



Living Donor Kidney Transplantation Preceding Pancreas Transplantation Reduces Mortality in Type 1 Diabetics With End-stage Renal Disease

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ABSTRACT

Background. Simultaneous pancreas-kidney transplantation (SPK) is a definitive treatment for type 1 diabetics with end-stage renal disease (ESRD). Because of the shortage of deceased donors in Japan, the mortality rate during the waiting period is high. We evaluated mortality risk in patients with type 1 diabetes waiting for SPK, and the benefit of living-donor kidney transplantation (LDK) preceding pancreas transplantation, which may reduce mortality in patients awaiting SPK.

Methods. This retrospective study included 71 patients with type 1 diabetes. Twenty-six patients underwent SPK, 15 underwent LDK, and 30 were waiting for SPK. Their cumulative patient and graft survival rates were retrospectively evaluated. Risk factors contributing to mortality in patients with type 1 diabetes awaiting SPK were evaluated with the use of a Cox proportional hazards model.

Results. The 5-year cumulative patient survival rates in the SPK and LDK groups were 100% and 93.3%, respectively ($P = .19$), and 5-year kidney graft survival rates were 95.7% and 100% ($P = .46$), respectively. The cumulative survival rate in patients awaiting SPK was 77.7% at 5 years after registration. Duration of dialysis was the only factor significantly associated with patient and graft survivals according to both univariate and multivariate analyses.

Conclusions. Patient and graft survival rates were similar in the SPK and LDK groups, but the survival rate of patients awaiting SPK decreased over time. Duration of dialysis was an independent risk factor for patient and graft survival. LDK preceding pancreas transplantation may be an effective therapeutic option for patients with type 1 diabetes and ESRD.

DESPITE the increase in brain-dead organ donors in Japan after the amendment of the organ transplantation law in 2010, a severe shortage of donors remains a serious problem. This has resulted in long waiting periods and high mortality rates while waiting for transplantation [1].

According to the statistical data of the Japanese Pancreas and Islet Transplantation Association, the mean waiting period for pancreas transplantation in Japan is 1,305 days. This compares unfavorably with the mean waiting period in Europe and the United States, which is <1 year. Of 194 patients are waiting for pancreas transplantation in Japan at the time of writing, 53 (27.3%) have already been waiting for >5 years.

Long-term dialysis in type 1 diabetes is inevitably accompanied by cardiovascular complications, which can be one of the factors to worsen the prognosis of type 1 diabetes. Held et al have reported that patients with type 1 diabetes receiving dialysis have a life expectancy one-half that of a healthy person [2]. Longer duration of dialysis is generally associated with poorer patient prognosis [3], especially with type 1 diabetes

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Table 1. Demographic and Clinical Characteristics of the Patient Population

Characteristics	SPK (n = 26)	LDK (n = 15)	Awaiting SPK (n = 30)	P Value
Age, y	36.4 ± 7.4	41.5 ± 8.3	42.3 ± 8.3	.013
Sex (male:female)	6:20	6:9	15:15	.11
Age at onset of type 1 diabetes, y	15.7 ± 8.2	14.6 ± 6.5	14.6 ± 7.2	.86
Duration of type 1 diabetes, y	23.8 ± 6.0	27.2 ± 9.5	27.6 ± 8.1	.16
Duration of dialysis, y	5.6 ± 4.0	2.8 ± 3.0	12.4 ± 8.4	<.001
History of CVD, n (%)	2 (7.7%)	2 (13.3%)	7 (9.8%)	.85
History of infectious disease, n (%)	2 (7.7%)	0 (0%)	5 (16.7%)	.10
Hb _{A1c} , %	7.5 ± 1.5	7.6 ± 1.6	7.9 ± 1.6	.63
Hb _{A1c} ≥7.6%	50.0%	33.3%	60%	.23
Insulin level, U	30.5 ± 10.0	34.2 ± 13.8	28.6 ± 9.1	.25
Observation period, d	3685 ± 1333	1373 ± 1055	1837 ± 1094	<.001

Note. Results are presented as mean ± SEM unless otherwise indicated.

Abbreviations: SPK, simultaneous pancreas-kidney transplantation; LDK, living donor kidney transplantation; CVD, cardiovascular disease; Hb_{A1c}, glycosylated hemoglobin.

with ESRD. Therefore, early kidney transplantation from a living donor can be a leading option in Japan, where there are few brain-dead donors. Living-donor kidney transplantation (LDK) preceding pancreas transplantation would be expected to enhance patient prognosis. We therefore evaluated the therapeutic utility of LDK preceding pancreas transplantation in patients awaiting simultaneous pancreas-kidney transplantation (SPK).

MATERIALS AND METHODS

Seventy-six patients with type 1 diabetes were approved for pancreas transplantation at our institution by the Pancreas Transplantation Central Coordination Commission from April 1999 to March 2014. Five of these patients were excluded because of cancellation of registration. Approval for SPK was based on clinical diagnosis, current and earlier medical histories, family history, current medications, contraindications, evaluation of possible complications (including renal function, retinopathy, neural disturbance, arteriosclerotic lesions, and malignant disorders), and general medical condition. Approval also required pancreatic absolute endogenous insulin deficiency, as assessed by daily urinary C-peptide excretion or by a certain C-peptide level on glucagon stimulation tests.

Of the 71 included patients, 41 underwent transplantation, including 26 who underwent SPK and 15 who underwent LDK, including 3 who later underwent pancreas after kidney transplantation (PAK). The remaining 30 patients were still awaiting SPK.

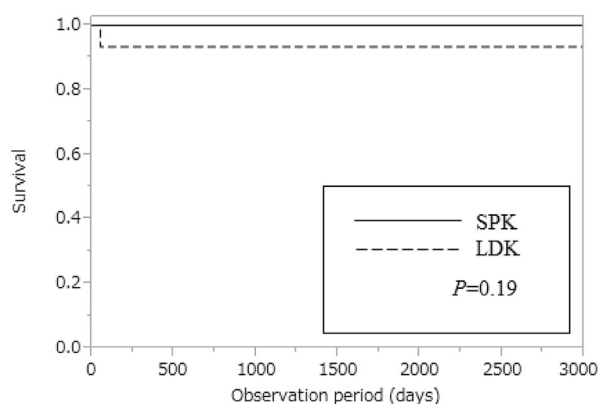
The cumulative patient survival rates were retrospectively calculated for 3 groups: SPK, LDK, and those awaiting SPK. The cumulative kidney graft survival rates in the SPK and LDK groups were evaluated and compared. The cumulative survival of all 71 patients registered for SPK was evaluated, and their long-term prognosis was evaluated by means of univariate and multivariate analyses.

JMP pro 11 (SAS Institute) was used for statistical analysis. Cumulative patient and graft survival rates were evaluated with the use of the Kaplan-Meier method and compared with the use of the log-rank test. The demographic and clinical characteristics of all 71 patients registered for SPK were evaluated, including age, sex, age at onset of type 1 diabetes, duration of type 1 diabetes (duration of insulin therapy), duration of dialysis, history of cardiovascular disease (CVD), history of infectious disease, glycosylated hemoglobin (Hb_{A1c}), insulin concentration, LDK, and history of pancreas or kidney transplantation. Potential risk factors were evaluated by means of univariate and multivariate analyses with the use of a Cox

proportional hazards model. χ^2 tests were used to compare the demographic and clinical factors. Differences between 2 groups were determined with the use of the Wilcoxon method. Statistical significance was defined as $P < .05$.

RESULTS

The demographic and clinical characteristics of the 71 patients registered for SPK are presented in Table 1. The cumulative survival rates of the SPK and LDK groups were 100% and 93.3%, respectively, at 1 year and 100% and 93.3%, respectively, at 5 years ($P = .19$; Fig 1). One patient who underwent LDK died from a hypoglycemic coma during the follow-up.



Survival rates in SPK and LDK groups

Category	N	1-year	5-year
SPK	26	100%	100%
LDK	15	93.3%	93.3%

Fig 1. Kaplan-Meier analysis of cumulative survival rates in simultaneous pancreas-kidney transplantation (SPK) and living-donor kidney transplantation (LDK) groups.

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