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[Original Article]

Clinical outcomes of simultaneous pancreas-kidney transplantation: experience of a single center

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Abstract

This study evaluated the outcomes of simultaneous pancreas-kidney transplantation (SPK) at Fukushima Medical University between 2001 and 2024. We retrospectively reviewed ten adult patients who underwent SPK. We aimed to clarify the important aspects of patient management in patients undergoing SPK, focusing on perioperative outcomes and long-term complications.

The median postoperative observation period was 1,968 days. Postoperative complications were observed in all patients. Most were classified as Clavien-Dindo (CD) grade I or II, but major complications, including CD grade IIIa or higher, were observed in four patients (40%) with zero mortality. Despite the loss of one kidney graft due to primary non-function, the 5-year survival rates for both patients and pancreatic grafts remained at 100%. However, there was one case each of pancreatic graft loss, kidney graft loss, and patient death after 5 years post-transplantation, all attributed to late-onset complications, including recurrent type 1 diabetes, focal segmental glomerulosclerosis, and cardiovascular disease. The short-term outcomes of SPK at our institution were favorable, with a trend toward a reduction in the comprehensive complication index (CCI) observed in the latter five cases compared with the first five cases, suggesting potential improvements in perioperative management. Long-term monitoring and collaboration with physicians are essential to enhance patient outcomes.

Key words : pancreas transplantation, graft survival, comprehensive complication index, late-onset complication

Introduction

Type 1 diabetes mellitus (T1DM) frequently manifests in the youth, and diabetes-associated complications, such as neuropathy and renal failure, significantly deteriorate the patient's prognosis and quality of life. Pancreatic transplantation, which is the only curative treatment for T1DM, normalizes glucose metabolism and prevents secondary complications[1-5].

According to the International Pancreas Transplant Registry (IPTR), approximately 66,000 cases have been performed worldwide by the end of 2021 since the first pancreas transplantation by Kelly *et al.* in 1966[6]. Pancreatic transplantation is categorized into three types : pancreatic transplantation alone (PTA), pancreas after kidney transplantation (PAK), and simultaneous pancreas/kidney transplantation (SPK), with the latter being the most commonly performed.

The first SPK in Japan was performed in 2000 after the enforcement of the "Organ Transplant Law." By the end of 2022, 518 pancreatic transplants were performed using organs from brain-dead donors (DBD, n=488), cardiac-dead donors (DCD, n=3), and living donors (n=27)[7]. Despite the

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higher incidence of marginal donors in Japan, the post-transplantation outcomes are comparable to those observed in other nations, including the United States[8].

Approximately 20% of the SPK cases involve pancreas graft loss[9]. The contributing factors include surgical complications (such as graft thrombosis, duodenal graft perforation, and other pancreatoduodenal graft-related factors), immunological complications (such as acute rejection, chronic rejection, and recurrence of T1DM), and death with functioning grafts (DWFG). The main causes of DWFG include infections, cardiovascular diseases, cerebrovascular diseases, and malignant tumors. Surgical complications are the primary cause of early perioperative pancreatic graft loss and underscore the importance of reducing perioperative complications[2,10-12]. However, immunological complications and DWFG present a risk for pancreatic graft loss not only in the perioperative period but also in the long term. As a correlation with the duration of T1DM has been demonstrated, long-term follow-up is crucial[5,13]. Despite the high number of marginal donors in Japan, few studies have evaluated the long-term outcomes and management strategies of SPK recipients in the Japanese context.

The pancreas transplantation program at Fukushima Medical University began in 2001, and by April 2024, 10 SPK procedures had been performed. This study aimed to evaluate the perioperative outcomes and long-term complications associated with SPK at our institute, with a particular focus on the primary outcome of pancreatic graft survival and the factors contributing to graft loss.

Materials and methods

Study population

We performed a single-center retrospective review of adult SPK cases between July 2001 and April 2024. Ten patients who underwent SPK were included in the study. This study was approved by our institutional review board (IRB) in accordance with the Declaration of Helsinki (approval number : REC2022-035).

Characteristics of the recipients and donors

Data on recipient demographics (age, sex, body mass index (BMI), HbA1c, duration of diabetes and dialysis, and duration on the waiting list), surgical data (graft-related [duration of transportation and total ischemic time (TIT)] and operative procedures), postoperative complications, and graft survival were collected from electronic medical records. Donor demographics (e.g., age, sex, BMI, cause of death, HbA1c level, extended-criteria donor status, and HLA mismatch) were obtained from documents provided by the Japan Organ Transplant Network (JOT NW).

Surgical details

The organs were procured after retrograde flushing with a UW solution through the abdominal aorta. The pancreas and kidneys were procured en bloc, separated on a back table, cold-preserved in UW solution, and transferred to our center by public transportation.

The pancreatic allograft was prepared on a back table. Gastroduodenal artery reconstruction using a donor arterial graft (I graft) was performed to maintain the blood supply to the head of the pancreas[14]. Portal vein extension was performed using the iliac vein harvested from the donor if the length of the portal vein was insufficient for anastomosis, although this was unnecessary in most cases. The duodenal segment of the pancreatic graft was shortened, and the staple line was inverted using seromuscular sutures. In all patients, the pancreatic graft was placed in the right iliac fossa in a head-up and tail-down manner. Arterial reconstruction was performed using a Carrel patch or an iliac Y graft to the right common iliac artery (CIA) or external iliac artery (EIA).

Exocrine drainage was achieved through enteric drainage, with the allograft duodenum anastomosed to the recipient jejunum or ileum, depending on arterial reconstruction. In cases where the anastomosis involved the CIA, the allograft duodenum was connected to the recipient jejunum using a side-to-side anastomosis. In all EIA cases except one, the allograft was connected to the ileum in a side-to-side fashion without additional placement of the graft duodenal decompression tube. Bowel anastomosis was sewn in two layers, with the inner layer using continuous full-thickness sutures and the back and front walls using interrupted seromuscular sutures. Intra-abdominal drains were routinely placed adjacent to the duodenal graft anastomosis and pelvic space. Subsequently, the kidney graft was transplanted into the left iliac fossa.

Immunosuppression and perioperative management

Immunosuppression was administered according to a protocolized regimen. Basiliximab (20 mg/body), an anti-IL-2 receptor antibody, was adminis-

tered intraoperatively and on the fourth operative day as an induction therapy. Maintenance immunosuppression consisted of a triple regimen of a calcineurin inhibitor (tacrolimus), an antiproliferative agent (mycophenolate mofetil (MMF)), and steroids. Intravenous administration of tacrolimus was initiated during surgery, after which it was switched to oral intake postoperatively, with a target trough of 10–15 ng/mL (1–7 days after transplantation), 8–10 ng/mL (8 days to one month after transplantation), 5–8 ng/mL (1–12 months after transplantation), and 3–5 ng/mL (after 1 year).

MMF was initially administered at 2000 mg/day, with adjustments made based on the patient's postoperative condition. Steroids (methylprednisolone) were administered as a single intraoperative dose of 250 mg/kg body weight, followed by a postoperative regimen starting at 50 mg/day. Methylprednisone was administered intravenously, and prednisolone was administered orally. The steroid dose was gradually tapered according to the protocol and maintained at 5 mg/day starting at 2 weeks postsurgery onwards.

Standard prophylaxis, including antibacterial (ceftazidime, trimethoprim sulfamethoxazole), antifungal (micafungin), and antiviral therapies (ganciclovir), were protocolized and modified based on the surveillance culture results.

Anticoagulation therapy with intravenous heparin was initiated based on the results of the activated partial thromboplastin time (APTT) after confirming that there were no signs suggestive of postoperative bleeding. Heparin was continued until day 14 (APTT target : 60–80 s). Aspirin and antiplatelet agents (clopidogrel sulfate) were administered to all patients.

Doppler ultrasonography (US) was performed two or three times a day for the first 7 days and at least once during the hospital stay. We routinely confirmed that the blood flow to the graft was maintained and that there was no abnormal fluid collection around the graft. Blood glucose levels were measured according to the protocol described by a diabetes specialist. Contrast-enhanced CT was routinely performed by day 7 if the renal function after transplantation was acceptable.

Postoperative complications and endocrinologic evaluation of the pancreas graft

Postoperative complications were classified using the Clavien-Dindo (CD) grading system. Complications of the highest grade were recorded in patients with more than one complication. Furthermore, the comprehensive complication index (CCI) was calculated for each patient to summarize the burden of multiple complications occurring within 90 days of transplantation[15]. In CCI, raw points are allocated according to the grade of the complication, summed, and scaled from 0 to 100[15]. A free online tool was used to calculate the cumulative CCI for each patient based on the number of complications per CDC grade (https://www.cci-calculator.com/cciCalculator). Complications occurring over one year post-transplant were defined as late-onset complications (LOC). The incidences of LOC were also assessed.

Pancreatic graft function was evaluated based on insulin-free status and HbA1c level. Pancreatic graft loss was determined when the patient required exogenous insulin to remain euglycemic and in the absence of detectable C-peptide levels (serum C-peptide < 0.3 ng/mL). To assess long-term outcomes, pancreatic and patient survival probabilities were calculated using Kaplan–Meier analysis. Kidney graft function was evaluated based on dialysis-free status and serum creatinine levels. Kidney graft loss was determined when a patient required dialysis.

Statistics

The Mann-Whitney U test was used to compare continuous variables between the groups because the data were not normally distributed and the sample size was small. This nonparametric test is appropriate for small sample sizes and does not assume normality, making it suitable for comparing medians between independent groups. Simple linear regression analysis was used to explore the relationship between the two variables. The analysis involved fitting a linear equation to the observed data, in which the independent variable (Post-Transplant Hospital Stay, plotted along the x-axis) predicted the dependent variable (CCI, plotted along the y-axis). The strength and direction of the relationship are indicated by the slope of the regression line, and the goodness-of-fit of the model is assessed using the R^2 value. Kaplan–Meier analysis was used to assess the survival probabilities of pancreatic grafts, kidney grafts, and patients. Statistical analyses were performed using SPSS software (version 28).

Results

Characteristics of the donors

Table 1 summarizes the characteristics of the ten donors. The median patient age was 47 years (18–59 years). Six donors were > 45 years old.

The median BMI was 22.8 kg/cm^2 (17.3–28.4), and the median HbA1c level was 5.6% (5.1–6.1). Brain death was caused by head trauma in four patients, anoxic brain injury in four, and cerebrovascular accident (CVA) in two. Three donors had histories of cardiopulmonary arrest (CPA) that required resuscitation. Half of the donors had unstable hemodynamics, which necessitated the administration of high doses or multiple vasopressors. All but one case involved marginal donors as defined by Kapur's criteria.[16)]

Recipient-related characteristics

The characteristics of all recipients are summarized in Table 2. The median postoperative observation period was 1968 days (96–8071). The recipients had a median diabetes duration of 25 years and had been on dialysis for 5.1 years. The median post-transplant hospital stay (PTHS) was 56 days.

The median TIT values for the pancreas and kidneys were 604 min and 951 min, respectively. Reconstruction of the GDA and portal vein extension were required in six and two cases, respectively.

Enteric drainage was predominantly performed via duodenoileostomy with side-to-side anastomosis. Enteric drainage was performed using the Roux-en-Y method in a patient with a history of peritonitis due to appendicitis because of the need for partial resection of the ileum.

Postoperative complications of SPK

Postoperative complications were observed in all the patients (Table 3). Most of these complications were classified as Clavien-Dindo (CD) grade I or II. Major complications classified as CD grade IIIa or higher were observed in four patients (40%); however, mortality was zero. Major complications included postoperative bleeding from the kidney graft zero-hour biopsy site, primary nonfunctioning kidney graft, wound dehiscence, and peritonitis due to perforation of the ileal stump after Roux-en-Y anastomosis. The first three major complications were successfully treated with surgical intervention. However, one patient with peritonitis required two additional surgeries and temporary intensive care unit (ICU) management because of sepsis resulting from peritonitis. The cause of the ileal stump perforation was obstruction associated with adhesions of the ileum on the anal side of the anastomosis. However, none of the patients experienced duodenal graft perforation.

The median CCI for all cases was 37.9, and a correlation was observed between the CCI and the PTHS (Fig. 1). An R^2 value of 0.5876, corresponding to an R-value of approximately 0.77, suggests a moderate correlation between the CCI and length of postoperative stay. The ten patients were divided into two groups: the early group (2001–2018) and the late group (2019–2024), with five patients in each group. A comparison of CCI between the groups showed a trend toward reduction in the late group compared to the early group (early group: 41.8 vs. late group: 29.6; $p=0.056$). (Fig. 2). The median PTHS of all patients was 56 days.

Table 1. Clinical characteristics of deceased donors for pancreas transplantation

Factors	All cases (n=10)
Sex, % male	60% (n=6)
Age, y (Median (range))	47 (18–59)
BMI, kg/m^2 (Median (range))	22.8 (17.7–28.4)
Cardiopulmonary arrest	30% (n=3)
Cause of brain death	
Head trauma	4 (40%)
Anoxic brain injury	4 (40%)
Cerebrovascular accident	2 (20%)
HbA1C, %	5.6% (5.1–6.1)
ICU stay, days (Median (range))	4 (1–12)
Hemodynamic instability, %	50% (n=5)
Marginal donors based on extended donor criteria※, %	90% (n=9)
HLA mismatch number	3 (2–4)
Duration of transportation, min (Median (range))	312 (105–421)

※ Definition of marginal donor: over 45 years, hemodynamic instability (dopamine < 10 mg/kg/min or use of two or more vasopressors use), or DCD) (Kapur Sandip; Bonham 1999)
※ BMI, body mass index; ICU, intensive care unit; HLA, human leukocyte antigen

Table 2. Clinical characteristics of recipient-related factors in pancreas transplantation

Factors	All cases (n=10)
Observational periods, days (Median (range))	1968 (96-8071)
Gender, % male	60% (n=6)
Age, y (Median (range))	49 (32-65)
BMI, kg/m^2 (Median (range))	21.4 (17.3-27.3)
HbA1C, % (Median (range))	7.9 (7.1-8.9)
Duration of diabetes, y (Median (range))	25 (19-41)
Duration on dialysis, y (Median (range))	5.1 (1.5-15.1)
Duration on the waiting list, days (Median (range))	1187 (78-2625)
Operation time, mins (Median (range))	711 (570-830)
Estimated blood loss (EBL) g (Median (range))	1405 (340-2130)
Blood transfusion, %	60% (n=6)
TIT-pancreas, min (Median (range))	604 (478-954)
TIT-kidney, min (Median (range))	951 (762-1145)
Artery (carrel patch), %	90% (n=9)
Reconstruction of GDA, %	60% (n=6)
Portal vein Extension, %	20% (n=2)
Enteric drainage procedure	100% (n=10)
Duodeno-jejunostomy, %	30% (n=3)
Duodeno-ileostomy, %	70% (n=7)
Roux-en Y, %	10% (n=1)
Postoperative hospital stays, days (Median (range))	56 (19-228)

BMI, body mass index; TIT, total ischemic time; HBA1c, glycosylated hemoglobin

However, similar to the trend observed with the CCI, the PTHS tended to be shorter in the late group than in the early group (early group : 67 days vs. late group : 30 days ; p=0.056). We believe that the reduction in the PTHS may be related to a decrease in perioperative complications.

Outcomes of pancreas transplantation and late-onset complications

Patient, pancreatic, and kidney graft survival rates are shown in Fig. 3. The pancreatic and kidney functions are shown in Figs. 4a and 4b. Despite the loss of one kidney graft due to primary nonfunction, the 5-year outcomes for both patient survival and pancreatic graft survival remained 100%. However, we encountered one case each of pancreatic graft loss, kidney graft loss, and patient death, all of which were attributed to LOC.

Among the 10 cases, six LOCs were observed in five cases. LOC onset occurred between one- and 16-years post-transplant. One patient with acute pancreatitis was treated with medication. Two patients required reoperation because of incisional hernia and strangulation of the bowel obstruction. One patient developed hyperglycemic acidosis and resumed insulin therapy 5 years post-transplantation. Although histological confirmation was not obtained, the patient was diagnosed with recurrent T1DM based on blood tests (no elevation of serum amylase and lipase levels), seroconversion of the anti-IA-2 antibody, and imaging findings (no graft pancreatitis or thrombosis). A case of kidney graft loss 6 years post-transplantation resulted from the progression of focal segmental glomerulosclerosis (FSGS). One patient suddenly died of cardiovascular disease 8 years after undergoing SPK with a functioning graft.

Discussion

The treatment outcomes of SPK performed at a single institute between 2001 and 2024 were analyzed. Postoperative complications were relatively frequent ; however, the short-term outcomes of SPK were favorable, with a decreasing trend in CCI in the last five cases compared to the first, suggesting improved perioperative management. No patient deaths or graft losses directly related to the surgery occurred. Except for one case of kidney graft loss due to primary nonfunction, all patients achieved insulin independence and were free from hemodialysis. Conversely, during long-term follow-up, we encountered one case of pancreatic graft loss likely related to T1DM recurrence, one case of

Table 3. Postoperative complications

Postoperative complications	All cases (n=10)
CMV infection	4 (40%)
Diarrhea (severe)	4 (40%)
Anemia	3 (30%)
Ileus	2 (20%)
Gastrointestinal bleeding	2 (20%)
Surgical site infection	2 (20%)
Delayed gastric emptying	2 (20%)
Mental disorder	2 (20%)
Peritonitis due to perforation of ileal stump	1 (10%)
Portal thrombosis	1 (10%)
Wound dehiscence	1 (10%)
Catheter related blood stream infection	1 (10%)
Others	7 (70%)
Kidney graft related complications	
Postoperative bleeding	1 (10%)
Macro-Hematuria	1 (10%)
Acute cellular rejection	1 (10%)
Primary non-function	1 (10%)
Clavien-Dindo grade (highest grade/patient)	
II	7 (70%)
IIIa	1 (10%)
IIIb	2 (20%)
IVa	1 (10%)
Readmission	2 (20%)
Postoperative CCI, median	33.5 (29.6-67.4)

Comprehensive complication index (CCI) (Slankamenac K, et al. Ann Surg. 2013; 258(1): 1-7)

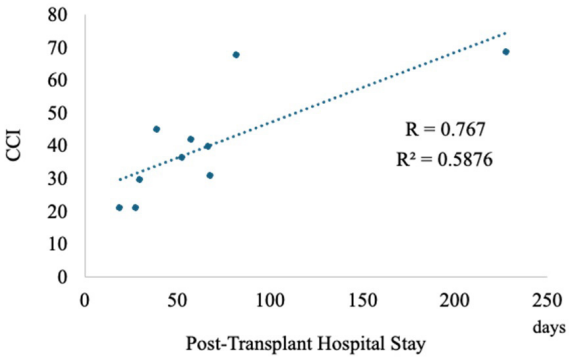

Fig. 1. Association Between Post-Transplant Hospital Stay and CCI.
A correlation was observed between the CCI and post-transplant hospital stay. An R^2 value of 0.5876, corresponding to an R-value of approximately 0.77, suggests a moderate correlation between the CCI and the length of postoperative stay.
CCI, comprehensive complication index.

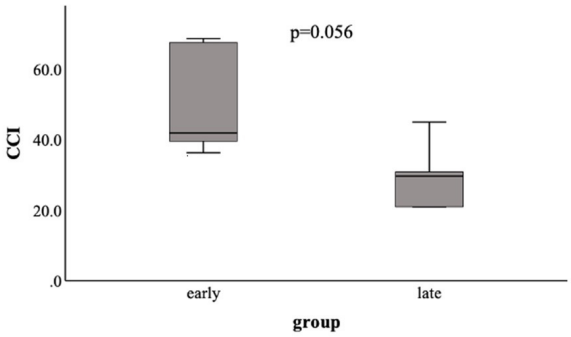

Fig. 2. Comparison of Mean CCI Values Between Group A and Group B.
The ten patients were divided into two groups : the early group (2001-2018) and the late group (2019-2024), with five patients in each group. A comparison of CCI between the groups revealed a trend toward a decrease in CCI in the late group (early group : 41.8 vs. late group : 29.6 ; p=0.056).
CCI, comprehensive complication index.

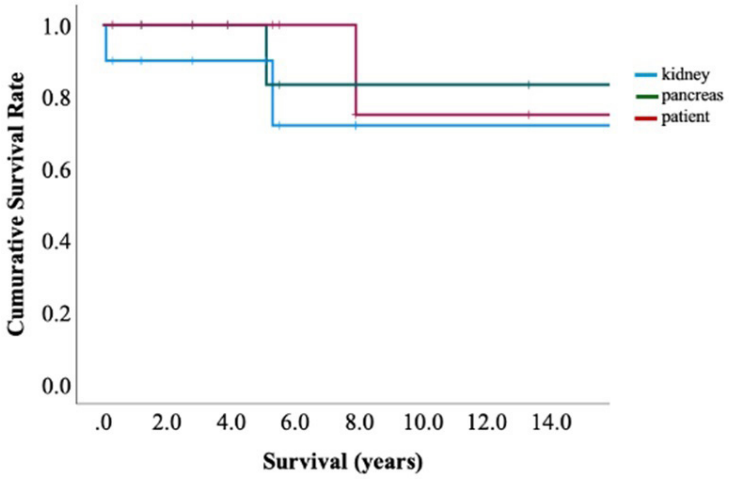

Fig. 3. Patient Survival Rate, Pancreas Graft Survival Rate, and Kidney graft Survival Rate.
Patient, pancreatic, and kidney graft survival rates are shown. Despite the loss of one kidney graft due to primary nonfunction, the 5-year outcomes for both patient and pancreatic graft survival remained 100%. However, we encountered one case each of pancreatic graft loss, kidney graft loss, and patient death after 5 years post-transplantation, all of which were attributed to LOC.
LOC, late-onset complications.

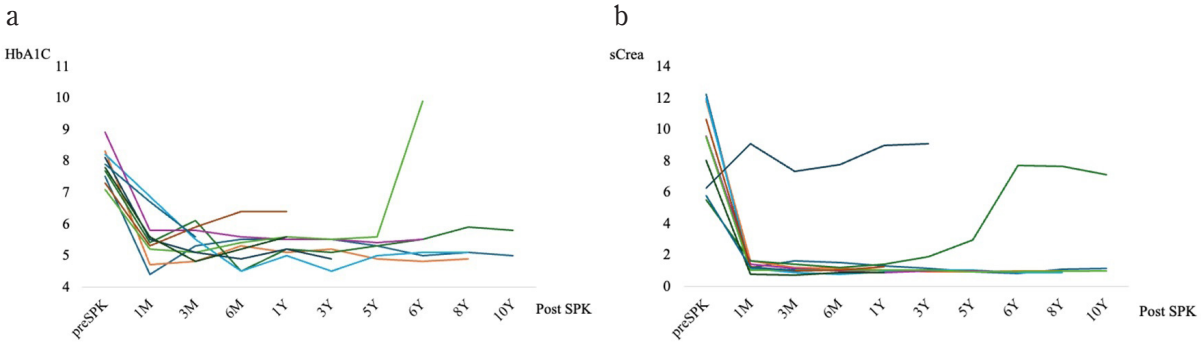

Fig. 4. Time Course of HbA1C (a) and sCrea (b).
The HbA1c level was maintained below 6.1% at 3M after SPK. HbA1c was elevated in one case due to recurrence of T1MD after 5-year SPK. All but one primary nonfunction kidney patient achieved a hemodialysis-free condition after SPK and maintained a sCrea level below 2.0 mg/dL for 3 years after SPK. One patient required hemodialysis because of end-stage renal disease caused by FSGS.
LOC, late-onset complications ; SPK, simultaneous pancreas-kidney transplantation ; FSGS, focal segmental glomerulosclerosis.

kidney graft loss likely resulting from FSGS, and one case of death because of cardiovascular complications. These findings highlight the challenges in managing long-term cases, particularly predicting T1DM recurrence and managing cardiovascular risks, which are known contributors to late morbidity and mortality in patients with SPK. Our experience underscores the importance of vigilant long-term follow-up, particularly for complications related to graft function and cardiovascular health.

Simultaneous pancreas-kidney transplantation has become the gold standard treatment for patients with T1DM and end-stage renal disease[1,8,13,17,18]. However, it is substantially more complex than other treatment options. Candidates for SPK usually have multiple comorbidities, and reducing postoperative complications is crucial. The incidence of major complications after SPK requiring surgical intervention has been reported 15-54% in previous studies[10,12,19]. The early graft loss rates in the pancreas and kidney were described as 2-20% and 0-13%, respectively[6,8,9,20].

Pancreatic graft loss is primarily attributed to complications, such as graft thrombosis and enteric leakage[9,11,19]. At this institution, one case of pancreatic graft thrombosis involved a venous thrombus

that was asymptomatic and resolved with the administration of anticoagulants and antiplatelet agents. In contrast, intestinal perforations required two reoperations. Enteric leakage, which occurs in 5–8% of cases, is a significant contributor to the need for graft pancreatectomy[21]. Various surgical reconstruction techniques have been investigated to mitigate enteric leakage. Most patients currently undergo pancreatic transplantation with enteric exocrine drainage[19,22,23]. A variety of procedures involving different small intestine sites for enteric anastomosis have been described. Some groups prefer using a Roux-en-Y loop, whereas others prefer direct anastomosis. The choice of anastomotic technique is determined by the surgeon's preference and the patient's condition[22]. At this institution, direct anastomosis of the jejunum or ileum is predominantly performed. In one case, Roux-en-Y was selected because of severe adhesions of the ileum within the pelvic cavity, and a decompression tube was placed in the graft duodenum. The patient experienced perforation of the ileal stump due to obstruction caused by adhesions in the efferent limbs. Pancreatic graft function was maintained through reoperation, perforation repair, and the creation of a diverting jejunostomy. To date, no multicenter studies have compared different anastomotic methods. However, the association between intestinal perforations and anastomoses remains unclear.

Currently, the most widely used method for grading postoperative complications is the CD classification, which grades postoperative complications on a scale from 1 to 5 based on the corresponding treatment[24]. Because only the highest-grade complication is reported, the overall medical burden is underestimated in patients who develop multiple complications. To overcome this limitation, Slankamenac *et al.* established the CCI. This allows for a more sensitive comparison of patient outcomes because the cumulative effect of all postoperative complications is captured in the final score[25-27]. The incidence of surgery-related complications (CD>IIIa) at our institution was consistent with that reported in previous studies, and no early pancreatic graft loss attributable to graft thrombosis or enteric leakage was observed. In this study, a decrease in the CCI was observed in the late group, suggesting improvements in perioperative management, including surgical techniques, immunosuppressive therapy, and infection control.

Four patients experienced five LOCs. Surgical intervention is required for patients with strangulated bowel obstruction or incisional hernias. Additionally, there was one case each of pancreatic graft loss, kidney graft loss, and patient death with a functioning graft (DWFG). Pancreatic graft loss occurred 5 years after SPK. The patient suddenly developed severe hyperglycemia and insulin dependence within a month and was diagnosed with irreversible pancreatic dysfunction. The cause of pancreatic dysfunction is speculated to be the recurrence of T1DM, based on the absence of C-peptide, absence of detectable DSA, seroconversion of anti-IA-2 antibody, and pancreatic exocrine destruction through serum and imaging studies[28]. Although subsequent blood tests revealed seroconversion to anti-IA-2 antibodies, the exact timing of seroconversion was unclear, as regular monitoring was not conducted post-transplant. Pancreatic graft loss due to immune-related factors is often attributed to autoimmunity, with increasing autoantibody levels potentially preceding graft function by several years. Although T1DM recurrence can occur, it is relatively rare compared to acute or chronic rejection. In this case, autoimmunity was suggested to have played a primary role in graft dysfunction, as evidenced by the absence of C-peptide, seroconversion of anti-IA-2 antibodies, and the absence of detectable donor-specific antibodies (DSA). Regular monitoring of autoantibodies post-transplantation might be crucial for identifying patients at risk of autoimmune graft loss. Although a percutaneous pancreatic biopsy is essential for a definitive diagnosis, its invasiveness limits the use of protocol biopsies in routine practice. Therefore, less invasive methods such as autoantibody monitoring may play an important role in the early detection of immune-mediated graft dysfunction[29,30].

Kidney graft loss was attributed to secondary FSGS. Because a 0-hour biopsy was not performed, the diagnosis remains speculative. However, based on the findings of a renal biopsy conducted one year post-transplant, the patient was diagnosed with chronic allograft nephropathy attributed to FSGS and nephrosclerosis, with no evidence suggesting rejection or calcineurin inhibitor nephrotoxicity. Over the subsequent five years, the proteinuria worsened, leading to end-stage renal disease (ESRD) and hemodialysis initiation. Treatment for secondary FSGS varies depending on the underlying cause but generally involves elimination of the cause and prevention of progression to ESRD. In this case, identifying the cause was difficult, and the patient progressed to ESRD after five years.

The cause of DWFG was a cardiovascular event that occurred seven years after SPK. At the time

of transplantation, the patient was 32 years old, with a 22-year history of T1DM and a 4.4-year history of dialysis. One year before the diagnosis of DWFG, a cardiovascular evaluation was performed because of chest discomfort and identified left ventricular hypertrophy, and the patient was subsequently prescribed β1-blockers. Tomimaru *et al.* reported in their analysis of Japanese SPK cases that the duration of T1DM is the only factor associated with death with functioning graft (DWGF)[9]. Although some reports suggest that SPK may contribute to a reduction in post-transplant cardiovascular events, many cases involve prolonged T1DM, making preventive measures against post-transplant cardiovascular events crucial[9,13]. However, even after successful pancreatic transplantation and subsequent normoglycemia, macrovascular disease may continue to progress. Peripheral vascular disease can worsen after pancreatic transplantation and may continue to worsen despite normoglycemia, suggesting that it is often too advanced to reverse[31]. For symptomatic cases such as the one presented here, regular follow-up by a cardiologist and an endocrinologist should also be considered.

This study has several limitations, including a small sample size and retrospective design, which may introduce bias and limit the generalizability of the findings. The lack of standardized autoantibody monitoring may have delayed the detection of autoimmune graft dysfunction, and the absence of post-transplant routine cardiovascular screening could have contributed to the late detection of cardiovascular events. Future prospective studies are required to confirm these results and clarify the role of autoimmunity in long-term graft outcomes.

Short-term outcomes of SPK at Fukushima Medical University were favorable, with a trend toward a reduction in the CCI observed in the latter five cases compared with the early five cases, suggesting potential improvements in perioperative management. To improve long-term outcomes, it is essential to develop regular monitoring programs in collaboration with physicians.

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Conflict of interest disclosure

All authors declare no conflicts of interest associated with this manuscript.

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