ORIGINAL ARTICLE

# Early intestinal complications following pancreas transplantation: lessons learned from over 300 cases – a retrospective single-center study

Joana Ferrer-Fàbrega[1,2], Brenda Cano-Vargas[1], Pedro Ventura-Aguiar[2,3], Gabriel Cárdenas[1], Ángeles García-Criado[4], Miguel Angel López-Boado[1], Ramón Rull[1], Rocío García[1], Miriam Cuatrecasas[2,5,6], Enric Esmatjes[2,7], Fritz Diekmann[2,3], Constantino Fondevila[1,2,6], Mª José Ricart[3], Laureano Fernández-Cruz[1], Josep Fuster[1,2,6] & Juan Carlos García-Valdecasas[1,2,6]

1 Hepatobiliopancreatic Surgery and Liver and Pancreatic Transplantation Unit, Department of Surgery, Institute Clínic of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Barcelona, Spain
2 August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain
3 Renal Transplant Unit, Nephrology and Kidney Transplant Department, Hospital Clínic, University of Barcelona, Barcelona, Spain
4 Department of Radiology, Hospital Clínic, University of Barcelona, Barcelona, Spain
5 Department of Pathology, Hospital Clínic, University of Barcelona, Barcelona, Spain
6 Network for Biomedical Research in Hepatic and Digestive Diseases (CIBERehd), Barcelona, Spain
7 Diabetes Unit, Department of Endocrinology and Nutrition, Institute Clínic of Digestive and Metabolic Diseases (ICMDiM), Hospital Clínic, University of Barcelona, Barcelona, Spain

**Correspondence**
Joana Ferrer-Fàbrega MD, PhD, HepatoBilioPancreatic Surgery and Liver and Pancreatic Transplantation Unit, Institute Clínic of Digestive and Metabolic Diseases (ICMDiM), University of Barcelona/Hospital Clínic Barcelona, C/Villarroel 170, Barcelona E-08036, Spain.
Tel.: +34 619755353;
fax: +34 93 2275589;
e-mails: 2008jff@gmail.com/ joferrer@clinic.cat

## SUMMARY

Enteric complications remain a major cause of morbidity in the post-transplant period of pancreas transplantation despite improvements surgical technique. The aim of this single-center study was to analyze retrospectively the early intestinal complications and their potential relation with vascular events. From 2000 to 2016, 337 pancreas transplants were performed with systemic venous drainage. For exocrine secretion, intestinal drainage was done with hand-sewn anastomosis duodenojejunostomy. Twenty-three patients (6.8%) had early intestinal complications. Median age was 39 years (male: 65.2%). Median cold ischemia time was 11 h [IQR: 9–12.4]. Intestinal complications were intestinal obstruction ($n$ = 7); paralytic ileus ($n$ = 5); intestinal fistula without anastomotic dehiscence ($n$ = 3); ischemic graft duodenum ($n$ = 3); dehiscence of duodenojejunostomy ($n$ = 4); and anastomotic dehiscence in jejunum after pancreas transplantectomy ($n$ = 1). Eighteen cases required relaparotomy: adhesiolysis ($n$ = 6); repeated laparotomy without findings ($n$ = 1); transplantectomy ($n$ = 6); primary leak closure ($n$ = 3); re-positioning of the graft ($n$ = 1); and intestinal resection ($n$ = 1). Of the intestinal complications, 4 were associated with vascular thrombosis, resulting in two pancreatic graft losses. Enteric drainage with duodenum–jejunum anastomosis is safe and feasible, with a low rate of intra-abdominal complications. Vascular thrombosis associated with intestinal complications presents a risk factor for the viability of pancreatic grafts, so prevention and early detection is vital.

*Transplant International* 2021; 34: 139–152

**Key words**
early intestinal complication, enteric drainage, graft survival, pancreas transplantation, vascular thrombosis

Received: 27 July 2020; Revision requested: 27 August 2020; Accepted: 16 October 2020;
Published online: 10 November 2020

© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd
doi:10.1111/tri.13775

## Introduction

Pancreas transplantation has been recognized as the standard treatment for improved glucose homeostasis in selected diabetic patients, particularly for those with end-stage renal disease [1]. Throughout its history, recent years have been coined the "decade of decline" because of the decreased number of cases [2,3]. Therefore, a re-evaluation to optimize patient outcomes and re-instill confidence in this procedure is required [4,5].

The propensity of the pancreatic allograft to vascular thrombosis and the need to adequately drive exocrine secretions have conditioned the development of surgical techniques for pancreas transplantation [6–13]. Whole pancreaticoduodenal graft with primary enteric exocrine drainage is currently the norm [14]. A variety of procedures have been described using various small-bowel sites in the intraperitoneal space [14–16]. Most groups prefer a direct side-to-side anastomosis between donor duodenum and jejunum, while others elect to use a Roux-en-Y intestinal limb [8]. After almost a decade, new modifications focusing on physiological technique are being developed [17]. One of these consists of placing the whole pancreaticoduodenal graft in the retroperitoneal space, with a duodenum–duodenum anastomosis [18–20]. Similarly, a duodenum–stomach anastomosis technique was reported for particular patients [21,22].

However, enteric drainage complication rates ranging from 2% to 20% have been reported, such as: intra-abdominal infections; anastomotic dehiscence; duodenal ischemia, and obstruction. Related morbidities pose more management challenges and could entail urgent relaparotomy and thus carry a greater risk of graft loss and mortality [16]. In general, these complications, considered the Achilles' heel of early attempts at pancreas transplantation, are poorly discussed and described in the literature. Some studies suggest that surgical and image-guided interventions can salvage some enterically drained grafts. However, their generalizability and real effectiveness remain unclear [23–26].

Although no surgical technique has achieved universal acceptance, contributions in the search for the "perfect technique" have nevertheless been made by principle transplant centers over time, our group included.

The first pancreas transplant in Spain was performed at the Hospital Clínic of Barcelona in 1983 [27]. To date, some 600 pancreas transplants from deceased donors have been performed within the leading program in the country [28]. Whole pancreaticoduodenal grafts have now been the standard since the early 2000s.

The objective of this study was to analyze over sixteen years, single-centre surgical complications associated with enteric drainage, and their clinical impact on patients' outcomes, taking into account that surgical technique and immunosuppression protocols have been standardized. As vascular thrombosis is one of the principal causes of graft loss, it would be interesting to search for relations between early intestinal complications and adverse post-transplant vascular events. This information could be highly effective for the detection and prevention of the potential risk factors affecting graft survival. It also provides an opportunity for the proposal of changes in the surgical technique with a view to improving results.

## Materials and methods

Between January 2000 and April 2016, a retrospective analysis including all pancreas transplants performed at Hospital Clínic of Barcelona was conducted, focusing on enteric drainage early surgical complications. Data were obtained from a prospective database and, where missing, collected from medical records. The institutional ethics board approved the study (HCB/2020/0498), and it was performed in accordance with the declarations of Helsinki and Istanbul.

### Patient population

Criteria donor selection is based on the consensus of pancreas and islet transplant of the National Transplant Organization [28]. In all transplant cases, organs were procured from deceased brain-dead donors. The indications and contraindications for pancreas transplant are subject to our institution criteria published elsewhere [29].

### Antibiotic prophylaxis

Initially, the prophylaxis was based on third-generation cephalosporin plus vancomycin for anti-Gram-positive bacterial activity. As a result of bacterial resistance, this was modified in 2015 to ertapenem plus vancomycin. Fungal prophylaxis with fluconazole 200 mg/day was universally used in all recipients. Cytomegalovirus prophylaxis was provided by intravenous ganciclovir at doses up to 5 mg/kg/12 h, or valganciclovir 900 mg/day



Transplant International 2021; 34: 139–152
© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

for 3–6 months, depending on glomerular filtration rates.

### Thrombosis prophylaxis

The scheme for all types of transplants is based on low molecular weight heparin at doses of 20 mg every 12 h, starting 8 h post–pancreas reperfusion. This regime is maintained until patient discharge (in the absence of thrombotic/hemorrhagic complications), with administration of acetylsalicylic acid pretransplant and 12 h postsurgery at doses of 50 mg every 24 h. The patient is then discharged with a 100 mg dose per day.

### Immunosuppression regimens

In simultaneous pancreas–kidney (SPK) patients, anti-interleukin-2 monoclonal antibody (basiliximab) 20 mg at Day 0 and Day 4 was used as standard induction therapy until July 2013, and thereafter replaced by rabbit anti-human lymphocyte polyclonal antibodies (either thymoglobulin 1.25 mg/kg/day or ATG 2.5 mg/kg/day) for four consecutive days. In pancreas after kidney (PAK) patients, these doses are extended to seven consecutive days. Maintenance immunosuppression was based on triple therapy with a calcineurin inhibitor (Cyclosporine A was used until 2005. Tacrolimus was introduced in the late 90s and is the current choice), mycophenolate and steroids.

### Surgical technique

The whole pancreatoduodenal graft is prepared on the back table. In our institution, the arterial anastomosis of the graft is created either by (i) end-to-end anastomosis between the splenic artery and the distal superior mesenteric artery [30]; or (ii) arterial reconstruction with an iliac arterial "Y" graft. In addition, the donor duodenum is dissected by mechanical staple to approximately 8–10 cm in length, and the edges are reinforced using a continuous, hand-sewn nonabsorbable suture.

For recipient surgery, the access route is midline laparotomy. The pancreatic graft is placed intraperitoneally on the right side of the pelvis, with the duodenal segment pointing upwards (Fig. 1). Venous systemic drainage is via the grafted portal vein into the cava or common iliac vein of the recipient. The arterial supply is provided by anastomosis end-to-side between either the grafted superior mesenteric artery or the Y-graft (depending on the back-table reconstruction technique used) and the recipient common right-iliac artery.

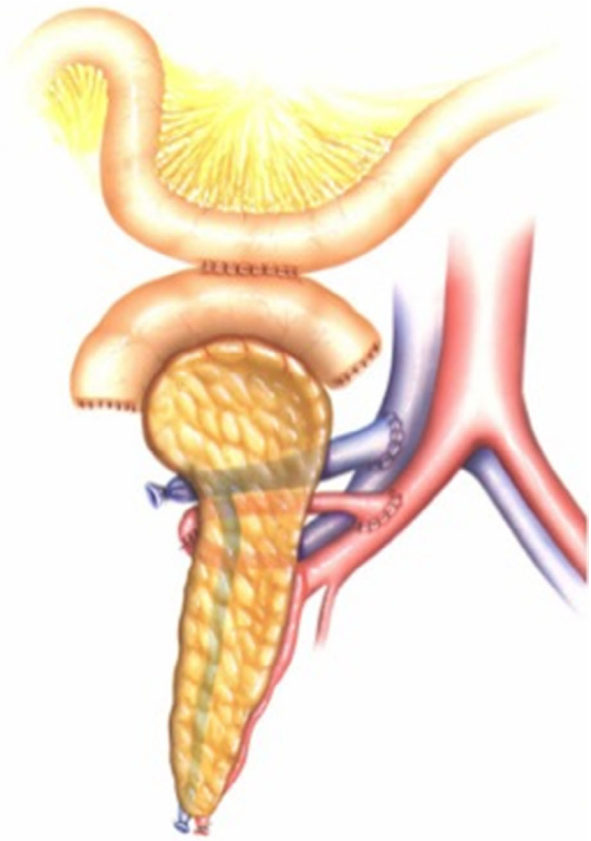


**Figure 1** Whole-organ transplant with systemic vein and enteric exocrine drainage (cephalad position). The grafted superior mesenteric artery (back-table arterial reconstruction: end-to-end anastomosis between the splenic artery and the distal superior mesenteric artery) is anastomosed to the recipient common right-iliac artery and the donor portal vein to the recipient vena cava/common iliac vein. A two-layer hand-sewn side-to-side duodenojejunostomy is constructed about 60-80 cm distal to the ligament of Treitz. Image courtesy of Prof. Fernández-Cruz.

For the exocrine secretion, intestinal drainage is performed with duodenum–jejunum anastomosis without Roux-en-Y loop, side to side for 60–80 cm from the Treitz, using a double layer continuous hand-sewn suture, the inner layer absorbable, and a nonabsorbable external layer.

### Surgical outcomes and follow-up

Early morbidity is defined as any complication within 90 days after pancreas transplant and is graded according to a standard classification [31].

A Doppler ultrasound is performed, 24 h post-transplant and the day before discharge in the case of an uneventful postoperative course, to assess the following: the vascular patency; the state of the graft, and any presence of asymptomatic fluid.


© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

Computed tomography (CT) is used in the case of abnormal ultrasound findings or worsening of clinical presentation, for example, fever or unresolved abdominal pain, in order to evaluate graft parenchyma, pancreatic duct, vascular structures, and enteric anastomosis.

Follow-up data during inpatient hospital stay include laboratory values for reperfusion injury in addition to pancreas and kidney graft function. Complete immunologic and virologic work-ups are also performed. Biopsies are taken when clinically indicated. Rejections are classified according to Banff criteria [32].

### Statistics

Categorical variables are described as frequencies (%) and percentages. Continuous variables are expressed as median and interquartile range [IQR]. Categorical variables were analyzed by use of Fisher's exact or chi-square test, and continuous variables were analyzed by unpaired Student's *t*-test, Mann–Whitney *U*-test, or other nonparametric tests.

Patient survival was calculated from the time of transplant to death or the end of follow-up. Pancreas graft survival was calculated from the time of transplant until the return to permanent insulin therapy dependency, or death/end of follow-up with a functioning graft. Both patient and graft survival analyses are estimated by Kaplan–Meier method. A $P$ value $< 0.05$ was considered to indicate statistical significance. Data are collected and analyzed with SPSS statistical software (SPSS 20.0, 1989-1995; Chicago, IL, USA).

## Results

### Patient characteristics

During the study period, 337 pancreas transplantations were performed, including 276 SPK, 23 PAK, three pancreas transplant alone (PTA) and 35 pancreas retransplantations. The whole series specific donor and recipient data are listed in Table 1.

A total of 23 patients (6.8%) presented at least one complication associated with enteric drainage and were selected for the present study (Table 2). The transplantation type was SPK in 17 patients, PAK in one patient, and pancreas retransplantation in five patients (4 were PTA and 1 was SPK). Median donor age was 29 years [IQR: 19–37], and gender distribution was mostly for male donors ($n = 15$), with a median body mass index of 23.7 kg/m$^2$ [IQR: 23–26.2]. The preservation solution used for organ perfusion was diverse, University of Wisconsin being the most frequent, and the median cold ischemia time was 11 h [IQR: 9–12.4]. Indications for pancreas transplantation were mainly type-1 diabetes mellitus. Recipient gender distribution was 65.2% male, with a median age of 39 years [IQR: 33–43]. Seventeen patients presented prior abdominal surgery. Distribution for the immunosuppressive therapy details is reported in Table 2. Differences between those patients with and without intestinal complications are depicted in Table 1. The two groups were comparable in terms of donor-related and preservation injury factors. Although the serum peak of amylase/lipase levels after transplantation as a marker of pancreas reperfusion injury did not show a significant difference between both groups, there was a trend toward a higher cold ischemia time for the intestinal complications group. Interestingly, the recipient's prior abdominal surgery ($P = 0.016$) and longer hospitalization time were significantly associated with early intestinal complications ($P < 0.0001$).

### Surgical technique

For back-table arterial reconstruction, end-to-end anastomosis of the distal superior mesenteric artery to splenic artery was used in 95.7% of cases and in one case, a Y-graft.

In recipient surgery, the type of arterial anastomosis distribution was superior mesenteric to right common iliac end to side anastomosis in 21 cases. One case was the arterial "Y" graft to the stump of the superior mesenteric artery of previous pancreatic graft anastomosis. In another case, the superior mesenteric artery was anastomosed to a donor iliac graft placed on the right common iliac artery. In all cases, systemic endocrine drainage was by portal vein anastomosis to the most distal part of inferior vena cava. Enteric drainage was performed with a 2.5 cm duodenum–jejunum side-to-side anastomosis.

### Intestinal complications

In our series, the various types of enteric complications ocurred within the first 30 postoperative days. The clinical presentation depended on the diagnosis of the intra-abdominal event. Moreover, negative cytomegalovirus antigenemia was confirmed in all recipients.

The type of complication and its presentation in a total of twenty-three patients are described as follows:


© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

**Table 1.** Whole series donor and recipient characteristics.

| | Total ($n$ = 337) | No intestinal complications ($n$ = 314) | Intestinal complications ($n$ = 23) | $P$ value |
|---|---|---|---|---|
| Donor | | | | |
| Cause of death | | | | |
| Trauma | 182 (54%) | 167 (53.2%) | 15 (65.2%) | 0.388 |
| Anoxic damage | 19 (5.6%) | 18 (5.7%) | 1 (4.3%) | |
| CVA | 121 (35.9%) | 116 (36.9%) | 5 (21.7%) | |
| Others | 15 (4.5%) | 12 (4.1%) | 2 (8.7%) | |
| Age (years) | 31 [21–40] | 32 [21–40] | 29 [19–37] | 0.304 |
| Gender (M/F) | 206 (61.1%)/131 (38.9%) | 191 (60.8%)/123 (39.2%) | 15 (65.2%)/8 (34.8%) | 0.826 |
| Body mass index (kg/m$^2$) | 23.4 [21.6–25.4] | 23.4 [21.5–25.4] | 23.7 [23–26.2] | 0.284 |
| Previous cardiac arrest | 48 (14.2%) | 45 (14.3%) | 3 (13%) | 1 |
| Intensive care unit stay (days) | 3 [1.7–7] | 2 [1–5] | 3 [2–7] | 1 |
| Amylase (IU/l) | 84 [48.7–170] | 84 [48–171.2] | 112 [55.7–155] | 0.518 |
| Lipase (IU/l) | 45 [17.5–115] | 45 [18–120] | 16.5 [8.2–85.7] | 0.121 |
| P-PASS total | 16 [14–18] | 16 [14–18] | 15.5 [14.2–18] | 0.913 |
| Preservation solution | | | | |
| UW | 256 (76%) | 243 (77.4%) | 13 (56.5%) | 0.157 |
| CS | 67 (19.9%) | 59 (18.8%) | 8 (34.8%) | |
| HTK | 7 (2.1%) | 6 (1.9%) | 1 (4.3%) | |
| IGL-1 | 7 (2.1%) | 6 (1.9%) | 1 (4.3%) | |
| Cold ischemia time (h) | 10.3 [8–12] | 10.3 [8–12] | 11 [9–12.4] | 0.542 |
| Recipient | | | | |
| Age (years) | 40 [35-45] | 40 [35-45] | 39 [33–43] | 0.464 |
| Gender (M/F) | 220 (65.3%)/117 (34.7%) | 205 (65.3%)/109 (34.7%) | 15 (65.2%)/8 (34.8%) | 1 |
| Type of diabetes | | | | |
| DM-I | 333 (98.8%) | 311 (99%) | 22 (95.7%) | 0.247 |
| Others | 4 (1.2%) | 3 (1%) | 1 (4.3%) | |
| Time of diabetes (years) | 26 [21–31] | 26 [21–31] | 26 [19–32] | 0.649 |
| Dialysis duration (months) | 27 [19.4–37.7] | 27 [18.6–37.5] | 26.5 [21.8–44.2] | 0.539 |
| Type of dialysis | | | | |
| Predialysis | 27 (8%) | 26 (8.3%) | 1 (4.3%) | 0.542 |
| Peritoneal dialysis | 75 (22.3%) | 70 (22.3%) | 5 (21.7%) | |
| Hemodialysis | 187 (55.5%) | 177 (56.4%) | 10 (43.5%) | |
| Hemodialysis/PD | 3 (0.9%) | 1 (0.3%) | 2 (8.6%) | |
| No dialysis | 45 (13.4%) | 40 (12.8%) | 5 (21.7%) | |
| Abdominal surgery | 160 (47.5%) | 143 (45.5%) | 17 (73.9%) | 0.016 |
| Transplant type | | | | |
| SPK | 276 (81.9%) | 259 (82.5%) | 17 (73.9%) | 0.296 |
| PAK | 23 (6.8%) | 22 (7%) | 1 (4.3%) | |
| PTA | 3 (0.9%) | 3 (1%) | – | |
| Retransplant | 35 (10.4%) | 30 (9.6%) | 5 (21.7%) | |
| Postreperfusion amylase (IU/l) | 195 [111–349] | 196 [119–351.5] | 177 [75–231] | 0.155 |
| Postreperfusion lipase (IU/l) | 183.5 [100–389.2] | 184 [100–391] | 160 [59–290] | 0.480 |
| Time of hospital stay (days) | 14.5 [11–22] | 14 [11–21] | 29 [22–37] | 0.000 |

CS, celsior; CVA, cerebro-vascular accident; F, female; HTK, Histidine-tryptophan-ketoglutarate; IGL-1, Institut Georges Lopez-1; M, male; PTA, pancreas transplant alone; PAK, pancreas after kidney transplant; PD, peritoneal dialysis; P-PASS, preprocurement pancreas suitability score; SPK, simultaneous pancreas–kidney transplant; UW, University of Wisconsin.

Continuous variables are expressed as median [IQR] and categorical variables as frequencies (percentages).

*Intestinal obstruction* presented in seven patients, as depicted in Table 3. From this group, one patient had diabetic gastroparesia as a comorbidity and two more patients were on immunosuppression therapy as a result of a previous SPK and a living donor kidney transplant, respectively. Two others had surgery as a result of a hydatid liver cyst and tubal sterilization, respectively. All patients presented symptoms of distention and


© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

**Table 2.** Analysis and description of cases with enteric drainage complications after pancreas transplantation.

| Case | Recipient gender/age (years) | Transplant Indication | Donor gender/age (years) | Preservation solution | Induction/immunosuppression protocol | Previous abdominal surgery |
|---|---|---|---|---|---|---|
| #1 | Female | DM 1 | Male | UW | Thymo | No |
| IO | 39 | HD | 39 | | Tac-MMF-Cs | |
| #2 | Male | DM 1 | Male | UW | Bs | No |
| IO | 29 | HD | 21 | | Cy-MMF-Cs | |
| #3 | Female | DM 1 | Female | UW | Thymo | SPK |
| IO | 34 | PFKT | 14 | | Tac-MMF-Cs | |
| #4 | Male | DM 1 | Male | UW | Thymo | LDKT |
| IO | 33 | PFKT | 15 | | Tac-MMF-Cs | |
| #5 | Male | DM 1 | Male | IGL-1 | Thymo | No |
| IO | 37 | HD | 19 | | Tac-MMF-Cs | |
| #6 | Male | DM 1 | Male | UW | Thymo | Hepatic cyst resection |
| IO | 39 | PD | 24 | | Tac-MMF-Cs | peritoneal dialysis catheter |
| #7 | Female | DM 1 | Male | UW | Thymo | Tubal sterilization |
| IO | 49 | Predialysis | 16 | | Tac-MMF-Cs | |
| #8 | Male | DM 1 | Female | UW | Bs | SPK |
| PI | 33 | HD | 35 | | Tac-MMF-Cs | Intestinal obstruction<br>Colecistectomy<br>Pancreas and kidney transplantectomy |
| #9 | Male | DM 1 | Female | CS | Bs | Bilateral aorto-femoral |
| PI | 47 | PD | 29 | | Tac-MMF-Cs | Goretex-Y bifurcation grafts<br>Appendectomy<br>Peritoneal dialysis catheter |
| #10 | Male | DM 1 | Male | HTK | Bs | Peritoneal dialysis catheter |
| PI | 56 | PD | 33 | | Tac-MMF-Cs | |
| #11 | Male | DM 1 | Male | CS | Thymo | Peritoneal dialysis catheter |
| PI | 42 | PD | 27 | | Tac-MMF-Cs | |
| #12 | Male | DM 1 | Female | CS | Thymo | Peritoneal dialysis catheter |
| PI | 36 | PD | 45 | | Tac-MMF-Cs | |
| #13 | Female | DM 1 | Female | UW | Bs | No |
| IF | 30 | HD | 28 | | Tac-MMF-Cs | |
| #14 | Male | DM 1 | Male | UW | Thymo | Peritoneal dialysis catheter |
| IF | 56 | PD + HD | 42 | | Tac-MMF-Cs | Repeated peritonitis |
| #15 | Male | Diabetes 2° pancreatitis | Male | CS | Thymo | Twelve abdominal surgeries (hemorrhagic pancreatitis). (drainage of pancreatic necrosis, cholecystectomy hepaticojejunostomy) |
| IF | 48 | HD | 29 | | Tac-MMF-Cs | |
| #16 | Female | DM 1 | Male | UW | Thymo | No |
| ID | 33 | HD | 15 | | Tac-MMF-Cs | |
| #17 | Male | DM 1 | Female | CS | Thymo | SPK |
| ID | 43 | PFKT | 37 | | Tac-MMF-Cs | Sigmoidectomy with protection ileostomy with later ileostomy closure (acute colonic diverticulitis) |
| #18 | Male | DM 1 | Male | UW | Thymo | No |
| ID | 39 | HD | 19 | | Tac-MMF-Cs | |
| #19 | Female | DM 1 | Male | UW | Bs | Peritoneal dialysis catheter |
| DA | 33 | HD + PD | 30 | | Tac-MMF-Cs | |
| #20 | Male | DM 1 | Male | UW | Thymo | Peritoneal dialysis catheter |
| DA | 41 | PD + HD | 23 | | Tac-MMF-Cs | Appendectomy |
| #21 | Male | DM 1 | Male | UW | Bs | Peritoneal dialysis catheter |
| DA | 34 | PD + HD | 31 | | Tac-MMF-Cs | Omentectomy |




© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

**Table 2.** Continued.

| Case | Recipient gender/age (years) | Transplant Indication | Donor gender/age (years) | Preservation solution | Induction/immunosuppression protocol | Previous abdominal surgery |
|---|---|---|---|---|---|---|
| #22<br>DA | Female<br>40 | DM 1<br>PFKT | Male<br>43 | CS | Thymo<br>Tac-MMF-Cs | SPK |
| #23<br>JF | Female<br>37 | DM 1<br>PFKT | Female<br>48 | CS | Thymo<br>Tac-MMF-Cs | SPK |

Bs, basiliximab; CS, celsior; Cs, corticosteroid; Cy, cyclosporine; DA, dehiscence of duodenum–jejunum anastomosis; DM 1, type 1 diabetes mellitus; HD, hemodialysis; ID, ischemia duodenum; IF, intestinal fistula; IGL-1, Institut Georges Lopez-1; IO, intestinal obstruction; JF, recipient jejunum fistula after previous graft transplantectomy; LDKT, living donor kidney transplantation; MMF, mycophenolate mofetil; PD, peritoneal dialysis; PFKT, previous functioning kidney transplant; PI, paralytic ileum; SPK, simultaneous pancreas–kidney transplant; Tac, tacrolimus; Thymo, thymoglobuline; UW, University of Wisconsin.

**Table 3.** Intestinal obstruction.

| Transplant/year | Postoperative amylase/lipase IU/l CIT (h) | Vascular event | Clavien–Dindo Classif. | Treatment Hospital stay (days) | Graft/patient Survival (months) |
|---|---|---|---|---|---|
| #1<br>SPK/2001 | 668/496<br>CIT: 4 | NO | IIIb | Adhesiolysis<br>*Pancreatitis tail pancreas* (8° day postop.)<br>HS: 17 | 73.9/228.9<br>Chronic rejection<br>Alive |
| #2<br>SPK/2001 | 750/633<br>CIT: 12 | NO | IIIb | Laparotomy: No cause founded (17° day postop.)<br>HS: 32 | 22.3/224.9<br>Recurrence DM 1<br>Alive |
| #3<br>Re-tx/2004 | 72/59<br>CIT: 15 | NO | IIIb | Adhesiolysis (14° day postop.)<br>HS: 23 | 58.7/58.7<br>Death (intestinal perforation) |
| #4<br>PAK/2010 | 222/160<br>CIT: 13 | NO | IIIb | Adhesiolysis (15° day postop.)<br>HS: 24 | 105.1/122.3<br>Chronic rejection<br>Alive |
| #5<br>SPK/2014 | 195/265<br>CIT: 8.5 | NO | IIIb | Adhesiolysis<br>*Drainage peripancreatic fluid* (19° day postop.)<br>HS: 29 | 67/67<br>Alive |
| #6<br>SPK/2014 | 64/135<br>CIT: 10 | NO | IIIb | Adhesiolysis<br>*Drainage peripancreatic fluid* (7ª day postop)<br>HS: 22 | 65.1/65.1<br>Alive |
| #7<br>SPK/2015 | 289/258<br>CIT: 15.1 | NO | IIIb | Adhesiolysis (13° day postop)<br>HS: 34 | 61.4/61.4<br>Alive |

CIT, cold ischemia time; DM 1, type 1 diabetes mellitus; HS, hospital stay; PAK, pancreas after kidney transplant; Re-tx, pancreas retransplantation; SPK, simultaneous pancreas–kidney transplant.

Normal value of amylase: 20–104 IU/l. Normal value of lipase: 13–60 IU/l.

abdominal pain. Imaging findings of pancreatic graft on Doppler ultrasonography was unspecific; hence, CT showed intestinal suboclusion in all cases. Relaparotomy was performed within a range of 7–19 postoperative days. Intraoperative findings were mainly with bowel adhesions around the pancreatic graft, in some cases with peripancreatic fluid. Adhesiolysis was performed on these patients.

*Paralytic ileum* was diagnosed in five patients, with a clear relation with previous abdominal surgeries. All


© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

cases presented with abdominal distension, pain, and vomiting. Imaging diagnosis was necessary to rule out other intestinal disorders. The symptoms were effectively resolved with conservative treatment (absolute diet + nasogastric tube), although in two cases nutritional support was necessary. Two out of five patients presented with acute pancreas rejection and were treated accordingly (Table 4).

*Intestinal fistula (duodenal leak) without anastomotic dehiscence* was presented in 3 patients. In the analysis, two patients had clinical presentation of abdominal pain, elevation of acute phase reactants, and hemodynamic instability. Diagnosis was confirmed by imaging (CT) of intra-abdominal abscesses. One patient required repeated laparotomies and, consequently, pancreas transplantectomy because of duodenal-edge perforations. The second patient had a satisfactory outcome after primary closure of duodenal perforation in spite of an apparent clostridium infection. The third case presented with abdominal pain and anemia, the CT showing peripancreatic hematomas with hemoperitoneum. A relaparotomy was necessary to clean the abdomen, but 6 days later, a subsequent surgery was performed to remove the graft because of duodenal fistula with peritonitis. Broad-spectrum antibiotics were crucial in the medical treatment of these patients. (Table 5).

*Ischemic of grafted duodenum*. In our study, three patients presented duodenal ischemia within the first 10 postoperative days. One patient had clinical presentation of abdominal pain following a systemic sepsis. During laparotomy, necrosis of the duodenum graft with perforation was found and a transplantectomy was required, despite the absence of evident vascular thrombosis. Another patient presented with venous thrombosis requiring a thrombectomy and anticoagulation. As a result, a first relaparotomy at 48 h was needed because of abdominal hematomas. Eight days later, the patient presented hypotension and elevation of the acute phase reactants. A reoperation was performed observing necrosis and perforation of the graft duodenum together with thrombosis in the venous anastomosis, resulting in a transplantectomy. The third case concerns a patient that presented with sudden abdominal pain, the CT showing evidence of a compromised duodenojejunal anastomosis. During the reintervention, rotation of the duodenum of the graft was evident. The graft was replaced in a more medial position, obtaining good macroscopic appearance (Table 6).

*Dehiscence of duodenum–jejunum anastomosis* was presented in four patients. One patient required four relapatomies because of a dehiscence in the intestinal anastomosis associated with peritonitis, resulting in a transplantectomy. The second patient presented with vascular thrombosis (partial splenic venous thrombosis plus partial arterial stenosis of the anastomosis between splenic and superior mesenteric artery of the pancreatic graft). Radiological thrombectomy and repeated laparotomies for retroperitoneal hematoma drainage were needed until a pancreas transplantectomy was deemed necessary because of dehiscence of the intestinal

**Table 4.** Paralytic ileum.

| Transplant/year | Postoperative amylase/lipase IU/l CIT (h) | Vascular event | Clavien–Dindo Classif. | Treatment Hospital stay (days) | Graft/patient Survival (months) |
|---|---|---|---|---|---|
| #8 Re-tx/2003 | 98/140 CIT: 11 | NO | I | Conservative (10° day) HS: 14 | 204.5/204.5 Alive |
| #9 SPK/2011 | 44/47 CIT: 8 | NO | I | Conservative (5° day) HS: 12 | 100.2/100.2 Alive |
| #10 SPK/2013 | 13/75 CIT: 8.3 | NO | II | Conservative (6° day) Treatment of acute rejection HS: 31 | 83.5/83.5 Alive |
| #11 SPK/2015 | 201/670 CIT: 11.3 | NO | II | Conservative (19° day) HS: 24 | 60.4/60.4 Alive |
| #12 SPK/2016 | 91/131 CIT:10.4 | NO | I | Conservative (5° day) Treatment of acute rejection HS: 25 | 49.1/49.1 Alive |

CIT, cold ischemia time; HS, hospital stay; Re-tx, pancreas retransplantation; SPK, simultaneous pancreas–kidney transplant. Normal value of amylase: 20–104 IU/l. Normal value of lipase: 13–60 IU/l.




© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

**Table 5.** Intestinal fistula (duodenal leak) without anastomotic dehiscence.

| Transplant/year | Postoperative amylase/lipase IU/l CIT (h) | Vascular event | Clavien–Dindo Classif. | Treatment Hospital stay (days) | Graft/patient Survival (months) |
|---|---|---|---|---|---|
| #13 SPK/2006 | 182/196 CIT: 10 | NO | IVa | 1°: Delayed primary closure 2°: Transplantectomy* (14° day) HS: 37 | 0.5/170.1 Alive |
| #14 SPK/2014 | 86/40 CIT: 11 | NO | IIIb | Primary closure (16° day) HS: 74 | 69.4/69.4 Alive |
| #15 SPK/2014 | 160/290 CIT: 12.4 | NO | IVa | 1°: Hematoma drainage 2°: Transplantectomy* (15° day) HS: 109 | 0.5/67.4 Alive |

CIT, cold ischemia time; HS, hospital stay; SPK, simultaneous pancreas–kidney transplant.

#13:* Pathology report: acute pancreatitis, peripancreatic fat necrosis, and duodenal perforation. #15:* Pathology report: duodenum ulcer perforation, and steatonecrosis. Normal value of amylase: 20–104 IU/l. Normal value of lipase: 13–60 IU/l.

**Table 6.** Ischemic of grafted duodenum.

| Transplant/year | Postoperative amylase/lipase IU/l CIT (h) | Vascular event | Clavien–Dindo Classif. | Treatment Hospital stay (days) | Graft/patient Survival (months) |
|---|---|---|---|---|---|
| #16 SPK/2003 | 177/32 CIT: 9 | NO | IVa | Transplantectomy* (6° day) HS: 27 | 0.2/70.6 Death (intestinal perforation) |
| #17 Re-tx/2013 | 231/162 CIT: 11 | Vein thrombosis | IVa | 1°: Hematoma drainage 2°: Transplantectomy* (10° day) HS: 84 | 0.3/84 Alive |
| #18 SPK/2016 | 226/286 CIT: 6.2 | NO | IIIb | Surgery (3° day) HS: 12 | 49.9/49.9 Alive |

CIT, cold ischemia time; HS, hospital stay; Re-tx, pancreas retransplantation; SPK, simultaneous pancreas–kidney transplant.

#16:* Pathology report: duodenal infarction, thrombosis of one, medium-sized arterial vessel. Pancreatic acinar changes with focal dilation and nonspecific chronic inflammation. #17:* Pathology report: venous thrombosis in vessels of medium and large size, ischemic necrosis of transmural duodenal wall, and necrosis in parenchyma and peripancreatic fat tissue. Normal value of amylase: 20–104 IU/l. Normal value of lipase: 13–60 IU/l.

anastomosis. The third patient presented with abdominal pain and leukocytosis thirteen days after transplant, the CT showing pneumoperitoneum, abdominal liquid and splenic venous thrombosis (>50%). The patient underwent relaparotomy for primary closure of a minimum orifice in the intestinal anastomosis, plus an intestinal bypass and endovascular thrombectomy, with a satisfactory outcome. Finally, the fourth patient presented with abdominal pain and fever, with an exploratory CT revealing the presence of pneumoperitoneum. During surgery, a dehiscence point in the anastomosis was repaired together with an intestinal bypass. The patient preserved pancreatic function until an arterial pseudoaneurysm was diagnosed requiring late transplantectomy (Table 7).

*Anastomotic dehiscence in recipient jejunum after previous graft transplantectomy* was diagnosed in one case of pancreas retransplantation because of chronic rejection. A pancreas transplantectomy of the first graft was needed as the new graft was placed in the same location. Pancreatic graft reperfusion was adequate and uneventful. However, imaging surveillance within the first 24 postoperative hours showed partial splenic distal vein and partial splenic artery thrombosis of the graft. The patient required relaparotomy for vascular thrombectomy. After eleven postoperative days, this patient presented with abdominal pain, with the CT confirming pneumoperitoneum with peritonitis. Repeated laparotomy was necessary and dehiscence of the enteric suture of the jejunum's recipient in the previous intestinal graft anastomosis site was found.


© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

**Table 7.** Dehiscence of duodenum–jejunum anastomosis.

| Transplant/year | Postoperative amylase/lipase IU/l CIT (h) | Vascular event | Clavien–Dindo Classif. | Treatment Hospital stay (days) | Graft/patient Survival (months) |
|---|---|---|---|---|---|
| #19 SPK/2007 | 789/710 CIT: 14 | NO | IVa | Surgery (×3)* Transplantectomy (18° day) HS: 48 | 0.9/95 Alive |
| #20 SPK/2008 | 75/48 CIT: 11 | Splenic vein thrombosis Splenic artery stenosis | IVa | Surgery (×3)* Transplantectomy (16° day) HS: 125 | 0.5/8.4 Death (respiratory infection) |
| #21 SPK/2009 | 41/142 CIT: 10 | Splenic vein thrombosis | IIIb | Primary closure + intestinal bypass + thrombectomy splenic vein (13° day) HS: 31 | 123.6/123.6 Alive |
| #22 Re-tx/2010 | 365/455 CIT: 15 | NO | IIIb | Primary closure + intestinal bypass (7° day) HS: 32 | 2.7/118.7 Alive |

CIT, cold ischemia time; HS, hospital stay; Re-tx, pancreas retransplantation; SPK, simultaneous pancreas–kidney transplant.

#19:* 1° Relaparotomy: drainage of abscess and primary closure of the anastomosis microperforation; 2° Relaparotomy: drainage of peritoneal liquid and intestinal bypass ("Y" Roux) because of dehiscence of intestinal anastomosis; 3° Relaparotomy: abdominal cavity washing; 4° Relaparotomy: transplantectomy. Pathology report: Acute focal pancreatitis, edema and chronic inflammation. Medium caliber arterial thrombosis. In the duodenum: Acute focal peritonitis. #20:* 1° Relaparotomy: drainage of retroperitoneal hematoma that compresses the vena cava and venous anastomosis; 2° Relaparotomy: drainage of residual hematoma; 3° Relaparotomy: pancreas transplantectomy because of dehiscence of intestinal anastomosis with peritonitis. Pathology report: Acute pancreatitis with steatonecrosis, focal vascular thrombosis in duodenum, acute inflammation unspecific in layers with peripheral fibrin deposits. Normal value of amylase: 20–104 IU/l. Normal value of lipase: 13–60 IU/l.

Therefore, intestinal resection of the affected segment and jejunum–jejunum anastomosis was necessary. At no time was insulin treatment required and the patient was discharged with both functional grafts.

### Patient and graft survival

After a median follow-up of the whole series of 131.6 months [IQR: 80.5–174.6], the 1, 3 and 5 year overall patient survival was 98.2%, 95.5%, and 94.6%, respectively. The patient survival at 1, 3, and 5 years for the group with intestinal complications vs. the group without was 95.7% vs. 98.4%, 95.7%; vs. 95.5%, and 91%, vs. 95%, respectively ($P = 0.289$; Fig. 2a).

Meanwhile, the 1, 3, and 5 year death-censored pancreas graft survival for the 337 patients was 87.5%, 83.5%, and 79.1%, respectively. The graft survival was significantly inferior for the group with intestinal complications compared to the group without: at 1, 3, and 5 years, namely 69.6% vs. 88.5%, 60.9% vs. 85.2%, and 60.9% vs. 80.5%, respectively ($P = 0.001$; Fig. 2b).

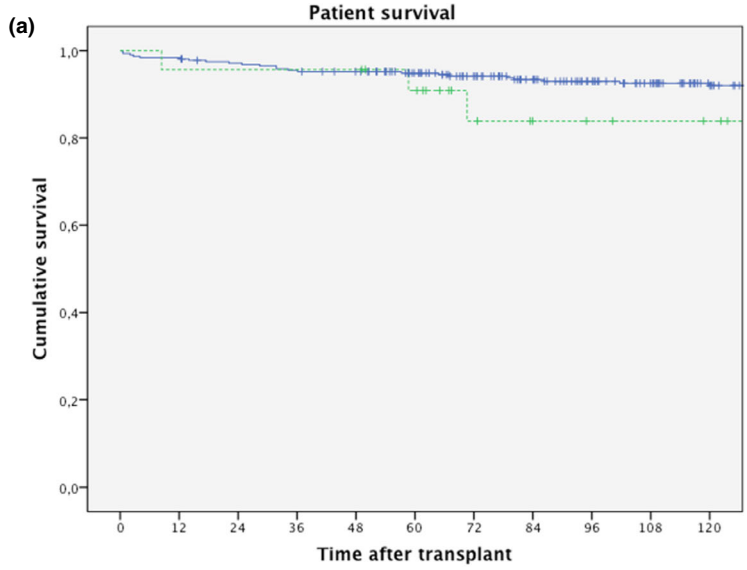
## Discussion

Pancreas transplantation continues to be a demanding procedure as it is associated with the highest technical failure rate of all solid organ transplants [11,33–36]. Regarding surgical morbidity, the impact of vascular thrombosis on the pancreatic graft survival is well documented [37]. Moreover, the role of early intestinal complications and their association with vascular events is an interesting field to explore in depth because of the inherent clinical repercussions and the lack of information on this topic in the literature.

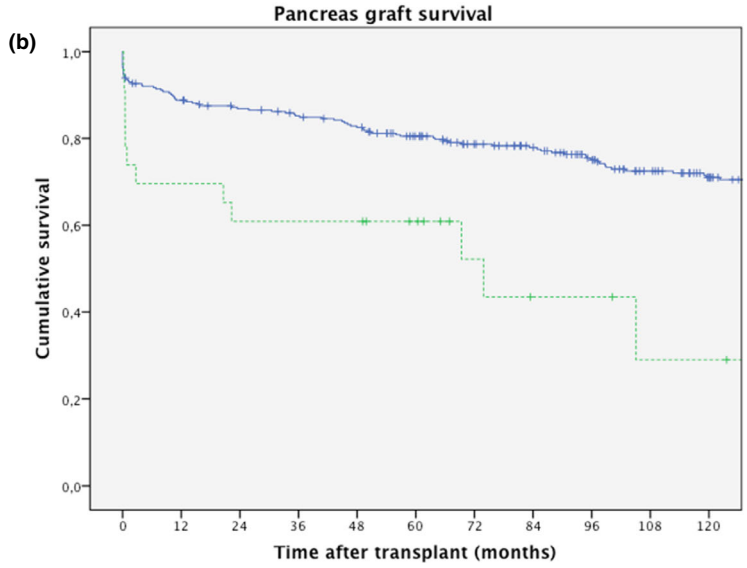
In the present large cohort study, we have found a post-transplant intestinal-related morbidity of 6.8% in the various transplant modalities. Some 18 patients required relaparotomy following transplantation as treatment for enteric complications. A total of 30.4% of cases were because of intestinal obstruction demonstrated by radiology, although no early pancreatic graft losses arose from this condition. These cases could be interpreted as a form of ischemia–reperfusion injury related to early pancreatitis, which contributes to




© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd




| Nº at risk | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No IC | 314 | 309 | 302 | 297 | 292 | 275 | 255 | 238 | 220 | 204 | 183 |
| IC | 23 | 22 | 22 | 22 | 22 | 19 | 12 | 9 | 8 | 7 | 6 |




| Nº at risk | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No IC | 314 | 276 | 265 | 257 | 247 | 229 | 209 | 198 | 178 | 160 | 143 |
| IC | 23 | 16 | 14 | 14 | 14 | 11 | 6 | 4 | 4 | 2 | 2 |

**Figure 2** (a) Patient survival for the group with intestinal complications (discontinuous line) compared to the group without intestinal complications (continuous line), ($P$ = 0.289). (b) Pancreas graft survival for the group with intestinal complications (discontinuous line) compared to the group without intestinal complications (continuous line), ($P$ = 0.001). IC, intestinal complications.

postsurgical adhesions and subsequent small-bowel obstruction. Furthermore, the intraperitoneal placement of the pancreas creates a potential site for an internal hernia [36,38,39]. At any rate, an accurate diagnosis is vital since prompt surgery is a sufficient measure to ensure bowel and allograft viability. Moreover, in the


© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

present study, a number of patients (21.7%) presented with paralytic ileus related with previous surgeries, all of which were successfully conservatively treated. In our experience, the chronologic onset of obstruction was not helpful in determining whether an adhesion or internal hernia was the likely cause, an observation also alluded to by Lall *et al.* [40]. It is worth noting that the intraperitoneal nature of pancreas operations increases the risk of bowel complications, a possibility that could be reduced by placing the graft in a retrocolic position, as previously reported in the literature [18–20,41].

Other scenarios in the field of enteric drainage resulting in a range of consequences for patient outcome are those complications related to grafted duodenum viability. In accordance with the literature [23,42,43], the rate of duodenal leakage is around 5–20% and may result in a significant rate of graft loss. In our series, intestinal fistula without anastomotic dehiscence originating from the duodenal edge accounted for three patients, with pancreas transplantectomy within 15 postoperative days being required in two. Interestingly, in both cases the pathological report showed acute pancreatitis and steatonecrosis. Primary closure was performed in one case, as the surrounding duodenum was viable and well vascularized. Al-Adra *et al.* [26] reported a rate of duodenal leakage in 33 of 426 pancreas transplantation recipients, with 8 patients needing graft pancreatectomy as primary therapy. Their study shows that, in selected patients, a duodenal leak can be repaired successfully in enterically drained grafts. Moreover, Sollinger *et al.* [11] described a leakage rate of 5.7% in 610 enterically drained transplants, of which up to 50% resulted in pancreas graft loss.

Interestingly, our study presented a concomitant vascular thrombosis diagnosed by imaging assessment in four of the 23 cases, with a significant correlation for graft loss in two of them. Ischemic of grafted duodenum represents a catastrophic event, as demonstrated in the present analysis, in which the majority of patients presented with vascular thrombosis either diagnosed by imaging or in the pathology report following transplantectomy. It must be stressed that poor graft reperfusion plays a significant role in graft loss. To prevent the possibility of this problem, the vascular branches of the superior mesenteric artery and celiac trunk must be kept intact, allowing for adequate perfusion of the gland during retrieval. Besides, in this series, one patient needed surgery because of torsion of the duodenum graft, which involved relocating the graft to a medial position. As previously reported [16], the decreased graft torsion arising from bladder drainage afforded a protective measure against technical failure. Nowadays, although enteric drainage is much more acceptable to the transplant community, it should be noted that when the pancreas is placed intraperitoneally, it may lead to twisting, predisposing venous thrombosis. Likewise, dehiscence of the duodenum–jejunum anastomosis presents some association with venous thrombosis and ischemic process. Ischemia–reperfusion injury is a potential risk factor for both vascular thrombosis and bowel leaks, in some cases resulting in a graft loss, as has arisen in half of our cases. Vascular events were diagnosed in up to 75% of cases, either by radiology or in the pathology after removal the graft. It is worth noting that two grafts were rescued after primary closure with intestinal bypass and thrombectomy when necessary. Notwithstanding, in selected patients, a total and partial graft duodenectomy may be conveniently employed with the aim of graft rescue as Pieroni *et al.* [44] demonstrated after 336 consecutive retroperitoneal transplantations. Anastomotic dehiscence in recipient jejunum after previous graft transplantectomy was diagnosed in one patient. Special attention should be taken in the case of retransplantation, as it is associated with greater technical difficulties.

To summarize, enteric drainage with an improved technique presents a low risk of nonimmunological pancreas transplant complications. The analysis of this series shows that enteric drainage as duodenum–jejunum side-to-side anastomosis is a safe and feasible technique. However, ischemic conditions could arise from venous thrombosis; arterial stenosis; inadequate revascularization; and retroperitoneal hematoma with extrinsic compression of vein anastomosis. What is interesting to evaluate are those complications related to a vascular event that could be avoided if an affective treatment is applied, as these are considered the Achilles' heel of pancreas transplantation. Close postoperative surveillance is mandatory as radiologic diagnosis of vascular thrombosis may be absent in the immediate postoperative period, as demonstrated when analyzing the pathology report in the case of transplantectomy.

In the present setting, treatment of leaking enteric-drained grafts has always mandated surgical exploration. If the leakage zone was well delineated and graft duodenum was not macroscopically compromised, a primary repair was initially attempted, with the creation of a intestinal bypass to exclude the anastomosis. Regrettably, in some of these cases, this approach was not sufficient to solve the problem because of worsening local conditions. Consequently, graft pancreatectomy was the procedure of choice.


© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

In spite of the retrospective nature of the present study, the low rate of enteric complications, and the absence of significant differences between groups regarding donor and recipient variables, our results stress the importance of primarily focusing on: the detection and control of the potentially risk factors related to donor characteristics; preservation injury (i.e., minimizing cold ischemia); back-table preparation of the graft or other technical issues; and later, prompt detection and treatment of bowel complications and potentially associated vascular events. It is true that a significant number of cases end in transplantectomy but in some, graft salvage may be possible, making operative repair an option that should be carefully considered. Further, non-related graft duodenum early complications (52.2%) did not have impact on graft survival, despite the fact that in some cases reoperation was required.

In May 2016, our group implemented a different technique with a view to improving outcomes. That is to say, graft position was modified by placing the pancreas in the space behind the right colon with a duodenoduodenostomy for exocrine secretions. The preliminary results have been recently published, and no complications related to the new surgical technique have been identified [41]. Taking into account that more cases have yet to be evaluated, it appears that retrocolic graft placement offers advantages concerning straightforward technical vascular reconstruction along with: minimizing the risk of torsion of vascular anastomoses; decreasing the risk of intestinal obstruction by separation of the small bowel from the pancreas graft; and allowing conservative treatment in case of anastomotic insufficiency or pancreatic fistula. Increasingly, more groups are implementing this technique, as the aforementioned advantages may also have an impact on the reduction of graft complications.

As many factors are implicated in the scenario of pancreas transplantation, long-term results are needed for valid interpretations of surgical technique, and efforts should be made with all potentially treatable factors from donor through to recipient.

## Authorship

JF-F, BC-V, JF and JCG-V: participated in research design. JF-F, BC-V and JF: participated in the writing of the paper. JF-F, BC-V, GC, JF and JCG-V: participated in the performance of the research. JF-F, BC-V, PV-A, GC, ÁG-C, MAL-B, RR, RG, MªJR, LF-C, JF and JCG-V: contributed to data acquisition and interpretation. JF-F, BC-V, MC, EE, FD, CF, JF and JCG-V: participated in data analysis. JF-F, BC-V, PV-A, GC, ÁG-C, MAL-B, RR, RG, MC, EE, FD, CF, MªJR, LF-C, JF and JCG-V: contributed to critical revision of manuscript.

## Funding

No direct or indirect financial support by extramural sources was received.

## Conflict of interest

The authors have declared no conflicts of interest.

## Acknowledgements

We thank Steve Illing, *Cambridge RSA CELTA*, for English language assistance.

## REFERENCES

1. Posegger KR, Linhares MM, Mucci S, *et al*. The quality of life in type I diabetic patients with end-stage kidney disease before and after simultaneous pancreas-kidney transplantation: a single-center prospective study. *Transpl Int* 2020; **33**: 330.
2. Stratta RJ, Fridell JA, Gruessner AC, Odorico JS, Gruessner RW. Pancreas transplantation: a decade of decline. *Curr Opin Organ Transplant* 2016; **21**: 386.
3. Stratta RJ, Gruessner AC, Odorico JS, Fridell JA, Gruessner RW. Pancreas transplantation: an alarming crisis in confidence. *Am J Transplant* 2016; **16**: 2556.
4. Gruessner AC, Gruessner RWG. Pancreas transplantation for patients with type 1 and type 2 diabetes mellitus in the United States: a registry report. *Gastroenterol Clin North Am* 2018; **47**: 417.
5. Dholakia S, Oskrochi Y, Easton G, Papalois V. Advances in pancreas transplantation. *J R Soc Med* 2016; **109**: 141.
6. Dholakia S, Mittal S, Quiroga I, *et al*. Pancreas transplantation: past, present, future. *Am J Med* 2016; **129**: 667.
7. Groth CG, Tydén G, Lundgren G, *et al*. Segmental pancreatic transplantation with enteric exocrine diversion. *World J Surg* 1984; **8**: 257.
8. Di Carlo V, Castoldi R, Cristallo M, *et al*. Techniques of pancreas transplantation through the world: an IPITA Center survey. *Transplant Proc* 1998; **30**: 231.
9. Desai NM, Markmann JF. Whole-organ pancreas and pancreatic islet transplantation. In: *Surgery of the Liver, Biliary Tract and Pancreas* 5th edn. edited by Leslie H. Blumgart, **2**, 1600 John F.Kennedy Blvd. Ste 1800. Philadelphia, PA 19103-2899: Saunders Elsevier , 2012: 1796–1804.


© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd

10. Boggi U, Vistoli F, Egidi FM, *et al*. Transplantation of the pancreas. *Curr Diab Rep* 2012; **12**: 568.
11. Sollinger HW, Odorico JS, Becker YT, D'Alessandro AM, Pirsch JD. One thousand simultaneous pancreas-kidney transplants at a single center with 22-year follow-up. *Ann Surg* 2009; **250**: 618.
12. West M, Gruessner AC, Metrakos P, Sutherland DE, Gruessner RW. Conversion from bladder to enteric drainage after pancreaticoduodenal transplantations. *Surgery* 1998; **124**: 883.
13. Sutherland DE, Gruessner RW, Dunn DL, *et al*. Lessons learned from more than 1,000 pancreas transplants at a single institution. *Ann Surg* 2001; **233**: 463.
14. Siskind EJ, Amodu LI, Pinto S, *et al*. Bladder versus enteric drainage of exocrine secretions in pancreas transplantation: a retrospective analysis of the united network for organ sharing database. *Pancreas* 2018; **47**: 625.
15. Boggi U, Amorese G, Marchetti P. Surgical techniques for pancreas transplantation. *Curr Opin Organ Transplant* 2010; **15**: 102.
16. El-Hennawy H, Stratta RJ, Smith F. Exocrine drainage in vascularized pancreas transplantation in the new millennium. *World J Transplant* 2016; **6**: 255.
17. Laftavi MR, Gruessner A, Gruessner R. Surgery of pancreas transplantation. *Curr Opin Organ Transplant* 2017; **22**: 389.
18. Walter M, Jazra M, Kykalos S, *et al*. 125 Cases of duodenoduodenostomy in pancreas transplantation: a single-centre experience of an alternative enteric drainage. *Transpl Int* 2014; **27**: 805.
19. Lindahl JP, Horneland R, Nordheim E, *et al*. Outcomes in pancreas transplantation with exocrine drainage through a duodenoduodenostomy versus duodenojejunostomy. *Am J Transplant* 2018; **18**: 154.
20. Horneland R, Paulsen V, Lindahl JP, *et al*. Pancreas transplantation with enteroanastomosis to native duodenum poses technical challenges–but offers improved endoscopic access for scheduled biopsies and therapeutic interventions. *Am J Transplant* 2015; **15**: 242.
21. Linhares MM, Beron RI, Gonzalez AM, *et al*. Duodenum-stomach anastomosis: a new technique for exocrine drainage in pancreas transplantation. *J Gastrointest Surg* 2012; **16**: 1072.
22. Shokouh-Amiri H, Zakhary J, Zibari G. A novel technique of portal-endocrine and gastric-exocrine drainage in pancreas transplantation. *J Am Coll Surg* 2011; **212**: 730.
23. Stratta RJ, Sindhi R, Sudan D, Jerius JT, Radio SJ. Duodenal segment complications in vascularized pancreas transplantation. *J Gastrointest Surg* 1997; **1**: 534.
24. Orsenigo E, Cristallo M, Socci C, *et al*. Successful surgical salvage of pancreas allograft. *Transplantation* 2003; **75**: 233.
25. Uva PD, Villavicencio Fornaciari S, Giunippero AE, *et al*. Case report: pancreas graft with a duodenal complication rescued using total duodenectomy. *Transplant Proc* 2014; **46**: 3068.
26. Al-Adra D, McGilvray I, Goldaracena N, *et al*. Preserving the pancreas graft: outcomes of surgical repair of duodenal leaks in enterically drained pancreas allografts. *Transplant Direct* 2017; **3**: e179.
27. Gil-Vernet JM, Fernández-Cruz L, Caralps A, Andreu J, Figuerola D. Whole organ and pancreaticoureterostomy in clinical pancreas transplantation. *Transplant Proc* 1985; **17**: 2019.
28. www.ont.es/publicaciones/Documents/pancreaseislotes. PDF Documento de consenso sobre trasplante de páncreas e islotes. Organización nacional de trasplantes.
29. Ferrer J, Ricart MJ. Indicaciones y contraindicaciones del trasplante de páncreas-riñón y del trasplante de páncreas aislado. Selección del candidato a trasplante. En: *Guía de Trasplantes de órganos abdominales*. Capítulo 24. Editor: Andrés Valdivieso. Guías clínicas de la Asociación Española de Cirujanos. Editorial Arán, 2017.
30. Fernández-Cruz L, Astudillo E, Sanfey H, *et al*. Combined whole pancreas and liver retrieval: a new technique for arterial reconstruction of the pancreas graft. *Br J Surg* 1992; **79**: 239.
31. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205.
32. Drachenberg CB, Odorico J, Demetris AJ, *et al*. Banff schema for grading pancreas allograft rejection: working proposal by a multi-disciplinary international consensus panel. *Am J Transplant* 2008; **8**: 1237.
33. Finger EB, Radosevich DM, Dunn TB, *et al*. A composite risk model for predicting technical failure in pancreas transplantation. *Am J Transplant* 2013; **13**: 1840.
34. Ziaja J, Krol R, Pawlicki J, *et al*. Donor-dependent risk factors for early surgical complications after simultaneous pancreas-kidney transplantation. *Transplant Proc* 2011; **43**: 3092.
35. Humar A, Ramcharan T, Kandaswamy R, Gruessner RW, Gruessner AC, Sutherland DE. Technical failures after pancreas transplants: why grafts fail and the risk factors. A multivariate analysis. *Transplantation* 2004; **78**: 1188.
36. Moya-Herraiz A, Muñoz-Bellvis L, Ferrer-Fábrega J, *et al*. Cooperative study of the Spanish Pancreas Transplant Group (GETP): surgical complications. *Cir Esp* 2015; **93**: 300.
37. Hakeem A, Chen J, Iype S, *et al*. Pancreatic allograft thrombosis: suggestion for a CT grading system and management algorithm. *Am J Transplant* 2018; **18**: 163.
38. Linhares MM, del Grande L, Gonzalez A, *et al*. Intestinal obstruction due to internal hernia following pancreas transplantation. *Transplant Proc* 2010; **42**: 3660.
39. Goodman J, Becker YT. Pancreas surgical complications. *Curr Opin Organ Transplant* 2009; **14**: 85.
40. Lall CG, Sandrasegaran K, Maglinte DT, Fridell JA. Bowel complications seen on CT after pancreas transplantation with enteric drainage. *AJR Am J Roentgenol* 2006; **187**: 1288.
41. Ferrer J, Molina V, Rull R, *et al*. Pancreas transplantation: advantages of a retroperitoneal graft position. *Cir Esp* 2017; **95**: 513.
42. Nymann T, Shokouh-Amiri MH, Elmer DS, Stratta RJ, Gaber AO. Diagnosis, management, and outcome of late duodenal complications in portal-enteric pancreas transplantation: case reports. *J Am Coll Surg* 1997; **185**: 560.
43. Spetzler VN, Goldaracena N, Marquez MA, *et al*. Duodenal leaks after pancreas transplantation with enteric drainage – characteristics and risk factors. *Transpl Int* 2015; **28**: 720.
44. Pieroni E, Napoli N, Lombardo C, *et al*. Duodenal graft complications requiring duodenectomy after pancreas and pancreas-kidney transplantation. *Am J Transplant* 2018; **18**: 1388.



© 2020 Steunstichting ESOT. Published by John Wiley & Sons Ltd