TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

125 Cases of duodenoduodenostomy in pancreas transplantation: a single-centre experience of an alternative enteric drainage

Martin Walter,[1] Martin Jazra,[1] Stylianos Kykalos,[1] Petra Kuehn,[1] Stefan Michalski,[1] Thomas Klein,[2] Andreas Wunsch,[1] Richard Viebahn[1] and Peter Schenker[1]

1 Department of General, Visceral and Transplant Surgery, University Hospital Knappschaftskrankenhaus Bochum, Ruhr-University Bochum, Bochum, Germany

2 Department of Medicine I, Marienhospital Herne, Ruhr-University Bochum, Herne, Germany

Keywords
duodenoduodenostomy, duodenum, enteric drainage, pancreas transplantation.

Correspondence
Peter Schenker MD, Department of General, Visceral and Transplant Surgery, University Hospital Knappschaftskrankenhaus Bochum, Ruhr-University Bochum, In der Schornau 23-25, 44892 Bochum, Germany.
Tel.: +49 234 2993201;
fax: +49 234 2993209;
e-mail: Peter.Schenker@rub.de

Conflicts of interest
The authors have declared no conflicts of interest.

The copyright line for this article was changed on March 23, 2015 after original online publication.

Received: 4 February 2014
Revision requested: 20 February 2014
Accepted: 14 April 2014
Published online: 24 May 2014

doi:10.1111/tri.12337

Summary

Several exocrine drainage procedures have been successfully developed to perform pancreas transplantation (PT). Retroperitoneal graft placement allows exocrine drainage via direct duodenoduodenostomy (DD). This technique provides easy access for endoscopic surveillance and biopsy. A total of 241 PT procedures were performed in our centre between 2002 and 2012. DD was performed in 125 patients, and duodenojejunostomy (DJ) in 116 patients. We retrospectively compared our experience with these two types of enteric drainage, focusing on graft and patient survivals, as well as postoperative complications. With a mean follow-up of 59 months, both groups demonstrated comparable patient and graft survivals. 14 (11%) of 125 cases in the DD group and 21 (18%) of 116 cases in the DJ group had pancreatic graft loss ($P = 0.142$). Graft thrombosis [5 (4%) vs. 18 (16%) $P = 0.002$], anastomotic insufficiency [2 (1.6%) vs. 8 (7%) $P = 0.052$] and relaparotomy [52 (41%) vs. 56 (48%) $P = 0.29$] occurred more frequently in the DJ group, whereas gastrointestinal bleeding [14 (11%) vs. 4 (3%) $P = 0.026$] occurred more often in the DD group. DD is a feasible and safe technique in PT, with no increase in enteric complications. It is equivalent to other established techniques and extends the feasibility of anastomotic sites, especially in recipients who have undergone a second transplantation.

Introduction

Pancreas transplantation (PT) has undergone remarkable development since its first implementation in 1966. It has become an accepted therapeutic option for diabetes mellitus owing to improvements in the procedure, progress behind organ conservation and intensive care medicine, and the increase in the availability of improved immunosuppressants [1]. Regarding surgical techniques, the bladder drainage method favoured until the mid-1990s has been increasingly replaced worldwide by enteric drainage [2]. Enteric drainage of the pancreas graft is considered the current standard method in PT; hence, in 2010, more than 90% of the patients with simultaneous pancreas–kidney (SPK) transplantation were treated with enteric drainage [2]. The most common method of enteric drainage is performing an anastomosis between the donor duodenum and the recipient jejunum, with the pancreas graft in an intraperitoneal position. This particular method has been modified in recent years.

Boggi *et al.* [3] achieved excellent results by means of a side-to-side duodenojejunostomy (DJ) with the Roux-en-Y method, including pancreas graft placement in a retroperitoneal position. If the pancreas is placed in the right retrocolic space, a further option is direct side-to-side duodenoduodenostomy (DD) [4–8]. Gastric-exocrine drainage techniques were also reported [9,10].

The advantage of DD is that both the small bowel anastomosis and the pancreatic head of the graft can be accessed endoscopically. This facilitates biopsy for diagnosis of rejection. In addition, in cases of intestinal bleeding at the anastomotic site, an endoscopic intervention for haemostasis may follow. Possible disadvantages appear in cases of anastomotic insufficiency or graft loss because subsequent leaks at the native duodenal site are more difficult to repair.

Because of these potential complications, the safety of DD has been controversial [5,6,11,12]. However, the few published reports on this topic generally involve small case sample sizes. Hence, the aim of this study was to review our experience with 125 DD procedures performed after PT. We focused on the results and complications of DD in comparison with DJ performed in a group of patients who had undergone PT.

In this study, we further aimed to describe DD as a surgical technique and its development over the years with respect to cases requiring treatment for duodenal leak after pancreas graft failure and removal. Here, we present data from 125 cases of DD in PT, the largest reported series of this technique to date.

Patients and methods

A total of 241 adult patients underwent PT at our centre between September 2002 and September 2012. SPK transplantation was performed in 219 patients; pancreas after kidney (PAK) transplantation, in 16 patients; and PT alone (PTA), in six patients. All the patients had C-peptide-negative type 1 diabetes. Between 2002 and 2005, DJ became the standard procedure in our centre. The first DD was then performed in 2005. Between 2005 and 2007, DD and DJ were applied. Since 2007, DD has been the standard procedure in our centre. This produced two groups of patients in our cohort as follows: patients with enteric drainage by DJ ($n = 116$) and those with DD ($n = 125$), who were analysed, retrospectively compared and evaluated for postoperative results and surgical complications.

Operative technique

Standard back-table preparation is performed before PT. The spleen is then removed, and the vessels are ligated, as well as the bile duct and gastroduodenal artery. The donor duodenum is reduced to a length of 8–12 cm and closed proximally and distally with a linear stapler. In our approach, these staple lines are inverted with seromuscular interrupted stitches using absorbable sutures. The mesenteric root that was previously transected by staple lines is sewed over in a double-row continuous technique (4-0 polypropylene). Arterial reconstruction of the pancreas graft, which includes the superior mesenteric and splenic artery, was performed using a donor iliac artery Y-graft. Venous extension graft of the portal vein was not necessary in any of the cases examined.

All the PT procedures were performed through a median laparotomy for surgical access. In case of planned DJ, the pancreas graft is placed intraperitoneally in a head-up position. The venous anastomosis is usually performed first and is placed to the proximal superior mesenteric vein, or alternatively to the inferior caval vein. The arterial graft is oriented caudally through a window made in the ileocecal mesentery. The arterial anastomosis is created between the Y-graft and the recipient's right common iliac artery (CIA) with an end-to-side anastomosis using two half-running sutures of 5-0 or 6-0 polypropylene. The DJ is placed at the second jejunal loop level by a two-layer, hand-sewn, side-to-side anastomosis with running sutures using 4-0 polydioxanone.

In case of a planned DD, the right colon is mobilized and a Kocher manoeuvre is performed. Exploration in the mesenteric root area of the superior mesenteric vein follows to assess the feasibility of anastomosis. In case of a small calibre mesenteric vein or distinct mesenteric root steatosis, venous anastomosis is created alternatively to the inferior caval vein. The pancreas is inserted vertically with the head upright. The arterial anastomosis is then created end-to-side between the donor's Y-iliac graft and the recipient's right CIA. After sufficient mobilization of the recipient duodenum, both duodena are approximated side-to-side, roughly at the level between the second and third portions of the recipient's duodenum. The external suture line is then applied to the posterior wall using 4-0 polydioxanone in a running suture style. Subsequently, a 2.5- to 3-cm longitudinal incision of both duodena is made (Fig. 1a). The inner layer is performed with a full-thickness running suture using 4-0 nonabsorbable polypropylene in consequence of the highly vascularized duodenum. Finally, the second external running suture line of the anterior wall is applied, again using 4-0 polydioxanone (Fig. 1b). The mobilized right colon is returned to its native position, thus completely covering the pancreas and making it a retroperitoneal organ. We do not routinely perform appendectomy. After reperfusion of the pancreatic graft and completion of the enteric anastomosis in cases of combined pancreas–kidney transplantation, the kidney

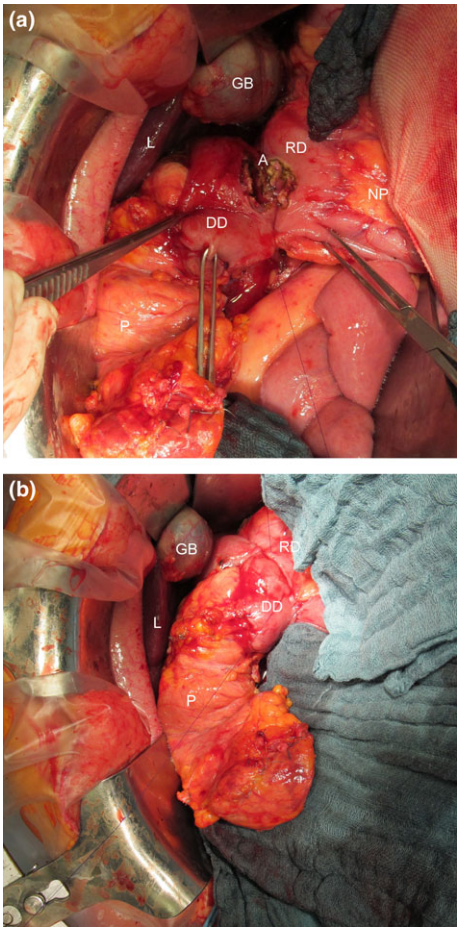

Figure 1 Duodenoduodenostomy. Incision of both duodena (a); the external running suture line of the anterior wall is applied (b). A, anastomosis; DD, donor duodenum; GB, gallbladder; L, liver; NP, native pancreas; P, pancreas graft; RD, recipient duodenum.

transplantation is performed with arterial and venous anastomosis to the recipient's left-sided pelvic vessels. Finally, two Jackson–Pratt drains are inserted routinely. One drain is placed in a retroperitoneal position beside the pancreas graft, ending behind the DD. A second drainage is positioned on the kidney graft.

In this study, all pancreas transplant operations were performed by a group of five surgeons. In the transition period between the two techniques (2005–2006), the leading surgeon selected which anastomosis to apply during the operating procedure. Since 2007, the target standard has been retroperitoneal placement of the pancreas graft with portal venous anastomosis and side-to-side DD. Exceptions were made in special situations (e.g. pronounced retroperitoneal adhesions after previous operations or if the superior mesenteric vein is found unsuitable for anastomosis). A gastric tube is intraoperatively inserted and maintained for 3–5 postoperative days, depending on the clinical course.

Immunosuppression

All the patients underwent quadruple immunosuppression comprising induction and triple maintenance therapy. Most patients received Thymoglobulin (Sanofi, Germany) antibody induction in doses of 1.5 mg/kg of body weight used as an intraoperative single-shot therapy. Since 2009, patients receive additional doses of Thymoglobulin (1.5 mg/kg of body weight) during the course of induction therapy. Additional doses were administered on the first and second postoperative days in target of a cumulative dose of 4.5 mg/kg of body weight according to blood leucocyte/thrombocyte levels and clinical course.

Twenty patients were given interleukin-2 receptor antagonists for induction [up until 2007, Daclizumab (Zenapax, Roche Pharma AG, Grenzach-Wyhlen, Germany); since 2007, basiliximab (Simulect, Novartis Pharma AG, Basel, Switzerland)]. On the day of the operation, the patients were intravenously administered 500 mg of prednisolone (Solu-Decortin H, Merck Pharma GmbH, Darmstadt, Germany). Patients were administered an additional 125 mg of intravenous prednisolone on postoperative day 1. Prednisolone was orally administered as of postoperative day 2, starting with a 20-mg dose. The oral dose was tapered to a maintenance level of 5 mg daily by week 8.

In most cases, maintenance immunosuppression comprised triple therapy with tacrolimus, mycophenolic acid and prednisolone.

Tacrolimus (Prograf, Astellas Pharma, Munich, Germany) therapy was started on the first postoperative day, with a dose of 0.15 mg/kg of body weight twice a day. Target blood trough levels during the first 2 months were 10–15 and 8–12 ng/ml subsequently. Mycophenolic acid therapy was also started on the first postoperative day, with either mycophenolate mofetil (CellCept, Roche Pharma AG) 2 g daily or mycophenolate sodium (Myfortic, Novartis Pharma AG) 720 mg twice daily.

All the patients received cytomegalovirus (CMV) prophylaxis with ganciclovir, followed later by valganciclovir for at least 3 months. In CMV high-risk constellations (D+/R−; D+/R+), CMV prophylaxis was performed for 6 months. *Pneumocystis jirovecii* prophylaxis was performed with trimethoprim/sulfamethoxazole for 3 months in total. Perioperative antibiotic prophylaxis was performed with ceftriaxone/metronidazole and fluconazole.

Anticoagulant therapy

Before pancreas graft reperfusion, all the patients received an intraoperative 1.500-U dose of antithrombin III. Anticoagulation with intravenous unfractionated heparin (400–600 U/h) was started within 4–6 h after the opera-

tion, following patient stabilization. The leading surgeon determined the start time of heparin therapy according to the intraoperative course. After 12 postoperative hours, if the patients were stabilized, partial thromboplastin time (PTT)-adapted heparin therapy was performed with a target PTT between 50 and 60 s. In addition, antithrombin substitution targeting >90% is performed. Anticoagulant therapy with unfractionated heparin was continued for 7–10 days and thereafter switched to thrombosis prophylaxis with a low molecular weight heparin (enoxaparin or fraxiparin). Moreover, all the patients received a platelet aggregation inhibition with oral acetylsalicylic acid at 100 mg starting from day 7.

Patient medical records, data from electronic laboratory recording system and Eurotransplant's donor records were gathered to determine donor and recipient characteristics. Furthermore, operative details, including use of different perfusion solutions, cold ischaemic time and total operative time, were reviewed. The primary observation target was patient and graft survivals within both groups. Secondary observation targets included occurrence rates of early postoperative complications such as bleeding, anastomotic insufficiency, graft thrombosis and necessity of relaparotomies. Occurrence of histologically confirmed rejection episodes was examined in both groups as well.

Statistical analyses

For statistical analysis, the chi-square test and Fisher's exact test were used to compare categorical variables, and the Mann–Whitney *U*-test was used to compare continuous variables. Patient and graft survivals were calculated using the Kaplan–Meier method with the log-rank test. A $P < 0.05$ was considered as statistically significant. Analysis was performed using SPSS (Chicago, IL, USA).

The local ethics board of the Faculty of Medicine, Ruhr-University of Bochum, approved the study.

Results

Between September 2002 and September 2012, a total of 241 PT procedures were performed (219, SPK transplantations; 16, PAK transplantations; and 6, PTA).

Donor characteristics are detailed in Table 1. Median donor ages, body mass index, sex distribution and cause of death were similar in both groups. Regarding the used perfusion solutions, the perfusion rate of the histidine–tryptophan–ketoglutarate solution (Custodiol HTK) to the pancreata was significantly higher in the DD group. This is owing largely to the fact that the HTK solution has been used exclusively in Germany since 2007 during visceral removal operations. In the DD group, only 8.8% of the removed pancreata were perfused with the University of Wisconsin solution. These organs were harvested outside Germany.

The recipients' characteristics are detailed in Table 2. Recipient age was a little higher in the DD group, although this difference was not statistically significant ($P = 0.084$). Recipient body mass index and pretransplant dialysis duration were significantly higher in the DD group. There was no difference in sex distribution. Portal venous drainage was performed significantly more frequent in the DD group (DD, 64% vs. DJ, 12%; $P < 0.001$).

No significant differences were observed between the groups regarding cold ischaemic time, both the pancreas and kidney grafts, and human leucocyte antigen mismatch. The DD group had a significantly longer operative time than the DJ group (Table 2).

Patient and graft survivals

The mean follow-up duration was 59.31 ± 37.81 months. The length of patient follow-up was shorter in the DD group than in the DJ group (33.2 ± 21.1 months vs. 87.4 ± 31.1 months).

The total patient survival rates were 96.1%, 93.1% and 91.2% after 1, 3 and 5 years, respectively. The total pan-

Table 1. Donor characteristics.

Donor characteristics	Duodenoduodenostomy ($n = 125$)	Duodenojejunostomy ($n = 116$)	*P*-value
Gender male/female	69/56	52/64	NS
Age (years)	35.5 ± 13.2	35.5 ± 12.6	NS
BMI (kg/m²)	23.5 ± 3.1	23.4 ± 3.0	NS
Preservation solution			
UW	12 (10)	95 (82)	<0.001
HTK	113 (90)	21 (18)	<0.001
Traumatic cause of death	34 (27.2%)	28 (24.1%)	NS

BMI, body mass index; UW, University of Wisconsin solution; HTK, histidine–tryptophan–ketoglutarate.
Values are given as mean ± SD or *n* (% of group).

Table 2. Recipient characteristics.

Recipient characteristics	Duodenoduodenostomy (n = 125)	Duodenojejunostomy (n = 116)	P-value
Gender (male/female)	83/42	66/50	NS
Age (years)	45.5 ± 7.7	43.7 ± 8.4	NS
BMI (kg/m²)	25.1 ± 3.8	23.5 ± 2.9	<0.001
CMV			
R−/D+	36 (28.8)	34 (29.3)	NS
R+/D+	29 (23.2)	26 (22.4)	NS
R−/D−	31 (24.8)	18 (15.5)	NS
R+/D−	29 (23.2)	38 (32.8)	NS
Duration of diabetes mellitus (years)	31 ± 8.8	29.9 ± 8.9	NS
Duration of dialysis (months)	37.5 ± 24.1 (n = 110)	32.1 ± 28.8 (n = 91)	<0.001
Venous drainage			
Systemic venous	45 (36)	102 (88)	<0.001
Portal venous	80 (64)	14 (12)	<0.001
Cold ischaemic time (min)			
Pancreas	683.2 ± 164.5	688.3 ± 171.8	NS
Kidney	784.9 ± 198.6	748.5 ± 183.7	NS
HLA mismatch			
AB	2.9 ± 0.9	3.0 ± 0.9	NS
DR	1.6 ± 0.6	1.5 ± 0.6	NS
ATG	113 (90.4)	104 (89.7)	NS
IL-2 RA	12 (9.6)	8 (6.9)	NS
Tacrolimus	122 (97.6)	113 (97.4)	NS
Type of transplantation			
SPK	115 (92.0)	104 (89.7)	NS
PTA	3 (2.4)	3 (2.6)	NS
PAK	7 (5.6)	9 (7.7)	NS
Operative time (min)	341.9 ± 81.4	270.2 ± 76.6	<0.001

BMI, body mass index; SPK, simultaneous pancreas–kidney transplantation; PAK, pancreas after kidney transplantation; PTA, pancreas transplantation alone; CMV, cytomegalovirus; R, recipient; D, donor; IL2-RA, interleukin 2-receptor antibody; ATG, antithymocyte globulin.
Values are given as mean ± SD or n (% of group).

creas graft survival rates were 79.7%, 77.4% and 73.2%, respectively. The total kidney graft survival rates were 90.1%, 88.6% and 84.9%, respectively. The cumulative patient survival rates (estimated with the Kaplan–Meier method) were 95.8%, 94.8% and 91.6%, respectively, in the DD group and 96.5%, 92.1% and 90.3%, respectively, in the DJ group, with no statistically significant difference (P = 0.624; log-rank test, Fig. 2a). The pancreas graft survival rates were 82%, 82% and 75.9%, respectively, in the patients with DD and 77.6%, 73.1% and 69.5% in the patients with DJ (P = 0.20; log-rank test, Fig. 2b). Accordingly, no statistically significant difference was observed in kidney graft survival after 1, 3 and 5 years (P = 0.924).

Surgical complications

In total, two anastomotic insufficiencies occurred in the DD group; both patients required reoperation. One patient underwent a new DD placement; the other patient merely underwent oversewing of a small leak. No further corrective surgery was necessary in these two patients. In total, eight anastomotic insufficiencies were observed in the DJ group, each requiring surgical treatment.

Two patients in the DJ group developed a small bowel obstruction from an internal hernia in the area of the pancreatic graft that required surgical treatment. Complications of gastrointestinal bleeding occurred more frequently in the DD group than in the DJ group. In total, 14 DD patients developed bleeding complications in the area of the enteric anastomosis. Of these 14 patients, seven could be treated with endoscopic haemostasis. Four patients required surgical correction following inefficient endoscopic haemostasis. Conservative therapy was successful in three cases (blood transfusion, reduction in anticoagulant therapy and increase in PPI medication, respectively).

Four patients in the DJ group developed anastomotic bleeding, two of which underwent corrective surgical pro-

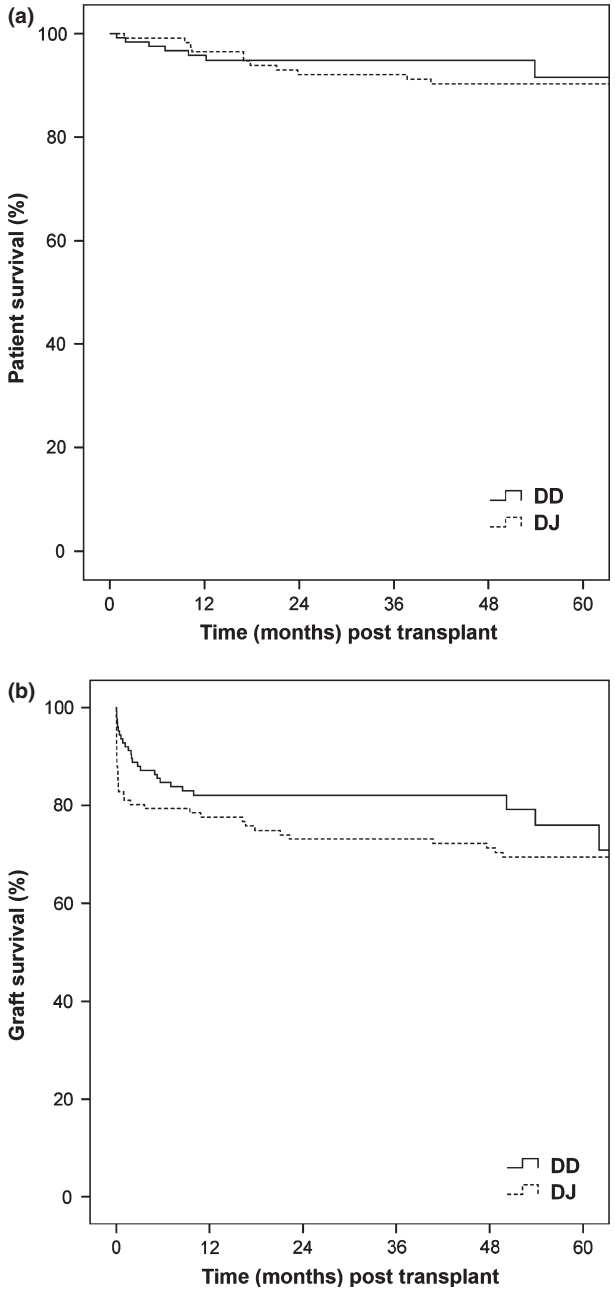

Figure 2 Kaplan–Meier curves representing patient (a) and pancreas graft survival (b) by enteric drainage technique. There was no significant difference between the DD and DJ groups [log-rank test, $P = 0.624$ (a); $P = 0.202$ (b)]. DD, duodenoduodenostomy; DJ, duodenojejunostomy.

cedures. Pancreatic graft removal was necessary for 14 cases (11.2%) in the DD group and 21 cases (18.1%) in the DJ group. This difference was not statistically significant ($P = 0.142$). The main cause of early graft loss was graft thrombosis (23/241, 9.5%), with five cases in the DD group and 18 cases in the DJ group ($P = 0.002$). When comparing portal venous (pv) versus systemic venous (sv) drainage within the DD group, no differences were found regarding pancreatic graft loss (pv 10% vs. sv 13.3%; $P = 0.568$) and relaparotomy rate (pv 41.2% vs. sv 42.2%; $P = 0.915$).

The hole in the recipient duodenum resulting from graft pancreatectomy was primarily treated in all the cases with a transverse, double-layer, interrupted suture using polydioxanone (3-0 or 4-0). Ten of the 14 patients had no complications during the postoperative course. Following pancreatectomy and oversewing the duodenum, three patients developed insufficiencies of the duodenal suture with consecutive duodenal leak. One female patient was treated with a Roux-en-Y-constructed DJ, forming a side-to-side anastomosis. In a second patient, the duodenal leak was treated with a side-to-side DJ. In a third patient, we were able to treat the duodenal leak conservatively while keeping the intra-abdominal drain in place for longer.

Pancreatectomy was performed in another patient who developed abdominal sepsis and mycotic erosion bleeding in the area of the pancreas graft. The patient showed undisturbed healing of the duodenal oversewing. However, the patient developed a complication involving a perforated peptic postpyloric duodenal ulcer. This complication required a distal gastric resection, including end-to-side gastrojejunostomy with blind closure of the proximal duodenum. The patient developed septic multiple organ failure and died 61 days after SPK transplantation after duodenal stump insufficiency and abdominal sepsis with evidence of a mycotic infection caused by *Candida glabrata*. The different complications caused by the two enteric drainage techniques are shown in Table 3.

Relaparotomy rates during the first three postoperative months (DD, 41.6% vs. DJ, 48.2%; $P = 0.29$) and inpatient stay [DD, 42.1 days (range, 14–116 days) vs. DJ, 42.3 days (range, 14–170 days); $P = 0.784$] were comparable in both groups. In the first post-transplant year, 142/241 (58.9%) inpatients were admitted again. No differences arose between the DD and the DJ groups (DD: 58.4% vs. DJ: 59.4%). The average number of inpatient admissions totalled 0.8 ± 1.02 in the DD group in the first year and 1.0 ± 1.09 in the DJ group, without a statistically significant difference. The most common three reasons for admission in both groups were urinary tract infections (DD: 29.6% vs. DJ: 21.5%), gastroenteritis (DD: 16% vs. DJ: 31.8%) and kidney transplant dysfunction (DD: 12% vs. DJ: 16.3%). During the first year, 5 (4%) and, respectively, 7 (6%) pneumonias were observed in the DD and DJ groups. The CMV infection rate was comparable in both groups (DD: 8%; DJ: 11.2%, $P = 0.511$).

After 1 year, the histologically confirmed overall rejection rate was 29.8%. These cases were mostly kidney biop-

Table 3. Complications by drainage technique.

	Duodenoduodenostomy (n = 125)	Duodenojejunostomy (n = 116)	P-value
Pancreas graft loss	14 (11)	21 (18)	NS
Pancreas graft thrombosis	5 (4)	18 (16)	$P = 0.002$
Anastomotic insufficiency	2 (1.6)	8 (7)	$P = 0.052$
GI anastomotic bleeding	14 (11)	4 (3)	$P = 0.026$
Blood transfusion	84 (67)	76 (66)	NS
Number of red cell concentrates/patient	4.28 ± 6.6	4.0 ± 5.5	NS
Obstruction	0 (0)	2 (1.7)	NS
Overall relaparotomy rate	52 (41)	56 (48)	NS
Due to bleeding, evacuation of haematoma	18 (14)	11 (9)	NS
Due to graft pancreatitis, peripancreatic fluid, intra-abdominal abscess, necrosectomy	17 (13)	13 (11)	NS
Pancreas graft thrombosis	5 (4)	18 (16)	$P = 0.002$
Anastomotic insufficiency	2 (1.6)	8 (6.9)	$P = 0.052$
Graft pancreatectomy	4 (3.2)	1 (0.8)	NS
Graft nephrectomy	2 (1.6)	1 (0.8)	NS
Fascial wound dehiscence repair	4 (3.2)	4 (3.4)	NS

Values are given as mean ± SD or n (% of group).

sies from the patients with combined pancreas–kidney transplantations (96%). Four patients in the DD group underwent trouble-free pancreatic graft endoscopic biopsies using a 21-gauge biopsy needle. The 1-year rejection rate was 28.8% in the DD group and 31% in the DJ group ($P = 0.705$). Of 36 cases in the DD group, 26 were considered borderline or Banff IA rejections. The 1-year rejection rate was 26.6% in patients with systemic venous drainage and 30.0% in patients with portal venous drainage within the DD group ($P = 0.837$). Of 36 rejections in the DJ group, 20 were borderline or Banff IA.

Serum creatinine, HbA1c and fasting glucose levels were measured and compared after 1 month, 6 months, 1 year and 2 years. With regard to pancreatic and kidney graft functions, no difference was found between both groups. The functional parameters for both groups are shown in Table 4.

Discussion

Safety management of exocrine pancreatic secretions has received the most attention in PT, as local release of activated pancreatic enzymes, similar to acute pancreatitis, can result in serious local tissue damage. The drainage of exocrine secretions into the urinary bladder dominated the 1980s and 1990s. This technique allows immunological monitoring of the graft through the determination of pancreatic enzymes in the urine or via cystoscopic biopsy [13,14]. In most centres today, bladder drainage is no longer used because of significant urological problems, reflux pancreatitis and potentially considerable bicarbonate loss. Bladder drainage has been increasingly replaced by enteric drainage; the proportion of patients undergoing PT with enteric drainage currently accounts for approximately 91% in the SPK transplantation group, 89% in the PAK transplantation group and 85% in the PTA group as per transplantation procedure [1]. Enteric drainage PT is usually performed as proximal DJ with or without Roux-en-Y limb [11]. Furthermore, exocrine drainage into the distal ileum [15] and gastric-exocrine drainage [9,10] were reported. DD emerges as another option for enteric drainage if the pancreas graft is placed in the right retroperitoneal space. DD in PT has already been described in single case reports and case series [4–8], all of them having in common a small number of patients.

The objective of this study was to describe our experience with 125 DD cases in PT to assess the comparative advantages or disadvantages between this technique and DJ. The study focused on cases in which pancreatic graft loss resulted in a duodenal leak that required treatment. This complication requires sophisticated surgical treatment and is the focal point of arguments from opponents of DD, thus spurring a controversy in the field.

Table 4. Graft function by drainage technique.

	Pre-Transplant			After 1 month			After 6 months			After 1 year			After 2 years		
	DD	DJ	*P*-value	DD	DJ	*P*-value	DD	DJ	*P*-value	DD	DJ	*P*-value	DD	DJ	*P*-value
Serum creatinine mg/dl	5.8 ± 2.5 (104)	5.2 ± 2.4 (67)	0.168	1.8 ± 1.1 (111)	1.6 ± 1.1 (103)	0.366	1.5 ± 0.6 (99)	1.5 ± 0.9 (97)	0.809	1.4 ± 0.5 (71)	1.3 ± 0.6 (93)	0.333	1.5 ± 0.7 (48)	1.5 ± 1.0 (91)	0.853
HbA1c%	7.7 ± 1.6 (87)	7.6 ± 1.3 (36)	0.894	6.4 ± 0.9 (95)	6.2 ± 0.8 (70)	0.870	5.9 ± 0.8 (89)	5.8 ± 1.1 (83)	0.938	5.9 ± 0.9 (75)	5.5 ± 0.7 (90)	0.109	6.0 ± 1.0 (44)	5.6 ± 1.0 (82)	0.186
Fasting glucose level mg/dl	n. a.	n. a.	n. a.	112.8 ± 42.5 (109)	112 ± 45.5 (101)	0.527	107.7 ± 42.1 (88)	104.0 ± 38 (97)	0.848	105.5 ± 31.2 (71)	102.6 ± 32.1 (92)	0.568	104.6 ± 32.2 (45)	97.0 ± 12.02 (79)	0.965

DD, duodenoduodenostomy; DJ, duodenojejunostomy.
Values are given as mean ± SD (*n*, number of patients).

Compared with the results from high-volume centres in the United States [16,17] and summarized data from the International Pancreas Transplant Registry [2], similarly good 1- and 5-year patient and graft survival rates could be achieved. In comparison with the US data, the complication rate (graft thrombosis, bleeding, rejection and relaparotomy rates) was slightly higher in this study. However, it must be noted that our recipient and donor groups had a significantly older age and that the donors exhibited a high proportion of death by cerebrovascular causes (>70%). In our opinion, the main reason for the relatively high rejection rate is a result of including the borderline rejections. For the overall collective of the study, there are at least 24 cases; that means exactly one-third of all reported rejections. If the borderline rejections are not included and rejection is defined as starting from stage BANFF I, as many authors do, there is a 1-year rejection rate of 18.4% (23/125) for the DD group and 21.5% (25/116) for the DJ group, respectively. Complications such as graft pancreatitis, intra-abdominal infections and required relaparotomies, which occurred more often in our patients, frequently necessitate a reduction in immunosuppressive therapy. It is also conceivable that the increased rejection rate could be due to this fact. After having analysed our data in 2009, we already noticed the increased rejection rates. For this reason and based on our positive experience with a repeated thymoglobulin dose in kidney transplantation within the Eurotransplant Senior Program, we extended the induction therapy in SPK from a single-shot therapy with 1.5 mg/kg/BW to two further postoperative administrations. The hospital stay of our patients is relatively long in relation to international standards, especially in the US. In our institution, we still have the opportunity to implement part of the rehabilitation during patients' initial admission, which results in a longer hospitalization period. The inpatients' stay is reported as a mean of 42 days in both groups. However, this value is distinctly inflated by 'long-stay patients' with a complicated recovery period. The median inpatient stay is 33 days in the DD group and 34 days in the DJ group. This value of inpatient hospitalization following pancreas transplantation can be found in most of the German transplantation centres.

Inspired by the results from Boggi *et al.* [3], applying retroperitoneal placement of pancreas grafts, the first DD cases in our centre were performed in patients with retransplantations or previous abdominal operations presenting distinct interenteric adhesion. Owing to the close anatomical location of both duodena, placement of a DD was the easiest and safest solution. Increasing experience with this technique and comparative results with DJ have established this surgical method as standard practice in our centre since 2007.

The 1 (DD, 82% vs. DJ, 78%)- and 5-year pancreas graft survival rates (DD, 82% vs. DJ, 73%) were slightly better in the DD group, although this difference was not statistically significant (log-rank test, $P = 0.202$). This is interesting because the patients in the DD group were on average older, showed longer diabetes and dialysis durations and had higher BMI compared with the DJ group. In addition, most of their organs were perfused with HTK Custodiol. All these factors are well known for their negative impact on the results of PT [18–23].

Removal of the pancreas graft was necessary in 14 (11.2%) of the 125 cases in the DD group compared with 21 of the 116 graft removals (18.1%) in the DJ group ($P = 0.129$). The main cause for early graft loss was graft thrombosis (23/241, 9.5%) with five cases (4%) in the DD group and 18 cases (15.5%) in the DJ group. Pancreas graft thrombosis occurred significantly less in the DD group ($P = 0.002$). As suggested by other authors, a potential advantage of the DD anastomosis is the avoidance of torsion or twisting of the allograft vessels [5].

The location of the graft in the retroperitoneum and anastomosis to the relatively fixed recipient duodenum may reduce graft mobility, which in turn may play a role in minimizing torsion on vascular anastomoses. In this regard, other investigators have noted a decrease in vascular thrombosis rate after placement of the pancreas in an upright, right-sided retroperitoneal position [3]. The higher number of portal venous anastomoses in the DD group offers another potential explanation for the low thrombosis rate in the DD group. Due to the high-flow and low-pressure systems, some authors discuss the portal venous drainage to be advantageous in the prevention of graft thromboses [3].

Depending on the thickness of the retroperitoneal space, the intraperitoneal positioning of the pancreas graft often involves a longer arterial Y-graft, whereas the retroperitoneal technique allows shortening the Y-graft to a minimum. Kinking or twisting of the graft vessels is thus greatly reduced. In this respect, our data confirm the previous results obtained by Boggi *et al.* [3].

As a rare complication, anastomotic insufficiency was identified in a total of 10 (4.1%) of 241 cases, occurring more frequently in the DJ group ($n = 8$). Anastomotic insufficiency occurred in only two cases in the DD group. Small bowel obstruction caused by internal hernia in the region of the pancreas graft and requiring surgery occurred only in the DJ group ($n = 2$). The DD group showed an increased incidence of gastrointestinal anastomotic bleeding. This trend was already noted by Gunasekaran *et al.* [5] who found that bleeding complications correlated with the application of circular staplers. In our approach, where all DD procedures were hand-sewn, the cause of this complication seems to have likely been the abundant blood vessel supply to the duodenum.

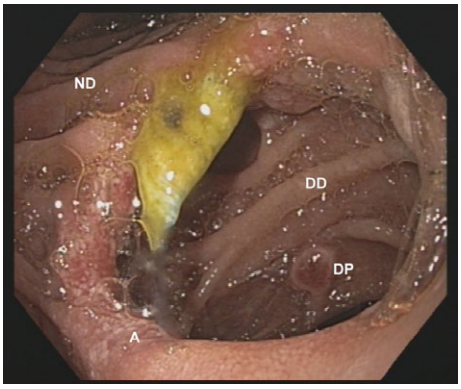

Figure 3 Endoscopic view of the anastomosis between both duodena. A, anastomosis; DD, donor duodenum; DP, donor papilla vateri; ND, native duodenum.

As mentioned earlier, cases of graft loss resulting in a duodenal leak requiring treatment is the most frequently discussed problem in DD. In our experience, severe surgical problems resulting from this issue are rare. After the 14 pancreas graft losses in the DD group, all duodenal leaks were primarily closed transversely, in two rows. The Gambee technique is a well-established method that can be used for at least the inner suture line. Three of these 14 patients showed insufficiency of the duodenal suture. Two of these patients had to undergo reoperation. In one case, the placement of Roux-en-Y DJ was performed, and in the other case, a side-to-side DJ was placed. In one case, with only slight biliary secretion, conservative therapy with keeping an abdominal drain in use for longer proved to be successful.

Therefore, we agree with other authors [5] that the longitudinal duodenotomy should not be longer than 2.5–3 cm to allow for a tension-free, transverse duodenal closure in case of graft removal. Otherwise, anastomosis must not be created too tightly to prevent stasis of secretions, and food or blood coagulum in the duodenal segment of the pancreas graft. Anastomosis should always be placed widely to allow easy passage by a standard gastroscope.

In recent years, histological examination of graft biopsies for rejection diagnostics has increasingly grown in importance. A biopsy is often indispensable, especially within the context of the increasing number of retransplantations in immunized patients, in PAK transplantation, or in isolated PT. However, isolated pancreas rejections not involving a kidney graft were also discussed in SPK transplantation [24]. These cases were most likely clinically inapparent rejections without any deterioration in renal function [25]. Although percutaneous ultrasound- or CT-guided pancre-

atic graft biopsies are now considered safer, there are still risks for bowel perforation, bleeding and pancreatic fistula formation. With the implementation of a retroperitoneal technique as described by Boggi *et al.* [3], these complications can be significantly prevented, as the pancreas graft is fixed and compartmentalized in the right retroperitoneal space. In our opinion, another essential advantage of the DD is the improved endoscopic accessibility of the pancreas graft for rejection diagnostics. In addition to the visual inspection of duodenal mucosa, there is opportunity for mucosal biopsy and ultrasound-guided pancreas biopsy (Fig. 3). Occurrence of bleeding can be visually checked immediately. Potential pancreatic fistula formation generally occurs with little consequence as the fistula intraluminally drains on its own into the duodenum. Other research groups also report successful therapy of pancreatic duct leaks in the pancreas graft by endoscopic papillotomy and stent insertion [5].

Endoscopic protocols are not kept at our centre. Endosonographically controlled biopsy of the pancreas graft with a 21-G needle was performed in four patients. In all the cases, sufficient tissue for histological examination was attainable. No complications were observed in any of the four patients.

According to our years of experience with more than 125 DD procedures in PT, we consider DD placement to be a simple and safe technique. Gastrointestinal complication rates were generally low (with exception of anastomotic bleeding). Our patient population even exhibited fewer complications with DD than with DJ. We could not confirm a special risk to patients, particularly those with graft loss. In fact, this technique produced advantages such as easy endoscopic access to the graft. With the introduction of this technique, occurrence of graft thrombosis could be significantly prevented. Nevertheless, potential benefits of this technique must be interpreted restrictively at the moment, as the present pool of 'DD drainage procedures' is still small and other enteric drainage techniques demonstrate similarly excellent results.

For patients undergoing pancreatic retransplantation procedures or patients exhibiting pronounced intestinal adhesions after previous abdominal operations, the DD represents a safe, alternative option for anastomosis compared with the already existing enteric exocrine drainage techniques.

Authorship

MW: collected and analysed the data and wrote the paper. MJ, SK, PK, SM, TK and AW: analysed the data and edited the paper. RV: analysed the results and edited the paper. PS: designed the study, collected and analysed data, and wrote the paper.

Funding

The study was performed without any financial support.

References

1. Gruessner AC. 2011 update on pancreas transplantation: comprehensive trend analysis of 25,000 cases followed up over the course of twenty-four years at the International Pancreas Transplant Registry (IPTR). *Rev Diabet Stud* 2011; **8**: 6.
2. Gruessner AC, Gruessner RW. Pancreas transplant outcomes for United States and non United States cases as reported to the United Network for Organ Sharing and the International Pancreas Transplant Registry. *Clin Transpl* 2012; 23.
3. Boggi U, Vistoli F, Signori S, *et al.* A technique for retroperitoneal pancreas transplantation with portal-enteric drainage. *Transplantation* 2005; **79**: 1137.
4. De Roover A, Coimbra C, Detry O, *et al.* Pancreas graft drainage in recipient duodenum: preliminary experience. *Transplantation* 2007; **84**: 795.
5. Gunasekaran G, Wee A, Rabets J, Winans C, Krishnamurthi V. Duodenoduodenostomy in pancreas transplantation. *Clin Transplant* 2012; **26**: 550.
6. Hummel R, Langer M, Wolters HH, Senninger N, Brockmann JG. Exocrine drainage into the duodenum: a novel technique for pancreas transplantation. *Transpl Int* 2008; **21**: 178.
7. Schenker P, Flecken M, Vonend O, Wunsch A, Traska T, Viebahn R. En bloc retroperitoneal pancreas-kidney transplantation with duodenoduodenostomy using pediatric organs. *Transplant Proc* 2009; **41**: 2643.
8. Viebahn R, Schenker P, Petersen P, *et al.* 40 cases of duodeno-duodenostomy in pancreas transplantation: single-center proof of a safe and simple technique. *Transplantation* 2008; **86.2S**: 50.
9. 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.
10. Shokouh-Amiri H, Zakhary JM, Zibari GB. A novel technique of portal-endocrine and gastric-exocrine drainage in pancreatic transplantation. *J Am Coll Surg* 2011; **212**: 730; discussion 8–9.
11. Boggi U, Amorese G, Marchetti P. Surgical techniques for pancreas transplantation. *Curr Opin Organ Transplant* 2010; **15**: 102.
12. De Roover A, Detry O, Coimbra C, Squifflet JP, Honore P, Meurisse M. Exocrine pancreas graft drainage in recipient duodenum through side-to-side duodeno-duodenostomy. *Transpl Int* 2008; **21**: 707.
13. Benedetti E, Najarian JS, Gruessner AC, *et al.* Correlation between cystoscopic biopsy results and hypoamylasuria in bladder-drained pancreas transplants. *Surgery* 1995; **118**: 864.

14. Prieto M, Sutherland DE, Fernandez-Cruz L, Heil J, Najarian JS. Experimental and clinical experience with urine amylase monitoring for early diagnosis of rejection in pancreas transplantation. *Transplantation* 1987; **43**: 73.
15. Sollinger HW, Messing EM, Eckhoff DE, *et al.* Urological complications in 210 consecutive simultaneous pancreas-kidney transplants with bladder drainage. *Ann Surg* 1993; **218**: 561; discussion 8–70.
16. 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.
17. 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.
18. Alonso D, Dunn TB, Rigley T, *et al.* Increased pancreatitis in allografts flushed with histidine-tryptophan-ketoglutarate solution: a cautionary tale. *Am J Transplant* 2008; **8**: 1942.
19. Farney AC, Rogers J, Stratta RJ. Pancreas graft thrombosis: causes, prevention, diagnosis, and intervention. *Curr Opin Organ Transplant* 2012; **17**: 87.
20. Kayler LK, Wen X, Zachariah M, Casey M, Schold J, Magliocca J. Outcomes and survival analysis of old-to-old simultaneous pancreas and kidney transplantation. *Transpl Int* 2013; **26**: 963.
21. Muthusamy AS, Vaidya A. Expanding the donor pool in pancreas transplantation. *Curr Opin Organ Transplant* 2011; **16**: 123.
22. Schenker P, Vonend O, Ertas N, *et al.* Incidence of pancreas graft thrombosis using low-molecular-weight heparin. *Clin Transplant* 2009; **23**: 407.
23. Stewart ZA, Cameron AM, Singer AL, Dagher NN, Montgomery RA, Segev DL. Histidine-tryptophan-ketoglutarate (HTK) is associated with reduced graft survival in pancreas transplantation. *Am J Transplant* 2009; **9**: 217.
24. Klassen DK, Hoen-Saric EW, Weir MR, *et al.* Isolated pancreas rejection in combined kidney pancreas transplantation. *Transplantation* 1996; **61**: 974.
25. Shapiro R, Jordan ML, Scantlebury VP, *et al.* Renal allograft rejection with normal renal function in simultaneous kidney/pancreas recipients: does dissynchronous rejection really exist? *Transplantation* 2000; **69**: 440.

