Standard Open Procedures from Deceased Donors

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Introduction

Since the first pancreas transplant in 1966 [1], a variety of surgical techniques for graft implantation have been reported. In fact, more so than with any other solid organ, the history of pancreas transplantation has predominantly revolved around the development and application of different surgical techniques [2]. And no other abdominal organ has seen such a variety of surgical techniques for the purpose of transplantation. The two most controversial issues in the past have been the management of exocrine pancreatic secretions (enteric vs. bladder drainage) and the type of venous drainage (systemic vs. portal venous drainage). Other issues have included pancreatic mass (whole vs. segmental transplants) and graft placement (intraperitoneal vs. extraperitoneal; and in SPK, bilateral vs. ipsilateral). According to the International Pancreas Transplant Registry (IPTR), an intra-abdominal whole-organ pancreas transplant with enteric and systemic venous drainage is now the preferred technique worldwide (see Chap. 66). However, the surgical technique may need to be adapted to the individual circumstances of donor and recipient to optimize the outcome.

Table 29.1 Comparison of bladder versus enteric drainage

	Enteric drainage (ED)	Bladder drainage (BD)
Advantages	Most physiologic techniques for drainage of exocrine pancreatic secretions No technique-related metabolic or urologic complications Duodenal and gastric drainage easily accessible for endoscopy	Monitoring of urinary amylase as a marker of rejection Less severe abdominal complications since leaks and abscesses are usually contained Access for cystoscopic biopsy
Disadvantages	No monitoring of exocrine pancreatic secretions Diffuse peritonitis is possible in case of a leak Jejunal drainage is slightly less accessible for percutaneous biopsy (because of midabdominal placement in case of portal drainage)	Nonphysiologic anastomosis, which causes a variety of metabolic and urologic complications, for example, metabolic acidosis and dehydration (because of loss of bicarbonate and fluids), high urinary tract infection rate, hematuria, genitourinary irritation; conversion to ED in 10–35% due to reflux pancreatitis and other reasons

General Considerations

Enteric Versus Bladder Drainage

A multitude of surgical techniques for diverting exocrine pancreatic secretions has been reported over time: enteric drainage, cutaneous graft duodenostomy, open intraperitoneal duct drainage, duct ligation, duct injection, gastric drainage, ureteral drainage, bladder drainage, and duodenal drainage (in chronological order). Of those, enteric and bladder drainage have been the most common techniques. Advantages and disadvantages of enteric vs. bladder drainage are depicted in Table 29.1.

After the introduction of tacrolimus and mycophenolate mofetil in the mid-1990s with a significant reduction in pancreas rejection rates, a major change in the management of pancreatic exocrine secretions took place: before then, enteric drainage was used in only about 10% of all transplants whereas now it is the predominantly used technique worldwide in about 95% of transplants. The reasons for this change are described below.

In their initial series of ten pancreas transplants, Lillehei et al. used enteric drainage (duodenojejunostomy via a Roux-en-Y loop) in six patients [3]. But, alternatives to enteric drainage were subsequently developed because of the high morbidity and mortality rates related to technical complications of the intestinal anastomosis. In 1973, Gliedman et al. described a technique of segmental pancreas transplantation in which the exocrine pancreatic secretions were drained via the native ureter into the recipient's bladder [4]. They also discussed the possible use of urinary amylase levels to monitor pancreas graft function. But, ureteral drainage of segmental pancreas grafts was hampered early on by three issues: (1) the technique was associated with a high anastomotic leak rate and, consequently, a high graft failure rate; (2) an ipsilateral nephrectomy was frequently required to use the native ureter; and (3) preferably segmental grafts were used. In 1983, Sollinger et al. reported a modified technique of direct drainage of the pancreatic duct into the bladder to divert exocrine secretions of segmental pancreas grafts, without an increased risk for anastomotic leaks or abscesses [5]. In 1985, Gil-Vernet et al. reported a whole-pancreas graft technique with successful anastomosis between the papilla of Vater (without duodenal conduit) and the ipsilateral recipient ureter [6]. Nghiem and Corry eventually described in 1987 the technique of bladder drainage via the graft duodenum for whole pancreaticoduodenal grafts [7]. Over the following 10 years, most centers adopted the technique of bladder-drained whole-organ pancreaticoduodenal transplants—considered safe, convenient, and usually sterile. According to the IPTR, through 1995 more than 90% of all pancreas transplants worldwide were bladder drained [8].

The advent of more potent immunosuppressive drugs (tacrolimus and mycophenolate mofetil) to prevent rejection and more efficient anti-microbial prophylaxis and treatment of infections along with improved surgical techniques in the second part of the 1990s led to the revival of the much more

physiologic enteric drainage. The following comprehensive review of the physiology of bladder drainage is, therefore, more of historical interest. However, since many pancreas recipients still enjoy good graft function with bladder drainage, the full spectrum of complications is listed here as they need to be managed competently when they arise.

The two main reasons for the widespread use of bladder-drained whole-organ pancreaticoduodenal transplants until well into the 1990s were (1) the relatively low complication rate, with no contamination from an enterotomy [which usually causes peritonitis] [9, 10], and (2) the ability to monitor urinary amylase levels to detect graft rejection [11]. In contrast to enteric drainage, surgical complications with bladder drainage are usually contained in the right or left lower abdominal quadrant: Leaks usually do not result in diffuse peritonitis because no abdominal spillage of enteral contents occurs. Duodenal segment or bladder leaks can frequently be managed conservatively, without surgical repair, by the placement of a Foley catheter and percutaneous drain(s). Serial urinary amylase measurements had been particularly helpful in solitary pancreas transplants (PTA, PAK) with their higher rejection rates and in which a simultaneously transplanted kidney from the same donor is not available as a harbinger to monitor serum creatinine levels for rejection [12]. Before it was shown that percutaneous computed tomography (CT)—or ultrasound (US)-guided biopsies of the bladder- or enteric-drained pancreas grafts could be successful, with a low complication rate [13–15], bladder drainage allowed cystoscopic biopsies of both the graft duodenum and the pancreas graft itself [16–19]. With percutaneous biopsies now being widely used, a bladder-drained pancreas graft in the right or left lower abdominal quadrant usually is easily accessible to percutaneous biopsies, whereas an enteric- and portal-drained pancreas graft in the mid-abdomen is less accessible with the exception of grafts that utilize duodenal and gastric drainage [20, 21].

However, bladder drainage is associated with unique metabolic and urologic complications. The loss of 1–2 L/day of (alkaline)exocrine pancreatic and duodenal mucosal secretions in the urine results in bicarbonate deficiency and electrolyte derangements, causing chronic (hyperchloremic) metabolic acidosis and dehydration. Permanent bicarbonate supplementation and increased fluid intake are the results of the nonphysiologic connection between the pancreaticoduodenal graft and the urinary bladder. Although most recipients can adapt to the need for increased fluid intake and bicarbonate supplementation, the altered physiology can challenge their patience and compliance. In extreme cases, this metabolic derangement can lead to malnutrition, lack of energy with easy fatigability, nausea and vomiting, anorexia, orthostatic hypertension and headaches, chronic abdominal pain and constipation, renal dysfunction, and failure to thrive. These severe symptoms may require long-term vascular access for intermittent bicarbonate and fluid supplementation, fludrocortisone for water and sodium retention, and acetazolamide or octreotide to reduce bicarbonate production of the pancreaticoduodenal graft [22].

Urologic complications are common because pancreatic enzymes are a permanent source of irritation to the transitional epithelium of the bladder and to the lower genitourinary tract. The consequences are altered integrity of the urothelium and an obligatory alkaline pH of the urine. Urologic complications include the following: chemical cystitis and urethritis (manifesting as dysuria), recurrent hematuria (in particular at the anastomotic site), bladder stones, and recurrent episodes of graft pancreatitis believed to be secondary to reflux. The high rate of urinary tract infections is a frequent cause of costly in- and out-patient treatment. But, most of these complications can be successfully managed nonoperatively (by Foley catheter placement, antibiotics, urine alkalization, and urinary tract analgesics) and usually resolve after the first 12 months posttransplant [22]. More serious, but less common, complications include severe perineal inflammation and excoriation and, more frequently in men, ureteral disruption, and strictures. Activation of the pancreatic proenzyme trypsinogen, by enterokinase present in the brush border of the duodenal mucosa, is considered the major cause [22, 23]. Autodigestion of the glans of the penis, the major labia, and the urethra as well as urethral strictures and preneoplastic bladder lesions have also been described [24–28].

The incidence of urologic complications because of activated proteolytic pancreatic enzymes is high. It may be further increased by an underlying neurogenic bladder (with incomplete emptying and causing urinary retention) and long blind duodenal segments (leading to urinary stasis and bacterial overgrowth) [29]. In a University of Wisconsin study, the incidence of recurrent urinary tract infections was as high as 35%; severe or chronic hematuria, 22%; anastomotic or duodenal segment leaks, 22%; reflux pancreatitis, 14%; and urethral lesions, 7% [30, 31]. Despite their high incidence, urologic complications rarely affect patient and graft survival rates.

The spectrum of complications caused by exposure of pancreatic enzymes to the urothelium has been extensively studied. But, the long-term consequences of exposure of urine to the duodenal graft mucosa have not been investigated in pancreas transplantation. In nontransplant patients, malignancies in intestinal conduits after a mean of 18 years were attributed to the carcinogenic effect of urine on the intestinal mucosa [32]. Duodenal biopsies obtained between 205 and 2264 days after pancreaticoduodenal transplants did not reveal any neoplastic lesions within 6 years posttransplant, but did reveal mild to moderate blunting of the villous epithelium; varying degrees of chronic lymphocytic, eosinophilic, and plasma cell infiltration of the lamina propria;

benign lymphoid aggregates; and intestinal metaplasia [33]. Nakhleh et al. noted crypt loss and villous atrophy of the graft duodenum but no neoplastic changes [34]. Yet, chronic bacteriuria, epithelial cell transformation caused by the juxtaposition of transitional and intestinal epithelium, and long-term use of immunosuppressive drugs are all considered potential carcinogenic factors, so long-term surveillance of the duodenal conduit is warranted [33]. Of note, at least one case of preneoplastic lesion in a bladder-drained pancreas allograft has been reported [28].

The therapy of choice for all persistent or refractory metabolic and urologic complications has been a conversion from bladder to enteric drainage (see section below: "Conversion from Bladder to Enteric Drainage"). According to US IPTR/United Network for Organ Sharing (UNOS) data, the rate of conversion for bladder-drained SPK transplants performed between 2008 and 2019 was 7% at 1 year, 18% at 5 years, and 18% at 10 years [8]. The rate was higher for solitary transplants (18% at 1 year, 35% at 5 years, and 35% at 10 years). Bladder drainage was more often used in solitary transplants and faster converted after stable graft function. But, conversion from bladder to enteric drainage requires another surgical procedure. Unfortunately, a few perfectly well-functioning grafts have been lost because of technical complications related to the conversion procedure, but overall graft survival in large patient series has not been worse after enteric conversion [22, 35–39].

In light of the potential complications of bladder drainage and possibly their negative impact on quality of life, interest in enteric drainage resurged in the mid-1990s thanks to improvements in surgical technique, immunosuppressive therapy, radiologic imaging, and interventional procedures, antimicrobial prophylaxis, liberal use of graft biopsies, and excellent results with enteric conversion after bladder drainage. Since then, additional variants of the original enteric or jejunal drainage have been introduced such as duodenal and gastric drainage.

The shift from bladder to enteric drainage, according to US IPTR/UNOS data, took place between 1995 and 2004: in 1995, 16% of pancreas transplants used enteric and 84% bladder drainage; in 2004, 84% used enteric and 15% bladder drainage; and in 2019, 97% used enteric and 3% bladder drainage. This shift from bladder to enteric drainage happened faster in the simultaneous pancreas and kidney (SPK) category (enteric drainage in 1995, 16%; in 2004, 87%; and in 2019, 97%) and later in the solitary pancreas transplant categories—pancreas transplant alone [PTA] and pancreas after kidney [PAK] transplant—(enteric drainage in 1995, 11%; in 2004, 81%; and in 2019, 95%). During the same time period, the rate of technical failures with enteric drainage significantly decreased. However, the rates have remained somewhat higher than with bladder drainage: in 1995, the overall rate of technical failures was 12% with enteric vs. 8% with bladder drainage; in 2004, 8% with enteric vs. 3% with bladder drainage; in 2019, 3% with enteric drainage; there were only 23 (!) bladder drained pancreas transplants performed in 2019, all without any technical complications [8].

Improvements in surgical technique largely contributed to the enteric drainage shift. In the past, pancreatic–enteric anastomoses of segmental grafts were associated with a high incidence of infections (peritonitis, abscess, mycotic aneurysm, and wound infection), pancreatic fistulas, or leaks. In the late 1980s, the Stockholm group reported, for segmental grafts, the routine use of (1) a Roux-en-Y loop for constructing the pancreatic-enteric anastomosis and (2) an external pancreatic duct catheter to temporarily protect the pancreatic–enteric anastomosis [40, 41]. A Roux-en-Y loop was advocated because it reduced the incidence and severity of surgical complications at the anastomosis between the graft duodenum and the inadequately prepared recipient bowel in the setting of high-dose immunosuppression. Graft pancreatectomy also causes less morbidity with a Roux-en-Y loop in place. In contrast, if the graft duodenum is directly anastomosed to the recipient's small bowel, at least one (temporary) enterostomy may have to be constructed. Hence, the use of a Roux-en-Y loop facilitates graft salvage in the event of graft duodenal complications and prevents the construction of an enterostomy.

An externally drained pancreatic duct catheter was initially used to protect the pancreatic–enteric anastomosis of segmental grafts and to monitor, early, the exocrine function of the graft (i.e., amylase content and juice cytology). A 6-French or 4-French catheter was inserted into the pancreatic duct and brought out through the recipient jejunum and abdominal wall; the catheter was removed 3–4 weeks post-transplant. But, the pancreatic duct catheter has also caused morbidity of its own, in particular graft pancreatitis.

With the reintroduction of enteric-drained whole-organ pancreaticoduodenal transplants by Starzl et al., according to the technique originally described by Lillehei [42], and with further improvements in immunosuppressive therapy and antimicrobial prophylaxis, the Stockholm group subsequently simplified the technique of enteric drainage again. First, they omitted the Roux-en-Y loop in favor of a direct side-to-side anastomosis; later, they also omitted the pancreatic duct catheter [43]. These changes did not result in an increased technical penalty.

Enteric drainage, the most physiologic technique to divert exocrine pancreatic enzymes even without the creation of a Roux-en-Y limb, is now established as the standard procedure [44–54].

At least three studies have prospectively compared bladder vs. enteric drainage [46–48]. In all three studies, patient and graft survival were not different for enteric vs. bladder drainage. However, in all retrospective and prospective

studies, the incidence of metabolic and urologic complications was significantly higher for bladder-drained grafts and was associated with a significantly higher number of hospital readmissions, thereby raising issues of cost and quality of life. Moreover, the conversion rate from bladder to enteric drainage is high; enteric drainage avoids reoperation [20, 29, 44–54].

One question remains: is there still an indication of bladder drainage? There is, but for different reasons. First, bladder drainage may still be indicated in patients with a high rejection risk: those with high PRA levels or undergoing retransplants, particularly in the solitary recipient categories (PAK and PTA). But, even these patients, once pancreas graft function is stable, tend to undergo conversion to the much more physiologic enteric drainage due to improved monitoring for rejection and more efficient immunosuppression [55]. Second, bladder drainage may be considered intraoperatively if after reperfusion the pancreaticoduodenal graft looks suboptimal and potential duodenal complications are of concern. In such cases, intended enteric drainage may be abandoned in favor of bladder drainage [56, 57]. It is quite evident that bladder drainage has turned into a niche technique for rare conditions and considerations.

A detailed analysis of outcome data for enteric vs. bladder drainage is provided in Chaps. 66 and 73.

Systemic Versus Portal Vein Drainage

Since the original descriptions (by Kelly et al. [1] and Lillehei et al. [3]) of the vascular technique, most pancreas grafts have been placed heterotopically in the pelvis, with vascular anastomoses to the recipient iliac artery and vein. It was recognized early that venous outflow of the pancreas graft into the systemic circulation, bypassing the liver, was less physiologic than venous outflow into the portal circulation. Yet, initially, portal vein drainage was not pursued because of the increased risk of technical complications. In theory, venous drainage of a low-flow organ (such as the pancreas graft) into the recipient's high-flow systemic circulation provides less risk for graft thrombosis, as compared with venous drainage of a low-flow organ into the recipient's low-flow portomesenteric circulation. Other reasons that prevented portal vein drainage from gaining more widespread application in the past included (1) the midabdominal position of the pancreas graft, (2) the need for an enteric anastomosis, with its historically higher incidence of leaks and of more severe intra-abdominal infections, and (3) the knowledge that portal drainage was not a fundamental requirement for euglycemia (in fact, euglycemia had been demonstrated in some of the first recipients with systemic drainage and long-term graft function). Over time, most of these early paradigms have changed.

In 1984, Calne et al. were the first to report venous outflow (of an intraperitoneally placed segmental graft) into the recipient splenic vein, draining the exocrine pancreatic secretions via a ductogastrostomy [58]. Gil-Vernet et al. drained a retroperitoneally placed segmental graft into the recipient splenic vein and performed a ductouterostomy for exocrine pancreatic drainage [59]. Subsequently, two other tributaries of the portal vein system were accessed for enteric-drained segmental grafts: the superior mesenteric vein [60] and the inferior mesenteric vein [61]. The latter study stated that if the β-cell mass is reduced below a critical level (e.g., because of rejection), portal drainage might provide an advantage over systemic drainage [46].

In 1989, Mühlbacher et al. were the first to use portal drainage in whole-organ pancreaticoduodenal transplants. They used a unique technique: The backside of the pancreas was flipped to the front, and the distal end of the donor splenic vein (extended by an 8-cm donor external iliac vein graft) was anastomosed to the recipient portal vein (end-to-side anastomosis in the hepaticoduodenal ligament); the graft duodenum was anastomosed to the bladder [62, 63]. In contrast to segmental transplants, such whole-organ transplants with portal vein drainage reportedly resulted in normal insulin secretion, glucose tolerance, and hepatic insulin extraction [63]. In 1992, Rosenlof et al. described the use of portal drainage in three recipients of enteric-drained whole-organ pancreaticoduodenal grafts [64]. After Gaber et al. presented a large series of pancreaticoduodenal transplants using portal vein and enteric exocrine drainage, an increasing number of transplant centers adopted that technique as their routine for venous drainage [20]. While Rosenlof et al. had used the recipient splenic vein, Gaber et al. used the superior mesenteric vein or one of its tributaries for venous drainage [20]. If the donor superior mesenteric vein—and not the distal splenicvein [62, 64]—is used for anastomosis, enteric drainage is used to divert exocrine pancreatic secretions.

According to US IPTR/UNOS data, the overall rate of portal vein drainage in enteric drained transplants decreased from 29% in 1995 to 10% in 2019 (see Chap. 66) [8].

A plethora of literature exists that demonstrates the metabolic advantage of portal vs. systemic drainage—more so in theory though due to the lack of serious clinical consequences with the use of systemic drainage. By bypassing the liver, systemic drainage causes peripheral hyperinsulinemia and portal hypoinsulinemia [65].

Peripheral hyperinsulinemia has been associated with the development of atherosclerosis, both directly (through stimulation of vascular smooth muscle growth [66–68]) and indirectly (through development and progression of dyslipidemia and hypertension [20, 69–73]). It has also been linked to increased concentrations of plasminogen activator inhibitor type 1 (PAI-1), which predisposes vessels to the formation of

lipid-laden rather than cell-rich plaques, rendering them particularly prone to rupture (and increasing the risk of the acute coronary syndrome) [72]. In addition, peripheral hyperinsulinemia has been associated with insulin resistance as a result of elevated basal hepatic glucose production, reduced postprandial peripheral glucose disposal, reduced insulin-stimulated glucose storage, resistance to the antilipolytic action of insulin, and immunosuppressive therapy [74–76]. Hyperinsulinemia also downregulates insulin receptors and postreceptor pathways in the muscle and adipose tissues, thus causing insulin resistance [77]. Clinically, peripheral hyperinsulinemia has been associated with hypertension, cardiovascular disease, weight gain, and, in women, polycystic ovary syndrome [78–81].

The second effect of systemic drainage, portal hypoinsulinemia, may cause lipid abnormalities because of the liver's role in the metabolism of lipoproteins. Hughes et al. retrospectively compared the lipoprotein composition after systemic (n = 20) vs. portal (n = 11) vein drainage: The group with portal vein drainage had substantial reductions in the low-density lipoprotein (LDL) apoB and intermediate-density lipoprotein (IDL) apoB subfractions [77]. In contrast, the group with systemic vein drainage had significant increases. Abnormalities of apoB-containing lipid proteins are believed to promote the development and progression of atherosclerosis. Further, in the group with portal vein drainage, the IDL triglyceride, cholesterol ester, phospholipid, and free cholesterol levels fell significantly at 1 year, as did the VLDL and LDL-free cholesterol to phospholipid ratios. In contrast, the group with systemic vein drainage had substantial increases in these parameters. Hughes et al. concluded that portal vein drainage leads to greater improvements in lipoprotein composition, lowering the risk of coronary vascular disease; in contrast, systemic vein drainage leads to a higher atherogenic potential [77]. Bagdade et al., in another retrospective study, noted that cholesteryl ester transfer (CET) levels were significantly higher for patients with systemic (vs. portal) vein drainage [82]. Increased CET levels (in the basal state) promote atherogenesis and have been associated with accelerated development of cardiovascular disease [82, 83].

In a retrospective study, Gaber et al. reported that hyperinsulinemia was evident in both fasting and stimulated tests for pancreas recipients with systemic vein drainage (n = 28), with values consistently two- to fivefold higher than with portal vein drainage (n = 19) [20]. In contrast, the Lyon group, in a randomized prospective study of systemic (n = 14) vs. portal (n = 16) vein drainage in recipients with enteric drainage, did not find significant differences in fasting insulin, C-peptide, cholesterol, or triglyceride levels [84]. Several centers have reported that glycosylated hemoglobin levels and fasting and stimulated glucose levels are not different between the two groups [20, 53, 84]. Havrdova et al. did not find any significant differences in fasting glycemia, HbA1c, homeostasis model assessment of insulin resistance (HOMA-I), standard IVGTT with coefficient of glucose assimilation (KG) calculation, parameters of C-peptide level, fasting insulin level, and response during IVGTT. Homeostasis model assessment of B-cell function (HOMA-B) and AUC of insulin level were higher in the group with systemic drainage [85]. These results were also echoed in a study by Alonso et al. [86]. Frystyk et al. showed that portal drainage raises insulin-like growth factor-I (IGF-I) and lowers glucose regulatory hormones (GH) secretion. They postulated that these changes might explain why glucose regulation is maintained despite lower peripheral insulin levels, compared with patients with systemic graft drainage and nondiabetic control subjects [87].

A study by Petruzzo et al. showed that systemic (n = 20) vs. portal (n = 24) drainage resulted in normal glucose tolerance. The area under the insulin curve was higher in the group with systemic drainage. Cholesterol, low-density lipoprotein-cholesterol, and triglycerides were higher in the group with portal drainage [88]. Another study by Petruzzo et al. showed that neither hepatic nor peripheral insulin resistance was detected in the systemic (n = 11) vs. portal drained (n = 12) groups. In the systemic drained group, only a lower insulin clearance was noted as well as slight decreased peripheral responsiveness to insulin without modifications of lipid status [89].

Bypassing the liver, where about 50% of the insulin is degraded during the first pass, does not significantly impair carbohydrate metabolism in patients with systemic vein drainage [20, 90]. In fact, carbohydrate metabolism in SPK recipients with bladder drainage is similar to that in nondiabetic solitary kidney recipients on the same immunosuppressive therapy [91]. Insulin may contribute to the development of hypertension by stimulating the sympathetic nervous system, promoting renal sodium retention, and stimulating the proliferation of arterial smooth muscle cells [20, 69]. Yet, the clinical consequences of peripheral hyperinsulinemia in pancreas recipients with systemic drainage have hardly been remarkable: Hricik et al. reported that hypertension at 1 year after systemic vein (and bladder) drainage was significantly less common and less severe in SPK recipients, as compared with solitary kidney recipients [92]. Fiorina et al. noted a significantly decreased intima-media thickness of the carotid artery posttransplant in SPK recipients, as compared with solitary kidney recipients [93].

Finally, in a systematic review and meta-analysis of the literature from 1989 through 2014 using PubMed, CINHAL, and Cochrane Library for portal versus systemic venous drainage, Oliver et al. noted significantly lower fasting insulin levels in the portal-drained group, but no differences in fasting blood glucose, hemoglobin A1C and cholesterol levels; other measures of lipids showed no difference as well.

They concluded that there is no significant difference in metabolic outcome in portal vs. systemic venous drainage [94].

In the late 1990s, discussion centered around the question whether portal vein drainage has beneficial effects on pancreas graft acceptance. Already 30 years earlier, it was postulated that antigen delivery via the portal vein favorably alters antigen presentation, with subsequent induction of immunologic hyporeactivity or even tolerance [95]. Subsequently, this finding was confirmed in several different transplant models—including intestinal transplants with concurrent donor cell augmentation via the portal vein [96–99]. Nymann et al., in a retrospective study, reported a higher incidence of rejection episodes for pancreas recipients with systemic vein (and bladder) drainage vs. portal vein (and enteric) drainage. The rate of pancreas graft loss from rejection was three times higher for recipients with systemic (20%) vs. portal (6%) vein drainage [100]. Similarly, Philosophe et al. in a retrospective study of 193 recipients with portal vein (and enteric) drainage vs. 133 recipients with systemic vein (and bladder) drainage, showed a significantly lower incidence of graft rejection episodes in those with portal vein (and enteric) drainage [101]. Both Nymann et al. and Philosophe et al. concluded that an immunologic advantage exists in favor of portal vein drainage. But, in two prospective studies of systemic vs. portal vein drainage in SPK recipients with enteric drainage, no differences in the incidence of rejection were found, thereby disputing an immunologic advantage in favor of portal vein drainage [102, 103]. Subsequent studies including IPTR analyses confirmed that there was no immunological advantage associated with portal vein drainage [86, 104–108].

Of note, Cattral et al. [109], disputing the perception that portal vein drainage might be more difficult to perform, did not notice any difference in mean surgical time and blood transfusion requirements for systemic vs. portal vein drainage. Furthermore, when portal vein and enteric exocrine drainage were combined, Bruce et al. [110] noted a short first-year hospitalization and a low relaparotomy rate.

In summary, portal vein drainage creates a more physiologic state of insulin metabolism. Peripheral hyperinsulinemia has been associated with atherosclerosis and portal hypoinsulinemia with lipoprotein abnormalities. Yet, no convincing evidence exists today that systemic vein drainage places pancreas recipients at a disadvantage by increasing their risk of vascular disease. Comparable metabolic control and graft outcome is achieved with portal vein and systemic vein drainage. As with enteric and bladder drainage, portal and systemic vein drainage should not be considered competing, but rather complementary, techniques. Obesity, thickened mesentery, and small mesenteric veins favor systemic vein drainage, whereas previous pelvic transplants or operations, severe iliac atherosclerosis, and short arterial grafts favor portal vein drainage [102]. Therefore, an individualized approach seems desirable.

Whole-Organ Versus Segmental Transplants

Whole-organ pancreaticoduodenal transplants in the late 1960s and early 1970s gave way to predominantly segmental transplants in the late 1970s and early 1980s. This change occurred because of greater technical ease in procuring, implanting, and managing complications of segmental grafts. With improvement in preservation solutions, surgical techniques, immunosuppression, and antimicrobial prophylaxis, the focus returned to whole-organ transplants in the late 1980s and 1990s. This change also occurred because of the greater islet mass: the greater functional reserve of whole-organ grafts makes rejection treatment more successful than for segmental grafts.

With a living donor, a segmental pancreas transplant remains the only option. The excellent long-term results (see Chaps. 38, 66, and 73) of technically successful segmental transplants from living (vs. deceased) donors are due to better HLA matching, a lower rejection rate, and shorter preservation time (resulting in little reduction in β-cell mass).

In a retrospective study by the Lyon group [111], segmental transplants (with duct injection) were compared with whole-organ transplants (with either bladder or enteric drainage). In terms of graft survival and metabolic control, better results were obtained with whole-organ transplants. With segmental grafts, glucose levels were significantly higher during the first year posttransplant. Because abnormalities in glucose metabolism further increased over time, the Lyon group postulated that the difference between segmental and whole-organ recipients was due to the smaller islet mass of segmental grafts. Thus, segmental transplants are technically simpler, but metabolic control is less satisfactory. Similarly, the Milan group reported that segmental recipients had a higher incidence of impaired glucose tolerance after oral glucose tolerance tests (OGTTs) and a less favorable lipoprotein profile [112, 113]. According to IPTR data, the use of segmental grafts has significantly declined over the last years, from 10% in 1966 to 1987, to 1% from 1988 to 1999, and to <1% between 2000 and 2015; segmental transplants were not performed in the United States after 2015 [8].

Intraperitoneal Versus Extraperitoneal Placement

The vast majority of pancreas grafts are placed intra-abdominally through a midline incision. This preserves all possible surgical options for transplantation and causes fewer wound infections; it also permits internal absorption of

peripancreatic secretions and lymphatic leaks. Few centers have used lower flank incisions in which the pancreas and kidney are placed extraperitoneal (with a slight retroperitoneal component). With the introduction of portal-enteric and donor duodenum to recipient duodenum drainage, retrocolic and retroperitoneal graft positioning through a transperitoneal approach has been instituted (see Chap. 31).

Extraperitoneal placement was initially advocated for segmental pancreas transplants using a J-shaped iliac (hockey-stick) incision, similar to the standard incision for solitary kidney transplants [114]. Although good exposure to the external iliac vessels was obtained, perigraft and wound infections were frequent. To reduce the technical complication rate, combined intra- and extraperitoneal graft placement was tried. Using the same J-shaped iliac incision, a 4-cm peritoneal incision was made after graft revascularization. The omentum was pulled through the peritoneal window and wrapped around the pancreas to facilitate the absorption of a potential leak [115]. This technique was eventually abandoned in favor of intra-abdominal graft placement.

In the 1990s, several groups advocated extraperitoneal (with partially retroperitoneal) placement of whole pancreaticoduodenal grafts. Three types of incisions were used: bilateral flank, lower abdominal transverse, and midabdominal transverse incisions. Barone et al., in a retrospective study, found that the transverse lower abdominal incision was associated with less pain, shorter duration of posttransplant ileus, fewer pulmonary complications posttransplant, and a low incidence of wound infections (12%) and hernias (6%) [116]. In a retrospective study by Barrou et al. of 22 SPK recipients, the overall results for a bilateral extraperitoneal approach were not different than for the intraperitoneal approach [117]. But, others have reported a wound complication rate three to ten times higher with the bilateral flank incision, as compared with the standard midline incision [118, 119].

Boggi et al. introduced retrocolic or retroperitoneal pancreas transplant placement with portal-enteric drainage in the early 2000s [120–122]. Through a midline intraperitoneal approach the right colon is fully mobilized to allow retroperitoneal access to the superior mesenteric vein (SMV) and the right common iliac artery. The donor portal vein is anastomosed to the recipient SMV, and the donor Y-graft is to the recipient's common iliac artery. The graft duodenum was originally anastomosed side-to-side to a diverting Roux-en-Y loop. Subsequently, a direct side-to-side without a Roux limb to the recipient jejunum, duodenum, or stomach was described [21, 120–127]. In their first series, Boggi et al. reported low morbidity and mortality rates. After donor duodenum to recipient duodenum drainage was introduced, retrocolic/retroperitoneal placement became more popular [120–127]. Complication and outcome data of retrocolic placement is detailed in Chaps. 31 and 66 [120–127].

For SPK recipients, Kuo et al. proposed extraperitoneal placement of the kidney graft and intraperitoneal placement of the pancreas graft [128, 129]. Their main argument for retroperitoneal placement of the kidney graft was easier access for a future kidney biopsy. But, this technique has not gained popularity because the simultaneously transplanted kidney—when placed intraperitoneally—is usually also anastomosed to the recipient's external iliac artery and vein; thus, it is positioned in the (lower) pelvis, allowing easy access for biopsy. Even if the intraperitoneal kidney graft cannot be biopsied (e.g., because of overlying bowel), the pancreas graft frequently can be. Computed tomography- and ultrasound (US)-guided biopsies of the pancreas graft carry no greater risk than kidney biopsies [13, 15].

Another variant of extraperitoneal placement is the use of a mid-abdominal transverse incision. In a retrospective study, Douzdjian et al. reported no differences in the incidence of wound complications with midabdominal transverse vs. midline incisions, but the rate of deep abscess formation was higher in recipients with midline incisions [130]. They found that a midabdominal transverse incision offers better exposure of the external iliac vessels and the bladder, as compared with a midline incision. However, because most pancreas grafts are anastomosed to the common iliac vessels, a lower transverse abdominal incision has not become popular. In addition, a midabdominal transverse incision and its closure take longer to perform and require transection of both rectus muscles.

In summary, intra-abdominal placement of the pancreas graft is by far the most common. Retrocolic, and in effect, retroperitoneal placement is usually preferred when duodenal/gastric drainage is performed. Extraperitoneal placement is rarely indicated; despite a few positive reports, the extraperitoneal approach—either through a lower-flank incision or a transverse abdominal incision—has not gained popularity and has been abandoned even by those groups that initially favored it.

Bilateral Versus Ipsilateral Placement of SPK Transplant

In the vast majority of SPK transplants, bilateral placement is preferred: the pancreas graft is placed on the right side and the kidney on the left side. Ipsilateral placement of SPK transplants is not commonly performed and was first performed in portal-enteric drained pancreas transplants, if the left side cannot be used for implantation due to vascular issues [131] or if one side should be "preserved for future retransplantation" [132].

A technique for ipsilateral and separate implantation of the two organs has been described by Fridell et al. [132]. The portal vein and the pancreatic Y-graft are anastomosed to the right common iliac vessels and the pancreatic tail is positioned towards the pelvis. The donor renal vessels are anastomosed to the recipient's external iliac vessels.

The creation of a common arterial conduit has been proposed if implantation of the kidney graft on the left side is "difficult or undesirable" [131]. Using this technique, both grafts are implanted on the right side in ipsilateral fashion. The renal artery is anastomosed end-to-end to the donor internal iliac artery of the Y-graft; the long external iliac artery of the Y-graft is brought through a window of the small bowel mesentery and anastomosed to a Carrel patch of the donor SMA. The pancreas graft is anastomosed to the recipient portal vein and the donor renal vein to the recipient right iliac vein [131].

Nghiem described a technique of ipsilateral placement using the right iliac artery as a single inflow vessel to both organs [133].

It has been shown that for portal-enteric drained SPK transplants ipsilateral placement of the pancreas and kidney grafts on the right side is safe and does not compromise recipient or graft survival. Ipsilateral placement is yet another technical variation that can successfully be used in pancreas transplantation.

Ipsilateral dual graft placement has also been used for systemic venous and enteric drained pancreas transplants (see Chap. 88). The Tianjin pancreas transplant group has described a technique in which a long donor iliac Y-graft (internal iliac artery-to-renal artery and external iliac artery-to-Carrel patch [encompassing the celiac and superior mesenteric arteries] anastomoses), systemic venous drainage (to the recipient vena cava), and enteric drainage of exocrine secretions were used (Chap. 88, Fig. 88.1).

Standard Procedures: Systemic Versus Portal Venous Drainage and Enteric Versus Bladder Drainage

Systemic Vein and Enteric Exocrine Drainage

Whole-Organ Pancreaticoduodenal Transplants with Systemic Vein and Enteric Exocrine Drainage on the Right Side in Caudad Position

The pancreas is placed intra-abdominally, preferably on the right side of the pelvis, for two reasons: (1) the iliac vessels are more superficial than on the left side and, therefore, dissection is easier on the right side and (2) the natural position of the right iliac vessels (vein lateral to artery) does not require vascular realignment or possible ligation and division of the internal iliac artery, although on the left side it might [134].

After induction of general and tracheal anesthesia, the patient is placed in a supine position on the operating table. A central vein line, an arterial line for constant blood pressure monitoring, and a nasogastric suction tube are all placed by the anesthesia team. A Foley catheter for bladder drainage, a sequential compression device, and prophylactic antibiotics are routinely used. Antibiotic coverage is repeated every 4 h intraoperatively. To facilitate bowel exposure and not to fight distended and gas-filled bowel loops, preoperative enemas are given, but usually, no formal bowel preparation is performed. The patient is placed in a slight Trendelenburg position.

The abdomen is entered through a midline incision, extending from a point midway between the xiphoid process and umbilicus down to the pubic bone. The abdomen is explored for any pathologic findings. If the abdominal contents appear normal, the dissection is started by mobilizing the cecum and distal portion of the ascending colon. The dissection is carried out in the avascular plane between the right colon and retroperitoneum, and all attachments are taken down using electrocautery. Doing so creates a comfortable retroperitoneal bed for the body and tail of the pancreaticoduodenal graft. During the dissection of the right colon, the right ureter is identified, isolated, and fully mobilized to a point midway between the iliac vessels and bladder.

The right common, external, and internal iliac arteries are dissected free all the way from the aortic bifurcation to a

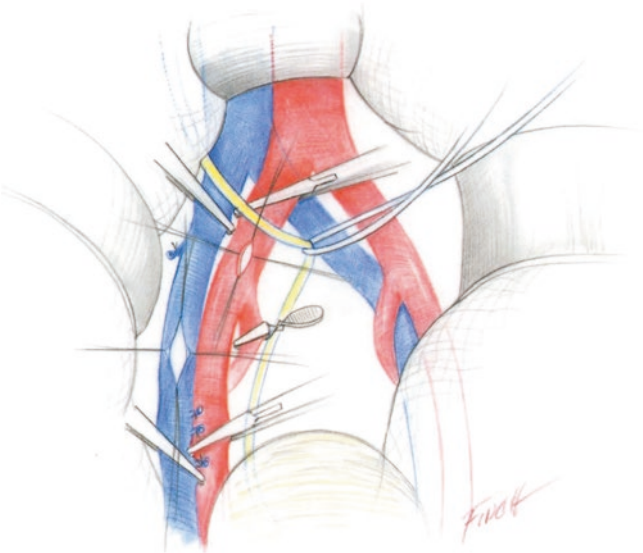

Fig. 29.1 Dissection of the recipient's right iliac vessels. The internal iliac veins are ligated and divided. The iliac artery is medial to the vein. The arteriotomy is proximal to the venotomy. The ureter is looped medial to the artery

level just proximal to the inguinal ligament (Fig. 29.1). Care is taken not to injure any nerve structures at the aortic bifurcation. Most diabetic patients have some degree of iliac atherosclerosis: the circular form is most worrisome, but posterior (and less commonly anterior) plaques > 180° can also cause clamp damage and may even result in distal embolization and limb ischemia. Usually, a 3–5 cm long segment of an iliac artery with no or only little (and preferably posterior) atherosclerosis must be identified for safe clamping.

The right common, external, and iliac veins are mobilized next. Major lymphatic vessels and lymph nodes overlying the iliac vessels are ligated; frequently, the gonadal or ovarian vein is also ligated to prevent possible impingement on the venous graft anastomosis. If the pancreas is placed in the caudad position, my recommendation is to ligate, stick tie, and divide all internal iliac (hypogastric) vein branches, on occasion including the first lumbar vein branch for complete mobilization of the vein from the inferior vena cava to just proximal to the inguinal ligament. Although not all pancreas transplant surgeons take the hypogastric veins routinely, I have found that this extensive dissection not only facilitates the venous graft anastomosis technically but also prevents tension on the anastomosis, possible tears in the donor portal vein, and anastomotic disruption. It also decreases the risk of venous thrombosis [135]. Manipulation of the iliac vein system can cause persistent vasospasm and application of topical papaverine may assist to resolve it.

Circumferential dissection of the iliac arteries must be performed with utmost care to not injure the iliac vein system or the inferior vena cava.

Once the dissection in the recipient is complete and the benchwork preparation of the pancreas is finished, intravenous heparin is given. I use 40–60 U/kg for nonuremic and 20–40 U/kg for posturemic recipients of solitary pancreas grafts and for SPK recipients who are not yet dialysis dependent. In uremic, dialysis-dependent SPK recipients, heparin is usually not given or only at a small dose of 20 U/kg. The proximal common iliac artery and vein and the distal external iliac artery and vein are usually clamped with atraumatic vascular clamps (e.g., Fogarty clamps with one soft and one hard insert). The internal iliac artery is separately clamped with a short atraumatic vessel clamp (e.g., Bulldog clamp) (Fig. 29.1). In patients with severe atherosclerotic disease, which is usually more pronounced in the common than in the external iliac artery, a suitable location for clamp placement can sometimes not be identified. Under those circumstances, the following options exist:

1. Only the external iliac artery is clamped proximally and distally; the arterial anastomosis is made as high on the external iliac artery as possible.
2. The internal (hypogastric) iliac artery is isolated and, after proximal branches are ligated and divided, mobilized all the way into the small pelvis. The internal iliac artery is clamped proximally; it is ligated, stick-tied, and divided distally. Dissection of the internal iliac artery usually provides 4–7 cm in vessel length. If the internal iliac artery also shows severe atherosclerotic disease, an (eversion) endarterectomy can provide adequate arterial inflow to the graft. Use of the hypogastric artery, with subsequent endarterectomy, avoids clamping of severely diseased common or external iliac arteries and thereby eliminates the risk of plaques breaking loose, causing distal occlusion or thrombosis.
3. A small arteriotomy is made at the site of the future arterial anastomosis. Balloon catheters are inserted, blocking both proximal and distal inflow. However, this technique makes the construction of the arterial anastomosis more difficult and usually results in a greater blood loss than with conventional techniques.

Clamping the iliac vessels does not change their natural position: The vein remains lateral and the artery medial. The position of the ureter after clamping is proximal and medial to the arterial anastomosis to avoid any impingement on the venous graft anastomosis. The venotomy is usually made first; four double-armed 6-0 nonabsorbable sutures are placed at the corners and sides of the venotomy. The arteriotomy is usually made in the common iliac artery proximal to the venotomy. Again, four double-armed 6-0 nonabsorbable sutures are placed at the corners and sides of the arteriotomy. Any plaques or intimal flaps are tacked at this time, usually with interrupted double-armed 6-0 or 7-0 nonabsorbable sutures. In case of arterial stenosis, proximal dilatations can be performed at this time. All manipulations on the arteries are made while the pancreas graft is not yet in the operative field, to avoid prolonged ischemia time. The iliac vein and iliac artery are both flushed with heparin until the effluent is clear.

In preparation for engraftment, the donor pancreas is wrapped in a wet, cold laparotomy sponge and brought into the operative field. This is the time to trim the portal vein. The portal vein is usually kept short to avoid kinking. The Y-graft is trimmed to an appropriate length. The end of the Y-graft may be cut in an oblique or "fish-mouth" fashion to enlarge the size of the anastomosis [21].

The venous anastomosis is completed first. The 6-0 nonabsorbable venotomy stitches are taken to their respective points on the donor portal vein; they are tied as the pancreas is lowered into the operative field. The end-to-side venous anastomosis is completed by running the 6-0 nonabsorbable corner sutures continuously from one end to the other and tying them at the corners. In identical fashion, the end-to-side arterial anastomosis is completed by running the 6-0 nonabsorbable corner sutures continuously from one end to the other and tying them at the corners. At the beginning of

the arterial anastomosis, mannitol (at 0.5 g/kg body weight), a colloid osmotic agent and free radical scavenger, is given to the recipient to minimize reperfusion edema. The amount of crystalloid fluid during the operation should be limited to diminish the risk of pancreatitis. In addition, octreotide (300 μg) is given intravenously at this time to also ameliorate the effects of reperfusion graft pancreatitis.

Crossmatched blood should be available before unclamping. Once the vascular anastomoses are complete, all clamps are removed (Fig. 29.2). Alternatively, and to test the integrity of the anastomoses first, spring clamps can be applied to the donor portal vein and donor Y-graft and released once both anastomoses have been proven to be "watertight." This "pre-testing" is helpful since it can be quite difficult to expose and repair anastomotic bleeding from the donor portal vein; once reperfusion occurs, attention can then be solely focused on achieving graft hemostasis [21]. Any bleeding sites are identified and carefully controlled with fine suture ligation techniques. Most bleeding arises from the mesenteric root, splenic hilum, or superior portion of the head of the pancreas. Gradual rewarming may identify additional bleeding sites.

After the graft is revascularized without any tension, torsion, or twist of the inflow and outflow vessels and hemostasis is achieved, a duodenojejunostomy is constructed either by direct anastomosis or by Roux-en-Y loop [136]. Historically, a Roux-en-Y limb was most commonly used to avoid contamination of the abdominal cavity with stool and causing generalized peritonitis in case of an anastomotic leak. The construction of a Roux-en-Y loop was also initially favored because it was believed that it could facilitate graft salvage in the event of graft duodenal complications. With improvements in surgical techniques and superior immunosuppressive protocols, anastomotic leaks are now rare and better controllable. Thus, the vast majority of pancreas transplants with enteric drainage are performed without the creation of a Roux-en-Y loop. However, if the graft duodenum does not appear to be well perfused, construction of a Roux limb is still recommended.

If the duodenum is directly anastomosed, a loop of jejunum is brought down to the level of the graft duodenum to ensure that the mesentery of the jejunum is long enough to reach the graft. In theory, the duodenojejunostomy should be made as proximally as possible (40–80 cm distal to the ligament of Treitz) to establish near-normal physiology and prevent discharge of pancreatic graft exocrine secretions into the distal ileum, which can result in diarrhea. If the jejunal loop reaches down to the graft easily, a side-to-side two-layer duodenojejunostomy is done (Fig. 29.2). Clamps are applied proximally and distally to the anastomotic site on the recipient's small bowel.

The outer posterior layer is constructed first, with interrupted 4-0 non-absorbable sutures. A donor duodenostomy just opposite from Vater's ampulla and a recipient jejunostomy (or ileostomy) of appropriate length are made. Closed suction drains are selectively used to remove exocrine secretions or bowel mucus from the field. The graft duodenum is cultured for aerobic, anaerobic, and fungal organisms. The inner layer is then constructed in a running fashion with a single 4-0 absorbable suture to achieve thorough hemostasis. Care is taken not to include the papilla of Vater in the suture line. The bowel clamps are removed after the inner layer is completed. The anastomosis is completed with an anterior outer layer with interrupted 4-0 nonabsorbable sutures.

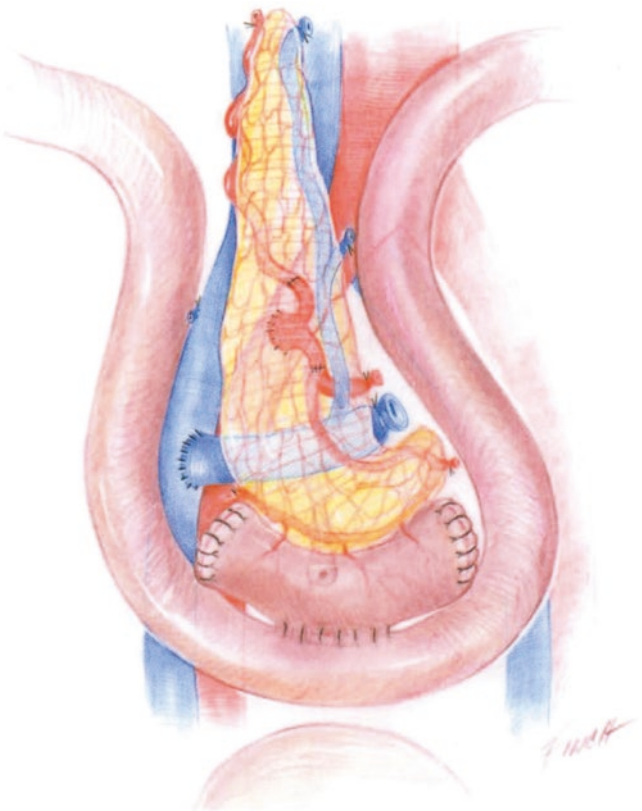

Fig. 29.2 Whole-organ transplant with systemic vein and enteric exocrine drainage: side-to-side two-layer duodenojejunostomy. The pancreas with its vascular anastomoses (donor Y-graft to recipient common iliac artery, donor portal vein to recipient common iliac vein) is implanted in the standard fashion on the right side of the pelvis

The side-to-side duodenojejunostomy can also be constructed by using a gastrointestinal anastomosis (GIA) stapler or an EEA stapler. If an EEA stapler is used, it is inserted through the open distal stump of the graft duodenum. The rod is punched through the antimesenteric wall, an enterotomy in the recipient bowel is made and purse-stringed around the anvil, and the stapler is fired in standard fashion. An EEA stapler anastomosis is reinforced externally with interrupted 4-0 nonabsorbable sutures. The distal stump of the graft duodenum is closed by stapler or hand-sewn technique. If a GIA stapler is used, the anastomosis is

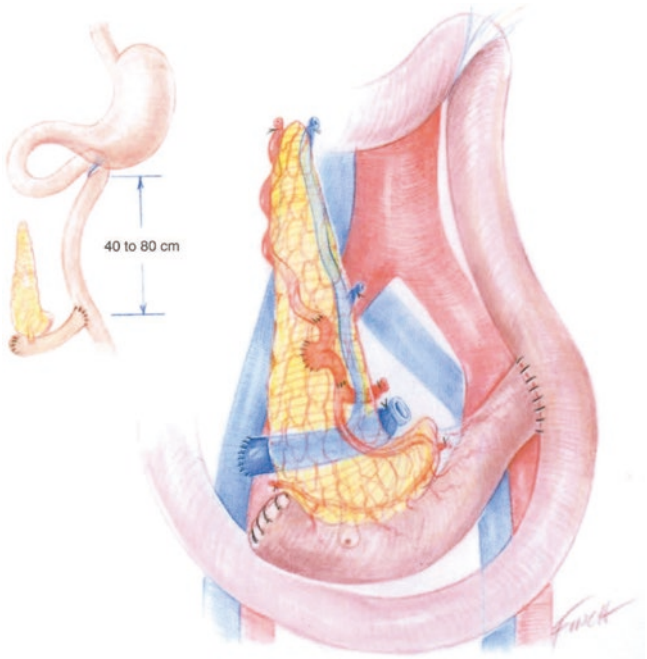

Fig. 29.3 Whole-organ transplant with systemicvein and enteric exocrine drainage: end-to-side two-layer duodenojejunostomy using the distal end of the graft duodenum. The anastomosis is located 40–80 cm distal to the ligament of Treitz (inset). The pancreas is implanted in the standard fashion on the right side of the pelvis

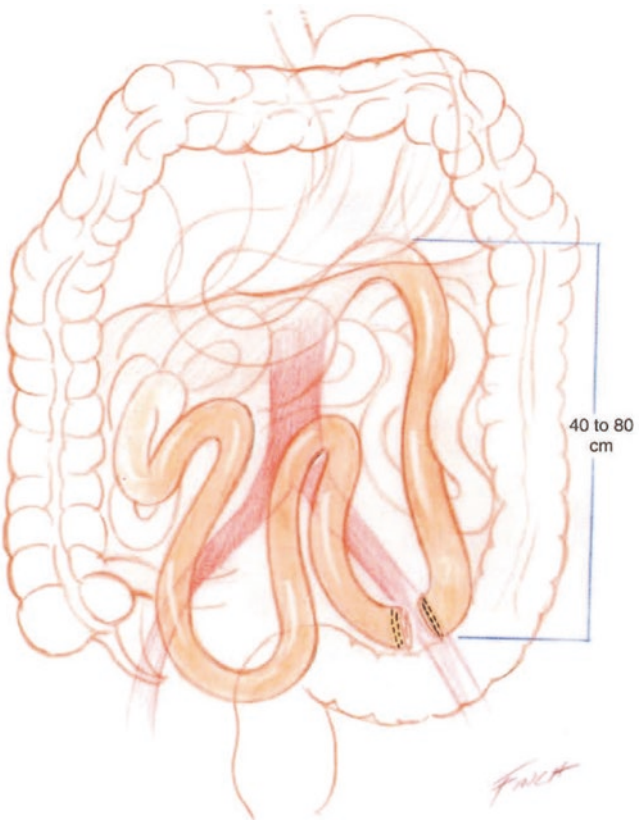

Fig. 29.4 Preparation of the Roux-en-Y loop for enteric exocrine drainage. The recipient jejunum is divided, using a GIA stapler, approximately 40–80 cm distal to the ligament of Treitz at a level that allows the construction of a tension-free duodenojejunostomy

reinforced internally with continuous 4-0 absorbable sutures to achieve thorough hemostasis and decrease the risk of anastomotic leaks. Alternatively, an end-to-side anastomosis can be constructed between the distal end of the graft duodenum and the recipient jejunum (Fig. 29.3); this end-to-side two-layer anastomosis can be hand-sewn or stapled with a GIA stapler.

If a Roux-en-Y loop is used, the proximal small bowel (40–80 cm distal to the ligament of Treitz) is brought down to the level of the graft duodenum to ensure that the mesentery of the jejunum is long enough to reach the graft. The jejunum is divided at a level that allows construction of a tension-free duodenojejunostomy. The jejunum is divided with a GIA stapler (Fig. 29.4). The stapled distal end of the jejunum is oversewn with 4-0 non-absorbable sutures. A bowel clamp is applied on the Roux limb distal to the anastomotic site. The two-layer side-to-side duodenojejunostomy is constructed in the same fashion as described above: either hand-sewn or stapled (with either a GIA or an EEA stapler) (Fig. 29.5). The bowel clamp is removed after the inner layer is completed. Alternatively, the distal stump of the graft duodenum can be anastomosed end-to-end to the distal end of the Roux-en-Y loop (hand-sewn two-layer anastomosis). The divided proximal end of the recipient jejunum is then anastomosed to a point on the distal bowel about 40 cm distal to the duodenojejunostomy. Doing so ensures an adequate defunctionalized limb for drainage of the exocrine pancreatic secretions. This jejunojejunostomy is a two-layer end-to-side or side-to-side anastomosis, either hand-sewn or stapled (with a GIA stapler).

The pancreas graft and all areas of dissection and mobilization are reexamined for bleeding. After complete hemostasis is accomplished, the abdomen is irrigated with 2–4 L of antibiotic solution (e.g., cephalothin sodium, 1 g/L of saline) and 2–4 L of antifungal solution (e.g., amphotericin B, 10 mg/L in sterile water). After all retractors are removed, the body and tail of the pancreas are covered by the cecum and ascending colon. The duodenojejunostomy and the head of the pancreas are covered by the small bowel and omentum. Usually, no drains are left in place.

However, if the pancreas graft reveals signs of hemorrhagic pancreatitis after unclamping, four drains (one for irrigation and three for drainage) are placed: one on top of the graft for irrigation, one lateral and parallel to the iliac vessels, one in the cul-de-sac, and one in the retrocecal position if the pancreas as implanted on the right side [137]. Postoperatively, the pancreas is irrigated for several days until the effluent is as clear as the influx.

The fascia of the midline abdominal incision is closed with #1 interrupted (or running) non-absorbable sutures. The

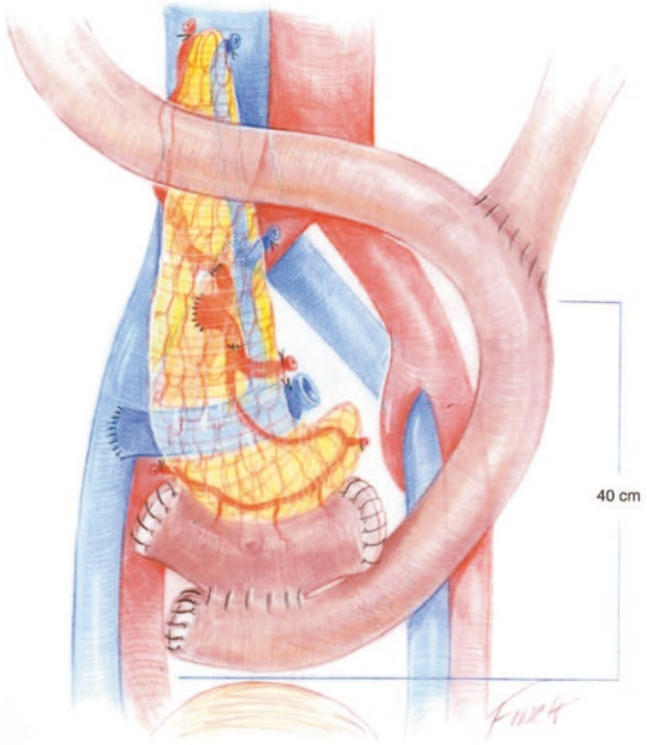

Fig. 29.5 Whole-organ transplant with systemic vein and enteric exocrine drainage: Roux-en-Y two-layer side-to-side duodenojejunostomy. The end-to-side jejunojejunostomy is made about 40 cm distal to the duodenojejunostomy. The pancreas is implanted in the standard fashion on the right side of the pelvis

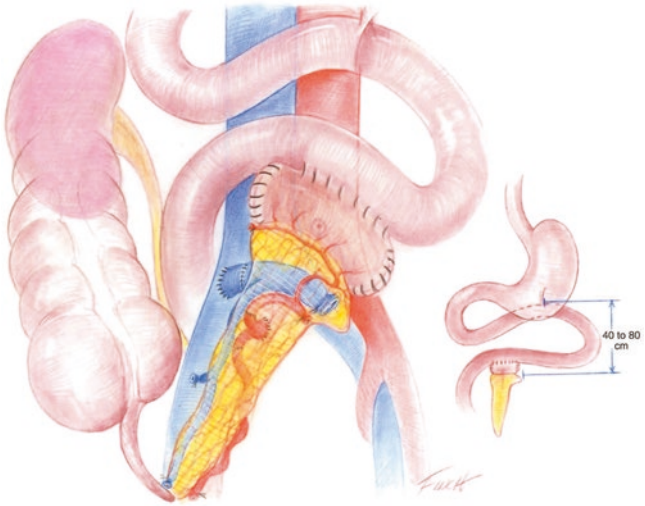

Fig. 29.6 Whole-organ transplant with systemic vein and enteric exocrine drainage (cephalad position). The donor portal vein (with an extension graft) is anastomosed end to side to the recipient's common iliac vein or infrarenal cava. The donor Y-graft is anastomosed to the recipient's common iliac artery. The arterial anastomosis is medial and distal to the venous anastomosis. A two-layer side-to-side duodenojejunostomy is constructed about 40–80 cm distal to the ligament of Treitz (inset)

subcutaneous tissue is irrigated with antibiotic and antifungal solutions. The skin is approximated with interrupted sutures or stapled. The Foley catheter remains for 10–20 days after the operation.

Although incidental appendectomies, cholecystectomies, and Meckel diverticulectomies at the time of pancreas transplantation have been performed and even recommended, there is no absolute need to perform any of these procedures unless there is evidence of acute or chronic disease [21, 138, 139].

Whole-Organ Pancreaticoduodenal Transplants with Systemic Vein and Enteric Exocrine Drainage on the Right Side in Cephalad Position

If the head of the pancreas is placed in a cephalad position, several options for vascular anastomoses exist. The following recipient vessels can be used:

1. Both common iliac vessels,
2. Vena cava and right common iliac artery, and
3. Vena cava and infrarenal aorta.

Most commonly, the first two options are been used; the third option may be an alternative for retransplants or if the common (and external) iliac arteries cannot be used.

If the proximal common iliac vessels are used for revascularization, the hypogastric veins are usually not ligated and divided [140]. The graft portal vein is anastomosed end-to-side to the common iliac vein or distal infrarenal vena cava. If the graft portal vein is short, an extension graft may be required to create a tension-free anastomosis. The arterial anastomosis to the proximal right common iliac artery is constructed in standard fashion (end-to-side) with 6-0 nonabsorbable sutures in running fashion; the infrarenal aorta (with a very short Y-graft anastomosis) may be used for retransplants or in case of severe atherosclerotic disease of the common iliac arteries on both sides (the right external iliac artery is rarely used in this circumstance as it requires a long arterial conduit for anastomosis). As with the caudad position, the arterial anastomosis is medial (to the venous anastomosis). But, unlike the caudad position, the venous anastomosis is proximal to the arterial anastomosis (Fig. 29.6).

With the cephalad position, the graft duodenum is easily anastomosed to the proximal jejunum (duodenojejunostomy) about 40–80 cm distal to the ligament of Treitz (Fig. 29.6), either side to side or with a Roux-en-Y loop. The intestinal anastomotic technique is the same as described above for the caudad position.

Whole-Organ Pancreaticoduodenal Transplants with Systemic Vein and Enteric Exocrine Drainage on the Left Side

If a previous kidney transplant was done on the right side (retroperitoneal placement via a hockey-stick incision), the pan-

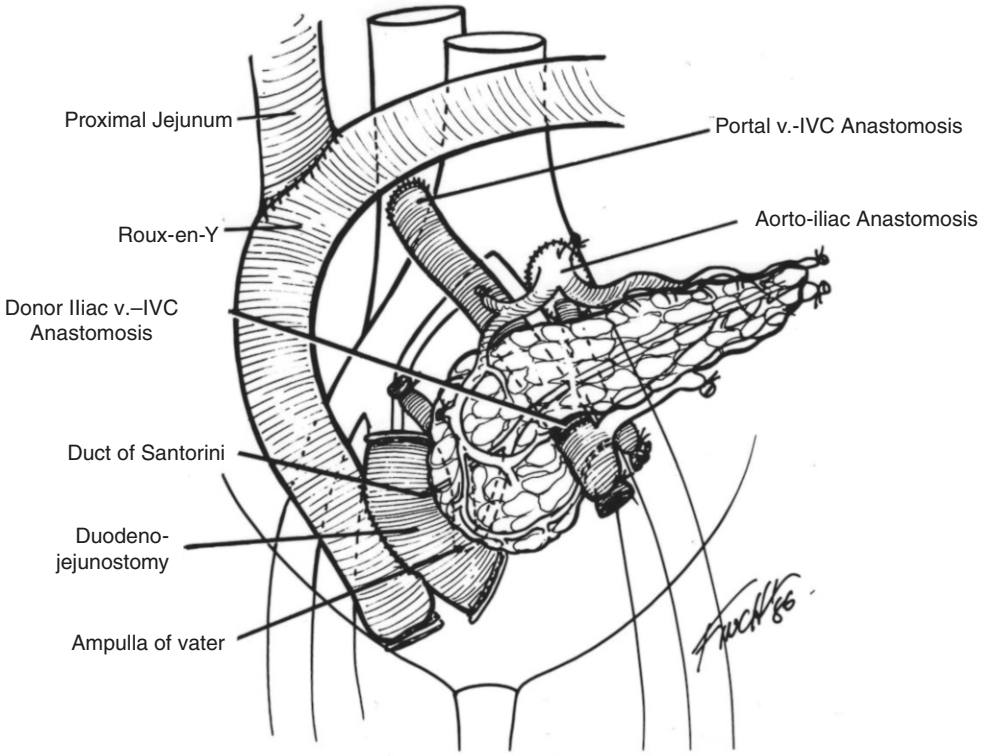

Fig. 29.7 Whole-organ transplant with systemic vein and enteric exocrine drainage: Roux-en-Y two-layer side-to-side duodenojejunostomy. The end-to-side jejunojejunostomy is made about 40 cm distal to the duodenojejunostomy. Implantation variant: the pancreas is engrafted on the left side with donor Carrel patch-to-left common iliac artery and donor portal vein (extension graft)-to-infrarenal vena cava anastomoses

creas is usually engrafted to the left iliac vessels (intraperitoneal placement via a midline incision) in either caudad or cephalad position. For caudad placement, the dissection and mobilization of the common, external, and internal iliac vessels may be done either lateral or medial to the sigmoid colon [134]. The medial position keeps the pancreas totally intraperitoneal. In the lateral position, the sigmoid colon and its mesocolon may impede peritoneal clearance of secretions from cut peripancreatic lymphatic tissues and increase the propensity for pseudocyst formation. An advantage of the lateral position is that only the retroperitoneal attachments of the sigmoid colon need to be taken down, whereas the mesocolon remains intact. If the pancreas graft is placed in the medial position, the dissection has to be carried out through an avascular window between the vascular arcades of the mesocolon. This approach usually provides good exposure to the common iliac vessels.

In contrast to the right side, the common left iliac vein is medial to the artery, and the internal iliac (hypogastric) artery may tether it down. To create a tension-free venous anastomosis and reduce the risk of thrombosis, the surgeon may elect to ligate and divide the internal iliac artery; doing so usually results in good mobilization of the common iliac vein. If the internal iliac artery on the right side, however, was used for the previous kidney transplant, the left internal iliac artery should be preserved. Under these circumstances, and if the donor portal vein is short, a portal vein extension graft of donor common iliac vein may be needed to create a tension-free venous anastomosis. If the left common iliac artery shows severe atherosclerotic disease except for a short proximal segment, the infrarenal vena cava can be used for portal vein anastomosis (Figs. 29.7 and 29.8). The technique for vascular engraftment

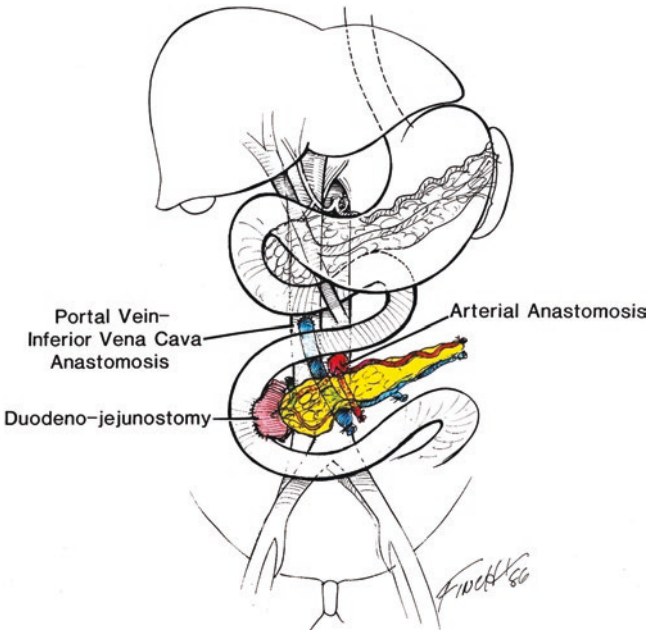

Fig. 29.8 Whole-organ transplant with systemic venous and enteric exocrine drainage (side-to-side duodenojejunostomy without Roux limb). Implantation variant: the pancreas is engrafted on the left side with donor Carrel patch-to-left common iliac artery and donor portal vein (extension graft)-to-infrarenal vena cava anastomoses

of the pancreas on the left side does not differ from the technique on the right side. Likewise, the technique of the duodenojejunostomy with or without the construction of a Roux limb is identical to the technique on the right side.

For the rare cephalad placement on the left side, the proximal common iliac vessels can be used or the infrarenal cava and the left common iliac artery. Usually, graft position medial to the sigmoid colon is preferred. The enteric anastomosis is the same as described on the right side.

SPK Transplants with Systemic Vein and Enteric Exocrine Drainage

If a kidney is transplanted simultaneously with the pancreas, the kidney is usually placed intra-abdominally on the left side of the pelvis.

For the kidney transplant, the recipient left external iliac vessels are preferred for vascular anastomoses; mobilization of the common iliac vessels is not required. Only on the rare occasion that the external iliac artery is completely calcified should the common or internal iliac artery be considered for an arterial anastomosis. The dissection of the left external iliac vessels is carried out lateral to the sigmoid colon, which is retracted medially during kidney engraftment. The left donor kidney is preferred because of its longer renal vein (vs. the right kidney), thus facilitating tension-free venous anastomosis. However, if the left kidney has multiple arteries (vs. a single artery on the right kidney), the surgeon may elect to use the right kidney and accept a shorter renal vein, which can usually be lengthened by using the attached donor vena cava as a conduit.

If the renal pedicle is long, I recommend prophylactic nephropexy to the anterolateral abdominal wall. Renal pedicle torsion after SPK transplants has been reported if the renal pedicle is ≥5 cm long and if there is a ≥2 cm discrepancy between the length of the renal artery and renal vein [141]. The paucity of adhesions secondary to steroid administration may further contribute to the development of renal pedicle torsion [142]. Nephropexy involves placing two to four non-absorbable sutures between the attached perirenal fatty tissue (or the renal capsule) and the anterolateral abdominal wall.

An alternative is to "retroperitonealize" the intra-abdominally placed kidney by anchoring the sigmoid colon mesentery to the lateral peritoneal reflection, using interrupted sutures [128, 129]. It has also been recommended to place the kidney completely extraperitoneally [128, 129]. The disadvantage is that a second incision is required. A modification of retroperitoneal placement of the kidney without a second incision was described by the University of Maryland group: After the midline incision is made, a retroperitoneal plane is developed to the (left) iliac vessels; the kidney is anastomosed in standard fashion and then remains in situ within this retroperitoneal pocket.

The optimal order of revascularization for pancreas and kidney grafts in SPK transplants has not been established but preservation time should be the determining factor:

1. If the preservation time is short (<12 h) the kidney can be implanted first to (1) diminish the risk of delayed kidney graft function, with the potential need for posttransplant dialysis, and (2) limit the amount of manipulation of the pancreas by placing retractors to obtain exposure for subsequent kidney graft implantation. The renal artery and renal vein are anastomosed end-to-side to the external iliac artery and external iliac vein, using the same technique as described for the pancreas graft anastomoses. If the preservation time is <12 h, the ureterocystostomy can be done before the pancreaticoduodenal graft is implanted.
2. If the preservation time is between 12 and 18 h, the kidney can still be implanted first. However, after completion of the renal vascular anastomoses, I recommend implanting the pancreas (vascular anastomoses and duodenojejunostomy) to diminish ischemia and reperfusion injury. The ureteroneocystostomy is performed after the pancreaticoduodenal graft is implanted. Alternatively, the pancreas is implanted first in light of a >12-h preservation time.
3. If the preservation time is long (>18 h) the pancreas should definitively be implanted first to decrease the risk of ischemia and reperfusion injury to the pancreas graft as well as to diminish the risks of graft pancreatitis and graft thrombosis.
4. If the pancreas graft is implanted first, it is important to avoid excessive traction on the pancreas graft when the kidney is implanted. Exposing the tail of the pancreas graft during this time to check perfusion can be very helpful [21].

An SRTR analysis of 12,700 SPKs investigated the influence of graft implantation order on graft survival [143]. The proportion of lost pancreas grafts at 3 months was significantly lower when the pancreas was implanted before the kidney (9.4% vs. 10.8%, $P = 0.011$). Increasing time lag (>2 h) between kidney and pancreas graft implantation—when the kidney was implanted first—accentuated the detrimental impact on pancreas graft survival (12.5% graft loss at 3 months, $P = 0.001$). Technical failure rates were reduced when the pancreas was implanted first (5.6% vs. 6.9%, $P = 0.005$). In contrast, graft implantation order had no impact on kidney graft survival.

To put this study in context with the preservation time as discussed above, it appears that—although observed differences are small—pancreas graft implantation first increases short-term pancreas graft survival and reduces rates of technical failure [143].

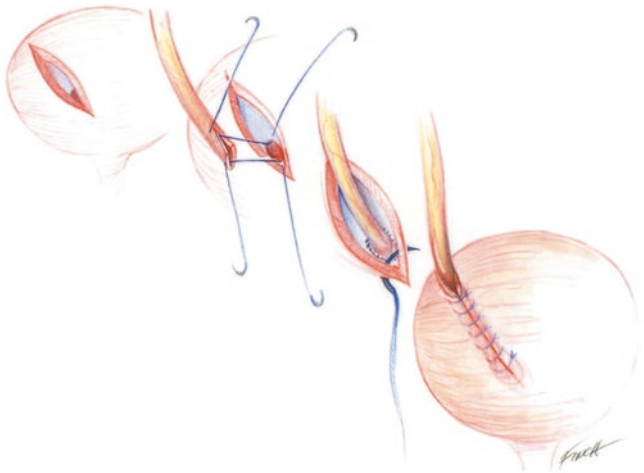

Fig. 29.9 Standard extravesical ureteroneocystostomy according to Lich. The seromuscular layer of the anterolateral surface of the bladder is incised for a length of 3–4 cm. The bulging urothelial layer is opened for only 0.5–1 cm at the distal end of the incision; the spatulated ureter is anastomosed using 5-0 or 6-0 absorbable sutures in running fashion. The muscle layer is closed over the ureter, thereby creating a submucosal tunnel

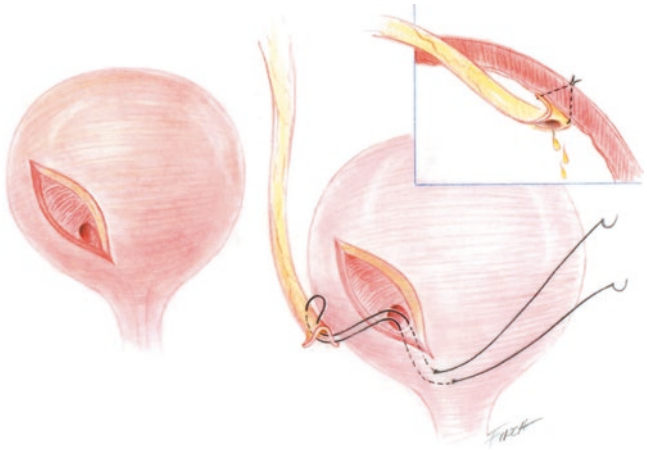

Fig. 29.10 Modified single-stitch extravesical ureteroneocystostomy. The seromuscular layer of the anterolateral surface of the bladder is incised for a length of 3–4 cm. The urothelial layer is separated from overlying muscle for 3–4 mm on each side of the incision. The bulging urothelial layer is opened for 0.5–1 cm at the distal end of the incision. A double-armed 3-0 nonabsorbable suture is passed from the outside (opposite the apex of the spatulation) into the ureter and brought through the ureteral tip. Both needles are then passed through the bladder opening and brought through the full thickness of the bladder, emerging 2–3 cm distal from the incision. The suture is tied, pulling the ureter into the bladder lumen, occluding the urothelial layer defect, and everting the tip. The seromuscular layer of the bladder is then closed over the ureter using 5-0 absorbable sutures, thereby creating a submucosal ureteral tunnel

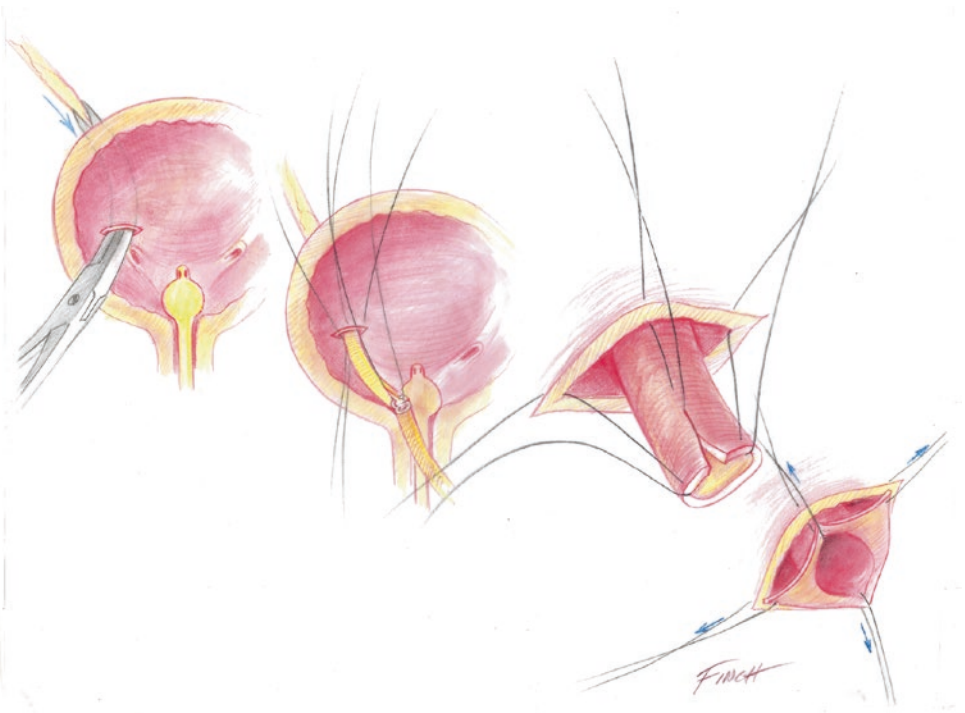

Fig. 29.11 Transvesical ureteroneocystostomy according to Politano–Leadbetter. The posterolateral bladder wall is transversely incised, a submucosal tunnel is created for about 2 cm, and, after a right-angle clamp is punched through the bladder, the ureter is drawn through the tunnel. The cut end of the ureter is incised (0.5 cm) and approximated with 5-0 absorbable sutures to the urothelial layer

The ureteroneocystostomy may be done by using an extravesical or anterolateral approach (standard Lich or modified one-stitch Lich technique) (Figs. 29.9 and 29.10)—or a transvesical or posterolateral approach (Politano–Leadbetter technique) (Fig. 29.11) [144–147]. The common goal of all techniques is the construction of a 2- to 3-cm submucosal tunnel to prevent reflux of urine up the ureter.

Ipsilateral placement of the SPK graft has been reported by Fridell et al. "to preserve the left iliac system side for future retransplantation" (Fig. 29.12). The donor

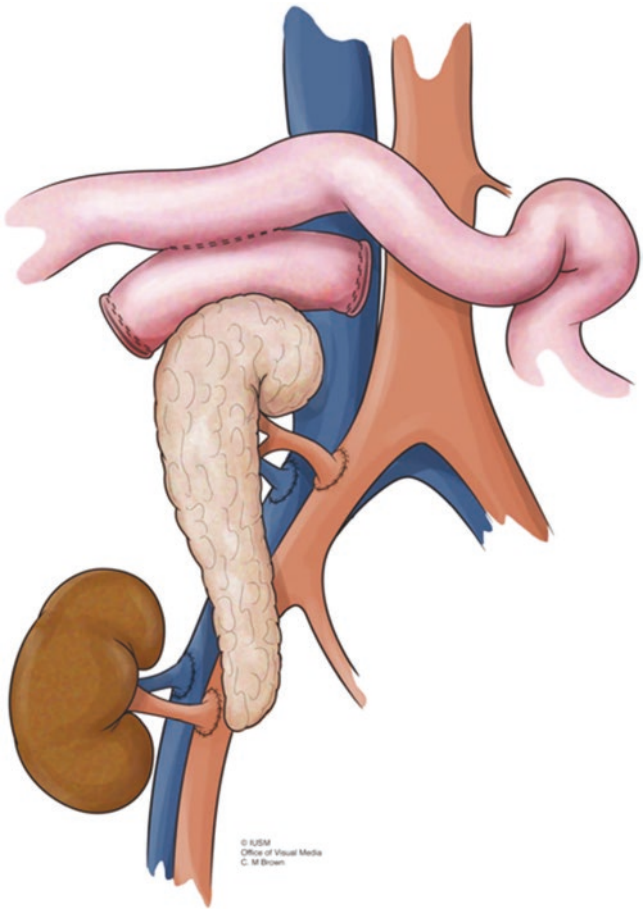

Fig. 29.12 Ipsilateral SPK placement. Donor Y-graft and portal vein are anastomosed to the recipient's right common iliac artery and vein. The head of the pancreas graft is directed cephalad. The donor renal artery and vein are anastomosed to the recipient's right external iliac artery and vein (reprinted with permission from Fridell et al. [132])

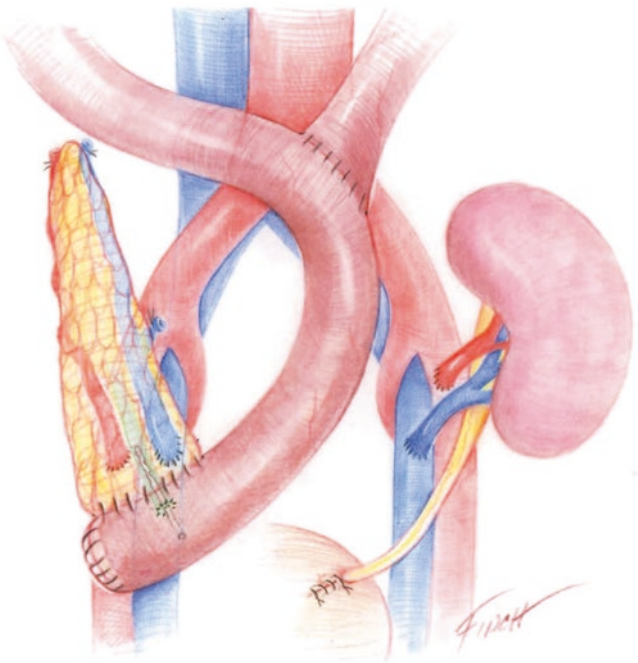

Fig. 29.13 Segmental transplant with systemic vein and enteric exocrine drainage in caudad position. The donor splenic artery and vein are anastomosed end to side to the recipient's external iliac artery and vein. The splenic artery anastomosis is lateral and proximal to the splenic vein anastomosis. The two-layer ductojejunostomy to a Roux-en-Y loop consists of an outer interrupted layer and an inner duct-to-mucosa anastomosis over a stent. The end-to-side jejunojejunostomy is made about 40 cm distal to the ductojejunostomy. The ureter of the simultaneously transplanted kidney is implanted into the bladder using the extravesical ureteroneocystostomy (Lich) technique

Y-graft and portal vein are anastomosed to the recipient's common iliac artery and vein. The head of the pancreas graft is directed cephalad. The donor renal artery and vein are anastomosed to the recipient external iliac artery and vein.

Segmental Pancreas Transplants with Systemic Vein and Enteric Exocrine Drainage

Segmental grafts are obtained from living donors, from split-pancreas deceased donors, or from deceased donors whenever the whole organ cannot be removed [134, 136].

The anatomy of the splenic artery itself and its blood supply to the tail of the pancreas is quite complex (see Chap. 16). It can be subdivided into three pancreatic segments: suprapancreatic (above the superior margin of the pancreas), retropancreatic (posterior to the superior margin of the pancreatic tail), and prepancreatic (anterior to the tail). The splenic artery gives rise to several intrapancreatic (parenchymal) branches: (1) The dorsal pancreatic artery (DPA) derives close (1–2 cm) to the origin of the splenic artery from the celiac trunk; the DPA passes downwards, dorsal to the neck/body and divides into right and left branches (the right branch supplies part of the head of the pancreas and connects with the pancreaticoduodenal arcades; the left branch becomes the transverse [or inferior] pancreatic artery, runs along the inferior pancreatic border and connects with other intrapancreatic vessels off the splenic artery); (2) the great pancreatic artery ("pancreatic magna"), the largest of two to ten pancreatic branches all of which originate distally of the DPA origin from the splenic artery; it also supplies the pancreatic duct in the tail; (3) the caudal pancreatic artery which usually originates from the inferior branch of the splenic artery in the hilum of the spleen; it runs inferiorly and back into the pancreas and connects with the transverse pancreatic artery; in contrast to deceased donor recoveries, it is rarely preserved in pancreas procurements from living donors.

Most segmental grafts comprise the body and tail of the pancreas, but on rare occasions, only the head of the pancreas (with the duodenum from a deceased donor) has also been engrafted. As with whole organ transplants, the right side is the preferred location.

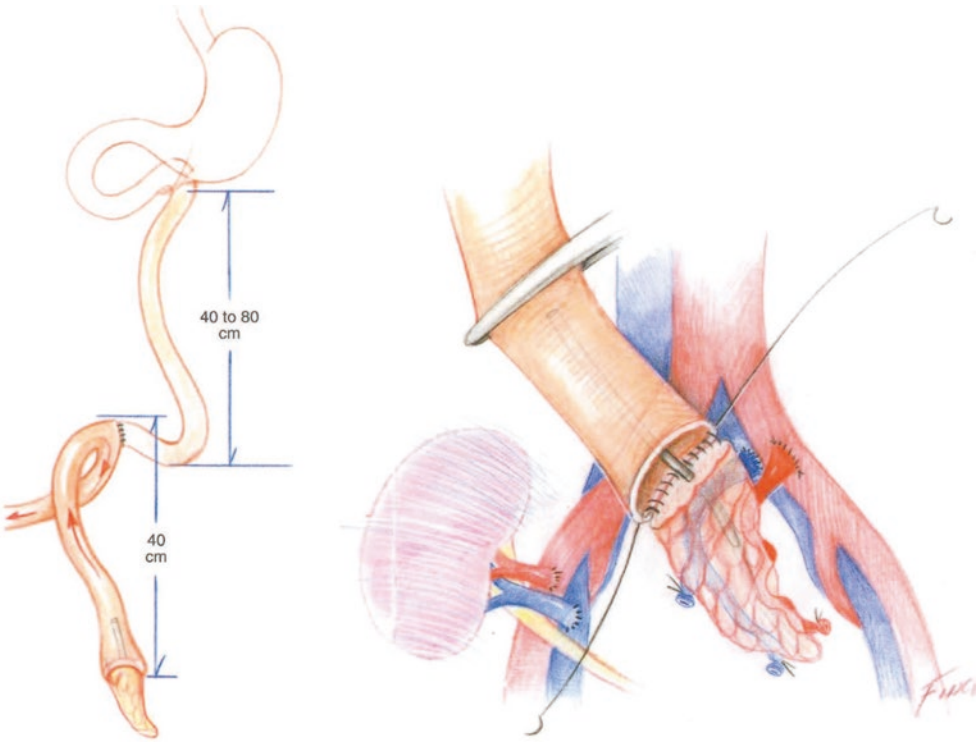

Fig. 29.14 Segmental transplant with systemic venous and enteric drainage in cephalad position. Because of the previous kidney transplant on the right side, the donor splenic artery and vein are anastomosed end-to-side to the left recipient common iliac artery and vein. The splenic artery anastomosis is lateral and distal to the splenic vein anastomosis. A two-layer Roux-en-Y pancreaticojejunostomy is created and a temporary stent is placed in the pancreatic duct. The Roux-en-Y limb is constructed in the standard fashion 40–80 cm distal to the ligament of Treitz; the jejunojejunostomy, 40 cm distal to the pancreaticojejunostomy (inset)

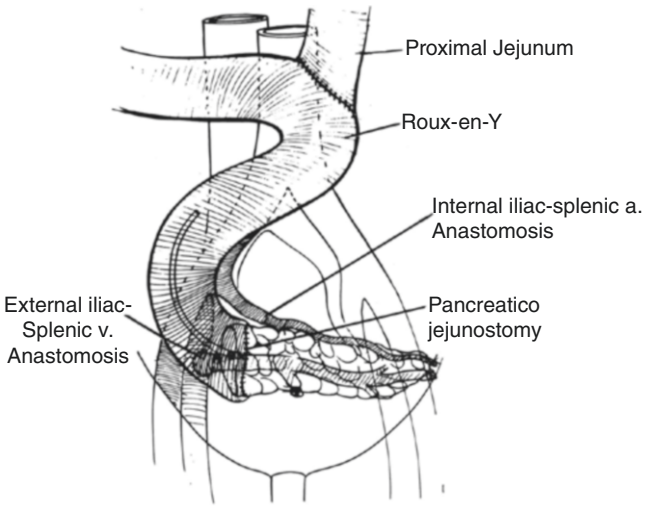

Fig. 29.15 Segmental transplant with systemic venous and enteric drainage. Implantation variant: the donor splenic artery is anastomosed end-to-end to the recipient's right internal iliac artery and the donor splenic vein end-to-side to the recipient's right external iliac artery

If the distal pancreas is transplanted, the splenic artery and splenic vein are anastomosed to the recipient's external iliac vessels (Figs. 29.13, 29.14, 29.15, and 29.16). The dissection of the recipient iliac vessels is as extensive as with a whole-organ transplant because of the importance of a tension-free venous anastomosis. In contrast to a whole-organ transplant, the external iliac vein is positioned medial to the external iliac artery; doing so reflects the natural position of the splenic

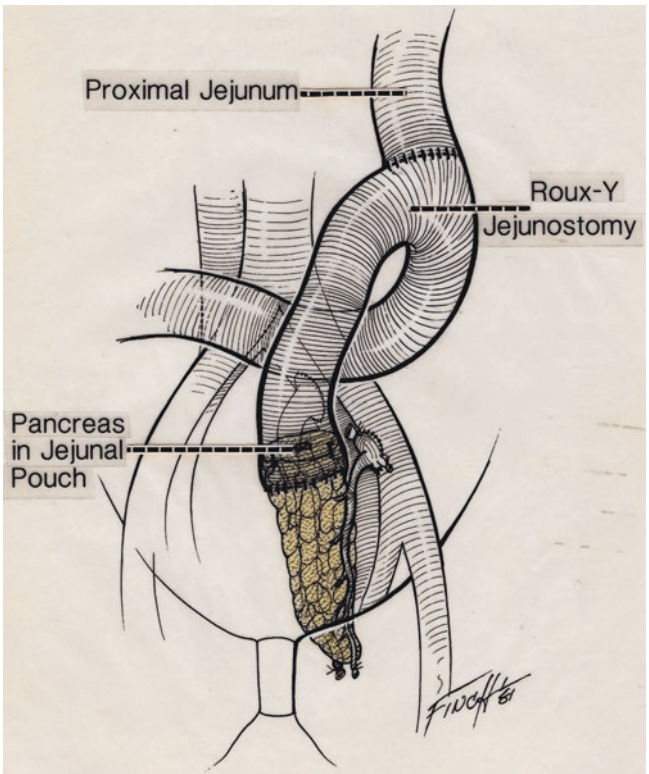

Fig. 29.16 Segmental transplant with systemic venous and enteric drainage in cephalad position. Implantation variant on the left side: the donor Carrel patch with the splenic artery is anastomosed end-to-side to the recipient's common iliac artery and the donor splenic vein with a donor portal vein cuff is anastomosed end-to-side to the recipient's left common iliac artery

artery and vein. If the iliac vein is completely mobilized and freed, a venous extension graft is usually unnecessary. The splenic vein is anastomosed end to side to the external iliac vein with running 6-0 or 7-0 nonabsorbable sutures. The splenic artery is then anastomosed lateral and slightly cephalad to the vein, either end to side to the external iliac artery or (less frequently) end to end to the internal iliac artery.

As with whole-organ pancreaticoduodenal grafts, two different placements of the segmental graft have been described when enteric drainage is used:

1. If the segmental graft is placed in a caudad position, the vascular anastomoses are constructed in the same fashion as described (Fig. 29.13).
2. If the segmental graft is placed in a cephalad position, the donor splenic artery and vein are anastomosed end-to-side to the recipient's common iliac artery and vein. The splenic vein anastomosis is medial and slightly cephalad to the splenic artery anastomosis (Fig. 29.15).

For enteric drainage of segmental grafts, a Roux-en-Y loop is routine [136, 148]. The proximal small bowel is drawn caudad to the level of the cut surface of the pancreas to ensure that the mesentery of the jejunum is long enough to reach the graft. The jejunum is then divided with a GIA stapler. The stapled distal end of the divided jejunum is oversewn with 4-0 non-absorbable sutures. In preparation for the pancreaticojejunostomy, interrupted sutures of 4-0 Prolene are placed on the posterior surface of the pancreas and jejunum to create the posterior outer layer of the anastomosis. A stab wound (0.5–1 cm) is made through all layers of the antimesenteric wall of the jejunum, several centimeters distal to the closed Roux-en-Y loop. The pancreatic duct is then anastomosed to the full thickness of the jejunal wall by invaginating the redundant end of the duct into the jejunal lumen (*ductojejunostomy*). Interrupted 7-0 or 6-0 absorbable sutures are used. Before the anterior row of the inner layer is completed, a stent is passed through the duct-to-mucosa anastomosis. Once the inner layer is completed, the anterior outer layer between the anterior surface of the pancreas and jejunum is constructed with 4-0 nonabsorbable sutures (Fig. 29.13). The stent is tagged to the anastomosis with one absorbable suture, which passes within several weeks through the distal bowel.

Alternatively, the Roux-en-Y limb is anastomosed to the whole cut surface of the pancreas (*pancreaticojejunostomy*), rather than to the duct itself, with the invagination technique (Fig. 29.14). This two-layer anastomosis is begun with an outer posterior layer with interrupted 4-0 non-absorbable sutures. The jejunum is incised transversely over a length of 3–4 cm. An inner layer between the cut surface of the pancreas and jejunal wall (full thickness) is constructed circumferentially with running absorbable 4-0 sutures. Doing so invaginates the whole cut surface of the distal pancreas into the Roux limb. An outer posterior layer of interrupted 4-0 non-absorbable sutures completes the anastomosis. A stent temporarily remains in the pancreatic duct, tagged to the anastomosis with an absorbable suture and extending into the jejunal lumen (Fig. 29.14). The stent usually passes with the enteric contents within a few weeks.

Finally, the divided and stapled proximal end of the recipient jejunum is anastomosed to a point on the distal bowel about 40 cm distal to the ducto- or pancreaticojejunostomy. Doing so provides an adequate defunctionalized limb for exocrine drainage of the distal pancreas. This jejunojejunostomy is a hand-sewn or stapled two-layer end-to-side or side-to-side anastomosis.

A number of variants for implantation of a segmental pancreas graft have been described including engraftment on the left side and the use of donor Carrel patches and/or portal vein cuffs (Figs. 29.15 and 29.16).

Systemic Vein and Bladder Exocrine Drainage

Whole-Organ Pancreaticoduodenal Transplants with Systemic Vein and Bladder Exocrine Drainage on the Right Side

As mentioned earlier in this chapter, bladder drainage is rarely performed nowadays. Since this niche or fall-back technique is technically unique and challenging, it still warrants a detailed description.

Before graft implantation and after complete dissection of the iliac vessels, the lower abdominal dissection is completed by mobilizing the bladder: the lateral attachments of the bladder are divided, including the round ligament in women. In men, care is taken to preserve the spermatic cord. Dissection of the bladder is limited to its upper third to prevent injury to its neural innervation. Even limited mobilization of the anterior and lateral portions of the bladder usually allows the creation of a tension-free duodenocystostomy.

Pancreas graft implantation on the right side (in the caudad position) is identical to the vascular anastomotic techniques used for enteric drainage on the right side.

After pancreas revascularization, if the distal stump of the graft duodenum is open, a clamp is placed for hemostasis and prevention of any spillage of duodenal contents. If the distal duodenal stump was stapled, the staple line is removed after revascularization and the edges are grasped with Babcock or Allis clamps. The duodenum is irrigated with amphotericin and antibiotic irrigation solutions; a pool-suction tip is used to prevent any spillage. The graft duodenum is cultured for aerobic, anaerobic, and fungal organisms to allow adequate antimicrobial prophylaxis posttransplant.

The duodenocystostomy can be done with either a stapler or a hand-sewn technique [149]; the complication rate is not different [150].

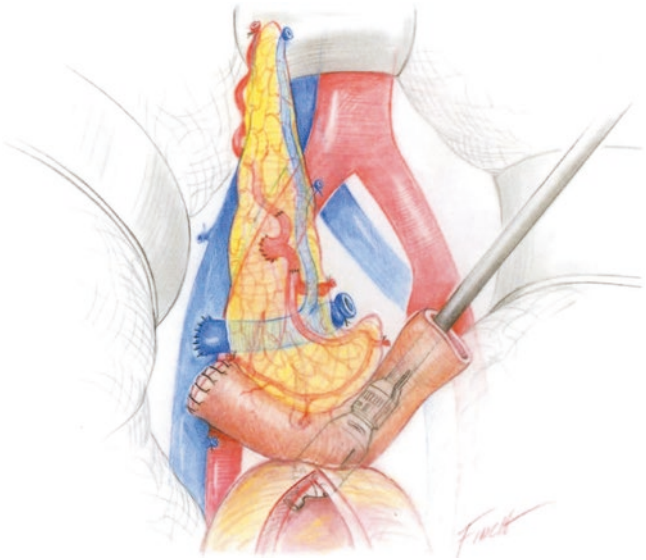

Fig. 29.17 Whole-organ transplant with systemic vein and bladder exocrine drainage: the arterial anastomosis (Y-graft) is medial and proximal to the portal vein (without an extension graft) anastomosis. The bladder is opened via an anterior cystotomy and the EEA stapler is inserted through the opened distal end of the graft duodenum. The rod of the stapler is punched through the antimesenteric wall of the duodenum and posterior wall of the bladder; the anvil of the EEA stapler is placed on the stapler rod. The stapler is ready to be fired, creating a circular staple line (duodenocystostomy)

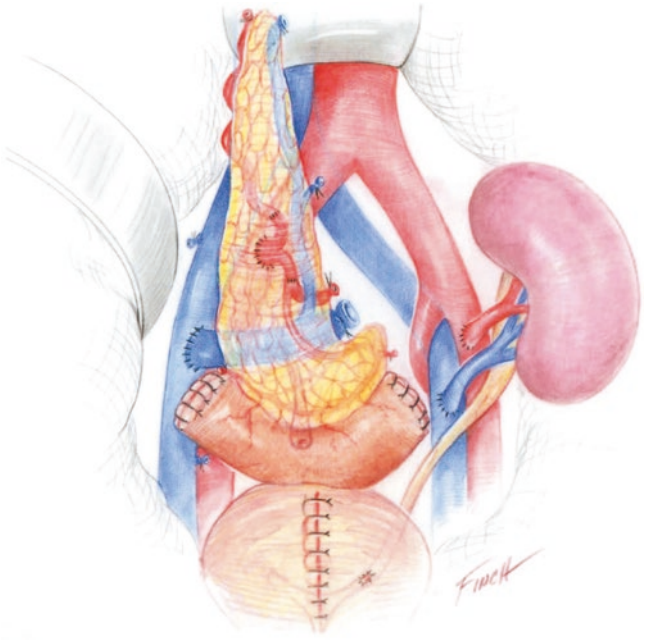

Fig. 29.18 Whole-organ transplant with systemic vein and bladder exocrine drainage: both the pancreas and kidney are placed intra-abdominally; the pancreas is on the right side of the pelvis. The donor Y-graft is anastomosed to the recipient's common iliac artery and the donor portal vein to the recipient's common iliac vein. Both duodenal stumps are oversewn, as is the anterior cystotomy. The donor renal artery and vein are anastomosed to the recipient's external iliac artery and vein; the ureter is implanted into the bladder using the Politano–Leadbetter technique

In patients without previous pancreas transplants or bladder surgery, the author prefers a side-to-end anastomosis (EEA) with a stapler (Fig. 29.17). Different sizes (21–31 mm) for the curved EEA stapler are used to dilate the duodenum and determine the size of the anastomosis. Usually, a 21- or 25-mm EEA stapler is used. After the anvil is removed, the curved EEA stapler is inserted into the open distal end of the graft duodenum and passed gently toward the proximal duodenum. The rod projecting from within the ring of staples, to which the anvil will later be attached, is punched through the antimesenteric wall of the duodenum with the aid of a cautery at a level just opposite the papilla. If a lateral duodenotomy to flush the duodenum was made at the time of the procurement, then a single 2-0 or 3-0 nonabsorbable purse-string suture is necessary to tighten the duodenal opening around the rod of the EEA stapler. The bladder is opened anteriorly, over a length of 3–5 cm, to create the anastomosis under direct vision. The rod of the EEA stapler is then pushed through the posterior wall of the bladder, several centimeters away from the cystostomy. This distance between the anterior and posterior cystostomy is necessary to avoid inadvertent narrowing of the duodenocystostomy when the anterior cystostomy is closed. The EEA anvil is placed on the stapler rod from within the bladder. The stapler is then tightened by stretching both walls of the duodenum and bladder over the ends of the stapler. The stapler is fired, creating a circular staple line.

On completion of the stapled anastomosis, the stapler is examined for the intactness of both rings. If either of the rings is not intact, the anastomosis needs to be redone (either with the hand-sewn technique or with a larger stapler). If the defect is small, the disrupted area can be reinforced only.

In general, the stapled duodenocystostomy is reinforced internally with continuous 4-0 absorbable sutures to facilitate hemostasis and decrease the risk of anastomotic leaks. The opened distal duodenal end is shorted to an appropriate length using a single throw of the TA-55 or TA-90 stapler. The staple line is oversewn with continuous 4-0 nonabsorbable sutures and then inverted with interrupted 4-0 nonabsorbable sutures in Lembert fashion (Fig. 29.18). Sometimes, the staple line is not oversewn and only Lembert sutures are placed; the distal duodenal segment is then closed in two or three layers. I have not found a difference in the rate of duodenal stump leaks according to the number of layers.

With the hand-sewn anastomosis, a horizontal posterior cystostomy 2–4 cm long is made. A two-layer anastomosis is created between the bladder and duodenum. The outer posterior layer is constructed first, with interrupted 4-0 nonabsorbable sutures. A horizontal graft duodenotomy of appropriate length is made antimesenterically at the level of the papilla. The inner layer is then constructed in a running fashion (to achieve hemostasis) with 4-0 or 3-0 absorbable sutures. The anastomosis is completed with the anterior outer layer with interrupted 4-0 nonabsorbable sutures. The opened

distal end of the duodenum is closed, as described above, with the stapler technique.

If only the pancreas is transplanted, the anterior cystostomy is closed in three layers (Fig. 29.18). The Foley catheter is clamped and the bladder is first irrigated and then filled with about 250 cc of antifungal and antibiotic solutions. Distention of the bladder reduces the risk of incorporating the back wall into the suture line. The bladder is closed in three layers: for the innermost layer, a running 4-0 absorbable suture is used to approximate the urothelium, submucosa, and muscularis; for the second, full-thickness layer, a running 3-0 absorbable suture is used; for the outer third, seromuscular layer, a running 3-0 absorbable suture is used and the suture lines are inverted.

The remainder of the operation is identical to the technique for enteric drained transplants as described above.

Whole-Organ Pancreaticoduodenal Transplants with Systemic Vein and Bladder Exocrine Drainage on the Left Side

Engraftment is similar to the technique for enteric drained transplants with dissection and mobilization of the common, external, and internal iliac vessels either lateral or medial to the sigmoid colon [134]. The medial position keeps the pancreas totally intraperitoneal and avoids interposition of the sigmoid colon between the pancreas graft and bladder. As mentioned above, an advantage of the lateral position is that only the retroperitoneal attachments of the sigmoid colon need to be taken down, whereas the mesocolon remains intact. If the pancreas graft is placed in the medial position, the dissection has to be carried out through an avascular window between the vascular arcades of the mesocolon.

The technique for vascular engraftment of the pancreas on the left side does not differ from the technique on the right side. Likewise, the technique of the duodenocystostomy is identical to the technique on the right side. Care must be taken not to accidentally transect the previously transplanted ureter while mobilizing the bladder. For that reason, the dissection of the lateral attachments of the bladder on the right side should be kept to a minimum. If the ureter of the transplanted kidney is inadvertently transected, a tension-free end-to-end anastomosis over a double-J stent (ends positioned in the renal pelvis and bladder) should be performed. The stent can be removed cystoscopically 3–4 weeks later.

SPK Transplants with Systemic Vein and Bladder Exocrine Drainage

As already mentioned, the kidney graft is usually placed intra-abdominally on the left side of the pelvis (Fig. 29.18). The technical details are identical to the techniques described above.

If bladder drainage is used and the duodenocystostomy is stapled (creating an anterior cystostomy), any ureteral implantation techniques may be used. If the duodenocystostomy is hand-sewn (without creating an anterior cystostomy), only the standard Lich technique or its one-stitch modification may be used.

Segmental Pancreas Transplants with Systemic Vein and Bladder Exocrine Drainage

If a segmental graft comprising the body and tail of the pancreas is engrafted, the right side is the preferred location (as with whole organ transplants).

If the distal pancreas is transplanted, the splenic artery and splenic vein are anastomosed to the recipient's external iliac vessels (Fig. 29.19). As described above, the dissection of the recipient iliac vessels is as extensive as with a whole-organ transplant because of the importance of a tension-free venous anastomosis. In contrast to a whole-organ transplant, the external iliac vein is positioned medial to the external iliac artery; doing so reflects the natural position of the splenic artery and vein. If the iliac vein is completely mobilized and freed, a venous extension graft is usually unnecessary. Upon completion of the vascular anastomoses, the bladder anastomosis is constructed. Given the proximity of the external iliac vessels to the bladder, a tension-free bladder anastomosis can easily be constructed. Two techniques for bladder drainage are used [134, 136]. Ductocystostomy and pancreaticocystostomy.

Ductocystostomy

A direct anastomosis is constructed between the pancreatic duct and bladder urothelium. The seromuscular layer of the bladder is transversely incised down to the urothelium (2–3 cm). Interrupted 4-0 non-absorbable sutures are placed seromuscularly through the bladder and on the posterior surface of the pancreas to create the posterior outer layer of the anastomosis, with the knots buried underneath. A small incision is made in the bladder urothelium (0.5–1 cm), and the bladder is opened (Fig. 29.19). The posterior row of the inner anastomosis is done between the pancreatic duct and bladder urothelium with interrupted 7-0 absorbable sutures. Before the anterior layer is completed, a stent is passed through the duct-to-urothelium anastomosis. The anterior layer of the anastomosis is completed with interrupted 7-0 absorbable sutures over the stent. The stent itself is tagged to the anastomosis with one of the interrupted sutures. An anterior outer layer between the seromuscular bladder wall and the anterior surface of the pancreas, with 4-0 non-absorbable sutures, completes the anastomosis (Fig. 29.19). The stent is either spontaneously excreted through the urethra or cystoscopically removed about 4 weeks posttransplant.

A variation of the outer layer has been described in which both an anterior and posterior muscular flap (each 2 cm wide) are created after the bladder is incised but while the urothelium is still intact [151]. This dissection results in a collar of bladder muscular tissue surrounding a broader area of the proximal and middle portion of the segmental graft.

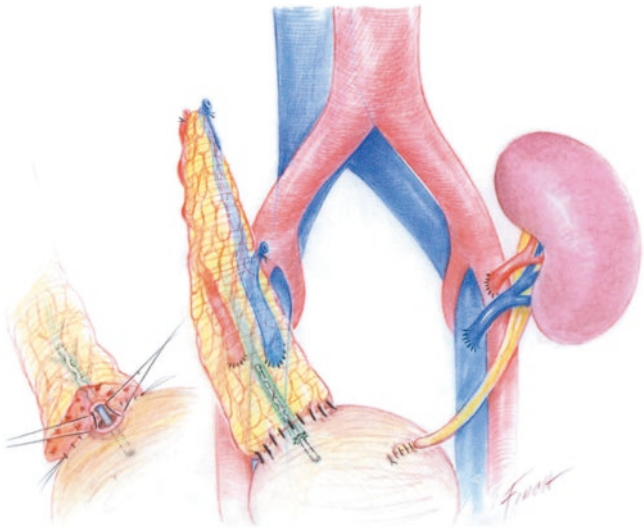

Fig. 29.19 Segmental transplant with systemic vein and bladder exocrine drainage. The donor splenic artery and splenic vein are anastomosed end-to-side to the recipient's external iliac artery and vein. The splenic artery anastomosis is lateral and proximal to the splenic vein anastomosis. A two-layer ductocystostomy is constructed: the pancreatic duct is approximated to the urothelial layer (inner layer) using interrupted 7-0 absorbable sutures over a stent (inset). The ureter of the simultaneously transplanted kidney is implanted into the bladder using the extravesical ureteroneocystostomy (Lich) technique

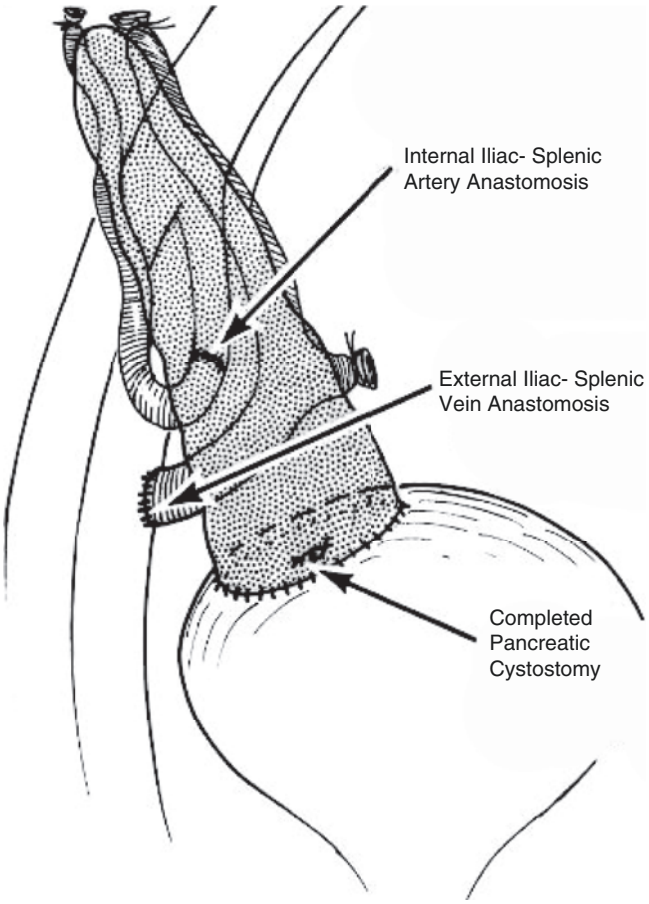

Fig. 29.20 Segmental transplant with systemic vein and bladder exocrine drainage. Implantation variant on the right side: the donor splenic artery is anastomosed end-to-end to the recipient's internal iliac artery and the donor splenic vein end-to-side to the recipient's external iliac artery and vein. A two-layer ductocystostomy is constructed: the pancreatic duct is approximated to the urothelial layer (inner layer) using interrupted 7-0 absorbable sutures over a stent (inset)

Pancreaticocystostomy

A two-layer anastomosis using the invagination technique is constructed. A first outer layer is begun with interrupted nonabsorbable 4-0 sutures between the posterior surface of the pancreas and bladder wall. The bladder is then transversely incised, over a length of 3–4 cm, and opened. A second inner layer of running 4-0 absorbable sutures is run around the entire circumference of the pancreas and cystotomy, thus invaginating the cut surface of the pancreas into the bladder. The anterior outer layer is finished with interrupted 4-0 nonabsorbable sutures. Stent management is identical to that of duct-to-mucosa anastomosis.

Variants for implantation of a segmental pancreas graft using bladder drainage have been described including end-to-end anastomosis between the donor splenic artery to the recipient's internal iliac artery (Fig. 29.20).

Portal Vein and Enteric Exocrine Drainage [152]

In contrast to systemic venous and enteric or bladder drainage techniques, the portal-enteric drainage procedure is a mid-abdominal rather than a pelvic procedure. There are several (relative) contraindications to portal-enteric drainage: BMI >35 kg/m^2, sclerosing encapsulating peritonitis, severe adhesions from previous laparotomies, a small recipient SMV (≤5 mm in diameter), a partially thrombosed or sclerotic SMV, a "deep" SMV embedded in extensive mesenteric fat, and portal hypertension [21].

Systemic vein drainage provides a choice between bladder or enteric diversion of exocrine pancreatic secretions. In contrast, portal vein drainage basically allows enteric diversion only. Except for the rare occasion in which the donor distal splenic vein is anastomosed (via an extension graft) to the recipient portal vein (see above [47, 48]), which places the head of the pancreas in a caudad position in proximity to the bladder, bladder drainage is technically not feasible with portal drainage. When the donor portal vein system is used for anastomosis, the head of the pancreas is in a cephalad position in the mid-abdomen.

For portal-enteric drainage, the donor duodenum and jejunum do not have to be shortened on the back table in order to preserve all options for the enteric anastomosis: small bowel, duodenal or gastric drainage [21].

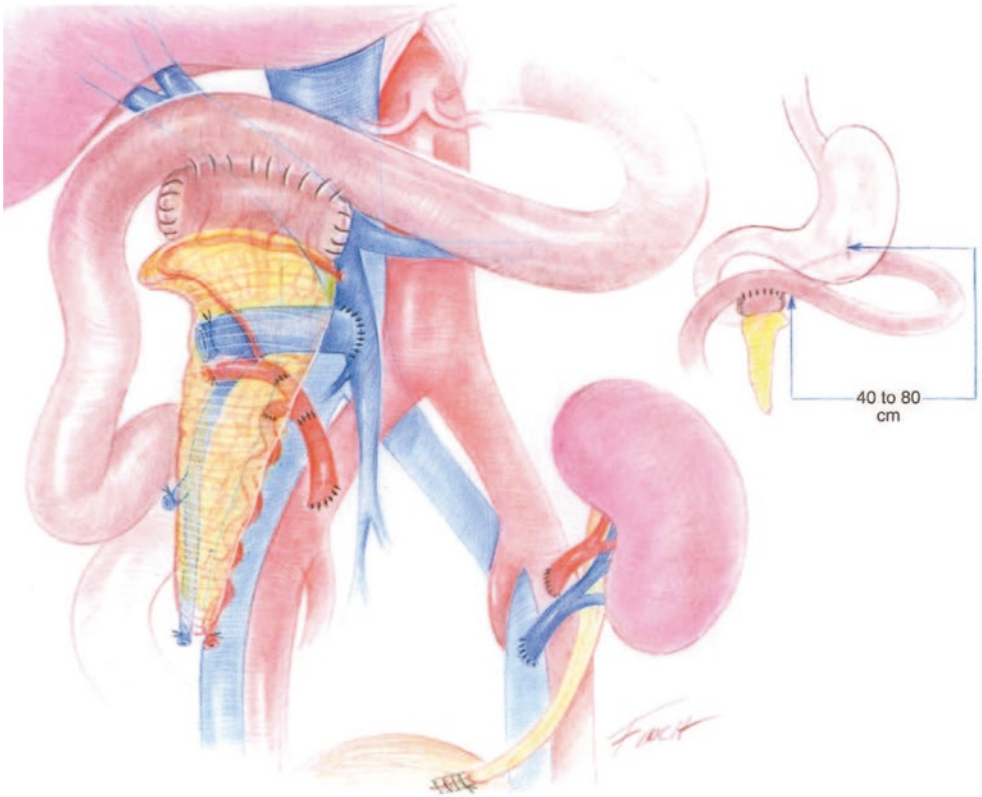

Fig. 29.21 Whole-organ transplant with portal vein and enteric exocrine drainage using the intraperitoneal approach. The pancreas graft overlies the root of the small bowel mesentery, with the duodenal segment below the transverse colon. The donor portal vein is anastomosed end-to-side to the recipient's superior mesenteric vein. The donor Y-graft (with an extension graft) is anastomosed to the recipient's common iliac artery through a mesenteric tunnel. A two-layer side-to-side duodenojejunostomy is constructed about 40–80 cm distal to the ligament of Treitz. In the final position, the jejunal limb usually lies anterior to the donor duodenum. The simultaneously transplanted kidney is anastomosed to the recipient's external iliac artery and vein. The ureter is implanted into the bladder using the extravesical ureteroneocystostomy (Lich) technique

Whole-Organ Pancreaticoduodenal Transplants with Portal Vein and Enteric Exocrine Drainage

Portal-enteric drainage can be accomplished with an intraperitoneal or retrocolic/retroperitoneal approach. Both techniques are described below. The intraperitoneal approach was described first.

Techniques of portal venous drainage have utilized the recipient portal vein directly [62], the splenic vein [58, 59, 62, 64] and the inferior mesenteric vein [61]. However, the vast majority of pancreas grafts with portal vein drainage are placed so that the donor portal vein connects to the recipient's proximal superior mesenteric vein (SMV) or to the SMV's main feeding vessel (Fig. 29.21). The head of the pancreas graft is directed cephalad and the tail and body caudad.

A small window in an avascular area of the small bowel mesentery is made so that the arterial Y-graft traverses the shortest distance to the arterial inflow (most commonly, the right common iliac artery). However, this distance may be as long as 6 cm; a short Y-graft could make this approach impossible and a "long" Y-graft is required [21].

If a large window is made in the ileal mesentery (preferably in a thin patient), both the venous and arterial anastomoses can be completed on the same side of the mesentery. Of note, the large window must be closed at the end of the procedure to avoid the development of an internal hernia [21].

As with back-table arterial reconstruction of pancreas grafts for systemic vein drainage, the donor internal iliac artery is anastomosed to the splenic artery, and the external iliac is anastomosed to the superior mesenteric artery (SMA). The "V" component of the Y-graft is kept short in case the portal position is not tenable and systemic drainage is necessary. A long "V" component in the iliac reconstruction leads to unnecessary buckling or kinking of the arterial conduit. By trimming the external iliac artery of an appropriately procured Y-graft, a significant remnant of external iliac is left over. During the bench preparation of the pancreas, this remnant of external iliac can be used as a Y-graft extension: It is sutured to the end of the common iliac artery with 6-0 non-absorbable sutures (Fig. 29.21). Alternatively, as discussed later, this remnant of external iliac may be anastomosed end-to-side to the

recipient's right common iliac artery before the pancreas is brought to the recipient field, marked anteriorly and brought retrograde through the mesenteric window for an end-to-end anastomosis with the donor Y-graft [21].

Another technique to maximize the Y-graft length is to construct anastomoses between the longer limb of the external iliac artery to the shorter splenic artery and the shorter limb of the internal iliac artery to the longer SMA [21].

Enteric drainage of the graft may be accomplished in several different ways. Gaber et al. popularized portal vein drainage with enteric exocrine drainage by using a defunctionalized Roux-en-Y limb connected in an end-to-end fashion to the distal portion of the donor duodenum [20]. Other techniques of enteric exocrine drainage of portally drained pancreas grafts have also been used. A simplified form of enteric exocrine drainage is the side-to-side anastomosis between the donor duodenum and a proximal loop of the recipient jejunum (Fig. 29.21).

After a midline laparotomy incision is made, the abdomen is explored for any unsuspected pathologic findings. The right common iliac artery is exposed overlying the inferior vena cava, taking care to avoid injuring the right ureter. The vessel is carefully palpated and enough is exposed to make the end-to-side anastomosis straightforward. Atherosclerosis is common in diabetic patients, so those with diminished femoral pulses at their transplant evaluation should undergo a preoperative arteriogram or magnetic resonance angiogram (MRA) preoperatively. Significant atherosclerosis may make the right common iliac unusable; if portal vein drainage is still desired, the left common iliac artery or aorta may be more suitable. If proximal arterial disease is severe and if the more distal external iliac arteries are relatively normal, systemic vein drainage should be considered. The external iliac arteries are in general not reachable even with very long Y-grafts when the pancreas is drained portally; however, they are easily accessible if iliac vein drainage is used.

Locating and mobilizing the proximal SMV or its main feeder vein for anastomosis is relatively straightforward. The transverse colon and its mesentery are elevated to expose the anterior root of the small bowel mesentery. Laparotomy pads and a self-retaining retractor system are used to place the transverse colon superiorly. The mesentery of the small bowel is laid flat using a wide malleable retractor from a self-retaining retractor system. With this positioning, the SMV lies in a superficial position. In some slender type 1 diabetics, this vessel can be seen through the serosa of the mesentery. It almost always lies to the right of the palpable SMA. The middle colic vein in the transverse mesocolon or distal branches in the small bowel can be traced to the SMV's origin, but doing so is rarely necessary. Manipulation of the SMV can cause vasospasm and an accurate assessment of its diameter should be made before starting the dissection; application of topical papaverine may assist in cases of persistent vasospasm [21]. The lymphatics overlying the SMV are usually ligated with fine ties. Dissecting the SMV requires a gentle technique: Its branches are small and, if torn, can cause troublesome bleeding. Small branches of the SMV are usually ligated, and larger branches are preserved.

The portal vein is kept short to avoid kinking. The venous anastomosis is completed first. The pancreas is wrapped in a wet, cold laparotomy sponge. Before clamping the SMV, a bolus of 50–70 U/kg of unfractionated heparin is administered in nonuremic patients and allowed to circulate for 3 min. In uremic patients, anticoagulation is individualized but usually does not exceed 30–40 U/kg. Fine vessel loops or a small vascular (spring) clamp is applied to the SMV; it is opened with an 11 blade and Potts scissors. The venotomy, sized to match the donor portal vein, commonly traverses branch points. The pancreas graft is brought to the field wrapped in an iced lap sponge, with the portal vein exposed. The graft is oriented with the donor duodenum facing superiorly toward the mesentery of the transverse colon. The end of the donor portal vein is anastomosed to the side of the SMV with 7-0 non-absorbable sutures. This delicate anastomosis is vulnerable to tearing and so should not be performed under tension. A vein extension graft can be used to decrease tension but is rarely necessary if the donor portal vein length is adequate and if the retractor is properly placed. After this anastomosis is completed, the SMV flow is restored and the graft's portal vein is occluded by using a Gregory or large (spring) Bulldog clamp. Release of the clamp from the SMV restores venous outflow in the native mesenteric circulation, diminishes the risk of bowel edema, and tests the integrity of the anastomosis [21].

Arterial reconstruction requires the creation of a plane for the Y-graft to traverse the mesentery to the right common iliac artery. Typically, a dime-sized defect is made in the mesentery, to the right and slightly inferior to the SMV. The Y-graft is pulled down through the mesenteric defect, taking care to avoid twisting. The end of the Y-graft (or of the arterial extension/jump graft) may be cut in an oblique or "fish-mouth" fashion to enlarge the size of the anastomosis [21]. A Gregory clamp is applied to the Y-graft and to a portion of the posterior mesentery to prevent twisting and retraction. The side of the right common iliac artery is then anastomosed to the end of the Y-graft with 6-0 non-absorbable sutures. One variation of this technique is to make a larger mesenteric defect over the right common iliac artery and position retractors so that both the arterial vasculature and SMV are exposed in the same field. Alternatively, the remnant of the donor external iliac artery can be anastomosed to the right common iliac before bringing the pancreas to the field. The external iliac remnant may then be drawn up through the mesenteric defect, allowing both venous and arterial anastomoses to be done in the same field on the top of the small bowel mesentery.

Mannitol (0.5 g/kg body weight) is administered intravenously before the arterial anastomosis is completed. A colloid osmotic agent and free radical scavenger, mannitol is given to the recipient to minimize reperfusion edema. Crossmatched blood should be available before unclamping. The lap sponge is removed from the gland, and the vein is unclamped first. Any gross bleeding is addressed. The arterial inflow is then unclamped. Exposure of bleeding is relatively straightforward for pancreas grafts with SMV drainage that are superficially located, as compared with pancreas grafts with systemic vein drainage that lie deep in the pelvis.

An alternate technique for unclamping that tests the integrity of the anastomoses first involves application of spring clamps to the donor portal vein and donor Y-graft. Hence, both anastomoses are proven to be "watertight" prior to clamp release. This "pre-testing" is helpful since it can be quite difficult to expose and repair anastomotic bleeding from the donor portal vein; once reperfusion occurs, attention can then be solely focused on achieving graft hemostasis [21]. Any bleeding sites are identified and carefully controlled with fine suture ligation techniques. Most bleeding arises from the mesenteric root, splenic hilum, or superior portion of the head of the pancreas. Once hemostasis is achieved, the correct orientation of the vessels is confirmed.

The enteric anastomosis can be constructed into a bowel loop, a Roux-en-Y loop, an omega loop, and the recipient duodenum or stomach [53, 101–103, 120–122, 153–158]. If the graft duodenum is not well perfused, diversion into a Roux-en-Y loop is safest. Most commonly, a suitable portion of jejunum (about 30–50 cm) distal to the ligament of Treitz is used for side-to-side anastomosis (Fig. 29.21). The main advantage of duodenal or gastric drainage is easy to access for endoscopic surveillance and graft biopsy. Although the rate of technical complications and graft loss has significantly decreased over time, many transplant surgeons still appear to be reluctant about these forms of pancreatic exocrine drainage [21].

If a side-to-side anastomosis is performed, the recipient jejunum is brought adjacent to the donor duodenum. In its final position, the donor duodenum sits under the transverse colon and is the most superior portion of the graft. The third or fourth portion of the graft duodenum should be used as anastomotic site in order to take advantage of dependent drainage of the denervated, atonic graft duodenum when the patient is in erect or supine position [21]. The jejunal loop is placed slightly inferior and anterior to the donor duodenum. A two-layer side-to-side duodeno-jejunostomy performed. First, a back row of 3-0 non-absorbable Lembert sutures is placed. Then, the donor duodenum and recipient jejunum are opened for 3–5 cm. A running circumferential 4-0 absorbable transmural suture is used for the inner layer of the bowel anastomosis; 3-0 non-absorbable Lembert sutures are used for the anterior wall to complete the anastomosis.

Opening of the (contaminated) small bowel requires maneuvers to minimize spillage. Linen-shod clamps are applied to the afferent and efferent jejunal limbs. Lap sponges are placed protectively around the anastomotic area to catch any spillage. The contents of the duodenum are evacuated and decompressed with suction after cultures have been obtained. After the bowel anastomosis is completed, the team's gloves are changed and the contaminated instruments are removed. The graft and anastomotic sites are inspected again for bleeding. The mesenteric defect (which was made to allow passage of the Y-graft) might require partial closure. After the graft is implanted, the abdomen is irrigated with bacitracin, kanamycin, and amphotericin B solutions. Drains are rarely, if ever, used; any "oozing" that suggests the need for a drain prompts a thorough search for surgical bleeding. Once the pancreas is well perfused and the abdomen dry, the abdomen can be closed (or a simultaneous kidney can be placed).

Postoperative care is similar after pancreas transplants with portal vein vs. systemic vein drainage (see Chap. 40).

There are several "disadvantages" associated with portal-enteric drainage using the intraperitoneal approach: the pancreas graft is surrounded by small and large bowel loops which may make it poorly accessible to ultrasound- or CT-guided biopsies. Complications may affect the entire mid-abdomen rather than the pelvis. A long interposition Y-graft may be necessary and there is the potential risk for venous graft torsion (which can be prevented by anchoring the tail of the pancreas to the anterior abdominal wall).

Some of these concerns can be addressed by using the retroperitoneal approach through a midline incision as described by Boggi et al. [120] (Fig. 29.22). This hybrid technique involves a midline intraperitoneal approach followed by access to the SMV through the right retrocolic region [120–122]. This not only allows the SMV to be approached from the lateral retroperitoneal (rather than the anterior) route but also assures good graft fixation in the right paracolic space with positioning of the graft posterior to the right colon. This technique, in contrast to the anterior intraperitoneal approach, improves accessibility for ultrasound/CT imaging and percutaneous biopsy. Because of the graft's retroperitoneal position, the Y-graft does not have to be long. One peritoneal window needs to be created in the right colon mesentery for the duodeno-jejunostomy and to facilitate absorption of potential leaks and perigraft fluid collections. Alternatively, a duodeno-duodenostomy can be constructed [21].

At the time of this writing, portal-enteric pancreas transplants using the retrocolic/retroperitoneal technique are performed by center-specific preference.

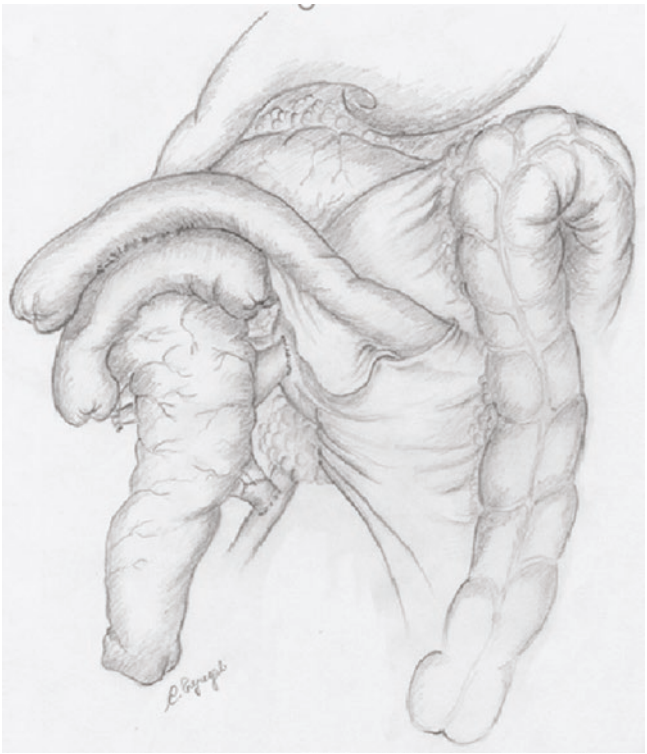

Fig. 29.22 Whole-organ transplant with portal vein and enteric exocrine drainage using the retroperitoneal approach. The pancreas graft is placed retroperitoneally and in right paracolic and cephalad position. The donor Y-graft is anastomosed to the recipients' right common iliac artery and the donor portal vein to the recipient's SMV. A long Roux limb is used to avoid compression of the SMV distally to the venous anastomosis (reprinted with permission from Boggi et al. [120])

Segmental Pancreas Transplants with Portal Vein and Enteric Exocrine Drainage

The combination of portal vein and enteric exocrine drainage has rarely been used for segmental pancreas transplants. In five patients, Sutherland et al. used the recipient's inferior mesenteric artery and vein for EEAs to the donor splenic artery and vein [61]. In each of these five patients, the inferior mesenteric artery was divided—at a point to preserve the collateral circulation of the colon—from the marginal artery of Drummond. In four patients, the exocrine secretions were managed by anastomosis of the neck of the pancreas to a Roux-en-Y limb to the recipient jejunum; in one patient, the pancreatic duct was injected with neoprene. Tyden et al. reported a technique in which the recipient's superior mesenteric artery and vein were anastomosed end to end to the donor splenic artery and vein. The neck of the pancreas was brought through a window in the transverse colon and anastomosed to the stomach (pancreaticogastrostomy) [60]. The recipient splenic artery and vein have also been used for a paratopically placed segmental graft, and the exocrine pancreatic secretions in this case were also diverted with gastric drainage [58]. Because of the high technical complication rate, none of these techniques gained widespread application. They are usually recommended only if the iliac arteries are severely atherosclerotic, which makes the anastomosis difficult, in particular when only the short splenic vessels of the segmental graft are available [61].

The only case of a segmental pancreas transplant with portal vein and bladder exocrine drainage was reported by Gil-Vernet et al. in 1985: they drained a retroperitoneally placed segmental graft into the recipient splenic vein and performed a ductouterostomy for exocrine pancreatic drainage [59].

Other Techniques to Divert Exocrine Pancreatic Secretions

Duodenal and, to a lesser degree, gastric drainage are newer techniques that are currently been used by some programs to divert exocrine pancreatic secretions. Both techniques provide easy access for endoscopic surveillance and biopsy. According to the IPTR, only <3% of all pancreas transplants utilize duodenal or gastric drainage (Chap. 66) [8].

Duct injection which became popular in the 1980s is rarely been used these days and if so, primarily as a rescue option for complicated enteric or bladder-drained pancreas transplants. Ureteral drainage as well as open duct drainage and duct ligation are basically of historical interest only.

Duodenal Drainage

Duodenal drainage (Fig. 29.23) with its modifications is described in detail in Chaps. 31 and 32 [120, 127, 156, 157, 159, 160]. In brief, duodenal drainage affords direct access to the allograft duodenum and pancreas for biopsy and for surveillance endoscopies including graft ERCP. It also expands the options for exocrine drainage sites, particularly in case of pancreas retransplantation after previous graft placement in the recipient's pelvis or lower abdomen. A disadvantage of duodenal drainage is the management of eventual leaks or graft pancreatectomies: closure of the native duodenum can be very challenging and is associated with morbidity and mortality (see Chap. 90). Duodenal drainage has been performed successfully with both systemic and portal venous drainage. It has reasonably grown in popularity over the past 10 years.

Gastric Drainage

In the first published case of portal vein drainage, Calne used the stomach for exocrine pancreatic drainage of a paratopically placed segmental graft (*pancreaticogastrostomy*) [58]. Using a transmesocolic approach, Tyden et al. described het-

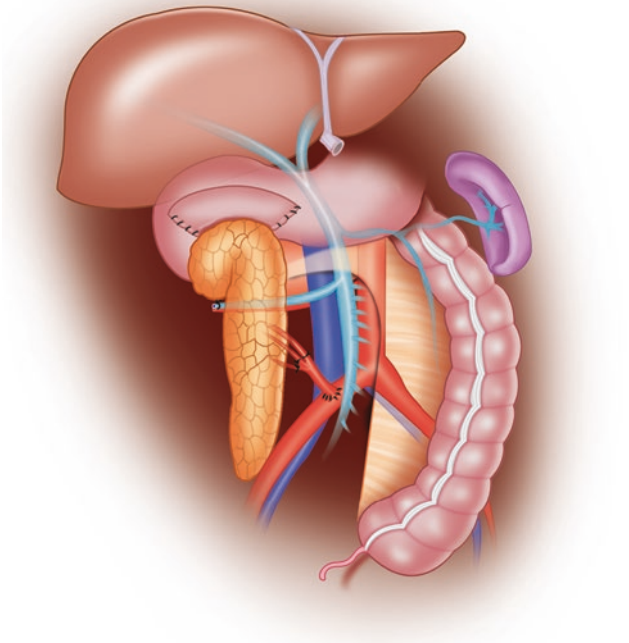

Fig. 29.23 Whole-organ transplant with portal venous and duodenal drainage (duodeno-duodenostomy) (reprinted with permission from Perosa et al. [160])

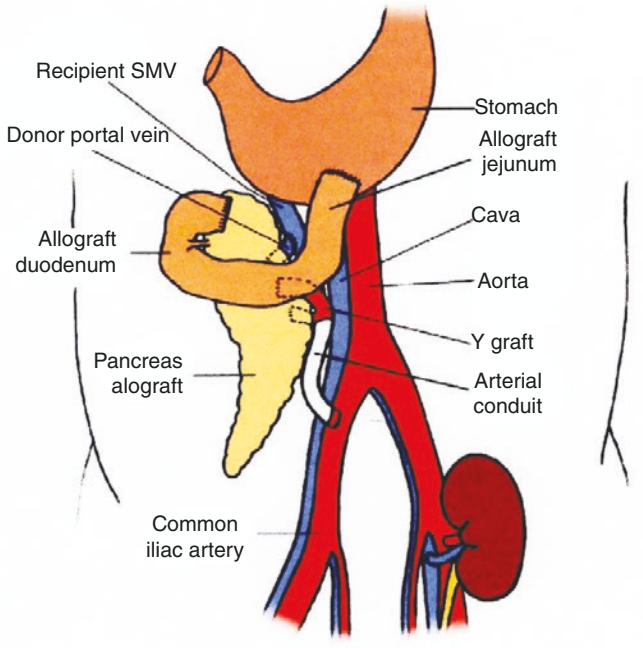

Fig. 29.24 Whole-organ transplant with portal venous and gastric drainage of the exocrine pancreatic secretions. Standard donor portal vein to recipient SMV anastomosis and long Y-graft conduit (using donor iliac or carotid Y-graft or combination thereof) anastomosis to the recipient's right common iliac artery. The end of the proximal "donor jejunum is anastomosed to the anterior aspect of the stomach close to the greater curvature in an antecolic fashion" (reprinted with permission from Shokouh-Amiriet al. [158])

erotopic placement of a segmental graft, with either systemic vein drainage (infrarenal vena cava and right common iliac artery) or portal vein drainage (superior mesenteric vein and artery) [161]. Gastric drainage was initially not widely applied because of the posterior position of the pancreas graft in the mid-abdomen and the potential for severe abdominal complications (e.g., diffuse peritonitis, leakage of gastric secretions).

However, gastric drainage using a novel technique has seen some revival since its re-introduction by Shokouh-Amiri et al. in 2011 (Chap. 30, Fig. 30.1) [158, 162, 163]. Gastric drainage with its modifications is described in detail in Chap. 30. In brief, gastric-exocrine drainage (most commonly combined with portal venous drainage) was developed to facilitate access to the graft duodenum and the pancreas (including the papilla) through the recipient's stomach by upper endoscopy for surveillance and biopsies (Fig. 29.24).

A similar technique of gastric drainage was described by Linhares et al. by "surgical necessity" [164]: the recipient infrarenal aorta had to be used for inflow due to intense perivascular fibroses of both iliac arteries and portal vein drainage was accomplished via the recipient SMV. Exocrine drainage was into the gastric antrum (Fig. 29.25). It appears that this technique can be considered a "salvage option" in case of re-transplant when massive adhesions and vascular scarring prohibit standard transplant techniques.

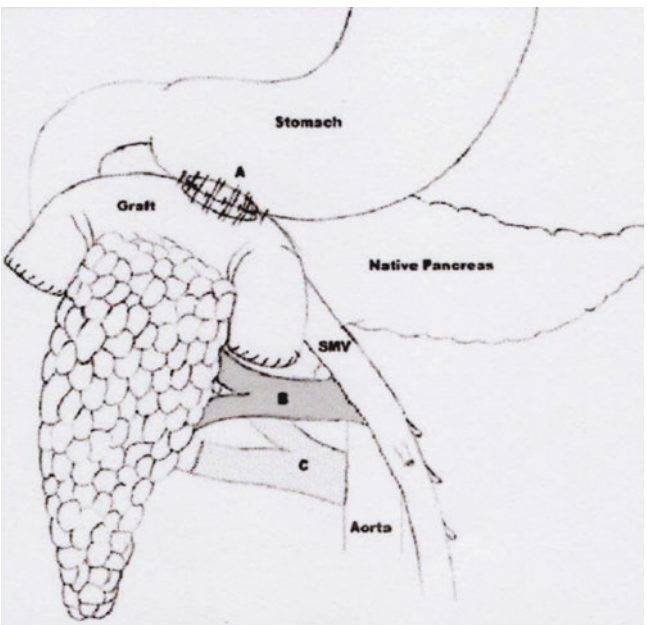

Fig. 29.25 Whole-organ transplant with portal venous and gastric drainage of the exocrine pancreatic secretions. Standard donor portal vein to recipient SMV anastomosis and donor Y-graft anastomosis to the recipient's infrarenal aorta. The duodenal portion of the graft to the anterior wall of the gastric antrum (reprinted with permission from Linhares et al. [164])

In general, advocates of gastric and duodenal drainage point out that these drainage techniques have the advantages of endoscopic monitoring, pancreas graft placement in a fixed position, and endoscopic access to both graft duodenum and pancreas. The main disadvantages of gastric and duodenal drainage are the challenges associated with leaks and/or graft pancreatectomies (Chap. 31).

Duct Injection

Synonyms used for duct injection include duct obstruction and duct occlusion. This technique was first reported by Dubernard et al. in 1978 for segmental grafts [165]. It entails the injection of the main pancreatic duct with up to 10 mL of neoprene, a liquid synthetic rubber that flocculates with changes in pH (Fig. 29.26). This technique was based on large animal studies in dogs in which progressive fibrosis of the pancreatic tissue was demonstrated after injection of neoprene in the main pancreatic duct, leaving the islets vascularized and functioning for prolonged periods. Although duct injection was initially used in many pancreas transplant centers around the world, it eventually became less popular than bladder or enteric drainage because it has a higher incidence of complications (e.g., obligatory graft pancreatitis after injection, and pancreatic fistulas). Concerns were also raised that exocrine fibrosis may impair long-term function of the vascularized islets [166]. According to US IPTR/UNOS data, duct injection was frequently used until 1983 (>50% of all cases). Since then, it has become a rarely performed technique and has been used in less than 1 % of all pancreas transplants.

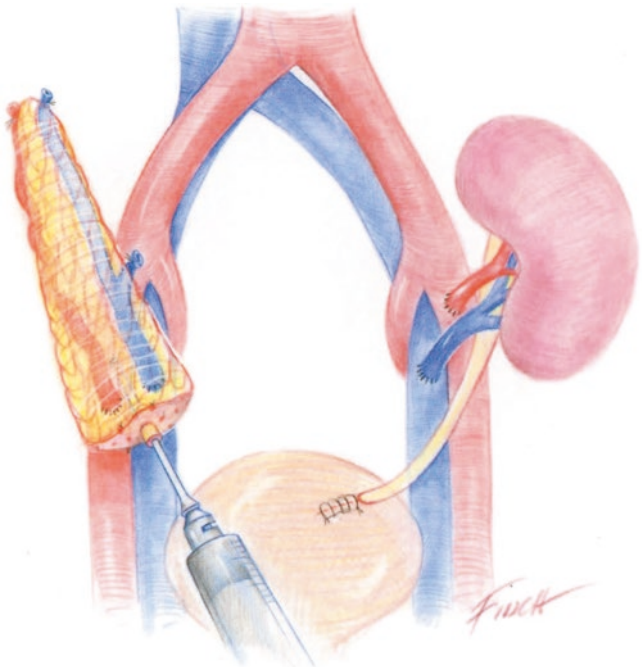

Fig. 29.26 Segmental transplant with duct injection. The donor splenic artery and vein are anastomosed to the recipient's external iliac artery and vein. The arterial anastomosis is lateral and proximal to the venous anastomosis. The duct is injected with a synthetic polymer. For ureteral implantation into the bladder, an extravesical ureteroneocystostomy (Lich) technique is used

As with other drainage procedures, duct injection has undergone a number of modifications over the years. A variety of synthetic polymers have been used besides neoprene, including prolamine, polyisoprene, and silicon [167–169]. Neoprene is easy to inject, adheres well to duct walls (in contrast to silicon), and solidifies when injected into the pancreatic duct [165]. Initially a dose of 10 mL was used, but 3–5 mL is usually sufficient with segmental grafts (Fig. 29.26). Duct injection can be performed on the bench or after revascularization. Under both circumstances, Wirsung's duct is cannulated with a small blunt-tipped catheter. Neoprene spillage should be avoided. After injection, the pancreatic duct is oversewn with a single 5-0 nonabsorbable suture. The cut surface is also oversewn with a single 4-0 absorbable suture, but total ligation of the pancreatic neck with a single purse-string suture has also been recommended.

Delayed injection until several weeks posttransplant has also been reported [170, 171]. A temporary catheter is placed in the duct and externalized, which allows monitoring of exocrine graft function early posttransplant. But, delayed (vs. immediate) duct injection has not resulted in better outcomes.

Duct injection has also been used with whole-organ transplants (Fig. 29.27). The injection technique itself is not different, as compared with segmental grafts, but the accessory Santorini's duct needs to be cannulated and injected separately if interductal connections are absent and if the accessory duct is not confluent with the main duct; a papilla minor with drainage of the accessory duct occurs in about 30% of cases [172]. Of note, duct injection can be successfully used with both systemic and portal vein drainage.

Over the years, most pancreas transplant centers that initially favored duct injection as their method of choice to divert exocrine pancreatic secretions have switched to either enteric or bladder drainage. In a retrospective study of 95 pancreas transplants with graft function >3 years, the Lyon group demonstrated inferior long-term outcomes with duct injection (using neoprene). At 3 years, overall pancreas graft survival was 65% with whole-organ enteric drainage, 60% with whole-organ bladder drainage, and only 47% with segmental graft duct injection [111].

Currently, duct injection is used as a (rescue) conversion technique for patients with surgical complications after enteric- or bladder-drained pancreas transplants. Conversion of bladder drainage (in the absence of systemic infection) to duct injection appears to be safe and effective [173].

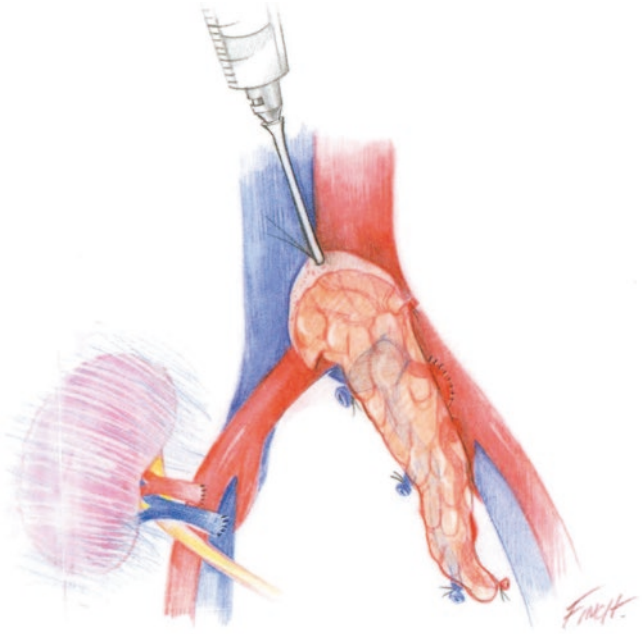

Fig. 29.27 Whole-organ transplant with duct injection: because of the previous kidney transplantation on the right side, the whole-organ pancreas graft (without the duodenum) is implanted into the left side; the Y-graft anastomosis is lateral and distal to the portal vein anastomosis. The pancreatic duct is injected with about 10 mL of a synthetic polymer

Ureteral Drainage

In the original description by Gliedman et al., the pancreatic duct of a systemic-drained segmental graft was directly anastomosed to the ipsilateral distal ureter of the recipient [4]. Gil-Vernet et al. described a modification with paratopic placement of the segmental graft and portal vein drainage via the recipient splenic artery and vein; after native nephrectomy, the renal pelvis was anastomosed to the tail of the graft [6]. Thus, ureteral drainage has been used with both systemic and portal vein drainage. It has also been used with whole-organ transplants, with the construction of an anastomosis between the pancreatic papilla (using only a small 0.5-cm rim of duodenum) and the native ureter [59]. Ureteral drainage has not become a widely used technique because of its high anastomotic complication rate and the frequent need for native nephrectomy. Of note, ureteral drainage was also used with living donor segmental grafts if the pancreatic duct and ipsilateral native ureter were a good size match and if neither enteric nor bladder drainage could be used (e.g., because of a short pancreatic neck and fear of possible injury to the donor splenic vessels) [148].

Open-Duct Drainage and Duct Ligation

Although completely different conceptually, open-duct drainage and duct ligation are discussed together, because neither technique gained widespread application. Technically, open-duct drainage involves only revascularization of the (segmental) graft with the duct left open, resulting in the preservation of functioning exocrine pancreatic tissue. The peritoneum can absorb pancreatic secretions and openly drain pancreatic juice, but there must be no microbial or enteric contamination at the time of operation [174]. In contrast, duct ligation after revascularization involves ligation or oversewing of the pancreatic duct, resulting in atrophy of the exocrine tissue. Consequences are (severe) graft pancreatitis and, on occasion, necrosis with infection [172]. Duct ligation did not prove to be superior to duct injection.

Less Common Types of Pancreas Transplants

Segmental Transplants

Segmental transplants from deceased donors are basically no longer performed due to reduced islet mass compared to whole organ grafts. They were most popular after duct injection was introduced in the late 1970s which eliminated the need for a tedious duct or pancreatic cut-surface anastomosis with its associated complications. At the time, segmental grafts were frequently procured with a Carrel patch encompassing the splenic artery and a donor portal vein patch to facilitate the constructions of the vascular anastomoses (Fig. 29.28).

If a rare deceased donor segmental transplant is performed, it is usually placed intra-abdominally on the right side (like a whole organ); if a kidney is simultaneously transplanted, it is placed on the left side.

The cuffs or patches of the splenic artery and splenic vein are usually anastomosed to the external iliac artery and vein as described above; on occasion, the hypogastric artery is used for arterial inflow. Alternatively, portal venous drainage

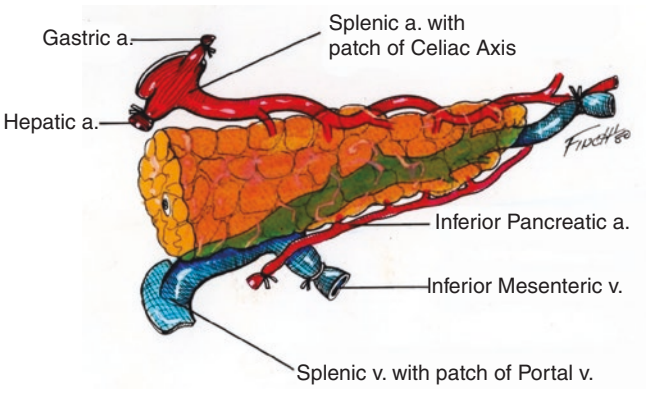

Fig. 29.28 Segmental graft from a deceased donor: the splenic vein is depicted with a cuff of donor portal vein and the splenic artery is attached to a Carrel patch

using the inferior or superior mesenteric vessels can be performed.

For diversion of exocrine pancreatic secretions, enteric or bladder drainage may be used—applying the same techniques as described above—as well as duct injection. For both enteric or bladder drainage, a two-layer anastomosis is created either by directly anastomosing the pancreatic duct to the jejunal mucosa (ductojejunostomy)or to the bladder urothelium (ductocystostomy) or by telescoping the whole cut surface of the pancreatic neck into the jejunum (pancreaticojejunostomy) or into the bladder (pancreaticocystostomy) (Figs. 29.13, 29.14, 29.15, 29.16, 29.19, and 29.20). The pancreatic duct is always stented with a small catheter and tagged with a single 6-0 or 7-0 absorbable suture to the anastomosis. The stent is either spontaneously excreted through the urethra or cystoscopically removed 3–4 weeks posttransplant.

Duct injection (Fig. 29.26) or ureteral drainage (e.g., size-matched pancreatic duct and ipsilateral ureter, short pancreatic neck) are no longer performed primarily but may be considered as rescue options.

Segmental transplants from living donors are now rarely performed due to substantial improvements in immunosuppressive therapy and advances in the diagnosis and treatment of rejection for whole-organ transplants from deceased donors. In contrast to segmental transplants from deceased donors, no donor cuffs are attached to the splenic artery and vein (Fig. 29.29) which increases the risk of thrombosis and technical failure of living donor segmental grafts. The surgical technique for segmental pancreas transplants from living donors is described in detail in Chap. 35.

Split-Pancreas Transplants

As with the liver, the vascular blood supply of the pancreas allows the splitting of one pancreas into two segmental grafts (see Chap. 14). A pancreas split procedure has been described from a donor whose liver was not simultaneously procured with the pancreas [175]. Arterial blood supply to the pancreas was provided via a Carrel patch encompassing the celiac artery (with the common hepatic, gastroduodenal, and superior pancreaticoduodenal arteries) and the superior mesenteric artery (with its inferior pancreaticoduodenal artery) (Fig. 29.30). Surgically, the split benchwork procedure was done by ex vivo division of the pancreatic neck between 4 and 0 absorbable sutures at 4 °C in University of Wisconsin (UW) solution. The arterial blood supply was divided by leaving the pancreatic tail and part of the body (distal segment) vascularized via the splenic artery and vein, and the pancreatic head, part of the body, and duodenum (proximal segment) vascularized via the superior and inferior pancreaticoduodenal arteries originating from the gastroduodenal and superior

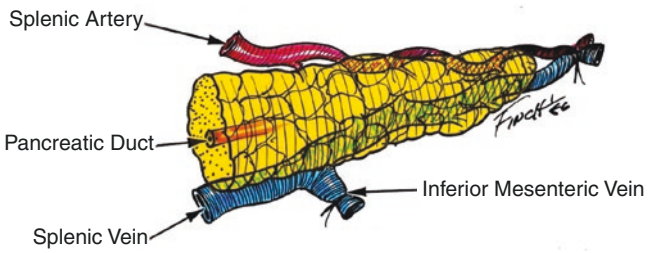

Fig. 29.29 In contrast, the segmental graft from a living donor: the cut surfaces (without cuffs) of the donor splenic vein and splenic artery are depicted

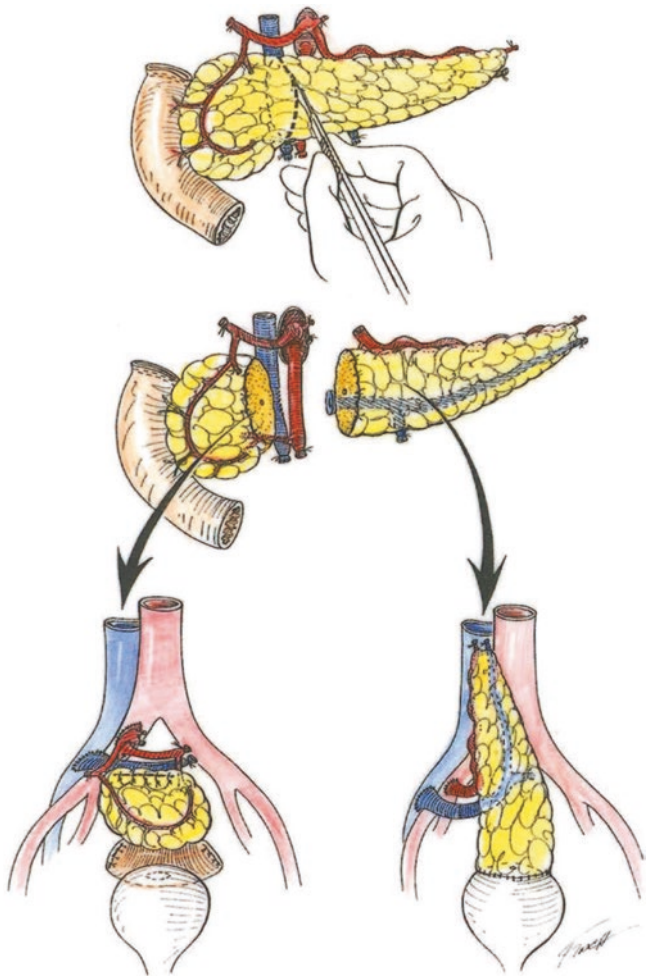

Fig. 29.30 Split-pancreas transplant with systemic vein and bladder exocrine drainage. The neck of the pancreas is divided above the portal vein using ligatures. The proximal segment (pancreatic head with duodenum) receives its blood supply via a Carrel patch encompassing the celiac artery and superior mesenteric artery; venous drainage is via the portal vein. (The orifice of the splenic is oversewn.) The distal segment (body and tail of the pancreas) receives its blood supply from the splenic artery and vein. The proximal segment was implanted on the right side of the pelvis in the standard fashion and a duodenocystostomy was created. The distal segment was also implanted on the right side and a ductocystostomy was created

mesenteric arteries. Thus, the Carrel patch along with the portal vein remained with the proximal segment. The orifice of the splenic vein in the portal vein was oversewn with a single 7-0 nonabsorbable suture in running fashion. For the proximal segment, the recipient common iliac artery and vein were used; for the distal segment, the recipient external iliac artery and vein were used. Exocrine drainage for both segments was into the bladder, via a duodenocystostomy for the proximal segment and via a ductocystostomy for the distal segment (Fig. 29.30). Bladder drainage was chosen because both recipients had high panel-reactive antibody (PRA) levels (76% and 100%, respectively); monitoring of exocrine secretions for early detection of rejection was crucial. If bladder drainage is not chosen or if a kidney is simultaneously transplanted, enteric drainage can be used with equal success. Thus, a split-pancreas transplant is an option, used rarely, for crossmatch-negative patients with high PRA levels.

Pancreas Transplants After Native Pancreatectomy

Pancreas transplants can successfully be done in patients who previously underwent total pancreatectomy for reasons other than pancreatic malignancies (see Chaps. 18, 80, and 81). The most common cause is chronic pancreatitis and the presence of diabetes mellitus. Total pancreatectomy results not only in endocrine but also in exocrine deficiency [176]. Although the latter can successfully be managed with oral enzyme supplementation, such patients frequently develop a very labile form of diabetes mellitus due to the complete absence of all glucose-regulatory hormones released by pancreatic islets (insulin, glucagon, somatostatin, and pancreatic polypeptide). Thus, the goal of a pancreas transplant for patients after total pancreatectomy is to re-establish full endocrine and exocrine function. Several single-center studies have shown that a pancreas transplant in patients with native pancreatectomy is a safe procedure resulting in long-term insulin independence with patient and graft survival rates similar to those of recipients of a primary transplant without native pancreatectomy [176–179].

According to US IPTR/UNOS data, <0.1% of all pancreas transplants have been performed in pancreatectomized patients (see Chap. 66) [8].

Given extensive previous surgery, in particular, in the mid-abdomen, placement of the pancreas graft in the pelvis with systemic vein drainage to the iliac vessels and enteric drainage via a side-to-side anastomosis or Roux-en-Y loop is usually preferred [176–179]. But at least one case of successful inferior vena cava, portal vein, and duodenal drainage has been reported [180]. This technique involves right-sided medial visceral rotation (i.e., an extended Kocher maneuver) with donor portal vein-to-recipient vena cava and donor Y-graft–to-recipient right common iliac artery anastomoses as well as a side-to-side anastomosis between the donor and the recipient duodenums.

If close monitoring for rejection early posttransplant is warranted (e.g., in patients with high PRA levels due to previous blood transfusions), the surgeon may elect to initially use bladder drainage and later convert to enteric drainage. But, for as long as the pancreas is bladder drained, oral supplementation of pancreatic enzymes is required. If portal vein (and enteric) drainage is used, the patient will also benefit from restoration of both endocrine and exocrine function, but the dissection might be more difficult because of adhesions from previous surgery. The surgical techniques for graft implantation in patients with native pancreatectomy are the same as described above.

En Bloc Transplants and Transplants from Pediatric Donors

En Bloc or Single-Unit Pancreas–Kidney Transplants

Combined pancreas–kidney transplants as en bloc or single units are relatively rare procedures. In those cases, the vascular sites in the recipient show advanced calcified peripheral vascular disease, are heavily scarred (due to previous use) or organs from a small pediatric donor are been used. The en bloc technique was initially described and successfully tested in a large animal (porcine) model (Fig. 29.31) [181, 182].

In general, single-unit pancreas–kidney transplants are technically feasible and can be successful.

It is important to point out that the arterial and venous sites should be chosen first to gauge the distance and configuration required for the donor's vessels and thus avoid twisting or kinking [184]. The disadvantage of this technique is that when a complication (e.g., thrombosis, abscess, and leakage) occurs in one graft, the other graft is automatically imperiled. Thus, en bloc pancreas–kidney transplants have basically been limited to highly selected transplant recipients.

Several techniques have been described:

- In one case report, the benchwork consisted of a standard Y-graft reconstruction with anastomoses of the external iliac artery to the superior mesenteric artery and of the internal iliac artery to the splenic artery. The renal artery then joined the Y-graft in an end-to-side fashion to provide a single arterial inflow vessel. A donor iliac vein was used to extend the portal vein. The renal vein was joined side-to-side to the extension graft to provide a single venous outflow vessel. In the recipient, the single-unit pancreas–kidney graft was implanted by suturing the conjoined venous graft to the left common iliac vein in an

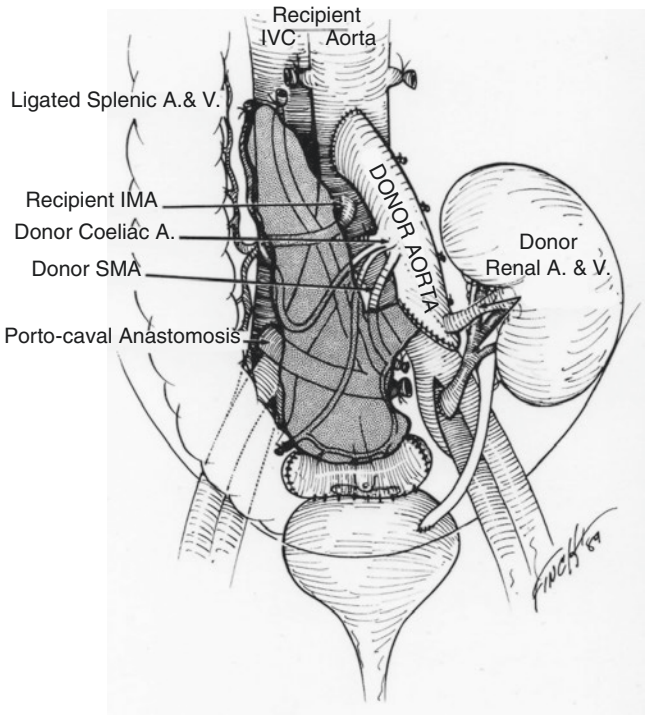

Fig. 29.31 En bloc transplantation of pancreas and kidney in a pig model. The donor aorta with the origins of celiac artery, SMA and left renal artery is anastomosed end-to-side to the recipient infrarenal aorta. The donor portal and renal veins are anastomosed separately from the recipient's common iliac veins (reprinted with permission from the author [182])

end-to-side fashion. The arterial graft was sutured to the only arterial site suitable for anastomosis on the left common iliac artery (end-to-side anastomosis). Exocrine pancreatic secretions were diverted to the jejunum in an end-to-side fashion [183].

- In another case report, the arterial reconstruction of both grafts was identical to the one described above. The donor portal vein, however, was directly anastomosed end-to-side to a long renal vein. The renal vein was then anastomosed to the distal inferior vena cava and the long Y-graft to the distal right common iliac artery. Exocrine pancreatic secretions were drained side-to-side to the recipient's jejunum [184].

As mentioned above, the construction of a common arterial conduit—rather than a true en bloc transplant—has been proposed if implantation of the kidney graft on the left side is "difficult or undesirable" [131]. Both grafts are implanted on the right side in ipsilateral fashion: the renal artery is anastomosed end-to-end to the donor internal iliac artery of the Y-graft and the long external iliac artery to the donor SMA. The pancreas graft is anastomosed to the recipient portal vein and the donor renal vein to the recipient right iliac vein (Fig. 29.32) [131].

Pediatric donors have been used in a few case reports using the en bloc technique. In one case, pancreas and both kidneys were procured en bloc with the abdominal aorta and cava; the donor (proximal) portal vein was anastomosed to the proximal end of the donor inferior vena cava. In the recipient, end-to-side anastomoses between the distal ends of the donor aorta and cava and the recipient iliac vessels were performed [185]. In another case of dual kidney–pancreas transplantation, the proximal donor aorta, and cava were first anastomosed end-to-side to the recipient's infrarenal aorta and cava. The donor portal vein and the donor SMA Carrel patch of the pancreas graft were then anastomosed end-to-end to the distal donor aorta and cava [186]. In a case of retroperitoneal en bloc implantation, only one kidney was used; the arterial anastomosis was between the donor distal aorta (encompassing the origins of SMA, celiac artery, and right renal artery) and the recipient's right internal iliac artery (due to severe calcifications of the common and external iliac arteries). The donor portal and renal veins were anastomosed separately end-to-side to the recipient's inferior vena cava [187]. In a modification of this technique the donor aorta was anastomosed to the recipient's right common iliac artery and the donor portal and renal veins were anastomosed separately to the recipient's right common iliac vein [188].

Transplants from Pediatric Donors

Another major change that has taken place in clinical pancreas transplantation since the first edition of this textbook is the now more widely-applied and successful use of pediatric donors for pancreas (and kidney) transplantation. In the first edition and around the time of the turn of the millennium, it was recommended that "deceased pancreas donors weighing ≤30 kg should only be used in selected situations, e.g., if the liver is not procured and the Carrel patch remains with the pancreas. Any arterial reconstruction of pediatric donor grafts, including the Y-graft technique, significantly increases the risk of pancreas graft thrombosis." [189]

However, after the turn of the millennium, several single-center studies showed in small patient series that pancreas transplants from pediatric donors ≤30 kg can be performed with excellent short- and long-term outcomes [190–199]. Most combined pancreas and kidney grafts from pediatric donors have been implanted separately with the exception of very small donors (≤10 kg) in which either (1) en bloc pancreas–dual kidney (see above) or (2) pancreas and separate en bloc kidney implantation techniques were used [190–199]. If two small kidneys are transplanted en bloc, both ureters can be anastomosed to the recipient's bladder using a small donor bladder patch comprising and preserving the

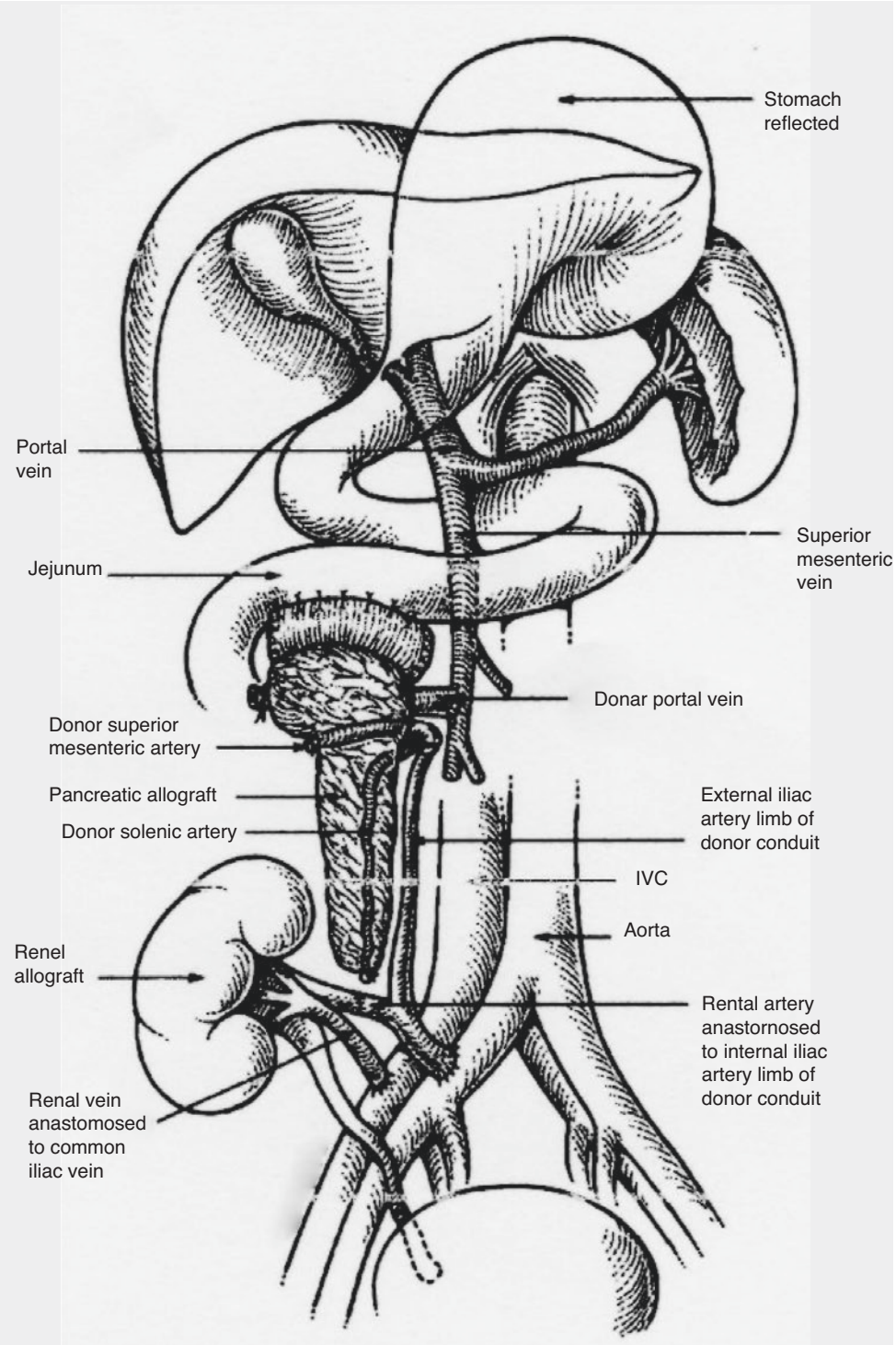

Fig. 29.32 SPK transplant using a common arterial conduit has been proposed if implantation of the kidney graft on the left side is "difficult or undesirable." Both grafts are implanted on the right side in ipsilateral fashion. The renal artery is anastomosed end-to-end to the donor internal iliac artery of the Y-graft; the long external iliac artery of the Y-graft is brought through a window of the small bowel mesentery and anastomosed to a Carrel patch of the donor SMA. The pancreas graft is anastomosed to the recipient portal vein and the donor renal vein to the recipient right iliac vein (reprinted with permission from Tso et al. [131])

bilateral donor orifices in the trigone: the anastomosis can be accomplished in one layer using 4-0 PDS sutures without ureteral stents [193]. According to one report, pancreatic grafts from pediatric donors may not grow in size posttransplant in adult recipients [200]. This interesting topic warrants further investigation since the smallest donor in that study was already 25 kg in weight.

Subsequently, a large single-center study of 33 pancreas transplants from donors' ≤30 kg (3%) showed no effect of donor weight on patient and graft outcomes when compared to donors >30 kg; pancreas graft survival was also not different for donors ≤20 kg vs. >20–30 kg [199]. Another study of 19 pediatric donors ≤30 kg also demonstrated excellent short-term outcomes with no surgical complications and

long-term patient and allograft survival that was comparable to that of adult donor pancreas transplants [197]. Of note, the vast majority of these grafts were implanted separately and with the construction of a Y-graft as done in pancreas transplants from adult donors.

These large single-center study results were echoed in a UNOS database analysis: short-term graft and patient survival rates were comparable between pediatric and adult donors. Ten-year patient and graft survivals were higher in the pediatric donor group: (70% and 54% vs. 68% and 51%, $p = 0.001$); only low-weight pediatric donors (≤30 kg) resulted in worse graft survival in the long term. Usage of small pediatric donors ≤30 kg was not associated with a higher incidence of technical complications or early graft loss [198].

In essence, pancreas grafts from pediatric donors should not be marginalized and can offset worsening organ shortage [197].

According to US IPTR/UNOS data, since 1995 pediatric donors ≤13 years of age were only used in 6% of all pancreas transplants, with 1-year graft survival rates of 88% for SPK, 80% for PAK, and 79% for PTA recipients [8].

Combined Pancreas and Extra-renal Solid Organ Transplants

According to US IPTR/UNOS data, the following combinations of pancreas and other solid organ transplants (except SPK) were performed in 1382 patients between October 1, 1988, and December 31, 2019: pancreas–liver–intestine ($n = 994$), pancreas–intestine ($n = 163$), pancreas–kidney–liver–intestine ($n = 101$), pancreas–liver ($n = 87$), pancreas–kidney–liver ($n = 11$), pancreas–kidney–heart ($n = 9$), pancreas–kidney–intestine ($n = 7$), pancreas–heart ($n = 5$), pancreas–lung ($n = 3$), and pancreas–liver–lung ($n = 2$). Only nine centers had performed >20 of those transplants [8].

Simultaneous Pancreas–Liver Transplants

Pancreas–Liver "Cluster" Transplants

In 1989, Starzl et al. reported on abdominal organ cluster transplants for the treatment of unresectable upper abdominal malignancies [201]. Those patients underwent resection of most or all of the stomach, liver, pancreas, spleen, duodenum, proximal jejunum, terminal ileum, and ascending and transverse colon. The void in the upper abdomen was filled with an organ cluster graft consisting of the liver, pancreas, duodenum, and variable segments of proximal jejunum. In the recipient, the supra- and infrahepatic vena cava anastomoses were performed first, followed by the placement of the donor Carrel patch at the site of the recipient's celiac artery. After revascularization of the graft, an end-to-end anastomosis was constructed between the donor and recipient's superior mesenteric veins. Although it was shown that abdominal organ cluster transplants were technically feasible and could be successful, long-term results were disappointing because of disease recurrence [202]. Pancreas graft complications were not uncommon and included severe pancreatitis and necrosis.

Combined Pancreas and Liver Transplants

According to US IPTR/UNOS data, 87 combined pancreas–liver were performed between October 1, 1988, and December 31, 2019, for various indications [8].

Combined pancreas–liver transplants have been performed both orthotopically ("en bloc") and heterotopically (Figs. 29.33, 29.34, 29.35, 29.36, 29.37, and 29.38) [203–226]. En bloc implantation offers certain advantages over separate implantation: it requires fewer vascular anastomoses, obviates the need for a separate biliary anastomosis and permits portal vein drainage of the pancreas graft. It is also associated with shorter operative time. Of note, a unique surgical complication of the en bloc technique has been reported: gastric outlet obstruction by a large donor aortic conduit [204]. This complication points to a key factor for the successful technical outcome of en bloc transplantation: the use of a donor that is smaller in size than the recipient [204, 208, 209].

Combined pancreas–liver transplants have been performed for a variety of pancreatic and hepatic disorders.

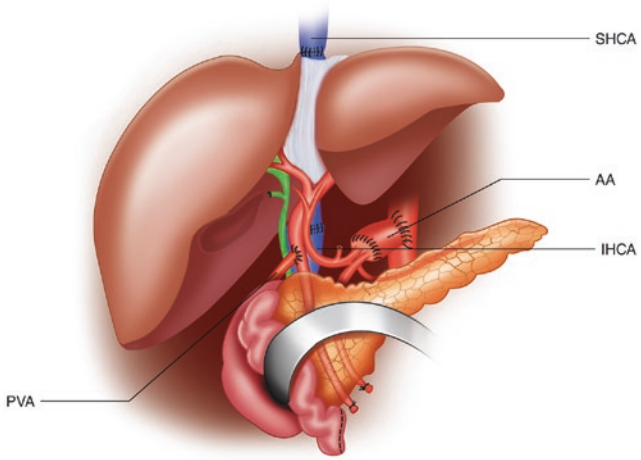

Fig. 29.33 En bloc pancreas/liver transplant with infrahepatic (IHCA) and suprahepatic vena cava (SHCA) anastomoses, interposition aortic conduit (AA) with Carrel patch of the celiac artery and SMA, and recipient-to-donor end-to-side portal vein anastomosis (reprinted with permission from Pirenne et al. [209])

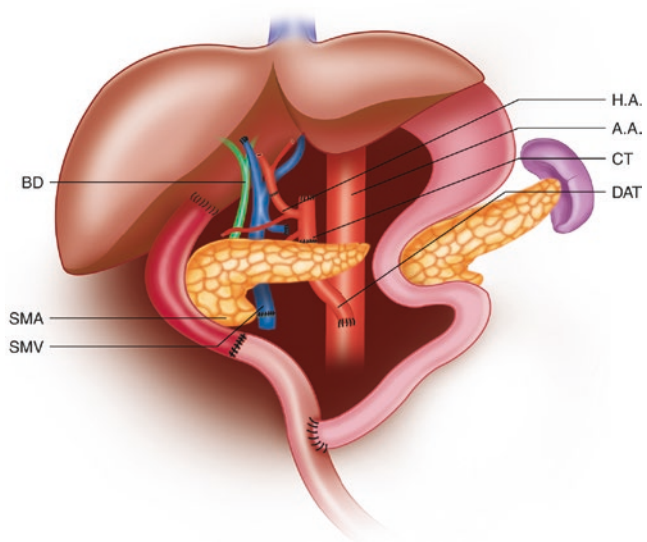

Fig. 29.34 En bloc pancreas/liver transplant with piggy-back caval anastomosis, interposition aortic tube (DAT) with Carrel patch of the celiac artery and SMA, and end-to-end anastomosis between donor SMV and recipient portal vein; Roux-en-Y anastomosis of the distal duodenal graft to the recipient proximal jejunum (reprinted with permission from Chen et al. [211])

Diabetes Mellitus

Twenty-three combined pancreas–liver transplants have been performed for the treatment of type 1 diabetes and end-stage liver disease [208, 209]. In addition, a series of 14 patients with insulin-dependent type 2 (rather than type 1) and end-stage liver disease has been reported [210]. The en bloc technique appears to be favored over separate implantation of pancreas and liver. Pirenne et al. (see Chap. 36) described a technique in which the supra- and infrahepatic caval anastomoses are performed first followed by a piggy-back anastomosis of the native portal vein onto the donor portal vein (Fig. 29.33) [208, 209]. A circular donor aortic patch comprising celiac artery and SMA is anastomosed end-to-end to a donor aortic tube that has been anastomosed to the recipient infrarenal aorta. An enterocolic side-to-side duodeno-jejunostomy is performed for exocrine pancreatic and biliary drainage.

Variations of the en bloc technique have been described primarily for arterial reconstruction and enteric drainage. A donor aortic patch encompassing the celiac artery and SMA can be anastomosed end-to-end to the recipient's common hepatic artery, celiac artery, or suprarenal aorta (Fig. 29.34) [211]. A donor iliac Y-graft connecting the celiac artery and the SMA can be anastomosed to the infrarenal aorta [212]. Duodeno-duodenostomy has been described for exocrine pancreatic and biliary drainage and offers the advantage of easy endoscopic access to the graft duodenum [210].

Eight combined pancreas–kidney–liver transplants have been reported in the literature [210]. These include patients with insulin-dependent diabetes mellitus and end-stage renal and liver disease. En bloc implantation of the pancreas, kidney, and liver grafts has been described [213] as well as en bloc implantation of the pancreas–liver grafts with separate (heterotopic) implantation of the kidney graft [212] as well as separate implantation of all three organs (Fig. 29.35) [214].

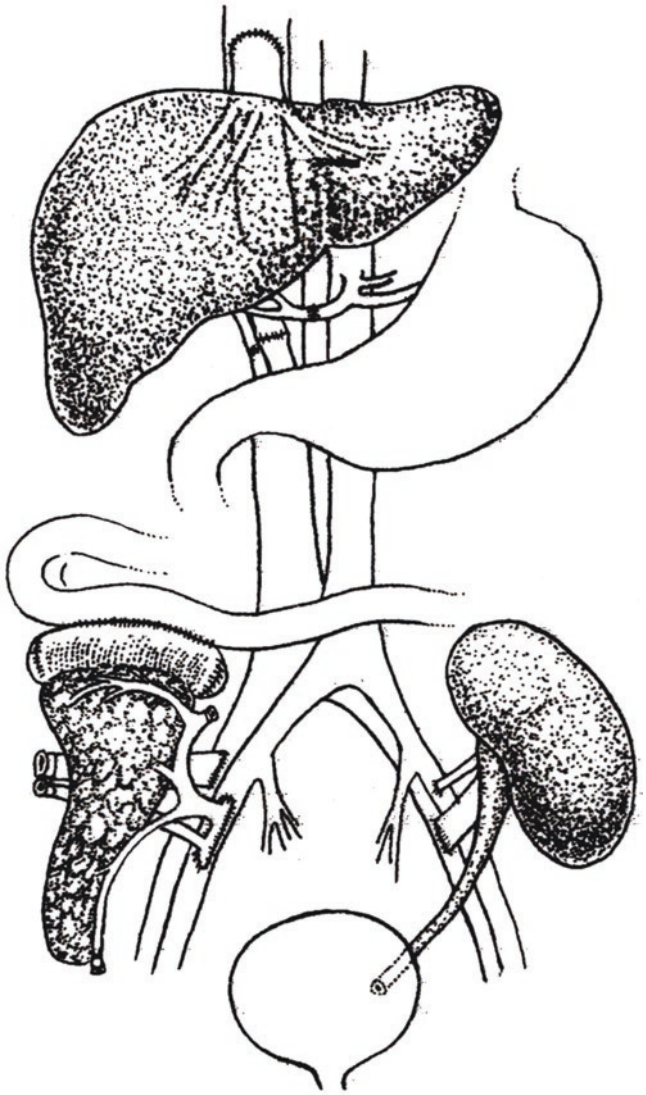

Fig. 29.35 Separate implantation of pancreas, liver, and kidney grafts: orthotopic liver transplant, standard heterotopic transplants of the enteric-drained pancreas and kidney grafts (reprinted with permission from Zhang et al. [214])

Cystic Fibrosis

Cystic fibrosis (CF), an autosomal recessive multisystem disorder that increases the viscosity of exocrine secretions—due to defective epithelial chloride transport—has been associated with pancreatic exocrine dysfunction in 85% and hepatobiliary complications in 30% of CF patients. Moreover, CF-related diabetes mellitus is a principal non-pulmonary

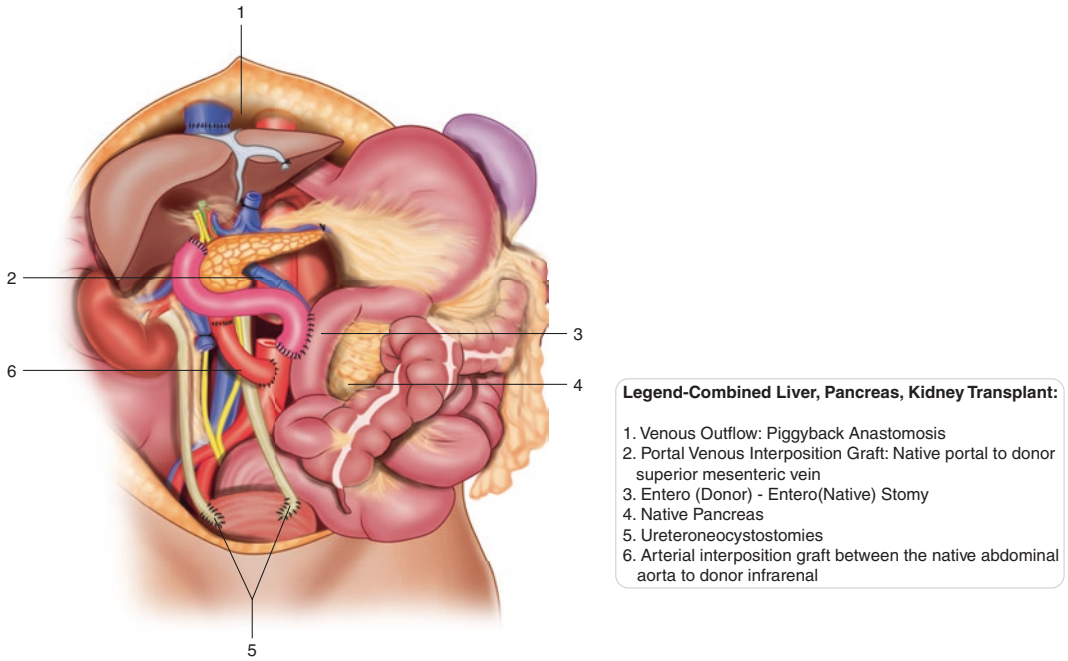

Fig. 29.36 First en bloc pancreas–liver and (dual) kidney transplant for Wolcott–Rallison syndrome. Arterial inflow through the donor infrarenal aorta (with an interposition graft of descending donor aorta) via the recipient infrarenal aorta. Venous outflow via piggyback technique (anastomosis of the donor suprahepatic inferior vena cava to the joint ostia of the recipients's suprahepatic veins). Portal vein continuity via venous interposition graft between the donor mesenteric vein and native portal vein. The donor duodenum was anastomosed antecolic to the recipient jejunum (enteric drainage) and bilateral extravesical ureteroneocystostomies were created (ureteral drainage) (reprinted with permission from Tzakis et al. [224])

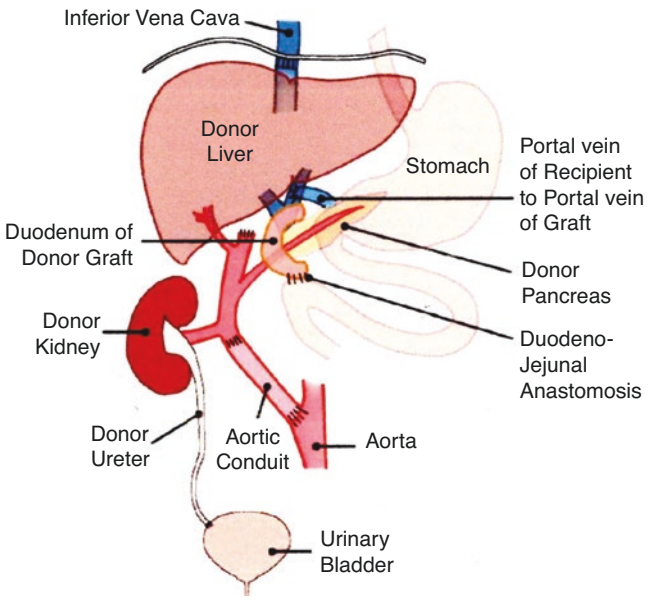

Fig. 29.37 En bloc pancreas–liver and (single) kidney transplant for Wolcott–Rallison syndrome. Arterial inflow through the donor infrarenal aorta (with an interposition graft of descending donor aorta) via the recipient infrarenal aorta. Venous outflow via piggyback technique (anastomosis of the donor suprahepatic inferior vena cava to the joint ostia of the recipients's suprahepatic veins). Portal vein continuity viaend-to-side anastomosis between the donor and recipient portal veins; enteric drainage and standard ureteroneocystostomy (reprinted with permission from Rivera et al. [225])

CF complication, with up to 50% of CF patients developing insulin-dependent diabetes mellitus before the age of 30 years (see Chaps. 72 and 80) [215–217].

The first combined pancreas–liver along with a kidney transplant for CF was performed in 1994; the patient underwent a heterotopic pancreas and kidney transplant and an orthotopic liver transplant [215]. Subsequent reports of combined transplants for CF describe separate and en bloc techniques, both of which are almost equally used [216–222].

Similar to combined pancreas–liver transplants for the treatment of diabetes and end-stage liver disease, a variety of surgical techniques for en bloc implantation in CF patients have been described. For caval venous reconstruction, end-to-end supra- and infrahepatic caval anastomoses as well as the piggyback technique have been used; for portal vein reconstruction, end-to-side or end-to-end anastomosis of the recipient portal vein to the donor portal vein (between the superior border of the pancreas and liver grafts) as well as recipient portal vein to donor SMV anastomosis (below the neck of the pancreas) [218–220]. Variations in arterial reconstruction include the use of a donor iliac artery Y-graft with anastomosis to the recipient infrarenal aorta (with or without a jump graft) or a donor innominate artery Y-graft directly anastomosed the recipient infrarenal aorta [218, 220]. Biliary continuity and

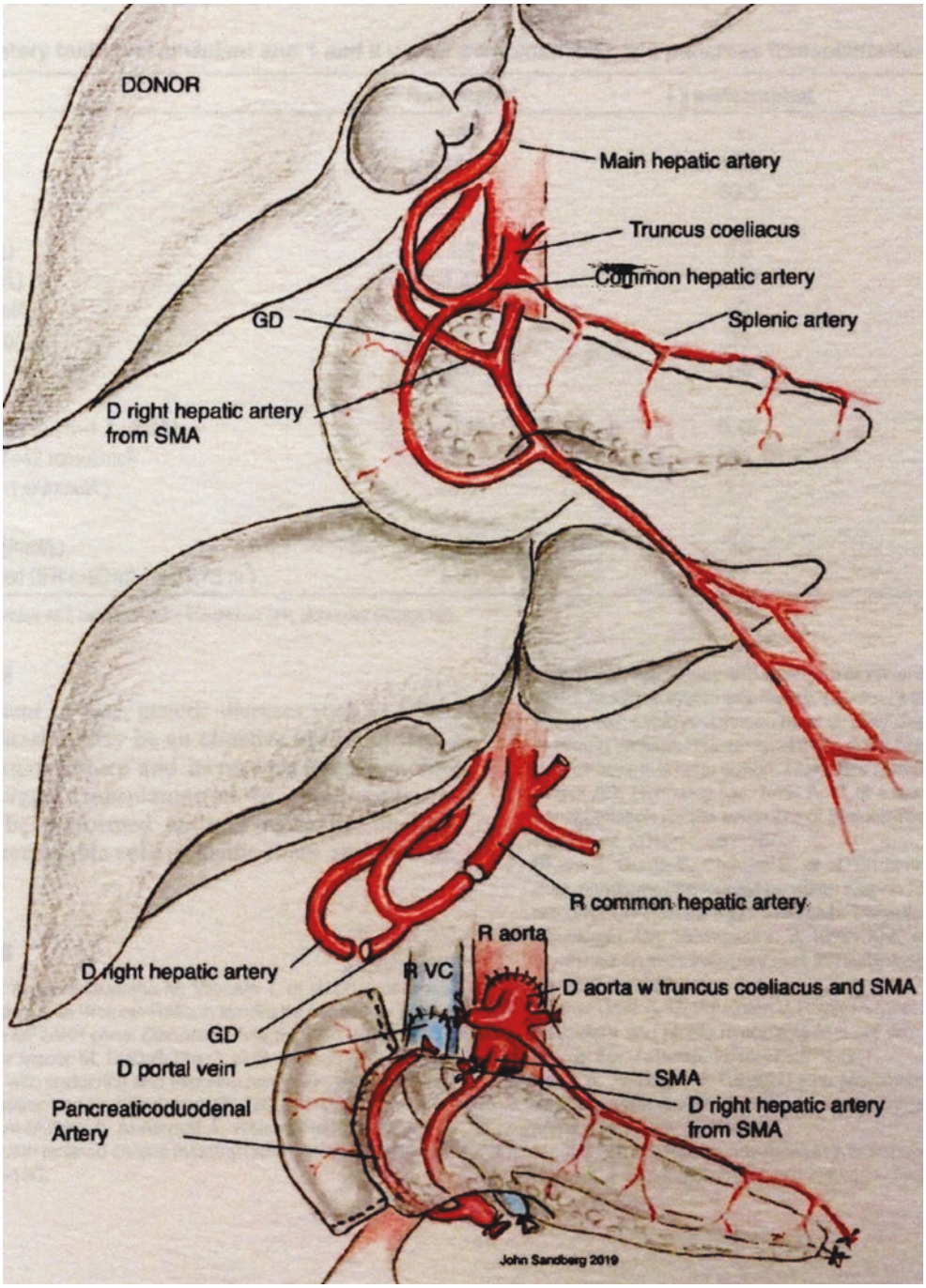

Fig. 29.38 Separate implantation of pancreas and liver grafts: orthotopic liver transplant with right accessory hepatic artery (from the SMA) anastomosed end-to-end to the gastroduodenal artery; heterotopic enteric-drained pancreas transplant with anastomosis of donor Carrel patch encompassing the celiac artery and SMA to the recipient infrarenal aorta and donor portal vein (with donor iliac vein extension graft) to recipient infrarenal vena cava (reprinted with permission from Nordström et al. [223])

drainage of pancreas exocrine secretions is usually re-established with a Roux-en-Y donor duodenum to recipient jejunum anastomosis or an anastomosis of the donor duodenum to a proximal loop of jejunum (with or without a Braun entero-enterostomy) [218, 220].

According to US IPTR/UNOS data, 26 CF-patients underwent pancreas with or without other solid organ transplants between January 1, 1988, and December 31, 2020 (see Chap. 72, Table 72.2). There were three SPK, 2 PAK, 1 PTA, 14 pancreas–liver, and 6 pancreas–multiorgan transplants (liver, lung, and/or intestine) [8].

Wolcott–Rallison Syndrome (WRS)

WRS is a rare, autosomal recessive disorder caused by a mutation of the EIF2AK3 gene on chromosome 2 that encodes the protein kinase R-like endoplasmatic reticulum kinase (PERK) [223]. This results in infantile-onset, insulin-dependent diabetes mellitus, recurrent liver dysfunction and liver failure, renal failure, and other symptoms all of which contribute to an overall poor prognosis. Few children survive beyond 10 years of age.

An en bloc technique for combined pancreas–liver and (dual) kidney transplantation has been reported in two cases.

In the first transplant performed for WRS, Tzakis et al. achieved arterial inflow to the composite graft through the donor infrarenal aorta which was connected to the recipient infrarenal aorta—below the origins of the donor renal arteries—via an interposition graft (donor descending aorta) that was pulled through the transverse mesocolon [224]. Venous outflow was accomplished using the piggyback technique (anastomosis of the donor suprahepatic inferior vena cava to the joint ostia of the recipient's suprahepatic veins). Portal vein continuity was established with the use of a venous interposition graft between the donor mesenteric vein and native portal vein. The donor duodenum was anastomosed antecolic to the recipient jejunum (enteric drainage) and bilateral extravesical ureteroneocystostomies were created (ureteral drainage) (Fig. 29.36) [224]. A similar technique with only one kidney allograft was used by Rivera et al.; the only modification was an end-to-side anastomosis of the native portal vein to the donor portal vein (Fig. 29.37) [225]. At least two other combined pancreas and liver transplants, but without concurrent kidney transplants, have been performed. In one case the en bloc technique as described above was used [226]. In the other case, the pancreas and liver grafts were implanted separately and the donor Carrel patch of the pancreas graft was anastomosed to the recipient infrarenal aorta and the donor portal vein to the recipient infrarenal cava (Fig. 29.38) [223].

Pancreas Transplants as Part of Multivisceral Transplants

Pancreas transplants as part of multivisceral transplants are described in detail in Chap. 36. According to US IPTR/UNOS data, combined pancreas–intestine transplants (with or without other solid organ transplants) were performed in 1265 patients between October 1, 1988, and December 31, 2019: pancreas–intestine–liver (n = 994), pancreas–intestine (n = 163), pancreas–intestine–liver–kidney (n = 101), and pancreas–intestine–kidney transplants (n = 7) [8]. From a historical perspective it is noted here only that after the introduction and subsequent abandonment of the pancreas–liver cluster transplants for the treatment of unresectable malignancies, the goal of multiorgan transplants shifted to the treatment of short bowel syndrome (secondary mainly to benign diseases) and associated total parenteral nutrition (TPN)-related liver failure [227, 228]. Since the vast majority of patients with short bowel syndrome and end-stage liver disease do not suffer from insulin-dependent diabetes, the pancreas is included in these en bloc transplants almost exclusively for technical reasons. To overcome separate liver and intestine implantation in the recipient with the need for bile duct reconstruction, the University of Nebraska group devised an elegant surgical technique. Initially used in pediatric combined liver–intestine transplants, this technique entails en bloc transplantation of the liver and small bowel along with a small portion of the head of the pancreas and duodenum: This allows implantation without additional construction of a Roux-en-Y loop for biliary anastomosis [229]. The University of Miami group modified this technique by including the whole pancreaticoduodenal complex with the liver–intestine transplants, again obviating the need for biliary reconstruction [230]. In addition, inclusion of the entire pancreas reduces operative time and pancreatic remnant-related complications by eliminating transection of the donor pancreas. As mentioned, the technical aspects of these en bloc multivisceral transplants including the pancreas are delineated in Chap. 36.

Simultaneous Pancreas–Lung Transplants

In patients with cystic fibrosis (see above), pulmonary failure and complete pancreatic (exocrine and endocrine) insufficiency can develop over time. Cystic fibrosis is an autosomal recessive genetic disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene (see Chap. 72). The CFTR protein is found in organs that produce mucus (lungs, pancreas, liver, pancreas, intestines, and sweat glands). Lung transplantation alone is the most common type of transplant performed in patients with cystic fibrosis, followed by liver alone and combined lung–liver transplants. In 2008, Fridell et al. reported the first three simultaneous pancreas and lung transplants [231]. All patients required insulin and because they were severely malnourished, enzyme supplementation pretransplant. The organs were procured from the same deceased donor. Bilateral lung transplants were performed first (using two separate thoracotomies). The pancreas transplant was engrafted intra-abdominally with portal venous and enteric exocrine drainage. None of the patients required insulin or supplemental pancreatic enzyme posttranplant [231]. Subsequently, the same group reported a successful simultaneous pancreas and kidney transplant after bilateral lung transplant for a recipient with cystic fibrosis. In 2018, the first successful combined lung–liver–pancreas transplant was reported in a 19-year-old male. The lung transplants were performed first using a bilateral clamshell incision. The pancreas and liver graft was implanted en bloc. An aortic conduit was fashioned by anastomosing the donor's thoracic aorta to the recipient's infrarenal aorta [232]. After completing the upper and lower caval anastomoses, the recipient portal vein was anastomosed to the left side of the donor portal vein, and the distal end of the abdominal aorta segment was anastomosed end-to-end to the thoracic aortic conduit. The donor duodenum was anastomosed side-to-side to the proximal jejunum. The patient had excellent exocrine and endocrine (as well as pulmonary) function 1-year posttranplant [232]. The indication for pancreas transplantation in this setting is also justified by the fact that diabetes mellitus is an independent risk factor for mortality in patients with cystic fibrosis [233].

According to US IPTR/UNOS data, three pancreas–lung and two pancreas–lung–liver transplants were performed between January 1, 1988, and December 31, 2020 [8].

Simultaneous Pancreas–Heart Transplants

The prevalence of cardiac disease in diabetic patients is extremely high (see Chaps. 26 and 27). It is a frequent cause of peritransplant morbidity and mortality. During the pretransplant evaluation, many pancreas transplant candidates undergo coronary artery angioplasty or a bypass procedure before being placed on the waiting list. But, a small percentage of patients have such advanced coronary disease that a heart transplant is the only therapeutic option. The number of patients who undergo a heart transplant because of surgically non-correctable, end-stage coronary artery disease secondary to diabetes mellitus (types 1 and 2) accounts for approximately 15% of all heart transplants. However, many transplant centers do not consider combined pancreas–heart transplants an option because of the advanced secondary complications of diabetes. According to US IPTR/UNOS data, nine pancreas–kidney–heart and five pancreas–heart transplants were performed between October 1, 1988, and December 31, 2019 [8]. Technically, the pancreas (with or without a kidney) is transplanted intra-abdominally in standard fashion after the heart transplant is completed.

Good long-term outcome after combined pancreas–kidney–heart transplantation can be achieved: one case with 11 years of follow-up and excellent graft function has been reported in the literature [234]. A successful pancreas after a combined heart–kidney transplant has been reported in a 32-year-old patient with brittle diabetes mellitus and end-stage cardiac (ischemic cardiomyopathy) and renal failure. The subsequent pancreas transplant was performed because of poor quality of life from diabetes and its risk to endanger the stable heart–kidney allografts. The pancreas was transplanted intra-abdominally with portal venous and enteric exocrine drainage 6 months after the combined heart–kidney transplant [235].

Other Technical Variations

Duodenal Button Versus Duodenal Segment

With the increasing popularity of bladder drainage in the late 1980s, the duodenal button technique was proposed as an alternative to the use of a whole duodenal segment [236, 237]. The duodenal button technique entails transplanting only a small rim (0.5–1 cm) of donor duodenum, surrounding the papilla of Vater (Figs. 29.39 and 29.40). The papilla is identified and a small catheter is introduced about 2 cm into the pancreatic duct. If Wirsung's duct cannot be easily identified, the ligated end of the common bile duct is opened, and the catheter is passed through the common bile duct to the papilla to reveal its location. The catheter is secured with two 5-0 or 6-0 absorbable sutures, either to the duodenal patch or to the anastomosis with the recipient jejunum or bladder.

As with the duodenal segment, the duodenal button technique allows either enteric or bladder enteric drainage (Figs. 29.39 and 29.40). If enteric drainage is used, the pancreatic duct catheter can be also externalized by tagging it at the anastomosis and bringing it out through the jejunal wall over a Witzel tunnel and the abdominal wall. The pancreatic duct catheter is then secured to the skin with a single suture. This approach allows temporary monitoring of exocrine pancreatic secretions in the early posttransplant period. The externalized catheter is left in place for about 3 weeks. If bladder drainage is used, the small catheter is either spontaneously excreted through the urethra or cystoscopically removed about 2–3 weeks posttransplant. One of the disadvantages of the duodenal button technique is that the extensive duodenal dissection and mobilization next to the head of the pancreatic graft increase the risk of devascularization, bleeding, and fistula formation. Since D'Alessandro et al., in a retrospective study, showed that graft survival was higher and the complication rate lower with the duodenal segment technique, the duodenal button technique has been, by and large, abandoned [237]. However, it remains an option if the duodenal conduit is damaged or devascularized.

The button technique was also used in a case of duodenal drainage: the donor Y-graft was anastomosed to the recipient's right common iliac artery and the donor portal vein to the recipient's vena cava. The head of the pancreas was oriented cranially and a donor duodenal button to the recipient duodenum (third portion) anastomosed was constructed (Fig. 29.41) [127].

Temporary Externalization of Pancreatic Secretions and Cutaneous Graft Duodenostomy

Temporary externalization of enteric-drained pancreas graft secretions was initially advocated by the Stockholm group (Fig. 29.42) [238]. Placing a small catheter in the pancreatic duct and bringing it out through the jejunum and skin allows monitoring of exocrine pancreatic secretions in the early posttransplant period. The catheter is usually pulled within 3–4 weeks posttransplant with little consequence. Because the placement of a catheter in the pancreatic duct creates morbidity of its own, in particular, graft pancreatitis, this technique has been abandoned by the same group that initially proposed it [239].

Of only historical interest is the construction of a cutaneous graft duodenostomy, a technique used by Lillehei et al. for their first four pancreas transplants and again used by Starzl et al. for the first enteric-drained whole-organ pancreas transplant [3, 42]. With the evolution of enteric and bladder drainage as safe and efficient techniques, and the development of simple percutaneous biopsy procedures, cutaneous duodenostomies have become obsolete. They are only considered an option in cases with intestinal leakages and diffuse peritonitis after direct side-to-side duodenojejunostomy.

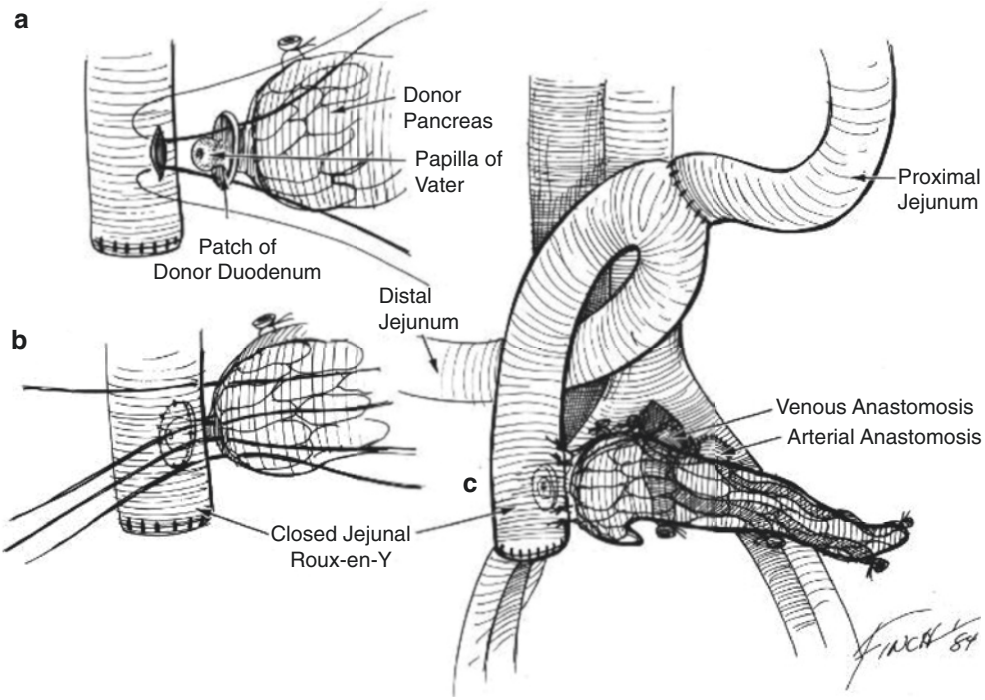

Fig. 29.39 Pancreas transplant with enteric drainage using the "button" technique. Only a small patch of donor duodenum is used for the anastomosis (**a**, **b**)

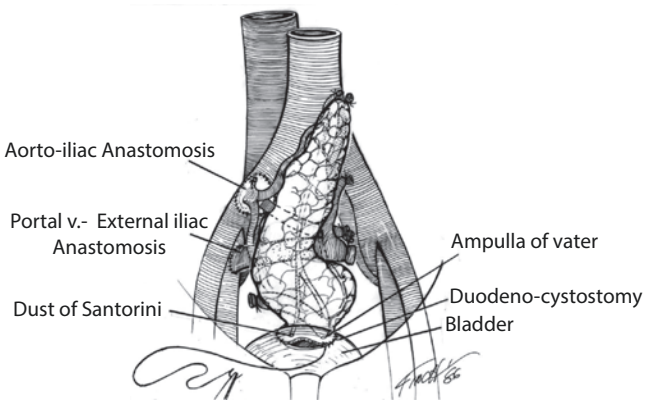

Fig. 29.40 Pancreas transplant with bladder drainage using the "button" technique. A relatively large patch of donor duodenum is used for the anastomosis

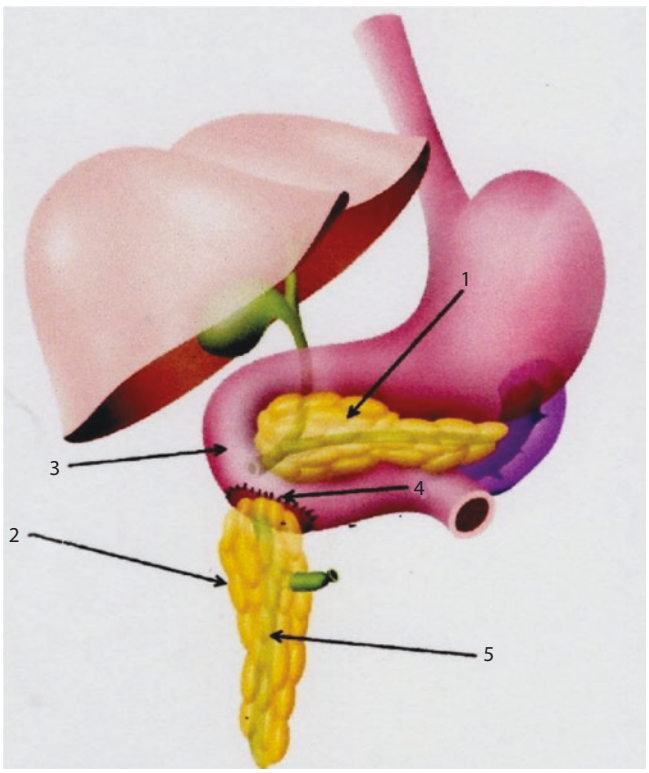

Fig. 29.41 Pancreas transplant with duodenal drainage using the "button" technique. A retroperitoneal approach is utilized (reprinted with permission from Pinchuk et al. [127])

Other Rare Technical Variants

Prior Aorto-Iliac or Ilio-Femoral Bypass Grafts

In my experience, pancreas transplants can be successfully performed in the presence of aorto-iliac or ilio-femoral bypass grafts. But, any duodenal graft spillage should be avoided. Patients should be placed on (broad-spectrum) antibiotic coverage for 7 days; antifungal coverage (fluconazole) should be provided for at least 14 days because *Candida* is a common microbe in the duodenum and has been associated with serious vascular complications [137]. Bladder (vs. enteric) drainage should be considered to avoid any additional risk of contaminating prosthetic material.

Intraoperative dissection or injury of the recipient iliac artery can be successfully repaired by using a donor iliac

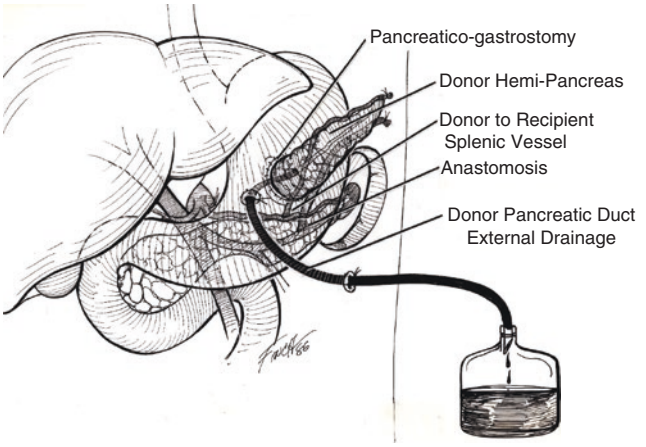

Fig. 29.42 Pancreas transplant with temporary externalization of gastric-drained exocrine graft secretions as initially advocated by the Stockholm group [238]. Placing a small catheter in the pancreatic duct and bringing it out through the gastric wall over a Witzel tunnel and the skin allows monitoring of exocrine pancreatic secretions in the early posttransplant period. The catheter is pulled within 3 weeks. Temporary externalization is basically only of historical interest and has been abandoned because of its complications

artery allograft as a conduit in the presence of posttransplant immunosuppression [240]. Prosthetic material for replacement should be used only in selected cases or if no donor or recipient's arterial graft is available.

Annular Pancreas Graft and Kidney Horseshoe Graft

Successful pancreas transplants have been reported with an annular donor pancreas; the first (rather than the second) portion of the duodenum was used for anastomosis [241]. Successful pancreas–kidney transplants have also been reported in the presence of a donor horseshoe kidney; the kidney was divided and showed good graft function 2 years posttransplant [242].

Double Arterial and Venous Bridge Anastomoses and Simultaneous Pancreas–Spleen Transplants

For segmental transplants, a technique using four vascular anastomoses (proximal splenic artery to aorta or common iliac artery, distal splenic artery to distal internal iliac artery, proximal splenic vein to inferior vena cava, distal splenic vein to distal internal iliac vein) has been developed in an attempt to reduce the high rate of posttransplant thrombosis. With this technique, blood flows from the aorta or common iliac artery through the splenic artery to the peripheral part of the hypogastric artery, and then returns from the pelvic organs through the hypogastric vein via the splenic vein of the graft to the inferior vena cava. This model assumes that the pelvic organs play the same role as the spleen under normal conditions; removal of the spleen decreases the blood flow in the splenic vessels to below one-third [243, 244]. Other surgical techniques aimed at improving splenic artery and vein flow rates have included the creation of a distal splenic arteriovenous fistula and interposition of the splenic artery [245, 246].

Another way to improve blood flow in the pancreas graft is to transplant both the pancreas and spleen. However, in particular, if the donor and recipient are not ABO identical, the spleen can cause a series of hematologic complications, such as hemolytic anemia and thrombocytopenia, as initially reported by Starzl et al. [42]. Another major concern is the potential development of graft-vs-host disease (GvHD) [247, 248]; in an attempt to avoid GvHD, some groups have irradiated the spleen in vitro before implanting it (see Chap. 54) [249, 250].

All of these surgical attempts to improve blood flow through the pancreas graft have been abandoned over time because of prolonged ischemia time, technical difficulties, or immunologic complications. Consequently, they have been replaced because of superior anticoagulation regimens and overall improvement in standard surgical techniques.

Splenomesenteric Arterial Anastomosis

Instead of the typical Y-graft anastomosis for arterial graft reconstitution, the arterial supply of the pancreas has also been reconstructed with a splenomesenteric anastomosis. This entails an end-to-end anastomosis between the proximal splenic artery and the distal end of the superior mesenteric artery (SMA) [251]. Although successful outcome has been reported, this technique has not found widespread application.

Conversion from Systemic to Portal Venous Drainage

Rarely has systemic vein drainage been converted to portal vein drainage. In the University of Minnesota series, one patient with a segmental transplant and slowly deteriorating glucose metabolism underwent anastomosis of the graft distal splenic vein to a recipient mesenteric vein; the previous spleno-iliac anastomosis was ligated. But, no significant improvement in glucose metabolism could be demonstrated after conversion [61].

Use of the Recipient Gallbladder and the Donor Superior Mesenteric Vein for Anastomosis

The use of the recipient gallbladder as the site for drainage of exocrine pancreatic secretions has been reported [252], but for obvious reasons not pursued in a large series.

For venous anastomosis, the donor superior mesenteric vein has been used after sewing the portal vein closed. This technique has not gained widespread application, and no advantage over the standard technique's use of the donor portal vein has been reported [253].

Conversion from Bladder to Enteric Drainage

Conversion from bladder to enteric drainage is a safe and therapeutic procedure in patients with metabolic, urologic, and technical complications after bladder-drained pancreas transplants. Since the vast majority of pancreas transplants are nowadays enteric drained, conversion from bladder to enteric drainage will become more of an uncommon procedure. Yet about 40–50% of all bladder-drained pancreas transplant recipients may ultimately require a conversion procedure and about 15–20% within the first year posttransplant [35, 36, 38, 257].

A detailed review of the advantages and disadvantages of bladder drainage was provided earlier in this chapter. In several single-center studies, the most common indications for enteric conversion were metabolic acidosis (33%), recurrent urinary tract infections (20%), reflux pancreatitis (19%), persistent hematuria (15%), urethritis (6%), anastomotic leaks and fistulas (4%), and duodenal perforation (4%) [35, 38, 254]. Other indications have included urethral disruption and recurrent urine leaks [18, 153, 154]. The timing for enteric conversion shows center-specific variation, between 1 and 72 months posttransplant [22, 35, 255–259]. One large study of 162 conversions reported that the median time to conversion varied by indication: 0.68 years for surgical, 3.1 years for urologic, and 2.7 years for metabolic disorders [38]. Several centers recommend delaying conversion beyond at least 6 months posttransplant to allow monitoring of urinary amylase levels for rejection as long as possible [22, 35]. In the rejection-prone PTA category, the incidence of rejection episodes and the rate of graft loss from rejection was significantly higher if conversion took place <6 (vs. ≥6) months posttransplant [35]. Thus, enteric drainage effectively treats complications related to bladder drainage, with an immediate resolution of symptoms, but increases the risk of undetected rejection after conversion.

The operative procedure comprises three steps: (1) division of the duodenocystostomy, (2) closure of the bladder, and (3) construction of a duodenojejunostomy. The following is a description of the technical aspects.

After induction of general endotracheal anesthesia, the patient is placed in a supine position on the operating table. A Foley catheter is placed, but the bladder is not filled with saline. Nasogastric suction, sequential compression devices, and prophylactic antibiotics are used. The abdomen is entered through the previous midline incision, and adhesions between the omentum, small bowel, and abdominal wall are carefully taken down. The patient is placed in the Trendelenburg position, and the duodenocystostomy is identified. Frequently, adhesions between the lateral portion of the duodenocystostomy and retroperitoneum have to be taken down; injury to the external iliac vessels must be carefully avoided. If the patient undergoes conversion because of a urine leak (either arising at the anastomosis itself or originating from the duodenal segment), cultures for aerobic, anaerobic, and fungal analysis are routinely obtained. In the absence of frank peritonitis or massive intra-abdominal abscess(es), the operative procedure continues with circumferential dissection of the duodenocystostomy.

Using electrocautery, the anterior portion of the duodenocystostomy on the bladder side is incised first. The duodenum with the anastomosis (including a small rim of bladder wall) is circumferentially disconnected from the bladder. The posterior cystotomy is closed transversely in three layers with 3-0 absorbable sutures in a running technique. The two innermost layers approximate the mucosa, submucosa, and muscularis. The outer third layer approximates the seromuscular tissue and inverts the two inner suture lines. Before the cystotomy is closed, the bladder is filled with about 200 mL of saline and the Foley catheter is clamped. If the patient previously underwent a kidney transplant, filling of the bladder prevents inadvertent inclusion of the neo-ureteral orifice in the suture line.

The graft duodenum can be anastomosed directly (side-to-side anastomosis) or to a Roux-en-Y limb of the recipient's small bowel. A Roux-en-Y loop is preferred if the patient requires high steroid doses or has a history of wound healing complications, a previous duodenal leak, or a thin and friable duodenum. For anastomosis, the recipient jejunum 40–100 cm behind the ligament of Treitz is preferred, but sometimes only an ileal loop reaches down to the graft easily.

If a side-to-side duodenojejunostomy without the formation of a Roux-en-Y loop is constructed, a two-layer anastomosis is made (Fig. 29.2). The outer posterior layer is constructed first with interrupted 4-0 nonabsorbable sutures. Bowel clamps are used on the recipient jejunum about 10–15 cm proximal and distal to the anastomosis. A jejunotomy (or ileotomy) of appropriate length is made antimesenterically, opposite from the graft duodenotomy. The inner layer is then constructed between the graft duodenum and recipient jejunum with 4-0 absorbable sutures in a running fashion to achieve thorough hemostasis. Care is taken not to include the papilla of Vater in the suture line. If a rim of bladder wall stays with the graft duodenum, no attempts are made to remove the small cuff or the staples; the rim is incorporated into the inner layer of the anastomosis. Closed-suction drains are selectively used. The bowel clamps are removed after the inner layer is completed. The anastomosis is completed with an outer anterior layer with interrupted 4-0 absorbable sutures. If the distal duodenal stump is long, an end-to-side duodenojejunostomy can be created; the previous duodenotomy should be closed in two layers (Fig. 29.3).

If a Roux-en-Y loop is used, the recipient jejunum is brought down to the level of the graft duodenum to ensure that the mesentery of the jejunum is long enough to reach the graft without tension. The jejunum is divided with a GIA sta-

pler, and the mesentery is divided between clamps (Fig. 29.4). The stapled distal end of the jejunum is oversewn with running or interrupted 4-0 nonabsorbable sutures. The technical aspects of constructing the duodenojejunostomy are described above. The proximal end of the Roux limb is then anastomosed to a point on the distal bowel 40 cm distal to the duodenojejunostomy (Fig. 29.5). Doing so ensures an adequate defunctionalized limb for drainage of the pancreas graft. If a segmental graft is converted from bladder to enteric drainage, a Roux-en-Y loop should be used to reduce the complications resulting from a leak at the pancreaticojejunostomy.

Foley catheter bladder drainage is usually maintained for up to 2 weeks. The nasogastric tube drain is maintained for a couple of days or until the return of bowel function.

Enteric conversion in large patient series has shown to be a safe procedure and to not increase the risk of pancreas (or kidney) graft loss [35, 36, 38, 257]. However, smaller patient series have reported postoperative morbidity including reoperation and graft loss [39, 254].

Technical complications are reported in 10–25% of patients after conversion, including anastomotic leaks, duodenal perforations, and graft pancreatitis [22, 36, 38, 39, 254]. Unusual complications such as enterovesical fistula and bladder rupture have also been noted after conversion [37, 260].

Perioperative treatment with octreotide has been reported to minimize technical complications after enteric drainage (150 mg three times/day for a total of 3 days) [261]. Postoperative monitoring of serum amylase levels appears to be helpful: Levels of ≥200 U/L for more than 4 days after conversion frequently indicate a technical complication, specifically in retransplants [262]. Under those circumstances, early reexploration is crucial because most recipients with complications after conversion can be successfully treated with primary repair and drain placement [263–266]. If primary repair is not technically feasible, exclusion of the graft duodenum to the abdominal wall is a viable alternative. In a retrospective study, West et al. reported no increased risk of graft loss with exclusion of the graft duodenum [35, 36].

Graft Pancreatectomy

Only about 20–50% of all pancreas graft failures require graft pancreatectomy [267]. The vast majority of these procedures are total graft pancreatectomies but segmental pancreatectomies have also been described, in particular, distal resections in case of partial allograft thrombosis.

Graft pancreatectomy can be a very challenging procedure given the proximity of the iliac vessels and/or the presence of extensive adhesions irrespective of whether the graft is swollen or shrunken in size. Several blood units should always be typed and crossed before the patient is taken to the operating room and intraoperative bowel and vascular injuries must be avoided.

Graft pancreatectomy can be categorized into three types according to the timing, technical difficulty, and cause of graft loss:

1. Early pancreatectomy (≤3 weeks posttransplant): Usually, adhesions are few and the pancreas can easily be mobilized from surrounding tissues. Most patients with early graft loss require graft pancreatectomy [268].

   Early graft pancreatectomy is usually required for graft thrombosis and much less frequently for severe graft pancreatitis. Graft thrombosis has traditionally been associated with "technical" complications, but acute pancreas rejection has also been implicated as a potential cause of early graft thrombosis. In fact, one study noted unsuspected acute pancreas rejection to be quite common in explanted grafts, but the case numbers were relatively small [269]. Of graft thromboses, about 60% are venous and 40% arterial. They differ in timing and symptoms. Most *venous* thromboses occur within the first week, and patients have severe and unrelenting abdominal pain. Clinical symptoms are consistent with an acute abdomen and include abdominal distention, tenderness to percussion and palpation (in particular over the graft), peritoneal guarding, and, after bladder-drained transplants, discharge of bloody urine that frequently contains duodenal debris. *Arterial* thrombosis occurs slightly later, with peaks in the first and second weeks posttransplant. Initially, patients are relatively asymptomatic, but symptoms develop once the necrotic graft becomes infected.

   A sharp increase in serum glucose levels over a short period of time is observed for both venous and arterial thrombosis. Although graft salvage has been reported, graft thrombosis usually mandates graft pancreatectomy. However, if graft thrombosis is limited to the splenic vein or to only one graft artery (superior mesenteric or splenic artery), only a partial pancreatectomy can be performed.

   In selected patients with early graft pancreatectomy (secondary to graft thrombosis), a concurrent or simultaneous pancreas re-transplant (synonyms: pancreas exchange, pancreas switch) can be considered [270] if (1) the recipient is clinically stable, with no evidence of intra-abdominal infection and (2) another donor organ is immediately available (see above).
2. Intermediate pancreatectomy >3 weeks and ≤3 months: adhesions between the graft and surrounding abdominal structures (bowel, omentum, ovaries, and colon) are common and frequently require sharp dissection.

   The most common causes are infection and graft pancreatitis. In contrast to graft thrombosis, infection and pancreatitis require graft pancreatectomy less commonly, thanks to improvements in antimicrobial prophylaxis and

therapy, placement of percutaneous drains, and surgical placement of irrigation and drainage systems. In this category, simultaneously retransplanting another pancreas graft is frequently not possible, because of the high rate of intra-abdominal infection (abscess, peritonitis), with or without peripancreatitis (tissue debris and necrosis). The rupture of a mycotic aneurysm with or without intragraft bleeding or necrosis, usually between >3 weeks and ≤3 months posttransplant, is an absolute emergency that requires both graft pancreatectomy and (frequently complex) vascular reconstruction of the recipient's blood vessels. If complete graft pancreatectomy is not safely possible, as much graft tissue as possible (including the graft duodenum) must be removed. Mycotic aneurysms with subsequent ruptures are frequently the result of infections and inadequate antimicrobial treatment. In such cases, an immediate retransplant is not an option for obvious reasons.

3. Late pancreatectomy (>3 months): The graft is frequently shrunken and is in close proximity to the recipient's vessels. Completely removing it without injury to the recipient's native vessels is challenging and sometimes not possible. The most common indication for late pancreatectomy is rejection, followed by infection and late (arterial) thrombosis. Other causes such as arterio-enteric (or vesical) fistula or pseudoaneurysm (with or without rupture) are rare and usually require intermediate or late pancreatectomy [268]. Graft pancreatectomy in the presence of an arterio-enteric (or arterio-vesical) fistula or a pseudoaneurysm (with or without rupture) can be technically a very challenging procedure and control of the recipient inflow and outflow vessels is crucial. Patients with chronic or irreversible acute rejection usually require graft pancreatectomy only when abdominal symptoms such as abdominal discomfort, pain, and/or nausea develop [268]. In the absence of intra-abdominal infection, these patients can undergo a simultaneous retransplant without an increased risk of surgical complications.

If graft pancreatectomy is performed due to thrombosis and if thrombotic material has been detected by imaging studies in the vena cava even before surgery, placement of a filter should be considered before taking the patient to the operating room in order to decrease the risk of pulmonary embolism.

Irrespective of the timing of graft pancreatectomy, preoperative preparation for patients undergoing graft pancreatectomy is no different than for any other major abdominal procedure. After induction of anesthesia, a central line catheter, a Foley catheter, and a nasogastric tube are placed; prophylactic antibiotics and sequential compression devices are routinely used. The abdomen is entered via the previous (midline) incision. All adhesions between the omentum, small bowel, abdominal wall, and pancreas graft are taken down by blunt and sharp dissection. The following is a description of pancreatectomy for grafts with systemic vein and enteric drainage.

Before the pancreas is fully mobilized, it is crucial to obtain both proximal and distal control of the iliac arteries and veins, in particular, if the graft is swollen and necrotic because of venous thrombosis. The common, external, and internal iliac vessels are identified, and vessel loops are passed around them in case they need to be clamped (e.g., bleeding). Propagation of the graft thrombus into the iliac vein results in leg swelling that can be profound and painful. If the patient has symptoms of deep venous thrombosis or even phlegmasia cerulea dolens, the leg should also be prepped and draped in standard fashion for venous thrombectomy, either from the site of the venous anastomosis or through a separate groin incision.

After control of the iliac vessels is obtained, the enteric anastomosis is taken down with electrocautery or stapled off if a Roux limb had been used for anastomosis. Doing so allows mobilization of the graft duodenum and head of the pancreas.

In case of venous graft thrombosis with a massively enlarged and immobile pancreas, control is best achieved by clamping the recipient's iliac arteries (common, external, and internal) and iliac veins (common and external) proximally and distally. If the graft thrombus has propagated into the iliac vein, the common iliac vein must be dissected with utmost care to avoid embolization of any thrombi. Therefore, placing the proximal venous clamp above the tip of any thrombotic material is crucial to prevent pulmonary embolism. Rarely, a thrombus extends all the way into the inferior vena cava; in most cases, clamping of the proximal common iliac vein suffices. But, sometimes it is necessary to use a curved Cooley clamp to gain additional control of the distal vena cava. Once all clamps are placed, the graft vessels are divided 1 cm distal to their respective anastomoses; all thrombotic material is removed, and the iliac vein and artery are flushed with heparin-containing solution. If the common iliac vein or distal vena cava cannot be identified and dissected free, a caval filter may be placed under fluoroscopy guidance via the internal jugular vein. Thrombotic material can then be removed via a separate groin incision, or thrombolytic therapy can be initiated.

If the patient has symptoms consistent with deep vein thrombosis, the thrombotic material can be removed either from the site of the venous anastomosis or through a separate groin incision. After proximal control of the iliac vein has been achieved, Esmarch rubber stockings are applied tightly from the ankle all the way up to the groin to squeeze out all thrombotic material. Once venous backflow is brisk, heparinized saline is injected distally and the vein is reclamped. Likewise, all thrombotic material that has extended proxi-

mally beyond the anastomosis is removed. The proximal vein is irrigated with the heparin-containing solution. The vein (or graft portal vein stump) is closed with a single running 4-0 or 5-0 nonabsorbable suture, avoiding any narrowing of the iliac vein. First the distal, and then the proximal, clamp on the iliac vein is removed.

Rarely, a thrombus in the graft artery extends into the common or external iliac artery. If so, a standard arterial thrombectomy is performed through the graft arterial stump or a separate groin incision. Once all thrombotic material is removed, the artery is flushed with heparin. The graft arterial stump is ligated with a silk tie and then suture ligated.

If the pancreas graft is not removed because of venous thrombosis and the operative field is dry, clamping of the iliac vessels may not be necessary. Under those circumstances, arterial anastomosis should be identified first. The inflow vessel should be ligated approximately 1 cm distal to the anastomosis on the side of the graft. The donor portal vein can then be clamped and divided. The pancreas graft is removed. The arterial and venous stumps are ligated and oversewn with running 4-0 or 5-0 nonabsorbable sutures.

With systemic vein and enteric drainage, the following options exist for taking down the enteric anastomosis:

1. If a Roux-en-Y limb was used, it should be shortened close to the duodenojejunostomy with a GIA stapler. The staple line is oversewn with interrupted 4-0 nonabsorbable sutures.
2. If a side-to-side anastomosis was constructed, a cuff of donor duodenum (if viable) with the stapled anastomosis should remain with the native jejunum. Usually, the jejunostomy can then be horizontally closed in two layers. If the jejunostomy is too big, this segment of bowel should be resected and a two-layer (end-to-end) anastomosis is constructed. In the presence of diffuse peritonitis, the jejunostomy can be externalized (loop jejunostomy); only if the jejunostomy is too big does this segment of bowel have to be resected, and two ostomies may have to be brought out. Depending on the patient's clinical condition, the ostomies are usually taken down 2–6 months after their construction.

With portal vein and enteric drainage, the technical concept of graft pancreatectomy is similar: After mobilization of the pancreas, the duodenojejunostomy is taken down. The recipient jejunum is closed horizontally (side-to-side anastomosis) or stapled across close to the jejunojejunostomy (Roux-en-Y loop). Ostomies are constructed in case of massive intra-abdominal infection. The long arterial Y-graft usually does not require proximal and distal control of the common iliac artery. The Y-graft is oversewn with a single running 5-0 nonabsorbable suture close to the recipient's common iliac artery. The venous anastomosis is taken down by placing a clamp on the graft portal vein (in the absence of venous thrombosis) or placing clamps proximally and distally on the recipient's superior mesenteric vein (in the presence of venous thrombosis). After the graft portal vein is divided about 1 cm distal to the anastomosis, the recipient's superior mesenteric vein is flushed with heparin and all thrombotic material is removed. The superior mesenteric vein (or the graft portal vein stump) is oversewn with a single running 5-0 nonabsorbable suture. Mesenteric thrombosis with bowel necrosis or liver failure is rare, given the location of the graft portal vein anastomosis (distal to the confluence of the superior mesenteric and splenic vein) and the presence of venous collaterals. In a retrospective study by Stratta et al., portal vein and enteric drainage did not place patients at an increased risk for pancreatectomy, but the incidence of pancreatectomy was higher than with systemic vein and bladder drainage [160].

With systemic vein and bladder drainage, the following approach to graft pancreatectomy should be chosen: after control of the iliac vessels is obtained, the bladder anastomosis is taken down with electrocautery. Doing so allows mobilization of the graft duodenum and head of the pancreas.

The bladder is closed in standard fashion using a three-layer closure (absorbable 3-0 or 4-0 sutures). The whole duodenum and the stapled anastomosis remain with the graft. In patients with a kidney graft, care is taken to not include the ureteral orifice in the bladder closure line. To avoid this complication, the bladder is filled with about 200–300 mL of saline for bladder expansion, and the Foley catheter is clamped. The pancreatic bed is then inspected, and the abdomen is irrigated with copious amounts of antifungal and antibiotic solutions. If the graft pancreatectomy is performed for infection or graft pancreatitis, cultures are taken and sent for aerobic, anaerobic, and fungal analysis.

If graft pancreatectomy becomes necessary >3 months or even years posttransplant (e.g., because of chronic abdominal pain from a rejected pancreas graft) and if the fibrotic graft is markedly shrunken and the graft vessels cannot be isolated, most of the pancreatic remnant should be removed. The cut surface is oversewn with a single running 3-0 or 4-0 absorbable suture. The graft duodenum should always be disconnected from the bladder and removed; it is frequently an ongoing source of infection (e.g., recurrent urinary tract infections) because of impaired blood supply. If the whole pancreaticoduodenal graft cannot be removed, the duodenum should be amputated at the head of the pancreas. The resection line is oversewn with 3-0 or 4-0 nonabsorbable sutures in running fashion. If the pancreas can be resected, proximal and distal control of the iliac vessels is as important for late as for early pancreatectomy.

In case of inadvertent damage to the iliac artery and vein during pancreatectomy, repair is crucial to prevent subse-

quent thrombosis. If a segment of the iliac artery or vein has to be resected, an interposition graft (internal iliac artery and saphenous vein) can be used. In the presence of infection, prosthetic material should be avoided because of the risk of anastomotic leaks and pseudoaneurysms.

Placement of drains after graft pancreatectomy is usually not necessary. Only in the presence of massive infection should an irrigation and drainage system be placed (see above). Once hemostasis is achieved, the abdomen is closed in standard fashion.

Since graft pancreatectomy can be a very challenging procedure, morbidity and mortality are not insignificant. Complications have included postoperative pulmonary embolism (resulting in death), pseudoaneurysm formation, bleeding, injury to the patient's vascular structures with the need for bypass procedures and more [268]. Of note, one large study of 50 late graft pancreatectomies showed that the procedure was not associated with a decrease in kidney graft survival in SPK recipients [267].

In the rare event of early distal graft pancreatectomy for the treatment of partial graft thrombosis, the distal segment is resected with or without the use of a stapler. The stump is closed in two layers in a typical fashion.

Rarely, graft pancreatectomy is performed simultaneously with an immediate islet retransplant (islets prepared from the same allograft). The resected allograft is digested in a collagenase preparation and the islets are harvested according to standard islet protocols (see Chap. 84). The main indication for this procedure is recurrent graft pancreatitis (especially if the patient already underwent conversion from the bladder to enteric drainage). However, islets from the same allograft should only be used in the absence of concurrent intra-abdominal infection. It has been hypothesized that successful engraftment and maintenance of islet function with standard immunosuppression are possible, given adequate islet mass and previous exposure of the peripancreatic lymphoid tissue to the recipient's immune system [271].

Pancreas Retransplants

The topic of pancreas retransplantation is covered in detail in Chap. 70.

This subchapter just provides a brief general overview with a focus on technical considerations for pancreas retransplantation.

According to US IPTR/UNOS data, the number of retransplants per year reached a peak of 9% in 2004 but declined constantly thereafter. In 2019, only 2% of all pancreas transplants were retransplanted. The decline is due to the decreasing number of PAKs which represents the most frequent retransplant category (see Chaps. 66 and 70). Most primary transplants are SPKs where the pancreas failed but the transplanted kidney continues to function [8, 272–285]. The most common indications for pancreas retransplants are technical failures (52%) (i.e., thrombosis [42%], infection/graft pancreatitis [7%], other [3%]) and rejection (35%). Retransplant outcome, as shown in Chaps. 66 and 70, is similar to that of primary transplants including technical and immunological graft loss rates despite the fact that retransplant candidates are usually more sensitized than primary transplant candidates [267, 276–278]. Similar outcome has been shown both for immediate retransplants (pancreas exchange or pancreas switch [270, 274, 279] and late retransplants [277, 278, 280]. Only one study using UNOS data showed worse outcomes with retransplants, but that study did not provide a comparison between primary and retransplants by recipient category. Hence, this analysis is flawed since most primary transplants are SPKs whereas most retransplants are in the solitary categories (mostly [re-] PAKs) [281]. As shown for primary transplants, re-SPKs provide better outcomes than solitary (PAK, PTA)-retransplants [267, 281–283]. Several single-center studies have also shown good outcomes with third and fourth pancreas transplants [284, 285]. Detailed outcome analyses are provided in Chaps. 66 and 70.

In general, pancreas retransplants can present challenges to the surgeon because of their technical complexity; previous (and sometimes multiple) transplants, laparotomies, and pancreatectomies make vascular dissection even more difficult. The need for additional procedures such as extensive adhesiolysis, removal of previously implanted grafts, and small bowel resection(s) can make retransplants technically very demanding [286]. In preparation for a retransplant it has been recommended to procure a greater number of vascular grafts from the donor since unusual and complex vascular reconstructions are more common [278, 280]. Nonetheless, the results of retransplants have significantly improved over time. A retransplant should now routinely be offered to recipients with a failed pancreas graft just as it is, for example, to recipients with a failed kidney graft. Yet pancreas retransplants are less practiced than for other solid organs. In fact, the quest for a pancreas retransplant is very frequently patient-driven: recipients who have experienced an insulin-free interval after their previous transplant are eager to pursue another one [280, 287].

From the surgical perspective, pancreas retransplants require versatility and technical competence to manange unexpected findings and apply unusual solutions [278, 280, 282]. Technically successful pancreas retransplants can be done with systemic or portal vein drainage and with enteric (including duodenal and gastric) or bladder exocrine drainage. For retransplants, the two different venous drainage techniques are even more complementary than for primary transplants, because access to previously undissected vascular structures decreases the risk of technical complications and reduces operative time. Thus, a patient with a failed graft

with systemic vein drainage may undergo a retransplant with portal vein drainage (and vice versa); portal vein drainage can be combined with enteric or duodenal drainage for the management of exocrine secretions. A patient with a failed graft with bladder drainage may undergo a retransplant with enteric drainage (and vice versa). The key word is technical flexibility because it may not be feasible to use the standard vascular sites in the recipient to connect the graft. Hence, the new pancreas graft may not be positioned where initially intended but where possible [280].

The two most common scenarios under which pancreas retransplants are performed are (1) graft loss for technical reasons which usually results in graft removal and (2) graft loss for immunological reasons which usually does not result in graft removal. The former permits the retransplant to be performed with greater technical ease and shorter operative time, the latter does not. These two scenarios can also determine whether the same or different drainage techniques are utilized [280]. If the reason for immunological graft loss was not rejection but recurrence of disease (diabetes), the prior graft can act as an antigenic stimulus and trigger an autoimmune response that can jeopardize the new graft; in this case, a different immunological protocol should be implemented [280, 288].

Preoperative preparation of patients undergoing a pancreas retransplant is basically no different than with a primary pancreas transplant or any other major abdominal surgery. Central vein and arterial lines, nasogastric suction, Foley catheter bladder drainage, prophylactic antimicrobial prophylaxis, and sequential compression devices are all routinely used. Immunosuppressive medication is per protocol; the first dose of anti-T-cell therapy is usually given after induction of anesthesia.

The previous (midline) incision is opened and all adhesions between the omentum, small and large intestine, and abdominal wall are carefully taken down to avoid any accidental enterotomies. Self-retaining retractors are placed and the abdomen is explored. If evidence of infection is noted, the procedure should be aborted at this time; cultures should be sent for analysis to allow specific and efficient treatment with antibiotics. Once the infection has cleared, the patient can be placed on the waiting list again.

If the previous graft used systemic vein drainage, is still in place, and is of (near) normal size, and if the new graft is to be implanted at the same site, the previous graft must be removed. The anastomosis of the graft duodenum to the recipient's small bowel or bladder is identified first.

If the previous graft used enteric drainage, the native bowel is clamped proximally and distally to the side-to-side anastomosis (or distally to the anastomosis if a Roux-en-Y loop was used), and the duodenojejunostomy is taken down. A small rim of graft duodenum with the previous side-to-side anastomosis remains with the native small bowel to facilitate horizontal closure of the jejunum. If a Roux-en-Y loop was used, the native bowel is stapled across, just distal to the duodenojejunostomy, and the stapler line is oversewn; the Roux limb can then be reused for the new duodenojejunostomy.

If the previous graft used bladder drainage, the duodenocystostomy is taken down by leaving a small rim of bladder wall with the previous anastomosis on the side of the graft duodenum. If enteric drainage is chosen for the retransplant, the bladder is closed in three layers as described above. If bladder drainage is chosen again, the bladder is left open for the construction of a new hand-sewn or stapled duodenocystostomy at the same site.

Once the anastomosis to the graft duodenum is taken down, the previous pancreas graft is fully mobilized by taking down all adhesions to the small and large bowel, omentum, and possibly the bladder. In female recipients, adhesions to the ovaries and the uterus may also have to be taken down.

In preparation for graft pancreatectomy, the proximal and distal iliac vessels are clamped. The arterial anastomosis is identified and divided about 1 cm distal to the anastomosis. The iliac artery is flushed with heparinized solution. Likewise, the donor portal vein is cut about 1 cm distal to the anastomosis. The portal vein stump and the recipient iliac vein are flushed with heparinized solution. The graft portal vein and artery stumps are only oversewn if different sites are chosen for the construction of the new anastomoses. Depending on the size of the new graft vessels, the previous anastomotic site can frequently be reused. The new anastomoses can be done either directly to the recipient iliac vessels at the previous anastomotic sites or to the stumps of the previous arterial and venous grafts. However, the infrarenal vena cava and the proximal iliac artery are frequently chosen for vascular implantation for sites [277, 280, 282, 289]. The technical aspects for construction of the vascular anastomoses are no different for retransplants (vs. primary transplants).

If the new graft also uses enteric drainage, the previous side-to-side anastomosis can be re-used or, in case of possible stenosis, a new two-layer side-to-side anastomosis needs to be constructed. If a Roux-en-Y loop was previously used, that limb can be used again. The technical considerations are the same if duodenal (rather than enteric/jejunal) drainage is used.

If the new graft uses bladder drainage again, it is usually safest to construct a hand-sewn two-layer duodenocystostomy. Only if the cystotomy after the takedown of the anastomosis is small can an EEA-stapler anastomosis be constructed. In preparation for a stapled anastomosis, the previous anterior cystotomy is reopened and the previous posterior cystotomy is purse-stringed around the rod of the stapler. The stapler is fired in standard fashion. The staple line is reinforced internally or externally using 4-0 nonabsorbable sutures.

If the retransplant is performed months or even years after the previous transplant, the previous graft is often fibrotic and completely shriveled down to the size of a large walnut or

plum. Graft pancreatectomy can then be extremely difficult. Under those circumstances, it might be prudent to leave the previous graft in place (in particular in asymptomatic recipients). The new graft can be implanted further proximally, either to the common iliac vessels or to the distal aorta and infrarenal vena cava. Only rarely it is technically feasible to implant the new graft distal to the previous graft. Irrespective of whether or not the previous graft duodenum is shriveled, the duodenocystostomy should be taken down in cases with previous bladder drainage. The graft duodenum must be amputated off the head of the pancreas, with the resection line on the pancreas side oversewn. Removal of the graft duodenum is important as it may harbor microbes that continue to cause recurrent urinary tract infections. In cases of previous enteric drainage, the duodenojejunostomy must only be taken down if the anastomosis is not widely patent, the graft duodenum is thin and friable (actually, most of the time, it is scarred and fibrotic from rejection and atrophy), or if there is a concern for the development of an enteric or arterio-enteric fistula [278].

If the previous graft had been removed earlier, in a separate procedure, a pancreas retransplant is obviously less time-consuming and requires only identification and dissection of appropriate sites for vascular implantation. The duodenojejunostomy, duodenoduodenostomy, or duodenocystostomy can be constructed in the same fashion as for primary transplants.

If a functioning kidney graft is still in place and had been anastomosed to the left external iliac artery and vein, every attempt should be made to use the proximal common iliac artery and vein on the right side for a pancreas retransplant. If doing so is technically not feasible, the aorta and vena cava and sometimes even the left common iliac vessels can be used for graft anastomoses. In preparation for kidney graft clamping (in case a side-binding clamp cannot be used on the aorta), the recipient should be fluid-flushed and given furosemide and mannitol as well as systemic heparin (30 U/kg). I have not lost a kidney graft to prolonged warm ischemia time, but adequate preparation and quick completion of the anastomoses are crucial. Under such circumstances, portal vein drainage of the pancreas graft may be considered a viable alternative since only the arterial anastomosis requires iliac or infrarenal aortic inflow whereas the donor portal vein can be anastomosed in undisturbed ("virgin") territory to the recipient portal/SMV complex.

Thus, unless an early pancreatectomy (usually secondary to thrombosis; see above) can be done with an immediate retransplant using the same recipient vascular sites for in- and outflow (pancreas exchange or pancreas switch) [270, 274, 279], the choice for appropriate vascular sites frequently requires some creativity. Not only can the iliac vessels proximally or distally to the previous sites be used, but also the contralateral iliac vessels (or a combination of ipsi- and contralateral vessels, e.g., long Y-graft to the left common iliac artery, graft portal vein to the right common iliac vein), the vessel stumps of previous grafts (both pancreas and kidney), or the infrarenal aortic and cava. In fact, if systemic vein drainage is again chosen for the retransplant, the right common iliac artery and the infrarenal vena cava are most commonly selected as vascular sites [280]. Alternatively, especially in patients with more than one retransplant, portal vein drainage should be considered in a previously undissected area of the abdomen, making optimal use of the different options for pancreas re-engraftment.

If the failed pancreas transplant used portal vein drainage, so can the next retransplanted graft. In most cases, the new site of the venous anastomosis (if the previous graft was removed in a separate procedure) should be proximal or distal to the previous anastomotic site on the superior mesenteric vein [275]. Alternatively, a large tributary to the SMV, a large IMV, or possibly the proximal splenic vein (via an extension or jump graft) can be used. If the previous graft is removed at the time of the retransplant, the stump of the previous graft vessel can also be used. Alternatively, to avoid extensive dissection in an area previously operated on, systemic vein drainage can be used, also utilizing the vena cava if the pancreatic head is already placed in a cephalad position and the common iliac vein cannot be reached. Again, the key to successful vascular reimplantation is technical flexibility on part of the transplant surgeon and considering all the different options for pancreas re-engraftment.

In case of inadvertent injury to the iliac artery or vein during the retransplant, an interposition graft of the donor iliac artery or vein can be used. Prosthetic material should be avoided to prevent subsequent infection.

If a prior kidney transplant is removed and replaced through a midline incision as part of a re-SPK, graft nephrectomy is performed using the extracapsular technique because only individual ligation of the renal artery and vein is required [282]. Even if the previous kidney graft is in a retroperitoneal position (PAK category), the extracapsular technique is preferred over intracapsular dissection since control of the major renal vessels, and not just of the renal hilum, is warranted. As for a pancreas retransplant, flexibility in determining the optimal site for implantation of the kidney retransplant is required [282].

Peritransplant care with either systemic or portal vein drainage is not different for pancreas retransplants vs. primary transplants (see Chap. 40). Likewise, the spectrum of surgical complications is as similar (see Chap. 42) as for primary transplants [277, 278, 280, 282].

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