World Journal of Transplantation

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DOI: 10.5500/wjt.v6.i2.255

World J Transplant 2016 June 24; 6(2): 255-271
ISSN 2220-3230 (online)

Exocrine drainage in vascularized pancreas transplantation in the new millennium

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Author contributions: El-Hennawy H and Stratta RJ studier conception, designs, acquisition of data, analysis and interpretation of data; all the authors do drafting of manuscript and critical revision.

Conflict-of-interest statement: The authors acknowledge that the above manuscript represents original work that has not been previously published or submitted for publication. There are no conflicts of interest, grant support, sponsorship, or other financial arrangements to report by any of the authors.

Manuscript source: Invited manuscript

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Received: February 16, 2016
Peer-review started: February 16, 2016
First decision: March 1, 2016
Revised: May 6, 2016
Accepted: May 31, 2016
Article in press: June 2, 2016
Published online: June 24, 2016

Abstract

The history of vascularized pancreas transplantation largely parallels developments in immunosuppression and technical refinements in transplant surgery. From the late-1980s to 1995, most pancreas transplants were whole organ pancreatic grafts with insulin delivery to the iliac vein and diversion of the pancreatic ductal secretions to the urinary bladder (systemic-bladder technique). The advent of bladder drainage revolutionized the safety and improved the success of pancreas transplantation. However, starting in 1995, a seismic change occurred from bladder to bowel exocrine drainage coincident with improvements in immunosuppression, preservation techniques, diagnostic monitoring, general medical care, and the success and frequency of enteric conversion. In the new millennium, pancreas transplants are performed predominantly as pancreatico-duodenal grafts with enteric diversion of the pancreatic ductal secretions coupled with iliac vein provision of insulin (systemic-enteric technique) although the systemic-bladder technique endures as a preferred alternative in selected cases. In the early 1990s, a novel technique of venous drainage into the superior mesenteric vein combined with bowel exocrine diversion (portal-enteric technique) was designed and subsequently refined over the next $\geqslant$ 20 years to re-create the natural physiology of the pancreas with first-pass hepatic processing of insulin. Enteric drainage usually refers to jejunal or ileal diversion of the exocrine secretions either with a primary enteric anastomosis or with an additional Roux limb. The portal-enteric technique has spawned a number of newer and revisited techniques of enteric exocrine drainage including duodenal or gastric diversion. Reports in the literature suggest no differences in pancreas transplant outcomes irrespective of type of either venous or exocrine diversion. The purpose of this review is to examine the

literature on exocrine drainage in the new millennium (the purported "enteric drainage" era) with special attention to technical variations and nuances in vascularized pancreas transplantation that have been proposed and studied in this time period.

Key words: Pancreas transplantation; Portal-enteric drainage; Simultaneous pancreas-kidney transplant; Systemic-bladder drainage; Enteric conversion; Solitary pancreas transplant; Systemic-enteric drainage

Core tip: The history of vascularized pancreas transplantation largely parallels advances in surgical techniques. Prior to 1995, most pancreas transplants were performed with delivery of insulin to the iliac vein and diversion of the pancreatic ductal secretions to the urinary bladder (systemic-bladder technique). Starting in 1995, however, a seismic change occurred from bladder to bowel drainage of the pancreatic secretions that was spurred in part by the success of enteric conversion. In the new millennium, most pancreas transplants are performed as pancreatico-duodenal grafts with either iliac vein and bowel exocrine diversion (systemic-enteric technique) or portal-enteric drainage. With refinements in surgical techniques, exocrine drainage is no longer considered the "Achilles' heel" of pancreas transplantation.

El-Hennawy H, Stratta RJ, Smith F. Exocrine drainage in vascularized pancreas transplantation in the new millennium. *World J Transplant* 2016; 6(2): 255-271 Available from: URL: http://www.wjgnet.com/2220-3230/full/v6/i2/255.htm DOI: http://dx.doi.org/10.5500/wjt.v6.i2.255

INTRODUCTION

Since the inception of the International Pancreas Transplant Registry (IPTR) in 1984, data on > 48000 pancreas transplants has been captured in the ensuing 30 years[1]. There exist 3 major types of vascularized pancreas transplantation; simultaneous pancreas-kidney (SPK), sequential pancreas after kidney (PAK), and pancreas transplantation alone (PTA). Solitary pancreas transplants refer to the PAK and PTA types. They are usually analyzed together because of similar outcomes coupled with the fact that these procedures are performed in the absence of uremia. However, the state of kidney function is quite different; post-uremic in PAK compared to non-uremic in PTA. In the past 3 decades, the results of SPK transplantation have been superior to solitary pancreas transplantation although the disparity in outcomes has decreased over time. In the United States, solitary pancreas transplants (PAK-17%, PTA-9%) represent the minority of activity while 74% are characterized as SPK transplants[1-3].

In uremic patients with type 1 diabetes mellitus, SPK transplantation is a highly regarded treatment alternative because it addresses both kidney failure and diabetes[3]. The number of United States annual pancreas transplants reached a high of 1484 in 2004 and had dropped to < 1000 by 2014[1-3]. The number of annual pancreas transplants reported to the Eurotransplant Network has similarly declined in the past decade whereas annual activity in the United Kingdom has remained relatively stable and activity elsewhere in the world has increased[1-3]. In spite of declining numbers, outcomes have continued to improve and include higher risk groups such as African-Americans, patients with a phenotype suggesting "type 2 diabetes" and solitary pancreas transplant recipients[1-5]. Five year patient survival rates are now nearly 90% across all three transplant types and 10-year patient survival is > 70% in all three groups. Moreover, insulin independence is sustained at 5 years in 73% of SPK, 64% of PAK, and 53% of PTA recipients. The pancreas graft half-life is currently 10-15 years, which is amongst the lengthiest for extra-renal transplants[2].

Evolution in surgical techniques has characterized and paralleled the growth and development of pancreas transplantation. In late 1966 at the University of Minnesota, Kelly *et al*[6] reported the first human pancreas transplant. The initial case was an SPK transplant with a segmental pancreas graft implanted in the iliac fossa with ligation of the pancreatic duct. In the ensuing 13 cases performed between 1966 and 1973, however, Lillehei *et al*[7] transplanted a pancreatico-duodenal graft with either an external ostomy/cutaneous fistula or connection between the recipient bowel and graft duodenum for exocrine drainage. Consequently, optimal management of the pancreatic ductal secretions was identified as a controversy very early in the development of pancreas transplantation. In the late 1970s and early 1908s, partial or segmental pancreatic grafts (based on the body and tail of the pancreas) with pancreatic ductal ligation or occlusion were the preferred methods of controlling the pancreatic secretions[8,9]. During this developmental phase, exocrine drainage techniques were considered to be the "Achilles' heel" of pancreas transplantation. The introduction of bladder diversion of the exocrine secretions into clinical transplantation in the mid-1980s revolutionized the safety and improved the success of pancreas transplantation[10]. From this point in time onward, whole organ pancreaticoduodenal largely replaced segmental pancreas grafts as the preferred method of transplantation. However, segmental pancreas grafts remain the only surgical option in pancreas transplantation from living donors[9,11]. From 1988 to 1995, > 90% of pancreas transplants in the United States were whole organ pancreatic grafts with iliac vein and bladder exocrine diversion (systemic-bladder technique), usually using a trimmed segment of donor duodenum inclusive of the ampulla of Vater as a channel for drainage of the exocrine pancreas[12].

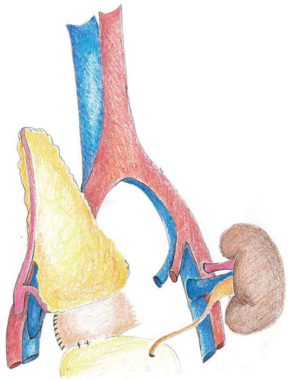

Figure 1 Technique of systemic-bladder drainage with creation of an anastomosis between the allograft duodenal segment and vesical dome of the recipient bladder.

To this day, there remains controversy regarding the optimal method for managing the pancreatic exocrine secretions. By review of data provided by the IPTR, it is evident that the overwhelming majority of pancreas transplants involve whole organ pancreatico-duodenal grafts with either bowel (systemic-enteric) or bladder diversion of the pancreatic ductal secretions coupled with systemic venous delivery of insulin[1,2]. However, starting in 1995, a seismic change from bladder to bowel exocrine diversion transpired coincident with improvements in immunosuppression, preservation techniques, diagnostic monitoring, general medical care, and the success and frequency of enteric conversion[13,14]. Enteric drainage usually refers to jejunal or ileal diversion of the exocrine secretions either as a direct anastomosis or in the presence of a defunctionalized Roux en y limb. By 1998, > 50% of SPK transplants were accomplished with bowel diversion and by 2003 this figure had risen to > 80% of cases in the United States although the systemic-bladder technique was still deployed in 50% of solitary pancreas transplants[13,15]. At present, pancreas transplantation with primary enteric exocrine drainage is performed in 90% of cases in the United States from 2010-2014 although the systemic-bladder technique is a reasonable alternative in selected cases and a preferred option at specific centers[1]. Roux limb diversion is performed in a minority of cases including 21% of SPK and 15% of solitary pancreas transplants[1].

To mimic the natural physiology of the endocrine pancreas, an innovative method of portal vein delivery of insulin (by anastomosing the donor portal vein to the recipient superior mesenteric vein for venous outflow) and bowel diversion of the exocrine secretions (portal-enteric technique) was pioneered in the early 1990s and refined over the past ⩾ 20 years[16,17]. At present, the proportions of enteric-drained cases with portal venous delivery of insulin are 22% in SPK, 11% in PAK, and 13% in PTA cases. Consequently, > 80% of bowel drained pancreas transplants in the United States are performed without a decompressing Roux limb of small bowel and with systemic (iliac or vena cava) venous delivery of insulin[1]. Although the promise of the portal-enteric technique has not been achieved, it has spawned a number of newer and revisited techniques of enteric exocrine drainage including duodenal or gastric diversion[18-32]. Previous reports have not shown any main variances in outcomes for bladder- or enteric-diverted pancreas transplants regardless of method of venous drainage[33-55]. Although one of the three described techniques is deployed in nearly all pancreas transplants at present, the prevailing viewpoint is that the most appropriate procedure to be used is best determined both by recipient and donor anatomy as well as the practicing surgeon's comfort level and experience. A number of previous excellent reviews have emphasized technical aspects of pancreas transplantation but few have been published in the past 6 years[52,56-64]. The purpose of this review is to examine the prevailing literature on exocrine drainage in the past 20 years (the purported "enteric drainage" era) with special attention to surgical techniques that have been introduced over time and with experience in pancreas transplantation.

Bladder drainage of the exocrine secretions (systemic-bladder technique)

Following the groundbreaking studies of Sollinger *et al*[65] and Nghiem *et al*[66] in the 1980s, bladder drainage with a donor duodenal segment became the preferred method of handling the pancreatic ductal secretions in pancreas transplantation until the mid- to late-1990s (Table 1)[67-74]. With this technique, the donor duodenum functions as an exocrine conduit and is anastomosed to the vesical dome either using a 2-layer hand sewn technique or a circular stapled anastomosis[75] (Figure 1). Bladder diversion gained wide acceptance owing to its safety, sterility, convenience, and ease of performance. In addition, bladder drainage enabled direct monitoring of the pancreatic secretions in the urine, permitted a direct approach for trans-cystoscopic biopsy of either the allograft duodenum or pancreatic parenchyma, and provided easy diagnosis and management of anastomotic problems with cystography and urethral catheter drainage[76]. Similar to the use of low pressure cystography to diagnose urine leaks following kidney transplantation, cystography facilitated the detection of anastomotic or duodenal segment leaks following pancreas transplantation with bladder drainage. Prolonged urethral catheter drainage in effect decompressed the anastomosis and enabled control of the exocrine leakage while promoting healing.

Bladder diversion of the pancreatic ductal secretions avoided the inherent bacterial contamination (*e.g.*, peritonitis) that occurred with bowel diversion leaks, contamination that lead to substantial morbidity and even mortality[77]. Consequently, it was associated with a lower risk of intra-abdominal infections and sepsis (because of the sterility of the lower urinary tract) compared to previous techniques of either segmental or whole organ pancreas transplantation with enteric

Table 1 Bladder drainage: Literature review

Center, authors, year, ref., study design, and follow-up	Number and type of transplant	Complications	Enteric conversion	1 yr patient survival	1 yr pancreas graft survival
University of Minnesota, Hakim *et al*[67], Retrospective, mean follow-up 55 mo	*n* = 425 with bladder drainage, SPK - 53%; PAK - 23%; PTA - 24%	Duodenal stump complications - 20%; Duodenal leak - 10%; Recurrent UTI - 9%; Hematuria - 6% (19% required surgery); Bladder stone - 0.5%; CMV duodenitis - 1.5%; Graft loss - 9%	16%	ND	ND
University of Nebraska, Stratta *et al*[68], Retrospective, mean follow-up 44 mo	*n* = 201 with bladder drainage	Duodenal stump complications - 19%; Duodenal leak - 6% (all required surgery); Hematuria - 13% (30% required surgery); CMV duodenitis - 3%	13%	94%	80%
University of Wisconsin, Sollinger *et al*[69], Retrospective	*n* = 500; 338 with bladder drainage, 112 with enteric drainage	Duodenal leak - 15.4%; Graft Thrombosis - 0.7%; Hematuria - 3%; UTI - 52.5%; Graft loss - 13%; Death with a functioning graft - 8%	24%	96.4%	87.5%
The Ohio State University, Henry *et al*[70], Retrospective, mean follow-up 16 mo	*n* = 300 with bladder drainage	CMV - 2%; Intra-abdominal infection - 15%; Wound infection - 8%; Rejection - 55%; Hematuria - 14%; Bladder leak - 10%	4%	92%	82%
University of Maryland, Del Pizzo *et al*[71], Retrospective, mean follow-up 35 mo	*n* = 140; SPK - 68%, PAK - 25%, PTA - 7%	Urological complication - 50%; Bladder stone - 10%; Duodenitis - 11%; Retained foreign bodies - 12%; Bladder tumor - 2%	21%	ND	ND
Mayo Clinic Rochester, Gettman *et al*[72], Retrospective, mean follow-up 44 mo	*n* = 65	UTI - 59%; Hematuria - 26%; Allograft pancreatitis - 19%; Duodenal leaks 17%, (all required surgery); Ureteral lesions - 9%	ND	92%	86%
Hospital Universitario Spain, Medina Polo *et al*[73], Retrospective, mean follow-up 52 mo	*n* = 107, all SPK, bladder drainage in 58, enteric drainage in 49	UTI - 72%; Hematuria - 20%; Bladder stone - 8%; Reflux pancreatitis - 48%	10%	92.7%	78.1%
University of Nebraska, Sudan *et al*[74], Retrospective, mean follow-up 60 mo	*n* = 57, all with bladder drainage	UTI - 15%; Dehydration - 20%; Rejection - 1%	ND	95%	88%

SPK: Simultaneous pancreas-kidney; PAK: Pancreas after kidney; PTA: Pancreas transplantation alone; UTI: Urinary tract infection; CMV: Cytomegalovirus; ND: Not determined/no data.

diversion. In addition, bladder drainage also provided a means to monitor for pancreas allograft rejection by measuring urinary parameters such as amylase, insulin or cytology[78]. However, bladder diversion created an abnormal linkage between the allograft pancreas with intervening donor duodenal conduit and the urinary bladder, which resulted in a number of unique metabolic, urologic, infectious, and miscellaneous complications. Disadvantages and advantages of bladder diversion are specified in Table 2.

With bladder drainage, anastomotic bleeding could be easily diagnosed by the presence of hematuria and usually managed non-operatively with urethral catheter drainage, alkalinization of the urine, administration of blood products, and correction of coagulation parameters. In refractory or persistent cases of hematuria secondary to anastomotic bleeding, however, administration of octreotide, bladder clot removal by cystoscopy with direct fulguration of bleeding sites, or enteric conversion might be indicated. Rates of hematuria are noted in Table 3.

In addition, bladder drainage resulted in obligatory fluid (up to 1-2 L/d of pancreatic exocrine secretions) losses and urinary bicarbonate wasting with consequent changes in the acid-base balance and enzyme-free environment of the lower genitourinary tract. Many patients were prone to dehydration, metabolic acidosis, erythrocytosis, and orthostasis, particularly in the setting of severe autonomic neuropathy secondary to diabetes. For these reasons, the length of donor duodenum transplanted with the pancreas was progressively shortened over time in an attempt to minimize protein

Table 2 Advantages and disadvantages of bladder drainage of the exocrine secretions

Advantages
Safety
Reduced infection rate because of relative sterility of lower urinary tract
Control of anastomosis by urethral catheter decompression
Technical considerations
Relative simplicity because of favorable anatomic location of bladder
Bladder mobilization permits tension-free, multi-layer anastomosis
Bladder vasculature and urothelium promote healing
Direct access to exocrine secretions for monitoring pancreas allograft function
Detection of rejection by urinary parameters (amylase, lipase, insulin, cytology)
Cystoscopic access for either duodenal or pancreatic parenchymal biopsy
Disadvantages
Urologic problems
Hematuria, dysuria, cystitis, urethritis, urethral stricture or disruption, balanitis
Increased risk of lower urinary tract infections, stone formation, and urine leaks (either from bladder or duodenum)
Metabolic and volume problems
Dehydration, orthostasis, constipation, erythrocytosis
Metabolic acidosis
Miscellaneous problems
Reflux-associated hyperamylasemia or pancreatitis
Transitional cell (urothelial) dysplasia
Need for enteric conversion for refractory, persistent, or recurrent problems
Medication burden (massive amounts of bicarbonate supplementation)

and bicarbonate loss from the allograft duodenal mucosa. In some patients, intractable, recurrent, or refractory complications would occur, which were then treated with open conversion from bladder to bowel diversion (enteric conversion) (Figure 2). Paradoxically, the success of "enteric conversion" paved the way for renewed enthusiasm in primary enteric drainage. Enteric conversion frequency ranged from 10% to 40% (Table 3)[79-86]. Several authors reported that enteric conversion resulted in superb long-term graft function coupled with marked symptom improvement even when performed several years following SPK transplant[84,87,88]. Despite urological morbidity and the finite risk of enteric conversion, 5-year actuarial patient and graft survival rates with bladder drainage were excellent and most complications could be managed with conservative (non-operative) therapy.

For diabetic patients with neurogenic bladders, episodes of reflux pancreatitis (managed with urethral catheter drainage) and recurrent urinary tract infections were not uncommon. In the setting of urinary tract infection, the pH of urine would become more acidic, which led to pancreatic enzyme activation and a variety of complications including hematuria, duodenitis, cystitis, urethritis, urethral stricture or disruption, and balanitis. In severe cases, some investigators even reported reduction cystoplasty and bladder re-anastomosis in an attempt to control persistent urologic problems.

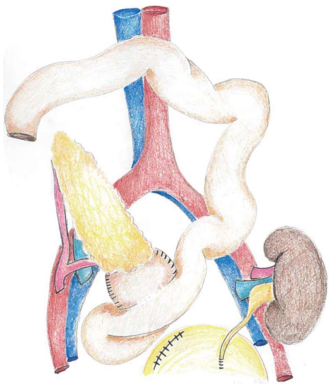

Figure 2 Technique of conversion from bladder to enteric exocrine drainage (enteric conversion) for persistent metabolic, urologic, or other problems.

Most patients required daily oral sodium bicarbonate supplementation and some received chronic suppressive antibiotics to limit the morbidity attributable to the abnormal physiology. Alternative treatments to reduce exocrine drainage side effects included the use of oral pancreatic enzymes or long-acting somatostatin analogues. Other late complications comprised duodenal leaks, stone formation, and the risk of urothelial dysplasia.

At present, bladder drainage remains an important option in selected cases, such as those in which pancreas graft quality in general or viability of the allograft duodenum in particular is suspect. In cases of duodenal ischemia or severe reperfusion injury, the bladder anastomosis can be performed by invaginating the duodenum into the bladder in order to minimize leaks (Figure 1). In addition, if the recipient has severe adhesions from multiple previous intra-abdominal procedures or sclerosing peritonitis, then a bowel anastomosis may be risky. Moreover, until recently, bladder drainage was preferred by many centers in solitary pancreas transplantation (PAK, PTA) because of the increased incidence of acute rejection (early and late) in this setting coupled with the established difficulty in the timely detection of pancreas rejection in the absence of either a urinary marker (with bladder drainage) or serum creatinine monitoring (with an SPK transplant).

A number of centers have reported excellent long-term outcomes in pancreas transplantation with the systemic-bladder technique[9,52,69,70,74,80,89]. For a period of time, the bladder drainage technique was also associated with lower incidences of thrombosis, early technical complications, and graft loss in IPTR reports compared to enteric drainage[12,13,15]. Consequently, many new centers (including those in developing countries) elected to embark on their experience in pancreas transplantation with systemic-bladder drainage owing to its technical simplicity and purported lower technical complication rate. In some instances, centers have adopted a 2-stage approach in which primary bladder diversion is followed by planned enteric conversion in order to avoid the immediate complications of primary enteric diversion

Table 3 Enteric conversion: Literature review

Center, authors, year, ref., and study design	Overall rate (%)	Urologic indications # (%)	Metabolic indications # (%)	Pancreatitis/other indications # (%)	Operative complications # (%)
University of Wisconsin, Van der Werf *et al*[79], Retrospective	95/449 (21%)	90 (95)	1 (1)	4 (4)	21 (22)
Sollinger *et al*[80], Retrospective	160/390 (41%)	93 (58)	1 (0.6)	47 (29)	ND
University of Minnesota, West *et al*[81], Retrospective	79/500 (16%)	43 (54)	26 (33)	15 (19)	12 (15)
University of Nebraska, Sindhi *et al*[82], Retrospective	25/195 (13%)	7 (28)	18 (72)	0	3 (12)
University of Barcelona, Spain, Fernandez-Cruz *et al*[83], Retrospective	16/74 (22%)	0	0	16 (100)	Death 1 (6); Wound infection 2 (12); Anastomotic leak 3 (18)
Leiden University Medical Center, Netherlands, van de Linde *et al*[84], Retrospective	51/ND	39 (76)	23 (45)	Pancreatitis 2 (3); Fistula 1 (1)	UTI 7 (13); Minor bleeding 1 (0.5); Phlebitis 1 (0.5); Paralytic ileus 1 (0.5); Relaparotomy 2 (3)
University of Cincinnati, Kaplan *et al*[85], Retrospective	26 (32%)	13 (50)	13 (50)	0	Death 1 (3); Anastomotic bleeding 1 (3)
Beaumont Hospital, Ireland, Connolly *et al*[86], Retrospective	6/ND	3 (50); 2 hematuria; 1 UTI	3 (50)	ND	Pulmonary edema 1 (16)

UTI: Urinary tract infection; ND: Not determined/no data.

(intra-abdominal infections, early graft loss) and the long-term metabolic and urologic problems related to bladder diversion[84,87]. For example, Marang-van de Mheen *et al*[87] routinely used a two-step approach in SPK transplant; primary bladder diversion followed by planned enteric conversion (Figure 2). They found that this approach resulted in urological complication rates similar to bowel-drained grafts with subsequent excellent survival rates. Conversions were performed by separating the graft duodeno-cystostomy, then re-establishing continuity and diversion by a side-to-side recipient jejunal-graft duodenal-anastomosis either without (most commonly) or with a diverting Roux limb.

The drawback to planned conversion is loss of urinary amylase as an immunological biomarker, especially in PAK and PTA recipients. In SPK transplant recipients, however, the renal allograft and serum creatinine can still be monitored as a biomarker for allograft rejection. Contrary to previous IPTR reports, however, there is no longer a survival, technical complication, or immunological monitoring advantage associated with bladder drainage, so the practice of "intentional" enteric conversion has been largely supplanted by primary bowel diversion[1-3].

Bowel diversion of the pancreatic ductal secretions (systemic-enteric technique)

Initial attempts at bowel exocrine diversion in the 1970-80s were fraught with complications including intra-abdominal sepsis and mortality because of limitations in preservation techniques, immunosuppression, diagnostic monitoring, and general medical care. However, the introduction of University of Wisconsin solution (that was initially developed as a pancreas preservation solution), tacrolimus, mycophenolate mofetil, ganciclovir, newer monoclonal and polyclonal antibody agents, biopsy-directed surveillance, and improvements in general medical and critical care (including higher resolution computerized tomographic scanning, more effective antibiotics, and the development of safe and more sophisticated percutaneous interventions) were pivotal in the re-emergence of primary bowel drainage as an alternative to bladder drainage. During the transitional phase from primary bladder to enteric drainage in the late 1990s to early 2000s, several studies (both prospective and retrospective) reported comparable outcomes with either technique although primary enteric drainage was not associated with the requisite long-term metabolic and urologic complications unique to bladder drainage (Table 4)[90]. In addition, the success of enteric conversion corroborated the safety and feasibility of primary enteric drainage following pancreas transplantation, which in essence eliminated the need for re-operation in 10%-40% patients with urinary bladder diversion. Moreover, bowel diversion of the pancreatic ductal secretions was much more acceptable to the medical community at large because it was more "physiologic" and logical to drain the pancreatico-duodenal secretions into the small bowel. Disadvantages and advantages of primary bowel diversion are noted in Table 5.

Potential risk variables for early bowel leaks include poor characteristics of the allograft duodenum (related to donor hemodynamic instability or trauma), ischemia-reperfusion and preservation injury (related to preservation solution as well as warm and cold ischemia), complications with either the vascular or bowel anastomosis because of adhesions or other technical issues, higher donor or recipient age or body mass index, peritoneal dialysis, and deconditioning in the recipient. In

Table 4 Bladder *vs* enteric drainage: Literature review

Center, authors, year, ref., and study design	Number and type of transplant	Complication/enteric conversion	Acute rejection/ graft loss	Reoperation and readmissions	1 yr patient survival	1 yr pancreas (and kidney) graft survival
University of Maryland, Kuo *et al*[35], Retrospective	23 SPK ED	ED: Fewer UTIs and urologic complications	ND	ND	ED 100%; BD 96%	ED 88%; BD 91%
University of Chicago, Newell *et al*[33], Retrospective	SPK; ED 12; BD 12	Acidosis and dehydration less with ED ($P < 0.005$); Hematuria; BD 25%; ED 0%; No anastomotic leaks in either group; No intra-abdominal infection in either group; Enteric conversion: 33%	ND	BD: 4 patients underwent enteric conversion	BD 100%; ED 83.3%	BD 91.7%; ED 83.3%
University of Wisconsin, Sollinger *et al*[80]; Retrospective	1000 SPK; BD 390; ED 610	Pancreas graft thrombosis; BD 2.3% ED 3.6%; Infection; BD 1.8% ED 0.8%; Pancreatitis; BD 1.3% ED 0.5%; Pancreatic leak BD: 12% ED: 5% ($P = 0.06$)	Kidney rejection; BD 29%; ED 19%; Pancreas rejection; BD 12.1%; ED 5.4%	ND	Similar in both groups	Similar kidney, and pancreas graft survival in both groups
Pirsch *et al*[37], Retrospective	48 BD; 78 ED	Opportunistic infections; ED: 12% BD: 31% ($P = 0.002$); CMV; BD 21% ED 4% ($P = 0.04$); Fungal infection; BD 17% ED 4%; UTI BD 63% ED 20% ($P = 0.0001$)	Kidney rejection; BD 38%; ED 30%; Steroid-resistant rejection; BD 19%; ED 17%			
University of Washington, Friedrich *et al*[90], Retrospective	34; ED 17; BD 17	ED 41%; BD 53%; Enteric conversion: 5%	ED 29%; BD 24%	Readmissions: ED 41%; BD 47%	ND	ND
University of Tennessee-Memphis, Stratta *et al*[41], Prospective	BD 16; ED 16	UTI BD 50% ED 19%; Urologic complications; BD 25% ED 12.5%; Dehydration BD 100% ED 44%	BD 44%; ED 31% P = NS	BD 25%; ED 25%; Readmissions: BD 2.6 ± 1.8; ED 1.75 ± 1.2	BD 88%; ED 94%	Kidney survival; BD 92%; ED 93%; Pancreas survival BD 81%; ED 88%
Albert Einstein Medical Center, Bloom *et al*[34], Retrospective	71 SPK; BD 37; ED 34	Dehydration BD 34% ED 3.4%; Acidosis BD 41% ED 0% Pancreatitis BD 40% ED 3.4% UTI BD 71% ED 27% ($P < 0.005$) Enteric conversion: 19%	BD: 13.5%; ED: 14.7%		Similar between groups	Pancreas allograft survival was similar between groups
Emory University, Pearson *et al*[36], Retrospective	SPK; BD 55; ED 11	BD; UTI 78%; Hematuria 27%; Dehydration 38%; ED no complication				
University of Pittsburgh Corry *et al*[43], Retrospective	BD 44; ED 199	Overall BD 41% ED 26%; Anastomotic bleeding; BD 16% ED 5%; Fistula BD 14% ED 6%		BD 24%; ED 16%		BD 44%; ED 69%
Toronto General Hospital, Cattral *et al*[40], Retrospective	SPK; BD 20; ED 20	UTI: Similar in both groups; CMV infections were significantly less in the ED group	BD 37%; ED 15%; ($P = 0.20$)	BD 1 patient to ligate an arteriovenous fistula in the pancreas graft; ED 4 patients; (bleeding in one, partial wound dehiscence in one, negative laparotomy in two)	BD 95%; ED 100%	Kidney graft survival; BD 95%; ED 100%; Pancreas graft survival; BD 95%; ED 100%

Wake Forest University, Stratta *et al*[46], Retrospective	297 SPK; SE 171 (58%); PE 96 (32%); SB; 30 (10%)	No differences were seen in surgical complications including pancreas thrombosis; Infections: SE 49%; PE 85%; BD 63%	SE 19%; PE 26%; BD 30%	Readmissions: SE 61%; PE 63.5%; BD 63%	SE 97%; PE 99%; BD 97%	Kidney; SE 94%; PE 98%; BD 93%; Pancreas; SE 87%; PE 92%; BD 87%

BD: Bladder drainage; ED: Enteric drainage; SB: Systemic-bladder; SE: Systemic-enteric; PE: Portal-enteric; UTI: Urinary tract infection; CMV: Cytomegalovirus; ND: Not determined/no data.

Table 5 Advantages and disadvantages of enteric drainage of the exocrine secretions

Advantages
Safety
Lower rates of urinary tract infections and urologic complications
More "physiologic"; fewer metabolic and volume problems
Fewer readmissions
Technical considerations
Treats exocrine insufficiency (in patients following total pancreatectomy or in patients with cystic fibrosis
Avoidance of need for enteric conversion; lower relaparotomy rate
Can be used with either systemic or portal venous outflow
Disadvantages
Safety
Higher incidence of leakage of pancreatic enzymes, pancreatitis, peri-pancreatic fluid collections
Higher incidence of intra-abdominal abscess, peritonitis, sepsis
Anastomotic leaks, GI bleeding
Increased risk of wound infections, wound healing problems (contaminated case with GI tract breach)
Technical considerations
Selective need for enterolysis or diverting Roux en y limb
Loss of direct access to anastomosis and allograft for diagnosis and treatment
Miscellaneous problems
Inability to directly monitor exocrine secretions

GI: Gastrointestinal.

addition, late intra-peritoneal infectious complications may occur in bowel-drained transplants[91-93]. In more recent series, however, the incidence of and outcomes associated with surgical complications following enteric diversion are similar to those following bladder drainage and the rates of early graft loss with either technique are comparable[1-3,52,62-64]. The incidence of surgical complications is also similar by type of transplant (SPK compared to solitary pancreas transplantation)[1-3]. Leaks from the allograft duodenum have been reported to occur in 5%-20% of bladder-drained and 5%-8% of bowel-drained pancreas transplants[9,33-52,67-73,80,91-95]. Increasing experience with enteric exocrine drainage is likewise associated with a decreased rate of technical complications[9,38,80,96-103].

Because of lingering concerns regarding the safety of enteric drainage based on historical precedent, the use of diverting Roux limbs was not uncommon in the late 1990s and many centers continued to direct the head and duodenum of the pancreas allograft toward the pelvis just in case "bladder conversion" was required.

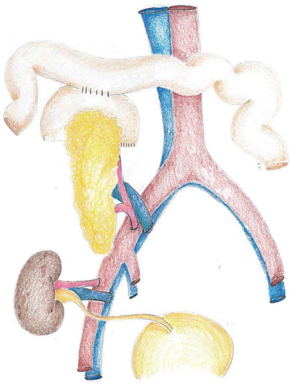

Figure 3 Technique of systemic-enteric drainage with side-to-side anastomosis between allograft duodenum and recipient small bowel.

Techniques that incorporated diverting Roux limbs with temporary external ostomies were also described in an attempt to permit direct endoscopic access and provide decompression of the enteric anastomosis and allograft duodenum[23]. However, with time and experience, most pancreas transplant surgeons evolved to directing the head and duodenum of the pancreas allograft away from the pelvis to simplify the enteric anastomosis, which was typically performed side-to-side between the allograft duodenum and either the recipient proximal jejunum or ileum without a Roux limb (Table 6)[104-108] (Figure 3). Safe techniques of using either the circular or linear stapler were described to simplify the enteric anastomosis[109,110]. If a Meckel's diverticulum was identified, some surgeons would excise the diverticulum and then use this site for the bowel anastomosis[111]. Placement ipsilateral of the kidney and pancreas allografts in SPK transplantation was also introduced to limit the dissection and expedite the procedure[106]. A potential side benefit of enteric drainage was elimination of the need to construct a duodenal segment, which meant less dissection during back bench preparation, less risk of devascularizing the head of the pancreas or duodenum by collateral disruption, and less time spent with the pancreas *ex vivo* and exposed. By transplanting the pancreas as a complete pancreatico-duodenal graft, collateral circulation to the pancreas and duodenum was preserved. Maintaining full duodenal length also facilitated numerous possibilities for performing the bowel anastomosis in the recipient. In addition, the distal donor duodenum could be used as access for stapler

Table 6 Systemic-enteric drainage: Literature review

Center, authors, year, ref., and study design	Number and type of transplant	Complications	Readmission/reoperation/ length of stay	1 yr patient survival	1 yr kidney/ pancreas survival
Medical University of South Carolina, Douzdjian *et al*[105], Retrospective	ED 16; BD 26	Recurrent/persistent urinary complications BD 46% ED 6% (P = 0.01); Dehydration BD 27% ED 6% (P = 0.05); Pancreatitis BD 8% ED 6% (P = NS); Wound infection BD 12% ED 19% (P = 0.5)	Readmissions BD: 1.7 ± 1.5; ED 1.2 ± 1.2 d (P = 0.2) Reoperations BD 23% ED 0 (P = 0.04); Length of stay BD: 12.9 ± 5.6 ED: 20.4 ± 9.6 d, P = 0.007	BD 96%; ED 94%; P = 0.6	Kidney BD 85%; ED 87%; Pancreas BD 90%; ED 85% (P = 0.6)
Institut de Malaties Digestives, Spain, Heredia *et al*[94], Retrospective	205 SPK; ED 97	Duodenal leaks: (n = 11); Acute rejection (n = 6); CMV infection (n = 3); Technical failure (n = 2); Death: (n = 2) as a consequence of sepsis	Reoperation for duodenal leak: Roux-en-Y technique: (n = 3) DJ technique: (n = 2) Transplantectomy: (n = 6)	ND	ND
Toronto General Hospital, Spetzler *et al*[95], Retrospective	Total 284; 191 SPK (67.3%); 93 PAK (32.7%)	Duodenal leak (incidence 6.3%), 12 (67%) occurred within the first 100 d after transplantation	Six grafts (33%) were rescued by duodenal segment resection;	ND	ND
Innsbruck University Hospital, Austria, Steurer *et al*[92], Retrospective	40 ED	Intra-abdominal infection - 11 (27.5%)	Reoperation for intra-abdominal infection Pancreatectomy: 5 Necrosectomy and drainage: 5 Percutaneous drainage: 1	ND	ND
Ruhr-University Bochum, Germany, Ziaja *et al*[104], Retrospective	30 SPK	Perioperative mortality 3.3%	Early relaparotomy was required in 20%; pancreatectomy in 10%	ND	ND
Indiana University, Fridell *et al*[106], Retrospective	49; SPK; All ED	Death: (n = 2) (1 patient died from multi-system organ failure and a second from graft *vs* host disease); Pancreatic graft failures: (2); renal graft failure: (1)	Relaparotomies: (n = 5) bowel obstructions: (2) anastomotic leak: (1) ureteral stricture: (1)	96%	Kidney 94%; Pancreas
University of Pittsburgh, Corry *et al*[107], Retrospective	104 SPK	Graft loss in 6 patients, Death in one patient	Splenic artery hemorrhage: (1) ND	98%	92%; Kidney 95%, Pancreas 83%
University of Maryland, Bartlett *et al*[108], Prospective	27; Solitary pancreas transplants	One graft lost to acute rejection in the tacrolimus group because of patient noncompliance	ND	ND	90% in patients receiving tacrolimus, 53% in patients receiving cyclosporine (P = 0.002)

BD: Bladder drainage; ED: Enteric drainage; CMV: Cytomegalovirus; ND: Not determined/no data; DJ: Duodeno-jejunostomy.

placement to perform the enteric anastomosis[109,110].

Bowel drainage of the pancreatic ductal secretions (portal-enteric technique)

To address the unusual anatomy of pancreas transplantation, Gaber *et al*[16] introduced a new technique in which an anterior intraperitoneal approach to the recipient superior mesenteric vein (SMV) was deployed for venous drainage. This procedure was later modified to a "retroperitoneal" approach to the SMV by Boggi' s group in Pisa. Both of these techniques combined bowel drainage of the pancreatic ductal secretions with portal venous delivery of insulin (portal-enteric technique)[16,17,112,113]. Alternative methods to achieve portal venous delivery of insulin have been reported using either the recipient portal vein directly, the inferior mesenteric vein, or splenic vein. However, in most cases, "portal venous" drainage usually infers that the allograft has a vertical orientation with the body and tail directed towards the pelvis, the head and duodenum directed cephalad, and the recipient SMV as the site for the venous anastomosis[18-22] (Figure 4). The bowel anastomosis is most commonly performed to a bowel loop that is not excluded from the transit of intestinal contents[4,16,17,33,39-42,44-46,49-53,112-121]. Alternatively, the allograft duodenum can be connected directly into the native stomach or duodenum, to a diverting Roux limb without or with a venting jejunostomy, or to an omega loop[23-32,122] (Table 7). Utilizing the native stomach or duodenum affords straightforward access to the allograft duodenum and pancreas for biopsy and surveillance by endoscopic techniques and also expands the possibilities for exocrine drainage sites, particularly in cases of pancreas retransplantation (Table 8)[25-32,123]. However, because up to 5%-10% of transplanted pancreata are at risk for early technical failure that may lead to leaks,

Table 7 Portal-enteric drainage: Literature review

Center, authors, year, ref., study design and follow-up	Number and type of transplant	Complications	Readmissions, reoperation, length of stay	1 yr patient survival	1 yr kidney and pancreas graft survival
University of Tennessee, Stratta *et al*[122], Retrospective, mean follow-up 3 yr	PE 126; 90 SPK; 18 PAK; 18 PTA; Era 1 (10/90-6/95); Era 2 (7/95-5/98); Era 3 (6/98-12/99)	In 3 successive eras, rates of acute rejection were 63%, 33%, and 39%, respectively; rates of major infection were 60%, 43%, and 44%, respectively	In 3 successive eras, rates of relaparotomy were 47%, 31%, and 33%, respectively; rates of thrombosis were 20%, 7%, and 6%, respectively. Mean length of stay: 12.5 d	In 3 successive eras, patient survival was 77%, 93%, and 100%, respectively	In 3 successive eras, kidney graft survival was 77%, 93%, and 94%, respectively; pancreas graft survival was 60%, 83%, and 83%, respectively
Università di Pisa, Italy, Boggi *et al*[17], Retrospective, mean follow-up 21 ± 20 mo	PE 110	10 grafts were lost; 3 acute rejection, 2 chronic rejection, 2 venous thrombosis, 2 deaths, 1 late thrombosis (6 mo). Incidence of pancreas acute rejection was 6%	Relaparotomy rate was 13.6%; Mean length of stay was 26 ± 14 d; One month readmission rate was 13%	98%	Pancreas graft survival was 91%
University of Chicago, Bruce *et al*[116], Retrospective, mean follow-up 16 mo	PE 70	Pancreas graft losses: Thrombosis (3), acute rejection (5), late duodenal perforation (2)	Total 1st year hospitalization: 37 ± 28 d; Relaparotomy in 14 (70%)	88%	Kidney 78%; Pancreas 79%
Louisiana State University, Zibari *et al*[23], Retrospective, mean follow-up 25 mo	PE 21	Postoperative Bleeding in 4, wound infections in 4, acute rejection in 9, pancreas graft loss in 2	Mean length of stay was 16 d	100%	Kidney 90%; Pancreas 90%
Wake Forest Baptist Medical Center, Rogers *et al*[4], Retrospective, mean follow-up 6 ± 3 yr	202; SPK 162, PAK 35, PTA 5; PE 179; SE 23	Thrombosis rate was 8%; acute rejection rate was 28%; major infection rate was 50%	Mean length of stay was 13 d; Relaparotomy rate was 38%	Overall patient survival was 87%; one-year patient survival was 97%	Overall kidney and pancreas graft survival rates are 76% and 65%; death-censored graft survival rates are 84% and 72%, and one year graft survival rates are 94% and 88%, respectively
Monash Medical Centre, Victoria, Australia, Kave *et al*[118], Retrospective, mean follow-up 2 yr	SB 37; PE 27	Pancreas graft thrombosis rates SB 10.8%, PE 7.4% (*P* = NS)		Two-year patient survival was SB 94.3% *vs* PE 96.0%	Two year kidney (SB 89.2% *vs* PE 85.2%); pancreas (SB 77.9% *vs* PE 71.4%)

SB: Systemic-bladder; SE: Systemic-enteric; PE: Portal-enteric.

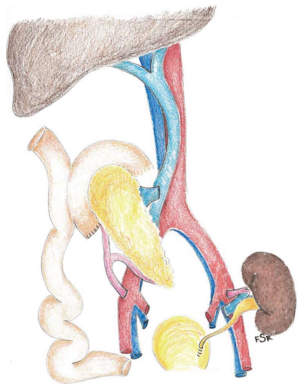

Figure 4 Technique of portal-enteric drainage with side-to-side anastomosis between allograft duodenum and small bowel; this technique is also amenable to using the native duodenum or stomach for exocrine diversion.

many centers are reluctant to perform enteric diversion either to the native stomach or duodenum. Following reperfusion of the transplanted pancreas, if the allograft duodenum does not appear well vascularized, bowel drainage with creation of a diverting Roux limb may be preferred to bypass the enteric stream and promote healing even though this procedure mandates an additional bowel anastomosis.

Although the rate of bleeding at the may be higher, some surgeons prefer to use either a circular or linear stapling device to create the bowel anastomosis[109,110]. However, most commonly, the connection between the allograft duodenum and recipient small bowel is performed using a 2-layer hand sewn technique that comprises a running continuous inner layer of interlocking absorbable suture coupled with an interrupted seromuscular outer layer of simple interrupted non-absorbable sutures to create a "watertight" and hemostatic closure[121]. The bowel anastomosis can be located anywhere between the distal ileum and native stomach although most commonly is performed as a primary side-to-side connection to the proximal jejunum (Figure 4). Other methods of reconstruction may include either an end-to-side or end-to-end anastomosis between the allograft duodenum and recipient gastrointestinal tract. When using portal-enteric drain-

Table 8 Portal-duodenal/gastric drainage: Literature review

Center, authors, year, ref., and study design	Number and type of transplant	Complications	Readmissions and reoperations	1 yr patient survival	1 yr pancreas survival
New York Medical College, Westchester Medical Center, Gunasekaran *et al*[28], Retrospective	DJ: 36; DD: 21; stapled 14, hand-sewn 7	Thrombosis: None in DJ, 2 in DD (P = NS); Enteric leak and small-bowel obstruction: 3 in DJ, 2 in DD (P = NS); Gastrointestinal bleeding: None in DJ, 4 in DD (P = 0.015)	ND	94% with DJ, 95% with DD	89% with DJ, 86% with DD
Louisiana State University, Shokouh-Amiri *et al*[27], Retrospective	Group 1: Allograft jejunum to stomach, n = 30; Group 2: Allograft duodenum to jejunum with Roux-en-Y venting jejunostomy, n = 30	In Group 1: Pancreatectomy in 3, CMV in 7, acute rejection in 4, death in 3; In Group 2: Pancreatectomy in 1, CMV in 2, acute rejection in 6, death in 2 (all P = NS)	Major complications: 4 in group 1, 10 in group 2	94% in group 1, 96% in group 2	85% in group 1, 83% in group 2
Bandeirantes Hospital, Sao Paulo, Brazil, Perosa *et al*[30], Retrospective	43 PAK, 10 PTA with DD	Thrombosis in 5 (9%); 4 additional pancreas graft losses (including 2 deaths with functioning grafts); Acute rejection in 9 (17%); major infection in 24 (45%)	Readmissions: Mean 1.1; Mean length of hospital stay: 11.8 d; Reoperations in 9 (17%)	96%	83%
University Hospital Bochum, Germany, Walter *et al*[31], Retrospective	DD in 125 (64% with portal outflow); DJ in 116 (12% with portal outflow)	GI bleeding in 14 with DD, 4 with DJ; Thrombosis in 5 with DD, 18 with DJ (P = 0.002); Acute rejection in 29% in DD *vs* 31% in DJ	2 anastomotic leaks with DD, 6 with DJ; Pancreatectomy in 14 with DD, 21 with DJ; Early relaparotomy in 42% DD *vs* 48% DJ, all P = NS	96% in both groups	82% with DD, 78% with DJ
Oslo University Hospital, Rikshospitalet, Norway, Horneland *et al*[32], Retrospective	20 SPK, 17 PTA, 3 PAK with DD (n = 40); 30 SPK 7 PTA, 3 APK with DJ (n = 40); In sequential eras	Thrombosis in 13% DD *vs* 5% DJ; Acute rejection in 23% DD *vs* 28% DJ, both P = NS	Reoperations in 40% DD *vs* 30% DJ; Mean length of hospital stay 19 d DD *vs* 16 d DJ, both P = NS	97.5% DD *vs* 92.5% DJ	Overall pancreas survival was 80% with DD, 87.5% with DJ (P = NS)
Scientific-Research Institute of Sklifosovsky, Moscow, Russia, Khubutia *et al*[123], retrospective	Group 1: 15 DJ; Group 2: 17 DD	Acute reject ion in 13% DJ *vs* 12% DD; Major infections in 20% DJ *vs* 6% DD, both P = NS	Surgical complications in 20% DJ *vs* 23.5% DD, P = NS	93% DJ *vs* 94% DD	Pancreas survival 93% DJ *vs* 94% DD; kidney survival 93% DJ *vs* 88% DD

DD: Duodeno-duodenostomy; CMV: Cytomegalovirus; ND: Not determined/no data; DJ: Duodeno-jejunostomy; NS: Not significant.

age, the recipient ileum can be anastomosed to the distal graft duodenum whereas the recipient jejunum can be anastomosed to the proximal graft duodenum. We prefer the former technique with the location of the bowel anastomosis on the posterior aspect of the 3rd or 4th portion of the graft duodenum to promote dependent drainage of the atonic, denervated graft duodenum when the patient is either in the erect or supine position[121]. Anastomotic length can be variable but usually ranges from 3-5 cm.

Unlike bladder drainage, however, anastomotic bleeding with enteric drainage is more occult and harder to diagnose in the absence of gastric, duodenal, or extreme proximal jejunal diversion or in the absence of a diverting jejunostomy. Because most enteric anastomoses are performed in the middle third of the gastrointestinal tract, endoscopic confirmation and treatment are not available. Consequently, the true incidence of anastomotic bleeding with enteric drainage is probably under-reported and the severity may be under-appreciated because of other causes of anemia in the immediate post-operative period. Fortunately, most cases are self-limited and respond to supportive measures such as decompression of the gastrointestinal tract, administration of blood products, and correction of coagulation parameters. In cases of persistent and significant lower (or rarely upper) gastrointestinal bleeding, administration of octreotide may be helpful by inducing vasoconstriction. Rarely, re-operation with revision of the enteric anastomosis (with or without Roux limb diversion) may be indicated for anastomotic bleeding. For severe gastrointestinal bleeding that occurs more than one week post-transplant, however, one must not assume it is secondary to anastomotic bleeding. In this setting, it is imperative to rule out a leaking pseudoaneurysm, which is best diagnosed and treated with angiographic techniques[124].

When using the retroperitoneal approach to the SMV for portal-enteric drainage, in order to perform an anastomosis to the small bowel, one must make a window in the mesentery of the right colon. Bowel drainage can then be accomplished without or with a diverting Roux limb in a standard side-to-side manner[17,113]. If one initially performs a side-to-side bowel

Table 9 Systemic *vs* portal-enteric drainage: Literature review

Center, authors, year, ref., study design and follow up	Number and types of transplant	Complications	Length of stay, readmissions and reoperations	1 yr patient survival	1 yr kidney and pancreas survival
University of Tennessee, Memphis, Stratta *et al*[44], Prospective, mean follow-up 17 mo	SE 27; PE 27	Incidences of acute rejection (33%) and major infection (52%) similar in both groups; Intraabdominal infections were slightly greater in the SE group (26% SE *vs* 11% PE); 2 deaths in SE group compared to one in PE group Pancreas Graft loss: 7 in SE compared to 4 in PE group, all *P* = NS	Readmissions (mean 2.8 SE *vs* 2.2 PE); Mean length of hospital stay: SE: 12.4 d; PE: 12.8 d; Relaparotomy: 8 in SE compared to 7 in PE group, all *P* = NS	SE 96%; PE 93%	Pancreas SE 74%; PE 85%; Kidney SE 96%; PE 93%
University of Maryland, Philosophe *et al*[45], Retrospective	SE: 63 SPK, 42 PAK, 26 PTA	Acute rejection: At 36 mo, the pancreas rejection rates were 21% for PE *vs* 52% for SE (*P* < 0.0001); the kidney rejection rates following SPK were 26% PE *vs* 43% SE (*P* = 0.017)	ND	36-mo patient survival rates were similar in both groups, 89% for PE *vs* 93% for SE	36-mo graft survival rates for all pancreas transplants were 79% with PE *vs* 65% with SE (*P* = 0.008)
Hospital Juan Canalejo, Coruña, Spain, Alonso *et al*[49] and Quintela *et al*[51], Retrospective, mean follow-up 23 mo	PE: 54 SPK, 55 PAK, 40 PTA; SE 18; PE 20	Incidences of intraabdominal infection and acute rejection episodes were not different between groups	Early relaparotomy no difference: SE: 34 d; PE: 20 d	PE: 80% *vs* SE: 86%	Death-censored pancreas (SKP and PAK) graft survival was 73% for PE and 81% for SE (*P* = NS)
Toronto General Hospital, Bazerbachi *et al*[53], Retrospective	SE 147; PE 45	In both groups, a complication occurred in 38% of patients in the first year; Major infections were not different between groups; 3-mo rejection rate was identical (6%) and the 1-yr rejection rate was 12.2% SE *vs* 13.3% PE; Most common reasons for pancreas graft loss in both groups were death with functioning graft (25%), graft thrombosis (13%), rejection (11%) and duodenal leak (9%)	Length of stay - mean 11 d *vs* 10 d in the SE *vs* PE; Most common causes of death in both groups were myocardial infarction (35%), cerebrovascular accident (13%) and cancer (13%); Most common causes of kidney graft loss in both groups were death with functioning graft (61%) and acute rejection (11%)	Patient survival did not differ at 5 yr (94% SE *vs* 89% PE) and 10 yr (85% SE *vs* 84% PE, *P* = NS)	Pancreas survival was similar at 5 yr (82% SE *vs* 76% PE) and 10 years (65% SE *vs* 60% PE); Kidney survival was similar at 5 yr (93% SE *vs* 84% PE) and 10 yr (82% SE *vs* 76% PE)
Medical University Innsbruck, Austria, Ollinger *et al*[120], Retrospective, Mean follow-up 8.3 yr	509 transplants in 4 eras including 34 PE and 146 SE (with DJ) in most recent era (2004-2011)	Thrombosis: 9% PE *vs* 5% SE, *P* = NS		5-yr patient survival 94%	5-yr pancreas survival 77% PE *vs* 74% SE
Hôpital Edouard Herriot, Lyon, France, Petruzzo *et al*[50], Retrospective	SE 36; PE 44; All SPK	No significant differences in long-term outcomes but the SE group had a higher incidence of pancreas graft loss secondary to thrombosis	No difference in total surgical complications	Patient survival rates 92% SE *vs* 95.5% PE	One-, 3-, 5-, and 8-yr pancreas survival rates were 75%, 60.6%, 56.7%, and 44%, respectively, in the SE group compared to 88.6%, 84.1%, 78.4%, and 31.3% in the PE group; One- 3-, 5-, and 8-yr kidney survival rates were 91.7%, 78.1%, 74.1%, and 57.9%, respectively, in the SE group compared to 93.2%, 88.6%, 78.4%, and 38.9% in the PE group

SE: Systemic enteric; PE: Portal enteric; ND: Not determined/no data; DJ: Duodeno-jejunostomy; NS: Not significant.

anastomosis, it is relatively straightforward to convert to a diverting Roux limb for whatever reason by separating the afferent limb with a gastrointestinal stapler just proximal to the anastomosis. The stapled and divided proximal limb can then be placed 40 cm or more distal to the anastomosis on the efferent limb and the second

bowel anastomosis can be constructed either in a side-to-side or end-to-side manner with either sutures or a stapler. A potential advantage of accessing the SMV for venous drainage is that the procedure is no longer pelvic but rather mid-abdominal in location, which is helpful in cases of retransplantation or in patients who have had previous pelvic irradiation or procedures[121].

With any method of enteric drainage, the efferent limb must be placed so as to remove any tension or traction on the bowel anastomosis. By careful positioning, an anastomotic "blow-out" or enteric leak can be averted by preventing bowel angulation just distal to the anastomosis. In addition, it is important close any mesenteric defects and to position the pancreas in such a way that the risk of internal hernia is minimized. Although some surgeons prefer to "wrap" omentum around the bowel anastomosis, we do not advocate this practice because of the concern for liquefaction necrosis that may develop from any fat that comes in direct contact with the pancreas following reperfusion. Fat necrosis may result in peri-pancreatic fluid collections that could subsequently require drainage or become infected.

Alleged gains of pancreas transplantation with portal venous delivery of insulin include immunological, technical, and metabolic, "advantages". However, neither large registry analyses nor prospective cohort studies have been able to corroborate these purported benefits (Table 9)[1,33,39-42,44-46,49-53,112-123]. Conversely, when comparing the three major techniques of pancreas transplantation, there are likewise no well controlled studies to suggest any major drawbacks of portal-enteric *vs* either systemic-bladder or systemic-enteric drainage.

One of most recent and exciting innovations in pancreas transplantation is the advent of laparoscopic pancreas transplantation with robotic support[125-127]. With the da Vinci Robotic system, Boggi *et al*[125] reported the first three whole pancreas transplants performed by using this technology. Their experience constitutes a proof of concept for pancreas transplantation with robotic-assisted laparoscopic surgery. In these cases, enteric drainage of was accomplished using a circular stapler to create an anastomosis between the proximal recipient small bowel and donor duodenum[126]. However, Boggi *et al*[127] have raised concerns regarding the influence of longer warm ischemia duration on viability of the graft because maintaining a cold graft temperature prior to reperfusion is difficult to accomplish laparoscopically. Although several "variations on a theme" exist in the procedural methodology of pancreas transplantation and novel approaches continue to be described, the prevailing viewpoint upholds that the technique with which the individual surgeon feels most confident and comfortable is the best one to be implemented based on donor pancreas quality and recipient anatomic considerations. With improved surgical outcomes over time, exocrine drainage techniques are no longer the "Achilles' heel" of vascularized pancreas transplantation.

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P- Reviewer: Chen ZS, Keller F, Marino IR, Rydzewski A, Salvadori M
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