

Current state of pancreas transplantation in Japan based on the nationwide registry

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Abstract

In Japan, 437 pancreas transplantations (PTx) were carried out between 2000 and 2019. Clinical data for all PTx cases are registered in the Japan Pancreas Transplant Registry of the Japan Society for Pancreas and Islet Transplantation. Here we analyzed the registry data to describe the current status of PTx in Japan. The 437 PTx included 410 from deceased donors (407 from brain-dead and 3 from non-heart-beating donors) and 27 from living donors. We investigated the clinical characteristics of the 410 PTx from deceased donors. The rate of marginal donors using expanded donor criteria was higher in Japan than in other countries. At 1/5/10 years post-PTx, the overall survival rates were 95.8%/94.2%/88.7%, and the graft survival rates were 85.9%/76.2%/67.4% for pancreas and 93.2%/90.8%/78.2% for kidney (non-censored for death). These rates were comparable to those in other countries. When stratified by PTx category, survival was significantly better following simultaneous pancreas-kidney transplantation (SPK) compared to pancreas-after-kidney transplantation (PAK) or PTx alone (PTA). Immunological rejection was more frequently the cause of graft loss in PAK/PTA cases than in SPK cases, potentially contributing to the poorer survival in PAK/PTA. These outcomes highlight two main concerns: substantial incidence of pancreas graft loss, and inferior outcomes after PAK/PTA. Overall, PTx outcome is favorable in Japan, despite the high rate of marginal donors. To improve outcomes, it is important to prevent and manage each cause of pancreas graft loss. Overcoming the poorer survival in PAK/PTA may require new immunosuppressive protocols or allogenic islet transplantation.

KEYWORDS

marginal donor, pancreas transplantation, pancreas transplantation alone, pancreas-after-kidney transplantation, simultaneous pancreas-kidney transplantation

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1 | INTRODUCTION

Pancreas transplantation (PTx) is an established therapy for patients with type 1 diabetes and uncontrollable glycemic dysfunction.¹⁻³ PTx can improve quality of life for patients with type 1 diabetes.⁴⁻⁶ The restoration of endogenous insulin secretion after PTx yields normal glucose metabolism in diabetic patients, thus eliminating the need for exogenous insulin, frequent daily blood glucose measurements, and the dietary restrictions imposed by the disorder. Additionally, in hemodialytic cases, simultaneous pancreas-kidney transplantation (SPK) may alleviate the need for hemodialysis. Restoration of normal glucose metabolism also has the secondary effect of potentially improving the life expectancy of PTx patients.^{7,8} Since the first PTx was carried out at the University of Minnesota in 1966, PTx has now been carried out worldwide.^{2,9} Posttransplant outcome is reportedly favorable. A study of PTx outcome in the USA between 2005 and 2014 demonstrated 1- and 3-year post-PTx patient survival rates of approximately 97% and 95%, and 1- and 3-year pancreas graft survival rates of 89% and 82% in SPK cases.¹⁰

Internationally, Japan ranks near the bottom in terms of organ donation, and thus the situation surrounding PTx in Japan is extremely different from that in other countries. Compared to many other countries, Japan has a substantially smaller number of deceased donors, as well as a vastly higher rate of utilization of marginal donors with expanded donor criteria. For example, the proportion of pancreas donors ≥ 50 years of age is approximately 30% in Japan, compared to $< 1\%$ in the USA.^{2,11} Therefore, investigation of the current PTx situation in Japan might elucidate novel findings in terms of the use of expanded donor criteria in PTx. In Japan, the clinical data for all PTx cases are registered in the Japan Pancreas Transplant Registry of the Japan Society for Pancreas and Islet Transplantation. In the present study, we described the current status of PTx in Japan by analyzing data extracted from this nationwide registry.

2 | PANCREAS TRANSPLANTATION HISTORY IN JAPAN

Since the first PTx procedure in 1966, over 50 000 PTx have been carried out worldwide.^{2,9} The first PTx procedure in Japan was performed in 1984 from a brain-dead donor. However, the concept of brain death became a social issue, and thus the next 14 PTx procedures in Japan were carried out from non-heart-beating donors.¹² In October 1997, the Organ Transplant Act was enforced in Japan, with corresponding organization of the Central Coordination Committee of Pancreatic Transplantation and its sub-committees. The first PTx after this enforcement was carried out at Osaka University Hospital in April 2000.¹³ However, even after enforcement, the number of PTx procedures performed in Japan remained low—with only 5-10 procedures annually. In 2010, to increase the use of brain-dead donors, the Revised Organ Transplant Act was enacted, which permits organ donation from brain-dead donors, even when the donor's intention is unclear, if written

consent is given by the donor's family. This yielded an approximately five-fold increase in the number of brain-dead donors, such that around 40-50 PTx procedures are now carried out annually. From 2010 to the end of 2019, 410 PTx procedures have been carried out from deceased donors for patients with type 1 diabetes,¹¹ along with 27 PTx from living pancreas donors.¹⁴

3 | INDICATION AND REGISTRATION SYSTEM FOR PTx IN JAPAN

Pancreas transplantation is classified into the following three categories: SPK, pancreas-after-kidney transplantation (PAK), and PTx alone (PTA). In Japan, SPK or PAK is performed for patients with severe type 1 diabetes with renal failure (estimated glomerular filtration rate [eGFR] < 30 mL/min per 1.73 m²). PTA is carried out for nonuremic patients with glycemic lability who are experiencing problematic hypoglycemia, such as severe hypoglycemia and impaired awareness of hypoglycemia, despite optimal diabetes management by certified diabetologists. Data from continuous glucose monitoring are required for proof of glycemic lability. For these indication criteria, severe type 1 diabetes is defined as a situation where the patient shows an insulin depletion status, with serum C-peptide levels of < 0.3 ng/mL at fasting, and < 0.5 ng/mL with glucagon (or ≤ 0.3 ng/mL). Unlike in other countries, in Japan, this definition of insulin depletion status is strictly fixed. Patients are essentially excluded from PTx if they show progressive proliferative retinopathy; active infectious, hepatic, or ulcerative disease; or malignant disease. A donor age of ≤ 60 years is desirable. Notably, in Japan, mainly due to the donor shortage, type 2 diabetes is not considered an indication for PTx.

After examination by the Expert Medical Board located in seven regions of Japan, and sub-committees of the Central Coordination Committee of Pancreatic Transplantation, all recipient candidates are registered with the Japan Organ Transplant Network (JOTNW). When a pancreas donor emerges, the JOTNW selects recipients for the donors based on several factors, including blood type, direct crossmatch test, time on the waiting list after PTx registration, number of human leukocyte antigen (HLA) mismatches, PTx category, and estimated transport time of the organ for PTx. When a kidney donor emerges, before offering the kidney organ to candidate recipients on the kidney-alone waiting list, the kidney organ is preferentially allocated for SPK.

4 | PANCREAS TRANSPLANTATION RESULTS IN JAPAN

4.1 | Pancreas transplantation procedures carried out in Japan

Between the enforcement of the Organ Transplant Act in 2010 and the end of 2019, 410 PTx procedures have been carried out in

Japan for type 1 diabetes from deceased pancreas donors, including 407 PTx from brain-dead donors and three from non-heart-beating donors.¹¹ The 407 PTx from brain-dead donors constitute 62% of the total of 662 organ donations carried out during this time period. Additionally, 27 PTx were performed from living pancreas donors during the same period. Figure 1 shows the annual number of PTx according to donor type. Notably, 49 PTx procedures were carried out in 2019—a larger number than in the other years. PTx from a living pancreas donor has not been carried out since 2014. Among the 410 PTx from deceased pancreas donors, SPK was performed in 344 cases (84%), PAK in 48 (12%), and PTA in 18 (4%). In contrast, among the 27 PTx from living pancreas donors, SPK was performed in 21 cases (78%), PAK in 1 (4%), and PTA in 5 (19%).

All PTx procedures were done at institutions approved from the Japan Society for Pancreas and Islet Transplantation—including Fujita Health University Hospital, Kyushu University Hospital, Tokyo Women's Medical University Hospital, Osaka University Hospital, Chiba-East-Hospital, Red Cross Nagoya Daini Hospital, Tohoku University Hospital, Hiroshima University Hospital, Kobe University Hospital, University Hospital, Kyoto Prefectural University of Medicine, Hokkaido University Hospital, Kagawa University Hospital, Niigata University Medical & Dental Hospital, Fukushima Medical University Hospital, Nagasaki University Hospital, Dokkyo Medical University Hospital, Kyoto University Hospital, and Tokyo Medical University Hachioji Medical Center. In 2018, institutional approval was withdrawn from Chiba-East-Hospital, whereas Saitama Medical Center newly received PTx institutional approval. As of August 2020, 18 institutions are approved for carrying out PTx. Table 1 presents the cumulative numbers of PTx performed at each institution.

4.2 | Clinical characteristics of PTx

Table 2 presents the clinical background characteristics of the 410 PTx from deceased donors. In terms of pancreas donor-related factors, median donor age was 43 years, with a range from 4 to 72 years. The majority of donors were 40-49 years of age (28%), followed by 50-59 years of age (22%) and 30-39 years of age (18%). Notably, 178 donors (43%) were ≥ 45 years of age, 117 donors (29%) were ≥ 50 years of age, and 27 donors (7%) were ≥ 60 years of age. The large number of older PTx donors is a unique characteristic of PTx in Japan compared to those in other countries. Additionally, 57% of donors were male and 43% were female. The median body mass index (BMI) was 21.8 kg/cm² (range: 11.4-34.3 kg/cm²). The predominant cause of death was cerebrovascular accident (208 of 410 cases; 51%). Among pancreas donors, median hemoglobin A1c (HbA1c) level was 5.6% (range: 4.3%-7.7%). Cardiopulmonary arrest occurred in 190 (46%) of the 410 cases and, among these cases, the median cardiopulmonary arrest duration was 36 min (range: 2-282 min). Among the 410 cases, 201 (49%) showed hemodynamic instability, defined by a requirement for high-dose dopamine (>10 $\mu\text{g}/\text{kg}$ per min) or at least two vasopressors at the time of procurement.¹⁵ In 291 (71%) of the 410 cases, the donors satisfied the criteria for a marginal donor using the expanded donor criteria defined by Kapur et al.¹⁵ Median number of HLA mismatches between donor and recipient was 3 (range: 0-6).

In terms of recipient-related factors, median recipient age was 44 years (range: 24-69 years). Notably, 16 recipients (4%) were ≥ 60 years of age, although ≤ 60 years of age is desirable for a PTx indication. The recipients included 161 male and 249 female patients. Median BMI was 20.9 kg/m² (range: 14.6-30.5 kg/cm²). Median HbA1c level among PTx recipients was 7.6% (range: 4.8%-15.2%).

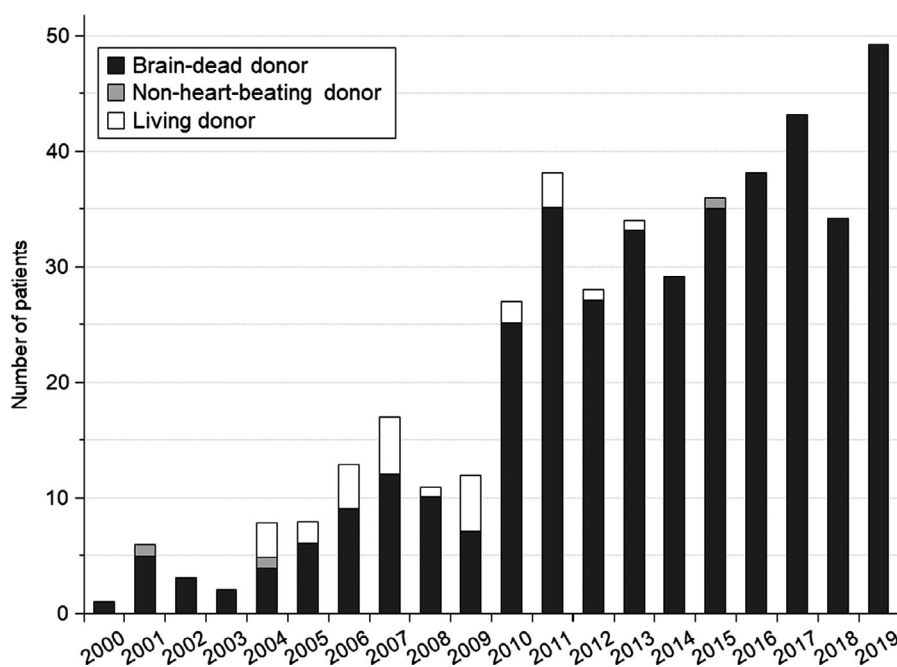


FIGURE 1 Annual numbers of pancreas transplantation (PTx) carried out in Japan between 2000 and 2019. The total of 437 PTx cases included 407 PTx from brain-dead donors, three from non-heart-beating donors, and 27 from living donors

TABLE 1 Numbers of PTx carried out in Japan at different institutions

Institution	PTx from deceased donor (n = 410)	PTx from living pancreas donors (n = 27)	Total (n = 437)
Fujita Health University Hospital	81	2	83
Kyushu University Hospital	68	4	72
Tokyo Women's Medical University Hospital	71	0	71
Osaka University Hospital	54	1	55
Chiba-East Hospital	23	18	41
Red Cross Nagoya Daini Hospital	25	0	25
Tohoku University Hospital	14	0	14
Hiroshima University Hospital	12	0	12
Kobe University Hospital	12	0	12
University Hospital, Kyoto Prefectural University of Medicine	10	0	10
Hokkaido University Hospital	9	0	9
Kagawa University Hospital	9	0	9
Niigata University Medical & Dental Hospital	7	2	9
Fukushima Medical University Hospital	6	0	6
Nagasaki University Hospital	4	0	4
Dokkyo Medical University Hospital	2	0	2
Kyoto University Hospital	2	0	2
Tokyo Medical University Hachioji Medical Center	1	0	1

Abbreviation: PTx, pancreas transplantation.

Among the 410 cases, 295 (72%) were positive for anti-cytomegalovirus IgG antibody. Median preoperative duration of diabetes was 28 years (range: 2-53 years), and the median hemodialysis period among SPK patients was 7 years (range: 0-29 years). The median waiting period from PTx registration to undergoing PTx was 1395 days (range: 6-5740 days).

Regarding PTx-related factors, median donor organ transport time was 227 minutes (range: 0-560 minutes). Median ischemic time was 718 minutes (range: 271-1381 minutes) for pancreas grafts, and 611 minutes (range: 196-1357 minutes) for kidney grafts. During PTx, arterial reconstruction was done with a Carrel patch in 355 cases (87%), and with a Y graft in 55 cases (13%). Portal vein extension was carried out in 87 cases (21%), and gastroduodenal artery reconstruction was performed in 219 cases (53%).¹⁶ For exocrine

drainage of the transplanted pancreas, bladder drainage was selected in 52 cases (13%), mostly during the initial part of the study period, whereas enteric drainage was selected in 358 cases (87%), mostly during the later part of the study period. Among the 52 cases with bladder drainage, 11 cases required enteric conversion surgery as a result of urinary infection, hematuria, and graft pancreatitis.

4.3 | Immunosuppression

We also examined the drugs used for posttransplant immunosuppression in the 410 cases of PTx from deceased donors in Japan. Tacrolimus (TAC)-based immunosuppression was predominant (405 of 410 cases; 99%), whereas cyclosporin A (CsA) was used in only a few cases during the initial part of the study period (5 of 410 cases; 1%). TAC was commonly combined with other drugs. In 293 (71%) of the 410 cases, TAC was used in combination with steroids, mycophenolate mofetil (MMF), and anti-interleukin-2 receptor (anti-IL-2R) chimeric monoclonal antibody (basiliximab). Anti-thymocyte globulin (ATG) (rabbit anti-human thymocyte immunoglobulin) has been increasingly given in the more recent cases, and was used in 92 (22%) of the 410 cases, including six cases in which both anti-IL-2R antibody and ATG were used.

4.4 | Posttransplant survival

To investigate long-term posttransplant outcome, we calculated the rate of postoperative survival after PTx, including overall survival and graft survival, in the 410 cases of PTx from deceased donors (Figure 2). Pancreas graft loss was defined as the return to a serum C-peptide level of <0.3 ng/mL, and kidney graft loss was defined as reintroduction of dialysis. For the assessment of graft survival, death with a functioning graft (DWFG) was considered graft failure. At 1, 3, 5, and 10 years after PTx, respectively, the overall survival rates were 95.8%, 95.8%, 94.2%, and 88.7%; the pancreas graft survival rates were 85.9%, 80.6%, 76.2%, and 67.4%; and the kidney graft survival rates were 93.2%, 92.9%, 90.8%, and 78.2%. These survival rates were almost comparable to the outcomes reported in the USA.¹⁰ The survival rates did not significantly differ between PTx from a marginal donor versus from a non-marginal donor. HLA mismatch number also did not affect survival. Causes of pancreas graft loss were as follows: graft thrombosis in 24 cases (5.9%), recurrence of type 1 diabetes in six (1.5%), chronic rejection in 19 (4.6%), acute rejection in nine (2.2%), duodenal graft perforation in six (1.5%), pancreaticoduodenal graft-related complication other than graft thrombosis and duodenal graft perforation in three (0.7%), and DWFG in 27 (6.6%) (Table 3). DWFG occurred due to cardiac disease in five cases, infection in five, malignancy in three, multiple organ failure in three, cerebral disease in two, pulmonary disease in two, renal insufficiency in two, gastrointestinal bleeding in one, graft-versus-host disease in one, accident in one, and unknown cause in two cases.

TABLE 2 Clinical background characteristics of 410 PTx from deceased donors in Japan

Factor		All cases (n = 410)
Donor-related factors		
Age, y		43 (4-72)
Gender	Male	234 (57%)
	Female	176 (43%)
Height, cm		165 (110-186)
Weight, kg		58.5 (18.5-94.1)
BMI, kg/cm ²		21.8 (11.4-34.3)
Cause of death	CVA	208 (51%)
	Anoxic brain injury	114 (28%)
	Head trauma	78 (19%)
	Heart disease	7 (2%)
	Other	3 (1%)
	HbA1c, %	
Cardiopulmonary arrest	-	220 (54%)
	+	190 (46%)
Cardiopulmonary arrest time, min		36 (2-282)
Hemodynamic stability	-	201 (49%)
	+	209 (51%)
Marginal donor using expanded donor criteria	-	119 (29%)
	+	291 (71%)
HLA mismatch number		3 (0-6)
Recipient-related factors		
Age, y		44 (24-69)
Gender	Male	161 (39%)
	Female	249 (61%)
Height, cm		161 (139-185)
Weight, kg		54 (36-87)
BMI, kg/cm ²		20.9 (14.6-30.5)
HbA1c, %		7.6 (4.8-15.2)
Anti-CMV IgG antibody	-	103 (25%)
	+	295 (72%)
Duration of diabetes, years		28 (2-53)
Duration of dialysis, years		7 (0-29)
Time from registration to PTx, days		1395 (6-5740)
PTx-related factors		
PTx category	SPK	344 (84%)
	PAK	48 (12%)
	PTA	18 (4%)
Transport time, min		227 (0-560)
Ischemic time of pancreas graft, min		718 (271-1381)

(Continues)

TABLE 2 (Continued)

Factor		All cases (n = 410)
Ischemic time of kidney graft, min		611 (196-1357)
Portal vein extension	-	323 (79%)
	+	87 (21%)
Arterial reconstruction	Carrel patch	355 (87%)
	Y graft	55 (13%)
GDA reconstruction	-	191 (47%)
	+	219 (53%)
Duct management	Bladder drainage	52 (10%)
	Enteric drainage	358 (90%)

Note: Data are presented as number of patients (percentage) or median (range).

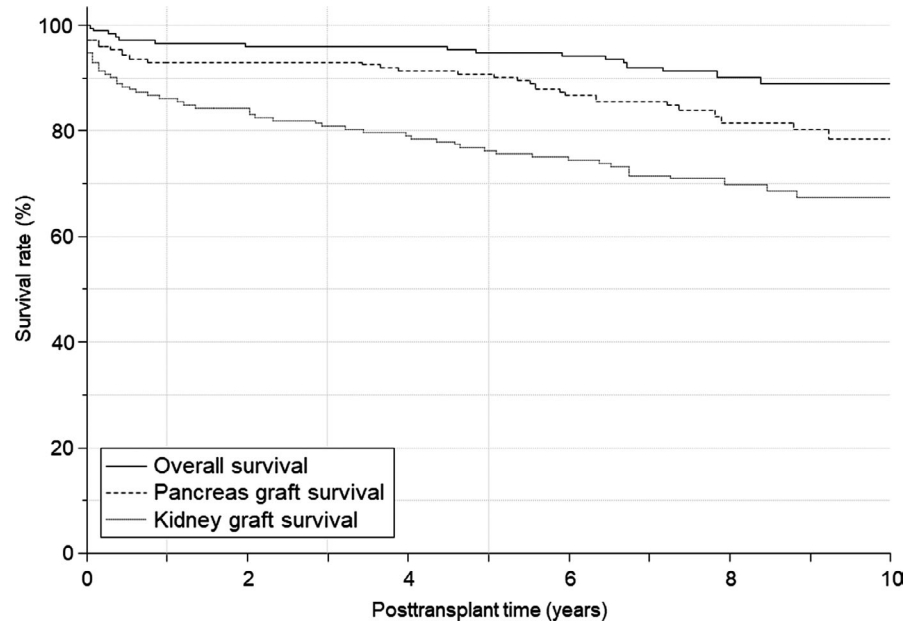
Abbreviations: BMI, body mass index; CMV, cytomegalovirus; CVA, cerebrovascular accident; GDA, gastroduodenal artery; HbA1c, hemoglobin A1c; HLA, human leukocyte antigen; PAK, pancreas-after-kidney transplantation; PTA, pancreas transplantation alone; PTx, pancreas transplantation; SPK, simultaneous pancreas-kidney transplantation.

We also examined pancreas graft survival after PTx according to PTx category (Figure 3). At 1, 3, 5, and 10 years after PTx, respectively, pancreas graft survival rates were 87.3%, 85.4%, 83.2%, and 74.6% among the 344 cases with SPK compared to 85.4%, 67.6%, 52.3%, and 41.8% among the 48 PAK cases. The 1-, 3-, and 5-year pancreas graft survival rates among the 18 PTA cases were 66.7%, 41.6%, and 31.2%, respectively. Survival was significantly better in SPK cases compared to PAK and PTA cases. The survival rates among SPK cases were similar between Japan and the USA, whereas the survival rates in PAK/PTA cases were inferior in Japan compared to the USA.¹⁰ Immunological rejection (including acute rejection and chronic rejection) was more frequently identified as the cause of pancreas graft loss in PAK/PTA cases compared to SPK cases, potentially contributing to the poorer pancreas graft survival in cases of PAK/PTA than SPK (Table 3).

5 | DISCUSSION

In the present study, we summarized the current status of PTx in Japan based on data from the nationwide registry. We found that posttransplant outcomes were good, and nearly comparable to the outcomes observed in the USA.¹⁰ This finding is particularly interesting considering that compared to the USA, Japan has much smaller numbers of deceased donors and performance of PTx procedures, and a higher rate of marginal donors using expanded donor criteria. Based on these findings, and considering that posttransplant survival did not significantly differ between PTx from a marginal donor versus a non-marginal donor, it may at least be speculated that the expanded donor criteria used to define marginal donors in this study

FIGURE 2 Patient and graft survival after pancreas transplantation in Japan. For graft survival analysis, death with a functioning graft was considered a graft failure



could be safely applied to donor selection for PTx in other countries, including the USA.

Our present results also highlighted unsatisfactory outcomes that should be improved. One issue was the substantial incidence of posttransplant pancreas graft loss, although this outcome was almost similar to that in the USA. Causes of pancreas graft loss included pancreaticoduodenal graft-related complications, such as graft thrombosis and duodenal graft perforation; immunological rejection; and death with a functioning graft. Thus, the reduction of pancreas graft loss will require preventative measures to address each cause. For example, with regards to graft thrombosis, one report shows the efficacy of contrast-enhanced ultrasonography for thrombosis detection.¹⁷ Postoperative monitoring of the blood flow in the pancreas graft is considered important, as early detection may enable pancreas graft rescue by interventional radiological therapy.^{18–20} However, duodenal graft perforation is reportedly associated with both immunological rejection and technical factors, such as poor blood supply, kinking of the intestinal anastomosis, and high pressure of the graft duodenum.^{21–23} Immunosuppression may be important for preventing immunological rejection-derived duodenal graft perforation. With regards to death with a functioning graft, it will be important to perform posttransplant screening for cardio-cerebrovascular disease and malignancy.²⁴

Another identified problem was poorer pancreas graft survival following PAK/PTA compared to SPK. The cause of this difference in survival remains unclear, but it may be related to the higher incidence of posttransplant immunological rejection in PAK/PTA than in SPK. Thus, it is clinically important to prevent the frequent development of pancreas graft immunogenic loss. Ito et al reported that immunosuppressive therapy using ATG resulted in reduced rejection in PAK cases.²⁵ This may indicate that immunosuppressive therapy is useful for regulating immunological rejection in PAK/PTA.

TABLE 3 Cause of pancreas graft loss based on PTx category

Cause	All cases (n = 410)	SPK (n = 344)	PAK/PTA (n = 66)
Graft thrombosis	24 (5.9%)	19 (5.5%)	5 (7.6%)
Chronic rejection	19 (4.6%)	6 (1.7%)	13 (19.7%)
Acute rejection	9 (2.2%)	4 (1.2%)	5 (7.6%)
Recurrence of type 1 diabetes	6 (1.5%)	3 (0.9%)	3 (4.6%)
Duodenal graft perforation	6 (1.5%)	6 (1.7%)	0 (0%)
Pancreaticoduodenal graft-related complication other than graft thrombosis or duodenal graft perforation	3 (0.7%)	2 (0.6%)	1 (1.5%)
Death with a functioning graft	27 (6.6%)	22 (6.4%)	5 (7.6%)
Cardiac disease	5 (1.2%)	5 (1.5%)	0 (0%)
Infection	5 (1.2%)	5 (1.5%)	0 (0%)
Malignancy	3 (0.7%)	1 (0.3%)	2 (3.0%)
Multiple organ failure	3 (0.7%)	3 (0.9%)	0 (0%)
Cerebral disease	2 (0.5%)	2 (0.6%)	0 (0%)
Pulmonary disease	2 (0.5%)	2 (0.6%)	0 (0%)
Renal insufficiency	2 (0.5%)	2 (0.6%)	0 (0%)
Gastrointestinal bleeding	1 (0.2%)	0 (0%)	1 (1.5%)
Graft-versus-host disease	1 (0.2%)	1 (0.3%)	0 (0%)
Accident	1 (0.2%)	0 (0%)	1 (1.5%)
Unknown reasons	2 (0.5%)	1 (0.3%)	1 (1.5%)
Total	94 (22.9%)	62 (18.0%)	32 (48.5%)

Note: Data are presented as number of patients (percentage).

Abbreviations: PAK, pancreas-after-kidney transplantation; PTA, pancreas transplantation alone; PTx, pancreas transplantation; SPK, simultaneous pancreas-kidney transplantation.

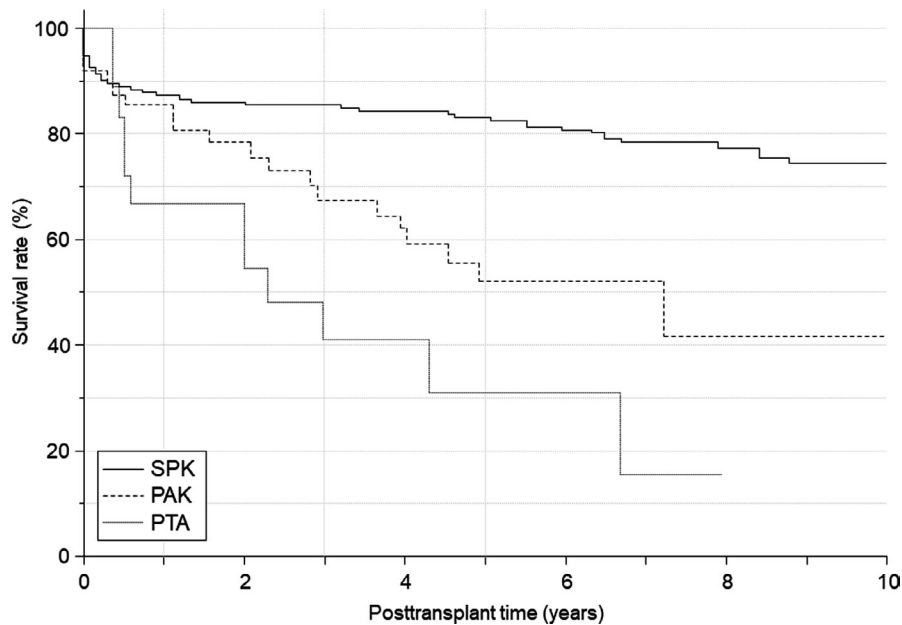


FIGURE 3 Pancreas graft survival after pancreas transplantation (PTx) according to PTx category. For pancreas graft survival analysis, death with a functioning pancreas graft was considered a pancreas graft failure. Abbreviations: PAK, pancreas-after-kidney transplantation; PTA, pancreas transplantation alone; SPK, simultaneous pancreas-kidney transplantation

Due to recent changes, allogenic islet transplantation for type 1 diabetes is now covered by the national health insurance system in Japan. Although PTx is highly invasive and frequently associated with severe complications, islet transplantation is a minimally invasive procedure that entails only the infusion of purified islet cells via the portal vein. In cases with end-stage renal dysfunction, SPK would be prioritized over islet transplantation. However, in cases of type 1 diabetes without renal failure (including cases of type 1 diabetes after renal transplantation), islet transplantation might be prioritized over PTx—particularly since, as described above, long-term pancreas graft survival is much poorer after PAK and PTA compared to after SPK. However, with existing immunosuppression protocols, multiple islet transplants are frequently required to obtain outcomes comparable to PTx.^{26,27} Therefore, at this time and until the development of improved immunosuppressive medicine, the indication for islet transplantation should be limited to patients with high risk for PTx procedure. As these procedures advance, future clinical assessment will be needed to determine whether PTx or islet transplantation is more effective for type 1 diabetes without renal failure.

6 | CONCLUSIONS

Here we have summarized the current state of PTx in Japan based on data from the nationwide registry. Our results showed favorable posttransplant outcomes which were comparable to those in the USA despite the high rate of marginal donors with expanded donor criteria in Japan. Our analysis also highlighted several issues that must be resolved, including the substantial incidence of posttransplant pancreas graft loss, and the poorer outcome in PAK/PTA compared to SPK. To improve pancreas graft survival, it is important to prevent and manage each cause of graft loss. Potential options for addressing the poor outcomes following PAK/PTA include the establishment of effective immunosuppressive therapy to regulate

immunological rejection in PAK/PTA, and the possible prioritization of allogenic islet transplantation over PAK/PTA.

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DISCLOSURE

Conflicts of Interest: Authors declare no conflicts of interest for this article.

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