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A single-centre experience of Roux-en-Y enteric drainage for pancreas transplantation

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SUMMARY

Exocrine drainage following pancreas transplantation can be achieved by drainage into the bladder or bowel, the latter typically by direct duodeno-jejunostomy; the use of Roux-en-Y enteric drainage is uncommon. We report a retrospective analysis of a single-centre experience of Roux-en-Y enteric drainage following pancreas transplantation. Over a 14-year period (2001–2015), 204 consecutive adult pancreas transplants were performed (96.6% simultaneous pancreas and kidney transplants), of which 26.0% were from donors after circulatory death (DCD). During a median follow-up of 67 months (range 13–183 months), 14 (6.9%) recipients experienced complications related to their enteric drainage. Complications during follow-up included early enteric anastomotic haemorrhage (five patients), non-anastomotic enteric bleeding (one patient), small bowel obstruction (four patients) and graft duodenal perforation (two within 6 weeks, five beyond 12 months). No recipient lost their graft as a direct result of complications related to enteric drainage. Patient and pancreas graft survival at 1 year was 99.0% and 94.0% and at 5 years 91.3% and 84.9%, respectively. We conclude that Roux-en-Y enteric drainage following pancreas transplantation is a safe and effective procedure and facilitates graft salvage in the event of graft duodenal perforation.

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Key words
anastomotic haemorrhage, duodenal perforation, enteric drainage, pancreas transplant, Roux-en-Y

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Introduction

Pancreas transplantation is the optimal treatment for achieving euglycaemia in selected patients with diabetes; it frees patients from the need to administer exogenous insulin, reduces metabolic instability, improves quality of life and may stabilize and reduce the long-term effects of diabetes [1,2]. The majority of potential recipients have advanced diabetic nephropathy and are candidates for simultaneous pancreas and kidney transplantation (SPK) [3]. A smaller number of patients may be candidates for pancreas after kidney transplantation (PAK) or pancreas transplantation alone (PTA) [2,4,5].

Clinical outcomes following pancreas transplantation have improved steadily over the last two decades, because of a combination of factors including improvements in patient selection, chemoprophylaxis, immunosuppression regimens and surgical technique [6]. In the UK, 1- and 5-year patient survival following SPK transplantation is 97% and 89%, respectively, and 1- and 5-year graft survival is 86% and 74%, respectively [7].

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A long-standing challenge in pancreas transplantation has been finding the optimal surgical technique for dealing with the exocrine drainage of the pancreas graft.

While bladder drainage was popular initially, most centres (>80% in the USA) now use enteric drainage (ED) into either the recipient duodenum or jejunum [3,6,8].

Direct anastomosis to the recipient duodenum has the advantage of allowing access to the graft duodenum via upper gastrointestinal endoscopy for surveillance and biopsy [9,10]. However, if an anastomotic complication arises, salvaging the graft and repairing the recipient duodenum can be technically challenging. Drainage to the jejunum is most commonly performed by fashioning a direct duodeno-jejunostomy, but can also be performed using a Roux-en-Y enteric limb. Gruessner *et al.* have reported 21% of SPK and 15% of solitary pancreas transplants using Roux-en-Y enteric drainage using data from the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR) [11,12]. The latter has two main potential advantages. First, it allows drainage of pancreas secretions into a defunctioned limb of bowel, thereby diverting the small bowel contents away from the transplant duodeno-jejunal anastomosis. Second, if the duodeno-jejunal anastomosis leaks when perforation occurs, graft salvage may be more easily achieved. Moreover, should removal of the pancreas graft prove necessary, the need for creation of intestinal stomas can be avoided, in contrast to direct ED techniques [13,14].

In the UK, surgical practice for management of the pancreatic exocrine secretion varies between the eight centres that undertake the procedure, with some units performing primary BD and others primary ED. Our routine practice since 2001 has been to perform Roux-en-Y enteric drainage of the pancreas graft, and in this paper we report our experience with this technique over that 14-year period.

Patients and methods

A retrospective analysis was undertaken of all adults undergoing pancreas transplantation at the Cambridge University Hospitals NHS Trust, between 01/01/2001 and 27/02/2015, using a prospectively maintained database. Recipient and donor demographic data were collected as were major postoperative complications and patient and graft outcomes (minimum follow-up period of 12 months). The analysis was undertaken as a service evaluation within Cambridge University Hospitals NHS Trust.

Surgical technique

All pancreas transplants were performed using a standard surgical technique. Back bench preparation of the pancreas was carried out with the organ immersed in ice-cold University of Wisconsin solution (Belzer UW, London, UK). The spleen was removed from the pancreaticoduodenal block and the duodenal segment shortened. The proximal and distal duodenal staple lines were oversewn with 3/0 polypropylene (Prolene, Ethicon), as was the small bowel mesentery. A "Y" conduit of donor iliac artery was used to anastomose the superior mesenteric artery and splenic artery of the graft. The pancreaticoduodenal allograft was implanted via a midline laparotomy, with anastomosis of the portal vein to the recipient inferior vena cava and the arterial "Y" conduit to the recipient right common or external iliac artery. The pancreas lay intraperitoneally, with the head in a cephalad direction and enteric exocrine drainage achieved via a jejunal Roux-en-Y loop. The proximal recipient jejunum was divided, and the donor duodenum was anastomosed to the jejunum of the Roux-en-Y loop by a hand-sewn two-layer side-to-side anastomosis, with an inner layer of continuous 3/0 polydioxanone (PDS, Ethicon) and an outer layer of interrupted 3/0 polypropylene. A side-to-side jejuno-jejunostomy was fashioned with two layers of 3/0 polydioxanone, no less than 30 cm from the transplant anastomosis. The appendix (and gallbladder if gallstones were present on preoperative US scan) was routinely excised, and a percutaneous feeding jejunostomy was inserted in most cases.

For SPK, the donor kidney was placed via the midline incision into an extra-peritoneal pouch in the left iliac fossa with anastomosis of the donor vessels to the recipient common or external iliac vessels and anastomosis of the ureter to the dome of the bladder over a double J stent.

Immunosuppression

The first 10 patients in the series received basiliximab induction with maintenance triple therapy comprising tacrolimus, mycophenolate and prednisolone. Thereafter, all patients received alemtuzumab induction (given subcutaneously to avoid a first dose reaction), with tacrolimus and mycophenolate maintenance without steroids.

Anti-microbial and anti-thrombotic therapy

CMV (cytomegalovirus) sero-positive recipients were given oral valganciclovir for 3 months, and CMV sero-negative

recipients of CMV sero-positive organs received oral valganciclovir for 6 months. CMV sero-negative recipients of sero-negative organs were given aciclovir prophylaxis against herpes simplex and varicella zoster viruses for 3 months. All recipients received 5 days of meropenem (2001–2015) or piperacillin/tazobactam (2015 onwards) and 7 days fluconazole anti-microbial prophylaxis. Epoprostenol (4 ng/kg/min intravenously) was started intraoperatively and continued for 48 h. Dalteparin (5000 U subcutaneously) was started on day one until discharge, and aspirin (75 mg) was started on discharge from hospital.

Statistical methods

Categorical data were analysed using Fisher's exact test and continuous data by Mann–Whitney using Prism (GraphPad Software Inc., La Jolla, CA, USA); P values <0.05 were considered statistically significant. Kaplan–Meier analysis was used for patient and graft survival.

Results

Clinical characteristics of the study cohort

Over the 14-year study period, 204 consecutive adult pancreas transplants were performed. Of these, 197 (96.6%) were simultaneous pancreas and kidney (SPK) and seven (3.4%) pancreas after kidney (PAK) transplants. The clinical characteristics of the organ donors and transplant recipients are shown in Table 1. The median donor age was 36 years (range 7–59 years) and median donor BMI 24 kg/m^2 (range 15–33 kg/m^2): 151 (74.0%) donors were donation after brain death (DBD) donors, and 53 (26.0%) were donation after circulatory death (DCD) donors. The median age of transplant recipients was 42 years (range 24–58 years), and their median BMI was 25 kg/m^2 (range 18–32 kg/m^2). Their median duration of diabetes was 27 years (range 11–53 years) and, for the 153 on dialysis, the median duration of renal replacement therapy 15 months (range 1–84 months).

Clinical characteristics according to development of enteric drainage complications

During the median follow-up period of 67 months (range 13–183 months), 14 (6.9%) of the recipients experienced postoperative enteric complications. The clinical characteristics of patients with and without Roux-en-Y related complications are shown in Table 1, and individual clinical details for patients with complications of enteric drainage are described in Table 2, which groups the patients according to whether they experienced early (within 30 days) or late (>30 days) complications post-transplant. The complications experienced (Table 2) comprised one or more episodes of enteric anastomotic haemorrhage (five patients), small bowel obstruction (four patients), graft duodenal perforation (seven patients) and non-anastomotic haemorrhage (one patient). There were no additional cases of pancreas graft fistulae apart from those recipients with graft duodenal perforation. Whereas all haemorrhagic complications occurred early, six of the seven graft duodenal perforations were late complications and five occurred beyond 12 months.

The gender, age and pretransplant renal status (predialysis, dialysis or existing renal transplant) of recipients were similar in those with and without enteric complications (Table 1). There was no difference in organ donor age, cold ischaemia time, donor BMI, HLA mismatch, recipient CMV status and recipient BMI according to whether or not recipients developed complications of enteric drainage (Table 1). Of the 14 patients who developed complications related to enteric drainage, nine (64.3%) received organs from DCD donors and five (35.7%) from DBD donors (P = 0.001).

Recipient outcomes, according to whether or not enteric complications occurred, are shown in Table 3. Recipients who developed enteric complications had a significantly longer cumulative hospital stay during follow-up (median 60 days, range 19–146 days vs. median 28 days, range 8–364 days, P = 0.002), and underwent a greater number of re-laparotomies (median 1, range 0–4 vs. median 0, range 0–2, P = 0.0001). The incidence of pancreas graft rejection did not differ significantly according to the presence or absence of enteric complications and neither did deep fungal infection or CMV infection.

Pancreas graft loss occurred in two (14.3%) recipients who developed enteric complications and 29 (15.8%) of recipients without enteric complications (Table 3). None of the recipients lost their pancreatic graft as a direct result of enteric complications. Overall the most common causes of graft loss in the study cohort were graft thrombosis, recurrence of type 1 diabetes and graft rejection (Table 3). Patient survival for the entire patient cohort, including those with enteric complications, was 99.0% at 1 year and 94.0% at 5 years (Fig. 1). Pancreas graft survival was 91.3% and 84.9%, and kidney graft survival was 99.0% and 98.6% at 1 and 5 years, respectively (Fig. 1). Kidney graft survival and graft function (serum creatinine) were similar in

Table 1. Donor and recipient clinical characteristics.

	Total $n = 204$	No complications related to enteric drainage (Group 1) $n = 190$	Complications related to enteric drainage (Group 2) $n = 14$	Groups 1 vs. 2 P value
Recipient age (years, median and range)	42 (24–58)	42 (24–58)	43 (27–51)	0.735
Male (*n*)	138 (67.6%)	128 (67.4%)	10 (71.4%)	1.00
Duration of diabetes (years, median and range)	27 (11–53)	27 (11–53)	29 (17–39)	0.858
Pretransplant renal status				
Predialysis (*n*)	51 (25.0%)	48 (25.3%)	3 (21.4%)	1.000*
Haemodialysis (*n*)	84 (41.2%)	77 (40.5%)	7 (50.0%)	
Peritoneal dialysis (*n*)	61 (29.9%)	58 (30.5%)	3 (21.4%)	
Existing renal transplant (*n*)	7 (3.4%)	6 (3.2%)	1 (7.1%)	
Duration of renal replacement therapy (months, median and range)	15 (1–84)	15 (1–84)	14 (6–42)	0.739
Recipient BMI (kg/m^2, median and range)	25 (18–32)	24 (18–32)	25 (20–29)	0.559
Deceased donor type				
DBD (*n*)	151 (74.0%)	146 (76.8%)	5 (35.7%)	0.001
DCD (*n*)	53 (26.0%)	44 (23.2%)	9 (64.3%)	0.001
Donor age (years, median and range)	36 (7–59)	36 (7–59)	35 (12–47)	0.482
Donor BMI (kg/m^2, median and range)	24 (15–33)†	24 (16–33)†	22 (15–29)†	0.217
Total HLA-A, HLA-B and DR mismatches				
1–3 (*n*)	64 (31.4%)	60 (31.6%)	4 (28.6%)	1.000
4–6 (*n*)	140 (68.6%)	130 (68.4%)	10 (71.4%)	1.000
Number of HLA mismatches (median and range)	4 (1–6)	4 (1–6)	4 (2–6)	1.000
Pancreas cold ischaemic time (hours, median and range)	10.2 (4.5–13.2)	10.1 (4.5–13.2)	11.0 (4.8–12.5)	0.567
Recipient CMV status pretransplant				
Sero-positive (*n*)	93 (45.6%)	88 (46.3%)	5 (35.7%)	0.581
Donor sero-positive/recipient sero-negative	47 (23.0%)	43 (22.6%)	4 (28.6%)	0.742

*Because of small numbers, the groups compared were predialysis v dialysis, (haemodialysis and peritoneal dialysis combined).
†Data available for 101/190 patients in Group 1 and 10/14 patients in Group 2.

recipients, irrespective of whether they developed enteric complications (Table 3). There were no cases of primary kidney graft non-function in the study group.

Details of complications related to enteric drainage

Enteric anastomotic haemorrhage

Five (2.5%) patients (#121, #132, #156, #161 and #200) experienced enteric anastomotic haemorrhage, and in all this occurred within 30 days of transplantation, (median 4.5 days, range 1–30 days). One patient (#156) had two episodes of anastomotic haemorrhage, one from the duodeno-jejunostomy and the other from the entero-enterostomy. In the remaining four patients, haemorrhage originated from the entero-enterostomy anastomosis in three (#121, #132 and #161) and from the duodeno-jejunostomy anastomosis in one (#200). The clinical presentation comprised melaena ($n = 2$), a drop in haemoglobin ($n = 2$) or both ($n = 1$). In one patient (#156), haemorrhage from the entero-enterostomy caused obstruction of the roux loop and a significant rise in lipase (2261 U/l) which resolved rapidly post laparotomy. Haemorrhage was treated successfully in all cases by re-laparotomy and re-fashioning of the enteric anastomosis.

Small bowel obstruction

Four (2.0%) patients developed small bowel obstruction as a direct result of the enteric drainage. Two patients (#81 and #201) developed early (days 8 and 14) acute small bowel obstruction because of an internal hernia. Both presented with abdominal pain and distension. Treatment comprised laparotomy with simple adhesiolysis in one case and resection of ischaemic bowel from the distal Roux limb in the second case.

Table 2. (a) Early complications (<30 days from transplantation). (b) Late complications (>30 days from transplantation).

No of cohort	Age/gender	Type of transplant	Time from transplant	Details of complication	Follow-up	Graft loss
(a) Enteric haemorrhage						
121	33F	DCD/SPK	1 day	1) Anastomotic haemorrhage from entero-enterostomy requiring laparotomy	5.5 years	No
132	44F	DCD/SPK	4 days	1) Anastomotic haemorrhage from entero-enterostomy requiring laparotomy	4.8 years	No
156	49F	DBD/SPK	3 days 5 days	1) Anastomotic haemorrhage from entero-enterostomy requiring laparotomy 2) Anastomotic haemorrhage from duodeno-jejunostomy requiring laparotomy	2.8 years	No
161	36M	DCD/SPK	12 days	1) Anastomotic haemorrhage from entero-enterostomy requiring laparotomy	2.6 years	No
200	47F	DCD/SPK	30 days	1) Anastomotic haemorrhage from duodeno-jejunostomy requiring laparotomy	1.2 years	No
152	49M	DBD/PA	20 days 24 days	1) Melaena—haemorrhage from donor duodenum—embolised 2) Subsequent ischaemic (iatrogenic) duodenal perforation—excision of duodenum and duodeno-jejunostomy re-fashioned	7 years	Yes, 9.8 m
Small bowel obstruction						
81	51M	DCD/SPK	8 days	1) Small bowel obstruction because of an internal hernia of the Roux-en-Y loop—bowel resection and re-fashioning of Roux-en-Y loop	6.9 years	No
201	32M	DCD/SPK	14 days	1) Small bowel obstruction—because of adhesions causing an internal hernia	1.2 years	No
Graft duodenal perforation						
152	49M	DBD/PA	20 days 24 days	1) Melaena—haemorrhage from donor duodenum—embolised 2) Subsequent ischaemic (iatrogenic) duodenal perforation—excision of duodenum and duodeno-jejunostomy re-fashioned	7 years	Yes, 9.8 m
(b) Small bowel obstruction						
126	31M	DCD/SPK	386 days 602 days 805 days	1) Duodenal perforation—serosal patch repair 2) Small bowel obstruction—transition point was at the entero-enterostomy—bowel resection 3) Duodenal perforation—resection and re-fashioning of Roux-en-Y loop	5 years	No
134	34M	DCD/SPK	1314 days 1435 days	1) Duodenal perforation—resection 2) Small bowel obstruction—intussusception at entero-enterostomy blind end—resection and re-fashioned	4.4 years	No

Table 2. Continued.

No of cohort	Age/gender	Type of transplant	Time from transplant	Details of complication	Follow-up	Graft loss
Graft duodenal perforation						
1	27M	DBD/SPK	46 days	1) Iatrogenic duodenal perforation—laparotomy and drainage	15.4 years	Yes, 5.2 m
34	43M	DBD/SPK	545 days	1) Duodenal perforation—T-tube inserted into duodenum and drainage	9.3 y	No
73	42M	DBD/SPK	467 days 488 days	1) Duodenal perforation—serosal patch repair 2) Subsequent duodenal resection	7.3 years	No
126	31M	DCD/SPK	386 days 602 days 805 days	1) Duodenal perforation—serosal patch repair 2) Small bowel obstruction—transition point was at the entero-enterostomy—bowel resection 3) Duodenal perforation—resection and re-fashioning of Roux-en-Y loop	5 years	No
134	34M	DCD/SPK	1314 days 1435 days	1) Duodenal perforation—resection 2) Small bowel obstruction—intussusception at entero-enterostomy blind end—resection and refashioned	4.4 years	No
164	45M	DCD/SPK	506 days	1) Duodenal perforation—primary closure, subsequent leak treated with drainage	2.5 years	No

Both of the other two patients developed late small bowel obstruction (805 and 1435 days) and had previously experienced graft duodenal perforation (see below). One of them (#126) developed acute intestinal obstruction as a result of adhesions related to the entero-enteric anastomosis. At laparotomy, a segment of ischaemic bowel was resected with primary re-anastomosis. The other patient (#134) developed intermittent small bowel obstruction because of intussusception of a short segment of bowel at the blind end of the entero-enteric anastomosis. Elective laparotomy was performed with resection of the short intussuscepting intestinal segment.

Graft duodenal perforation

Seven (3.4%) patients experienced graft duodenal perforations. They all presented with acute abdominal pain; CT scan showed a fluid collection adjacent to the graft duodenum and/or free intraperitoneal air, and duodenal perforation was confirmed at laparotomy in all cases. Two patients (#1 and #152) developed iatrogenic duodenal perforations (46 and 24 days, respectively): one of these (#1) suffered a duodenal perforation during a renal transplant biopsy and was treated with laparotomy and drainage, but required a subsequent laparotomy and oversewing of the graft duodenum at 147 days. The second iatrogenic perforation occurred 24 days post-transplant in a patient (#152) who had undergone radiological embolization of the graft duodenum to treat duodenal haemorrhage. At laparotomy, a limited duodenal resection was performed with re-anastomosis of the Roux-en-Y limb to the remaining viable duodenum. Neither of the iatrogenic duodenal perforations involved either the duodeno-jejunal anastomosis or the stapled ends of the duodenal graft.

The other five recipients developed late perforations (median 506 days, range 386–1314 days after transplantation). Three (#34, #134 and #164) of the five recipients experienced one duodenal perforation and two (#73 and #126) experienced a recurrent duodenal graft perforation. All of these perforations occurred in association with one or other of the oversewn stapled ends of the duodenal graft. In none of the five late duodenal perforations was the precise cause of the perforation identified; there was no evidence of rejection, and CMV PCR of peripheral blood was negative. Of the three patients who experienced only one perforation, one (#34) presented with abdominal pain and fever, and a CT scan showed a fluid collection in the right flank extending to the donor duodenum. At laparotomy a T-

Table 3. Recipient outcomes.

	Total *n* = 204	No of complications related to enteric drainage (Group 1) *n* = 190	Complications related to enteric drainage (Group 2) *n* = 14	Group 1 vs. 2 *P* value
Duration of follow-up (months, median and range)	67 (13–183)	69 (13–73)	55 (14–183)	0.109
Cumulative hospital stay (median and range)	30 (8–364)	28 (8–364)	60 (19–146)	0.002
Re-laparotomies/patient (median and range)	0 (0–4)	0 (0–2)	1 (0–4)	0.0001
Recipients—no re-laparotomy (*n*)	170 (83.3%)	169 (88.9%)	1 (7.1%)	
Recipients—1 to 2 re-laparotomies (*n*)	30 (14.7%)	19 (10.0%)	11 (78.6%)	0.0001
Recipients—3 to 4 re-laparotomies (*n*)	4 (2.0%)	2 (1.1%)	2 (14.3%)	
Recipients treated for pancreas graft rejection (*n*)*	49 (24.0%)	48 (25.3%)	1 (7.1%)	0.201
Deep fungal infection (*n*)	3 (1.5%)	2 (1.1%)	1 (7.1%)	0.193
CMV infection (*n*)	31 (15.2%)	30 (15.8%)	1 (7.1%)	0.699
Total pancreas graft loss (*n*)†	31 (15.2%)	29 (15.3%)	2 (14.3%)	1.000
Cause of pancreas loss‡				
Thrombosis	14 (6.9%)	14 (7.4%)	0 (0.0%)	
Recurrence of type 1 diabetes	6 (2.9%)	6 (3.2%)	0 (0.0%)	
Rejection	7 (3.4%)	6 (3.2%)	1 (7.1%)	
Pancreatitis	2 (1.0)	1 (0.5%)	1 (7.1%)	
Other	2 (1.0%)	2 (1.1%)	0 (0.0%)	
Kidney graft loss (*n*)	14 (6.9%)	14 (7.4%)	0 (0.0%)	
Serum creatinine (μmol/l)				
1 year (median and range)§	108.5 (55–258)	108 (55–258)	128.5 (72–162)	0.335
3 year (median and range)¶	109.5 (47–354)	108.5 (47–354)	122.5 (92–172)	0.730
5 year (median and range)**	120.5 (53–313)	123 (313)	81 (4–121)	0.032

*Defined as receiving high dose steroids, ATG or campath.

†Excludes death with a functioning graft.

‡No statistical comparison because of small numbers.

§Missing data for 24 patients in Group 1 and one patient in Group 2.

¶Missing data for 71 patients in Group 1 and five patients in Group 2.

**Missing data for 98 patients in Group 1 and eight patients in Group 2.

tube was inserted into the duodenum and a drain into the abscess cavity. The patient required a further three laparotomies and drainage procedures over a 4-month period and has a functioning graft at 9.3 years.

The second (#134) patient presented at 1314 days with fevers and a large fluid collection overlying the graft pancreas which was treated by limited resection of the donor duodenum.

The third patient (#164) presented at 506 days with fevers, abdominal pain and distension, and at laparotomy a donor duodenal perforation was closed. Ten days later he developed a controlled duodenal fistula which resolved with antibiotics and parenteral nutrition (PN); the patient is currently alive with a functioning graft 2.5 years later.

Two recipients experienced recurrent late graft duodenal perforations (#73 and #126). One recipient (#73) presented with a large pelvic fluid collection. At laparotomy, a perforation in the donor duodenum was closed with a serosal patch. Drain amylase levels remained high, and at repeat laparotomy 20 days later, the site of duodenal perforation was resected and oversewn. Duodenal histology from both laparotomies showed ischaemia with no evidence of graft rejection or CMV infection.

The second recipient (#126) with recurrent late perforation was treated with a serosal patch repair. At 85 days, he re-presented with duodenal perforation that was resected and oversewn and the Roux-en-Y loop revised. None of the above patients required the formation of an intestinal stoma during the management of their graft duodenal perforation or required a graft pancreatectomy.

Discussion

The findings from this large single-centre study demonstrate that Roux-en-Y enteric drainage is a safe and

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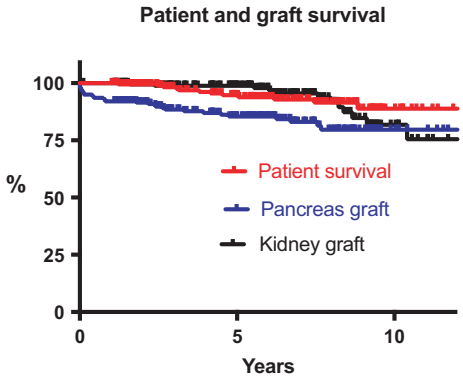

Time (Years)	1	5	10
Number at risk (Patient)	204	119	18
Number at risk (Pancreas graft)	185	102	12
Number at risk (Kidney graft)	201	110	16

Figure 1 Kaplan–Meier estimates of patient and graft survival (censored for patient death).

effective technique for pancreas transplantation. Only 14 (6.9%) of recipients encountered complications directly related to their enteric drainage during follow-up, which compares favourably with that reported following direct enteric drainage [3,10]. Early (<30 days) complications encountered following Roux-en-Y drainage comprised anastomotic haemorrhage, iatrogenic graft duodenal perforation and small bowel obstruction, whereas late complications comprised graft duodenal perforations and small bowel obstruction. All of these complications were treated successfully by surgical intervention, and none of the pancreas grafts were lost as a direct result of complications of enteric drainage.

Graft duodenal perforation is a serious complication of enteric drainage since it may result in the need for stoma formation and lead to graft loss. In a large North American series comprising 610 pancreas transplants with direct duodeno-jejunostomy drainage without a Roux-en-Y loop (primary or secondary following bladder drainage), the duodenal leak rate was 5.7% [3]. The potential advantage of Roux-en-Y enteric drainage is that management of duodenal perforations is less likely to require stoma formation or result in graft loss. However, Spetzler *et al.* [15] recently reported a Canadian cohort of 284 pancreas transplants; 6.3% of patients developed duodenal leaks after Roux-en-Y enteric drainage and almost half lost their pancreas graft because of the duodenal leak. Two thirds of the perforations in that series occurred within the first 100 days. In contrast, only two (1.0%) patients in our series suffered perforation within the first 100 days, and both those were iatrogenic. The remaining five perforations (2.5%) in our series occurred beyond 12 months post-transplant.

All of the graft duodenal perforations in our study presented with acute abdominal pain, often in association with diarrhoea or vomiting and raised inflammatory markers. The presence of such symptoms should prompt urgent abdominal CT, which in all of our cases of duodenal perforation demonstrated either free intraperitoneal air or a fluid collection associated with the pancreatic graft. If a clinical diagnosis of duodenal perforation is supported by the findings from CT, then we recommend urgent laparotomy. Management of duodenal leaks in our series evolved from attempts to create controlled fistulas with a T-tube or closure with serosal patches to treatment involving resection of the perforation and either direct primary closure of the defect or utilization of the Roux limb to close the defect, and this is now our recommended surgical practice.

None of the recipients in our series required stoma formation as a result of duodenal perforation. While the duodenal leak rate in our series is broadly comparable to that reported in the other series (5–8%) [16], it was striking that duodenal leaks did not require graft pancreatectomy in the present series, whereas in the other series, the pancreatectomy rate following duodenal leaks was 28–55% [15–17].

Graft duodenal perforation after pancreas transplantation may occur for a variety of reasons including graft rejection, CMV infection, ischaemia and distal obstruction, although the precise cause in a particular patient is often difficult to determine. In one series of late anastomotic leaks after pancreas transplantation, 40% of recipients had an identifiable antecedent event such as CMV infection or acute rejection that might have contributed to the perforation [18]. No obvious antecedent events to spontaneous perforation were apparent in the present series, and no patient in our series had evidence of CMV infection or graft rejection as the cause of duodenal perforation. A notable feature of the patient cohort in our series was that a quarter received grafts from DCD donors. While the overall complications related to enteric drainage were significantly more common in recipients of DCD donor organs, the numbers are too small to make any decisive conclusions about an

association between donor type and duodenal leak. Moreover, if DCD donor organs were more prone to duodenal perforation, it might be expected that this would occur early rather than late as observed in the present series. However, DCD donor pancreas grafts undoubtedly incur a greater reperfusion injury following transplantation, and this may conceivably lead to chronic ischaemia in some grafts that eventually manifests as spontaneous perforation. In cases where resection of the duodenal perforation was performed, histopathological examination typically showed either inflammation and/or chronic ischaemia, which is consistent with the findings reported in the series of late donor duodenal complications by Nymann *et al.* [19] and points to an ischaemic aetiology.

The other common complication related to enteric drainage after pancreas transplantation is early anastomotic haemorrhage, and this may relate, at least in part, to the anti-coagulation commonly used as prophylaxis against vascular thrombosis of the pancreatic graft. In our series, 2.2% of patients developed anastomotic haemorrhage which also compares favourably with other series of enteric drainage which typically report anastomotic haemorrhage rates of between 3% and 11% [10,14,20]. All of the cases of anastomotic haemorrhage in the present series were managed successfully by re-fashioning the enteric anastomosis.

It is well recognized that enteric drainage, with or without a Roux-en-Y limb, may result in intestinal obstruction through a variety of causes [21]. In our series, small bowel obstruction requiring surgical intervention and directly related to the Roux-en-Y drainage occurred in 1.7% of patients. The causes of obstruction were an internal hernia, intussusception and adhesions, all of which were treated successfully by either intestinal resection or adhesiolysis.

From our single-centre experience of Roux-en-Y enteric drainage following pancreas transplantation in a total of 204 cases over a 14-year period, we conclude that it is a safe and effective procedure with a relatively low rate of complications and associated with excellent long-term patient and graft survival rates.

Authorship

IA and CJEW: designed the study, analysed the data and wrote the paper. AJB, GD, NKR, SJFH, AJ, KSP and GJP: contributed to data collection and writing of the final manuscript.

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Conflicts of interest

None of the authors have any conflicts of interest to declare.

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