplant recipients registered in Japanese society for lung and heart-lung transplantation during 2000–2007 is illustrated in Fig. 9. The

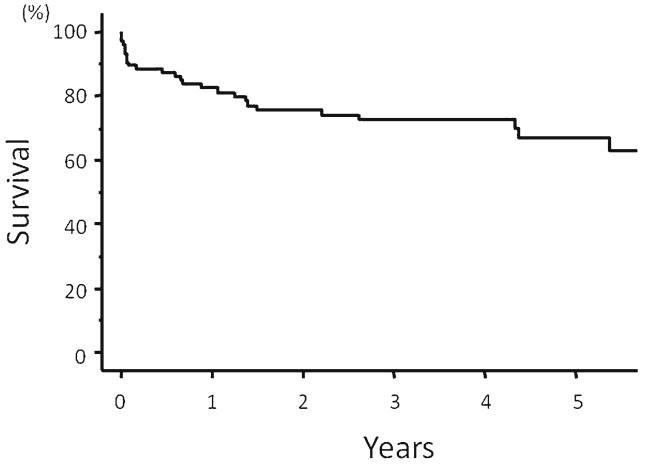

Fig. 9 Survival curves calculated by the Kaplan-Meier method after lung transplantation. Japanese Society of Lung and Heart-Lung Transplantation 1998–2007 ($n = 105$)

benchmark survival rates were 89.4% at 1 month, 88.4% at 3 months, 82.4% at 1 year, 72.5% at 3 years, and 67.0% at 5 years. Survival curves for DDLT and LDLLT are shown in Fig. 10. The 3- and 5-year survivals were, respectively, 61.1% and 53.4% for DDLT patients and 78.7% and 74.6% for LDLLT patients. There is a trend that the 5-year survival of LDLLT is somewhat better than DDLT, but the difference is not statistically significant ($P = 0.077$). The mortality rate for the deceased-donor bilateral lung transplantation (DDBLT) group was somewhat high, with the 3-month survival 73.7%, whereas 100% survival was achieved during the first 3 months after deceased-donor single lung transplantation (DDSLT); however, there was no significant difference in long-term survival between the groups (Fig. 11). The

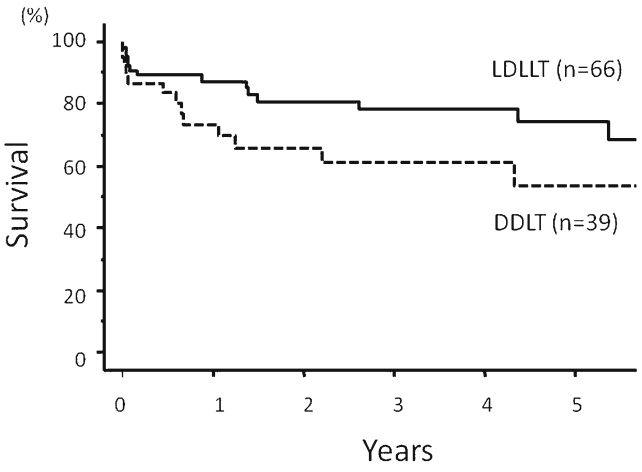

Fig. 10 Survival curves calculated by the Kaplan-Meier method after DDLT and LDLLT

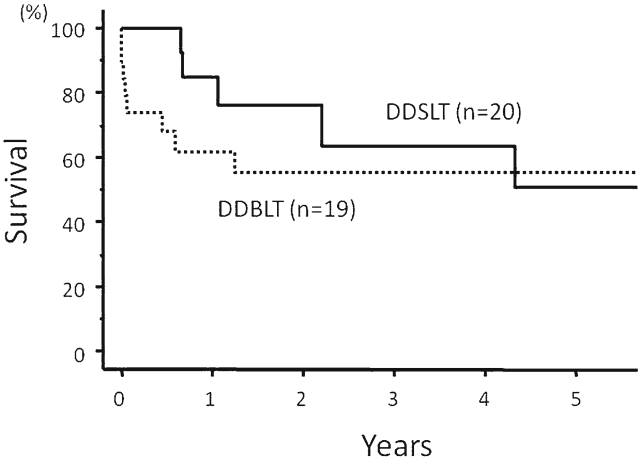

Fig. 11 Survival curves calculated by the Kaplan-Meier method after DDSLT or DDBLT

survival curves according to the recipients' disease in the four major Japanese indication categories for lung transplantation are shown in Fig. 12. The 5-year survival rates, by those diseases (BO, LAM, IPAH/PPH, IIPs) for the lung transplant recipients were 61.4%, 75.8%, 72.0% and 53.7%, respectively, with no significant differences between the disease groups.

Functional status

The functional status of those who survived more than 6 month was excellent (Figs. 13, 14). More than 90% of the recipients were restored to almost normal daily life with Hugh-Jones I or II classification in both DDLT and LDLLT groups. Increased respiratory activity was achieved by transplantation, resulting in an increased

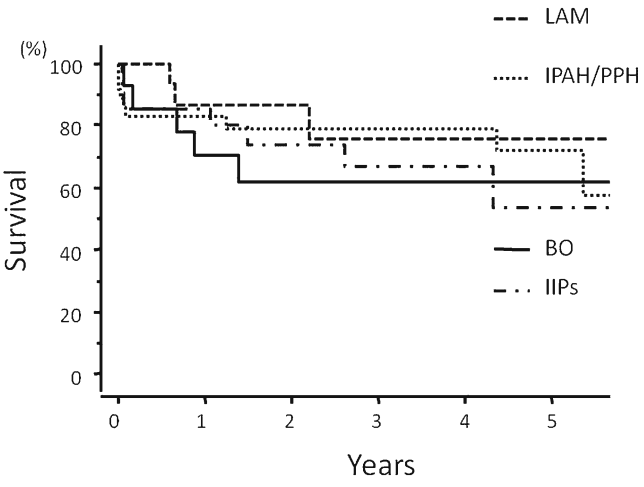

Fig. 12 Survival curves calculated by the Kaplan-Meier method after lung transplantation by recipient diagnosis. *IPAH/PPH*, idiopathic pulmonary arterial hypertension/primary pulmonary hypertension; *IPF*, idiopathic pulmonary fibrosis; *LAM*, lymphangioleiomyomatosis; *BO*, bronchiolitis obliterans

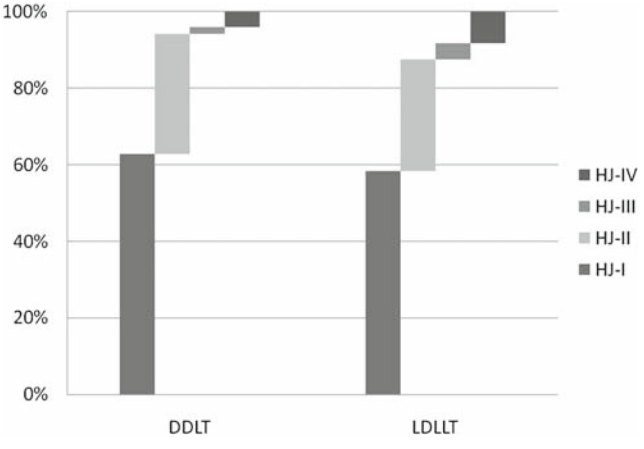

Fig. 13 Hugh-Jones classification (functional status), *HJ-I* to *HJ-IV*, of lung transplant recipients who survived longer than 6 months

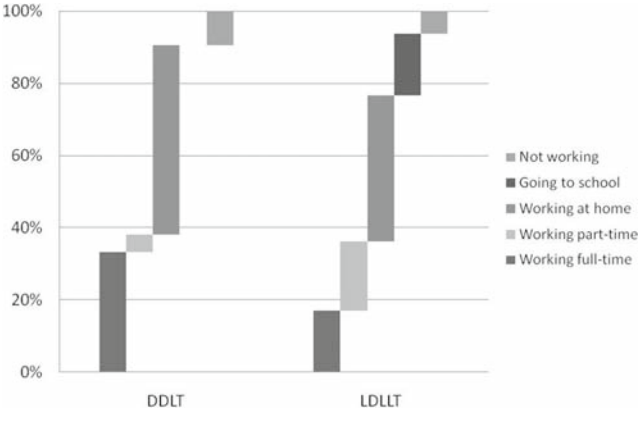

Fig. 14 Status of lung transplant recipients who survived longer than 6 months

Table 2 Cause of death after transplantation

Condition	Total no.	Primary graft failure	Operation-related	Infection	Acute or chronic rejection	PTLD	Other
DDLT	13	2 (15.4%)	2 (15.4%)	3 (23.1%)	1 (7.7%)	1 (7.7%)	4 (30.8%)
LDLLT	13	2 (15.4%)	2 (15.4%)	5 (38.5%)	2 (15.4%)	1 (7.7%)	1 (7.7%)

PTLD, posttransplantation lymphoproliferative disease; DDLT, deceased-donor lung transplant; LDLLT, living-donor lobar lung transplant

social life. More than 90% of the recipients were returned to either full-time or part-time work or school, or at least engaged in domestic help.

Cause of death

A total of 79 of 105 recipients were alive at the end of 2007. In all, 13 of 39 DDLT recipients and 13 of 66 LDLLT recipients died for a variety of reasons. The causes of death are illustrated in Table 2. Operation-related death was identified in four cases. Infection (10.1%) was the major cause of postoperative death, three DDLT recipients and 5 LDLLT recipients dying from a variety of infection problems. Death due to acute or chronic rejection occurred in three cases: one in the DDLT group and two in the LDLLT group.

Discussion and conclusion

The year 2008 marked the 10th anniversary of the Japanese lung transplantation program started in accordance with the Japanese Organ Transplant Law, which took effect in 1997. The first candidate for cadaveric transplantation was registered on the JOTNW lung waiting list in August 1998. The cumulative number of lung transplant candidates has continuously increased thereafter, and more than 110 candidates were actively awaiting a lung for transplantation at the end of 2007.

The first successful lung transplant (LDLLT) in Japan was performed by the Okayama group in October 1998.[5] Two years later, the Tohoku and Osaka groups succeeded in performing the first single-lung transplantation from a brain-dead donor by sharing lung grafts from the same donor.[6,7] The subsequent results during the first decade in the history of Japanese lung transplantation can be judged as either a great success or rather satisfactory. The overall 5-year survival rate was 67.0%, including 53.4% and 74.6% in the DDLT and LDLLT groups, respectively. The total operation-related and 1-month mortality rates after surgery were 3.8% and 10.4%, respectively. These data are better or at least acceptable in comparison to those in the international registry.[4]

The biggest problem with the Japanese lung transplantation program is the extreme shortage of brain-dead donors. Donor shortage is a universal problem with transplantation programs, including those in the United States and Europe; however, the Japanese situation is unique. A total of 63 brain-dead donations were performed in accordance with the Japanese Transplant Law during 1999–2007, with an average of only seven donations yearly from a population of 120 million. Despite the critical donor shortage, each lung transplant center has made great efforts to save patients waiting for a lung by sometimes accepting a marginal donor or considering living-related transplantation. Altogether, 57% of the possible lung donors were accepted from the entire brain-dead donor pool. Although it has not been clearly evaluated, a considerable number of marginal donor lungs seemed to be accepted and transplanted as the "lung graft acceptance ratio" from brain-dead donors is thought to be generally 10%–30%. On the other hand, the donor shortage encourages the Japanese centers to extend the lung transplant procedure to accept "living-related transplantation." Based on the data from the first decade of Japanese lung transplant history, 62.8% of lung transplants were performed as living-related transplantation.

At the time of this report, the rate of brain-dead donations seems to be gradually but steadily increasing. The lung transplant centers in Japan continue to make a special effort to save the candidates waiting for a lung by sometimes accepting marginal donors or by performing living-related transplantation.

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References

1. Bando T, Date H, Minami M, Kondo T, Shiraishi T, Miyoshi S, et al. First registry report: lung transplantation in Japan—The Japanese Society of Lung and Heart-Lung Transplantation. Gen Thorac Cardiovasc Surg 2008;56:1–2.
2. Christie JD, Edwards LB, Aurora P, Dobbels F, Kirk R, Rahmel AO, et al. Registry of the International Society for

Heart and Lung Transplantation: twenty-fifth official adult lung and heart/lung transplantation report—2008. J Heart Lung Transplant 2008;27:957–69.
3. Aurora P, Edwards LB, Christie J, Dobbels F, Kirk R, Kucheryavaya AY, et al. Registry of the International Society for Heart and Lung Transplantation: eleventh official pediatric lung and heart/lung transplantation report—2008. J Heart Lung Transplant 2008;27:978–83.
4. Hertz MI, Aurora P, Christie JD, Dobbels F, Edwards LB, Kirk R, et al. Registry of the International Society for Heart and Lung Transplantation: a quarter century of thoracic transplantation. J Heart Lung Transplant 2008;27:937–42.
5. Date H, Yamashita M, Nagahiro I, Aoe M, Andou A, Shimizu N. Living-donor lobar lung transplantation for primary ciliary dyskinesia. Ann Thorac Surg 2001;71:2008–9.
6. Miyoshi S, Minami M, Ohta M, Okumura M, Takeda S, Matsuda H. Single lung transplantation from a brain-dead donor for a patient with idiopathic pulmonary fibrosis: a breakthrough after new legislation in Japan. Jpn J Thorac Cardiovasc Surg 2001;49:398–403.
7. Fujimura S, Kondo T. The lung transplantation has come to be done in Japan. Kyobu Geka 2000;53:986–91 (in Japanese).