Surgical Aspects of Pancreas Transplantation

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Cadaveric Donor

General

The successful outcome of pancreas transplantation largely depends on the procuring surgeon's expertise [1]. It became obvious that perioperative coordination is essential, in particular when the pancreas and liver are procured by different teams.

A midline incision is made. After the falciform ligament is divided, the right colon is fully mobilized to expose the retroperitoneum, cava, aorta at its bifurcation, and duodenum. The infrarenal aorta is encircled, the inferior mesenteric artery is divided, the mesentery is reflected superiorly, and the superior mesenteric artery is identified at its base and encircled. The triangular ligament of the left lobe is mobilized to allow access to the supraceliac aorta.

After infrarenal and supraceliac control of the aorta is achieved, the porta hepatis is dissected. The common bile duct is divided close to the superior margin of the head of the pancreas. The hepatic artery is dissected from its bifurcation to the celiac artery; the gastroduodenal artery is ligated and divided. The splenic artery is identified and looped with a vessel loop. The portal vein is dissected free at its midpoint between the pancreas and liver. The nasogastric tube is advanced into the duodenum, and the duodenum is flushed with a solution of amphotericin, metronidazole, and gentamicin.

The patient is heparinized (20,000 U) and the distal aorta cannulated and ligated. The inferior mesenteric vein is cannulated, and the cannula is advanced up to the portal vein. The supraceliac aorta is clamped. Inferior vena cava is exposed supradiaphragmatically at its junction with the right atrium and incised. The right pleural cavity is opened. The aortic and portal cannulas are flushed with 3 and 2 L, respectively, of cold UW or other (HTK) solution. The abdomen is packed with slushed ice until the perfusion is complete.

Once flushing is complete, the ice is removed. The liver is carefully excised, taking the adjacent diaphragm. The portal vein is divided, leaving an adequate stump (1–2 cm) on the pancreas side. The splenic artery is divided close to its origin and tacked with a single nonabsorbable 6-0 suture to aid future identification.

The lesser sac is opened by sharp dissection along the greater curvature of the stomach toward the spleen. The short gastric vessels are divided with scissors. The spleen is mobilized carefully,

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dividing all its peritoneal reflections. The spleen is elevated. The avascular plane behind the pancreas is developed, both bluntly and sharply. The peritoneal reflection along the inferior border of the pancreas is divided. After removal of the perfusion cannula, the inferior mesenteric vein is ligated on the pancreas side. The attachments along the superior border of the pancreas toward the stomach are divided by sharp dissection. The Kocher maneuver is completed. Attachments to the anterior surface of the head of the pancreas, including the right gastric and gastroepiploic artery, are ligated. The duodenum is divided just distal to the pylorus using a GIA stapler. The third or fourth portion of the duodenum or proximal jejunum (right behind the ligament of Treitz) is divided in a similar manner. The mesentery and mesocolon are divided using a GIA stapler. The superior mesenteric artery is taken with a patch of the aorta without injury to the renal arteries. The pancreas is removed and packaged.

Meticulous surgical technique and attention to detail during the benchwork preparation are paramount to avoid grave technical complications posttransplant. Bench-work reconstruction involves these steps: splenic hilar dissection, duodenal segment preparation, ligation of mesenteric vessels, and arterial (or venous) reconstruction.

Korea

The most important aspect for the decision of whether the pancreas is appropriate for transplantation is the direct inspection of the pancreas at the time of recovery [2]. Initially, a portion of the head and body of the pancreas is exposed after dissection of the hepatogastric ligament. Subsequently, the greater omentum is separated from the transverse colon to open a lesser sac, and the whole pancreas is exposed for evaluation. The pancreas is given up for recovery if there is significant calcification, fibrosis, fat infiltration, and edema in the pancreas, or severe atherosclerosis in feeding arteries.

When the pancreas is considered to be suitable for recovery, dissection of the pancreas and duodenum is initiated. At first, the head of the pancreas, aorta, and inferior vena cava can be exposed after dissection with the Kocher maneuver. Anterior and posterior pancreaticoduodenal arteries are ligated. The right gastric artery is ligated as well as supraduodenal arteries. It should be cautious not to make an injury to an atypical right hepatic artery originating from a superior mesenteric artery. After ligation of supraduodenal arteries, a gastroduodenal artery from the common hepatic artery is exposed, which is tagged with prolene 6-0 at the time of recovery, and encircled with a vessel loop. Dissection should be progressed from gastroduodenal artery to celiac trunk to identify the origin of the splenic artery, which should be encircled with a vessel loop. The inferior mesenteric vein at the lower border of the pancreas should be identified and encircled with vessel loop. At the time of portal perfusion through the inferior mesenteric vein in liver harvest, it is important not to insert liver perfusion cannula deep into the pancreas.

The nasogastric tube is lowered to Treitz ligament, and proximal jejunum is clamped for duodenal irrigation with antibiotics and antifungals-mixed normal saline. After irrigation, the nasogastric tube is repositioned up to the stomach. The proximal duodenum is separated from the pylorus with GIA 60 stapler.

After perfusion of abdominal viscera with HTK or UW solution, the pancreas and the liver are usually separated in situ. The splenic artery is separated from the Celiac trunk at the origin, whereas the gastroduodenal artery is divided from the common hepatic artery at the origin. Both arteries should be tagged with 6-0 prolene before separation. The portal vein should be divided at an appropriate point to secure a proper length of the portal vein. After recovery of the liver, the superior mesenteric artery is separated at the origin from the aorta. At the time of the superior mesenteric artery division, it should be cautious not to injure both renal arteries. The inferior mesenteric vein is ligated at the lower border of the pancreas. Mesenteric root below uncinated process is divided with TA 90 stapler. Spleen is separated from the stomach by dividing short gastric arteries. Handling the spleen, distal pancreas and spleen are separated from adjacent

tissue. After recovery of the pancreas and followed by both kidneys, en bloc dissection of common, external, and internal iliac arteries should be performed and harvested for use as Y-graft in pancreas arterial reconstruction.

After identification of anatomy of the pancreas in bench procedure, distal portion of duodenum below the pancreatic attachment is separated from the mesentery. The proximal end of graft duodenum closed by stapler during the organ harvest is reinforced with 4-0 prolene suture. Stapled end of the mesenteric root is reinforced with 4-0 prolene continuous suture. Spleen is detached from the tail of the pancreas with double ligation of splenic artery and vein. Open end of gastroduodenal artery is closed. The divided portal vein is trimmed, and reconstruction of the splenic artery and superior mesenteric artery is carried out by Y-graft of donor bifurcated iliac artery into a single stoma as usual fashion. After ligation of trivial vessels and loose tissues surrounding the pancreas, the graft is kept in cold preservation solution until use (Fig. 1).

Japan

Because of operation by the certified 18 facilities under a multi-facility cooperation system for carrying out pancreas transplantation and performing a simulation of organ removal using pigs once a year, the procedure for procurement of pancreatic graft from the cadaveric donor is unified to some extent in Japan. Details procedure on the procurement of pancreatic graft from the cadaveric donor is published on the Japan Society for Transplantation website [3].

Laparotomy is made with from median sternotomy to the upper pubis following the chest thoracotomy. After Kocher's maneuver, the abdominal aorta and inferior vena cava (IVC) is taped just above the left and right bifurcations of

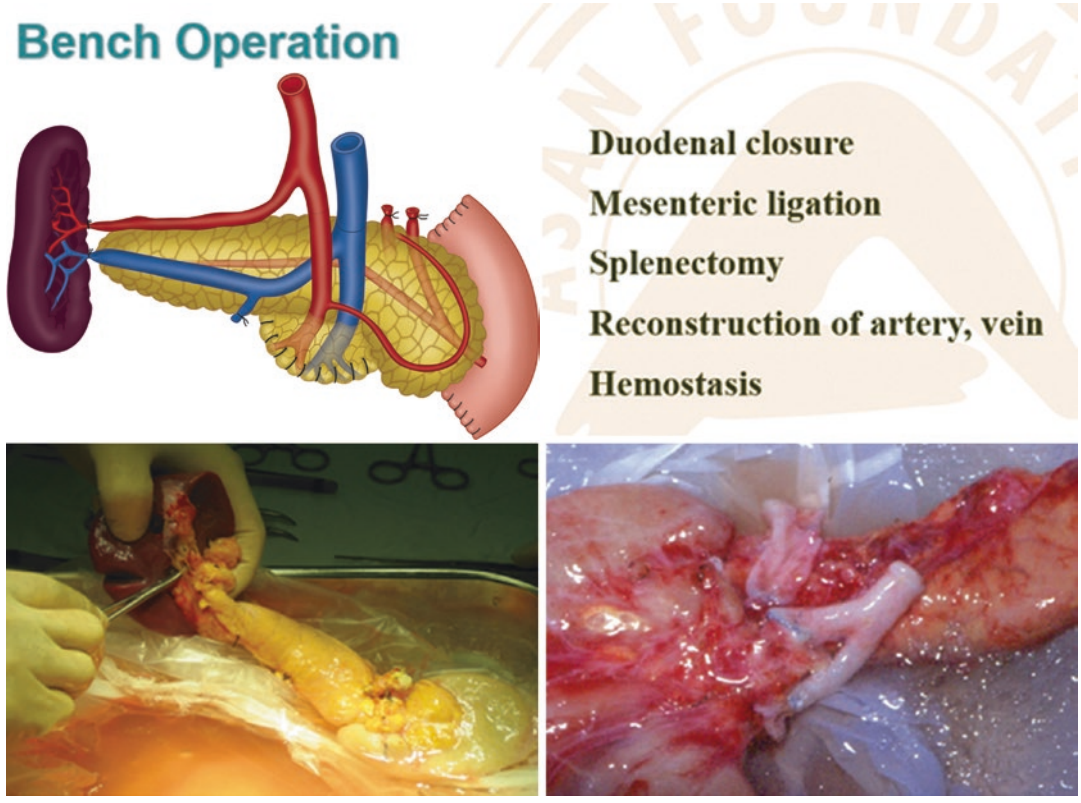


Fig. 1 Deceased donor pancreas transplantation-bench procedure (AMC)

the common iliac artery and vein. Then, the abdominal aorta is taped just below the diaphragm.

The greater sac is opened to observe the pancreas, and both kidneys are mobilized from the retroperitoneum to make a space for surface cooling. At 3 min after systemic heparinization (400 units/kg), cannulations to the abdominal aorta and inferior vena cava just above the bifurcations of the common iliac artery and vein are performed.

After the cannulation, the aorta is clamped (cross-clamp) at the position of just below the diaphragm. Blood is washed out from the cannula inserted to the inferior vena cava by perfusing of cold 2–3 L of UW solution by drip infusion from the cannula inserted from the abdominal aorta. Also, surface cooling of the abdominal organs is achieved with slush ice as soon as possible (Fig. 2).

Organ procurement is performed in the order of heart, lungs, small intestine, liver, pancreas, and kidneys. Since both liver and pancreas are procured in more than 90% of the donors, the common hepatic artery (CHA) is divided at 1–1.5 cm from the branch of the celiac artery and splenic artery. The gastroduodenal artery is divided at 5 mm from the branch of the CHA. As a result, the arteries of the pancreatic graft are procured with a Carrel patch containing CEA and SMA. The portal vein is also shared by the liver transplant team and is divided at a position of 5 mm from the upper edge of the pancreas. IVC is cut at the proximal side of the branch of renal veins (Fig. 3). After the procurement of the liver, en bloc procurement of the pancreas and both kidneys are performed. The pancreas is procured with the duodenum, spleen, aorta, and IVC. The proximal and distal sides of the duodenum are separated with an automatic suture device. Separation of pancreas and kidneys is performed on the back table (Fig. 4).

Since more than 80% of the pancreas transplantation is SPK, the pancreas and left kidney are used for SPK. In the case of using blood vessels for reconstruction in recipient operation, both sides' iliac arteries and veins are procured. Blood vessels are shared between the liver and pancreas transplantation team depending on their needs for the recipient operation.

After a closure of the abdominal wound of the donor, the pancreas and kidney are packed and

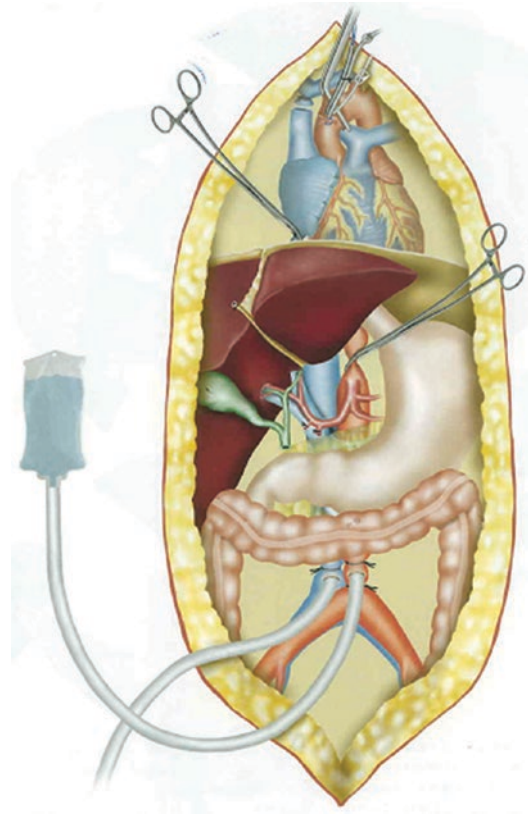


Fig. 2 Cross-clamp after the cannulation into the aorta and vena cava (Japan)

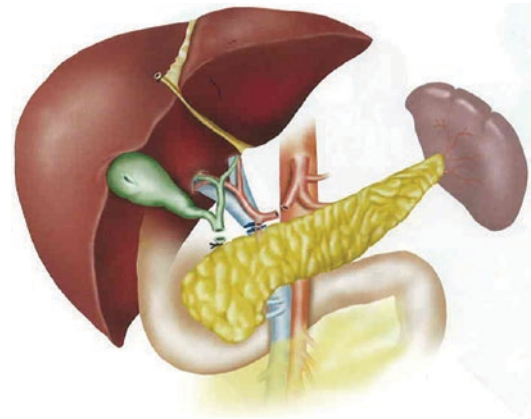


Fig. 3 Procurement of the liver (Japan)

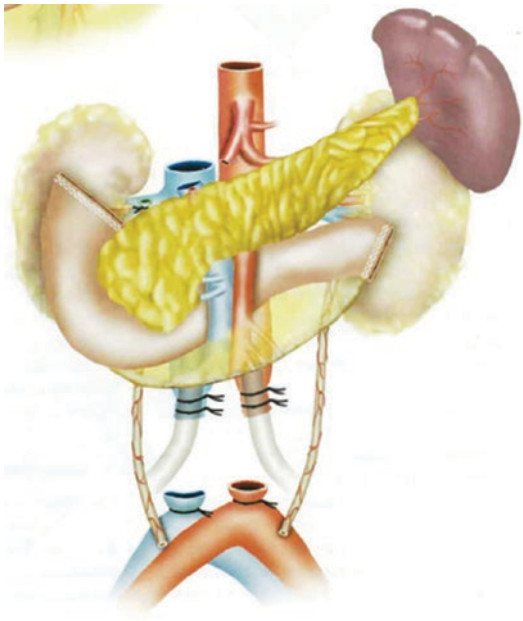


Fig. 4 En bloc procurement of the pancreas and kidney with duodenum and spleen (Japan)

transported to the transplantation center. Both organs are preserved in cold UW solution and placed on ice in a cooler box. Cold ischemic time of the pancreas may be approximately 24 h.

At our facility, we perform kidney transplantation first during the back table operation of the pancreas graft.

The tissues surrounding the pancreas, such as the small intestine, mesenterium, adipose tissue, and spleen, are removed. Treatment is performed in cold UW solution, and all dissections are performed by ligation or vessel sealing system (Ligasure™). For the spleen, it depends on the institution whether it is removed at the back table or during transplantation.

In Japan, >70% of the DBD donors for pancreas transplantation are classified as marginal donors according to the criteria proposed by Kuper et al. [1]. Therefore, in order to secure a good blood flow of the head of the pancreas head and maintain the graft function, I-graft, which was an iliac artery procured from the donor, was placed between the origin of the common hepatic artery and gastroduodenal (GDA) artery (Figs. 5 and 6). However, recently, if there is enough outflow from the GDA by perfusion from SMA on the back table, the reconstruction of blood vessels using I-graft may be omitted. In Japan, an aortic patch (Carrel patch) that includes the celiac artery and superior mesenteric artery is usually used for arterial anastomosis in the recipient operation (Fig. 7), and the cases of using a Y-graft is only 13.5%. Reconstruction of the Y-graft is performed using the iliac artery collected from the donor. If the portal vein of the pancreatic graft is short, the portal vein is extended using the iliac vein harvested from the donor. Recently, there are many cases where portal vein extension is not performed (Figs. 8 and 9).

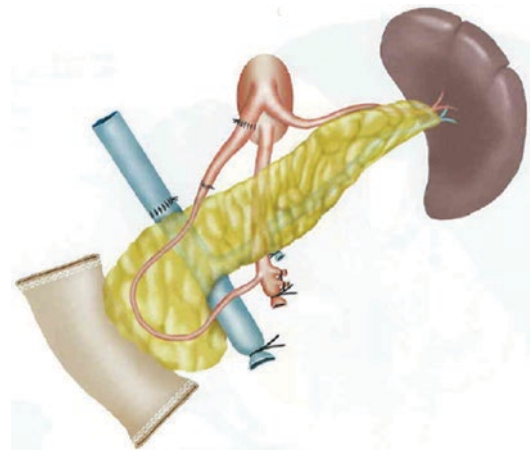
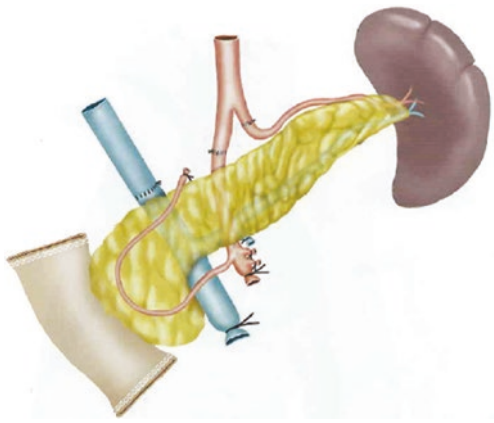


Fig. 5 Arterial reconstruction using I-graft (Japan)

Taiwan

Patients with a positive crossmatch against donor cells are excluded for pancreas transplantation. The pancreas grafts are procured in a "'no-touch" technique en bloc with the duodenum. The spleen is separated from the pancreas before aorta cross-clamping. Histidine-tryptophan-ketoglutarate (HTK) solution, 4000–6000 mL, is used for in situ perfusions via the distal aorta. Back table preparation includes removal of the peripancreatic fat and arterial reconstruction using a donor iliac arterial Y-graft. The gastroduodenal artery stump is remained ligated, and no reconstruction is attempted.



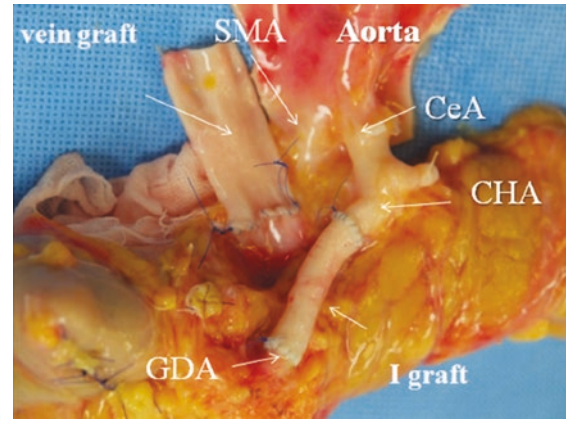


Fig. 6 I-graft and portal vein prolongation (*CeA* celiac artery, *CHA* common hepatic artery, *GDA* gastroduodenal artery, *SMA* superior mesenteric artery) (Japan)

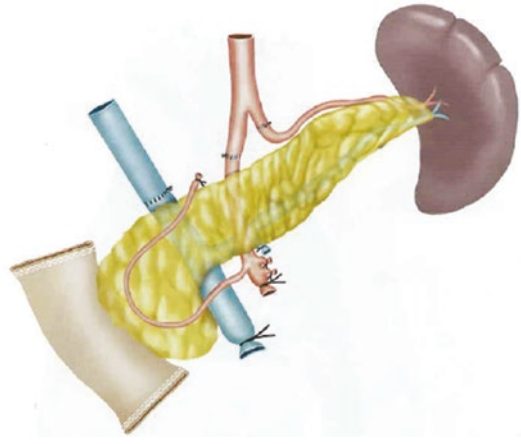


Fig. 7 Arterial reconstruction using Y-graft (Japan)

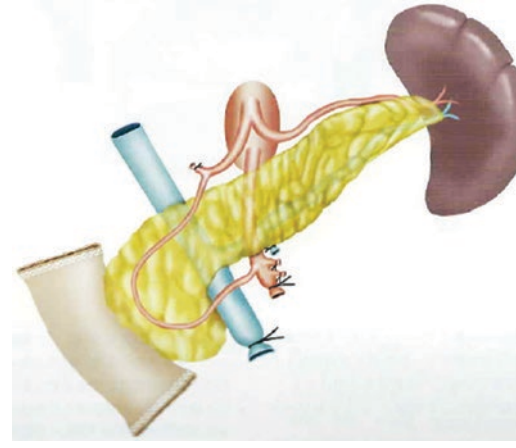


Fig. 9 No reconstruction of the artery by Carrel patch (Japan)

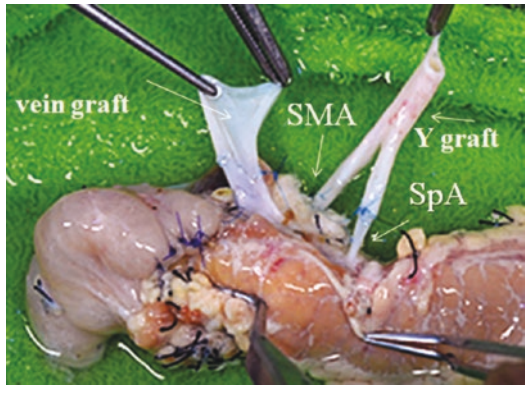


Fig. 8 Y-graft and portal vein prolongation (*SpA* splenic artery, *SMA* superior mesenteric artery) (Japan)

Recipient

General

Since the first pancreas transplant in 1966 [4] 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. The most controversial issues have been the management of exocrine pancreatic secretions (bladder vs. enteric drainage) and the type of

venous drainage (systemic vs. portal vein drainage). According to the International Pancreas Transplant Registry (IPTR), through 1995, more than 90% of all pancreas transplants worldwide were bladder drained [1].

Two main reasons for the widespread use of bladder drained whole organ pancreaticoduodenal transplants are the low complication rate, with no contamination from an enterotomy, and the ability to monitor urinary amylase levels to detect graft rejection [5, 6]. Contrast to enteric drainage, surgical complications with bladder drainage are usually contained to 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. Urinary amylase measurements have been particularly helpful in solitary pancreas transplants, in which a simultaneously transplanted kidney from the same donor is not available to monitor serum creatinine levels for rejection [7].

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 [8].

Urologic complications are common because alkaline pancreatic enzymes are a source of irritation to the transitional epithelium of the bladder and to the lower genitourinary system. Urologic complications include the following: chemical cystitis and urethritis, recurrent hematuria, bladder stones, and recurrent graft pancreatitis from reflux. The high rate of urinary tract infections is a frequent cause of morbidity. More serious but less common complications include severe perineal inflammation and excoriation and, more frequently in men, urethral disruption and strictures [8–11].

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. Currently, enteric drainage is increasingly used, thanks to improvements in surgical technique, immunosuppressive therapy, radiologic imaging and interventional procedures, and antimicrobial prophylaxis [12–17].

Portal vein drainage creates a more physiologic state of insulin metabolism [18]. While in systemic drainage, peripheral hyperinsulinemia has been associated with atherosclerosis and portal hypoinsulinemia with lipoprotein abnormalities [19–22]. Yet no convincing evidence exists today that systemic vein drainage places pancreas recipients at a disadvantage by increasing their risk of vascular disease [23, 24] or at a high risk of immunologic rejection [25–27]. The pancreas is placed intraabdominal, preferably on the right side of the pelvis, for two reasons: the iliac vessels are more superficial than on the left side and, therefore, dissection is easier on the right side, and the natural position of the right iliac vessels (vein lateral to the artery) does not require vascular realignment or possible ligation and division of the internal iliac artery, although on the left side it might. Currently, inferior vena cava can be a recipient site for venous anastomosis site with the advantage of easy exposure and high outflow venous system of IVC compared with the iliac vein limiting the postoperative venous thrombosis.

When the donor portal vein is used for anastomosis, the head of the pancreas is in a cephalad position in the mid-abdomen. The vast majority of pancreas grafts with portal vein drainage are placed so that the donor portal vein connects to the recipient proximal superior mesenteric vein (SMV) or to the SMV's main feeding vessel. A hole in 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). This distance may be as long as 6 cm.

Korea

Midline laparotomy was performed in the recipient. In the pelvic space, the iliac vein and artery were mobilized to avoid the tension of graft vessel anastomosis. The graft portal vein was anasto-

mosed end-to-side to the recipient's external iliac vein or distal IVC, which is preferred in use currently. The superior mesenteric and splenic arteries reconstructed by donor iliac arterial Y-graft were anastomosed to the recipient's common iliac or external iliac artery. Drainage of the exocrine pancreatic secretions was performed either by bladder or by enteric drainage.

In the case of bladder drainage, the pancreas graft duodenum was placed in a caudal position on the right side of the pelvis with an arterial anastomosis to the iliac artery and venous anastomosis to the iliac vein. The pancreas graft duodenum was then anastomosed to the urinary bladder using two-layer side-to-side hand-sewn sutures.

In the case of enteric drainage, the head of the pancreas graft was placed in a caudal position. Vascular anastomosis of graft portal vein is created to external iliac vein or distal IVC, and pancreas arterial Y-graft to external or common iliac artery. The pancreas graft duodenum was anastomosed to jejunum or ileum by the side to side fashion or Roux en Y limb of jejunum by the end to side fashion.

In SPK, a kidney transplant is performed in the left pelvic site initially, then a pancreas transplant in the right pelvis. The graft distal duodenum is shorted at the level of the junction between the second and third portion of the duodenum by GIA stapler. After meticulous hemostasis, JP drainage is inserted around the graft pancreas, followed by abdominal wall closure [2] (Fig. 10).

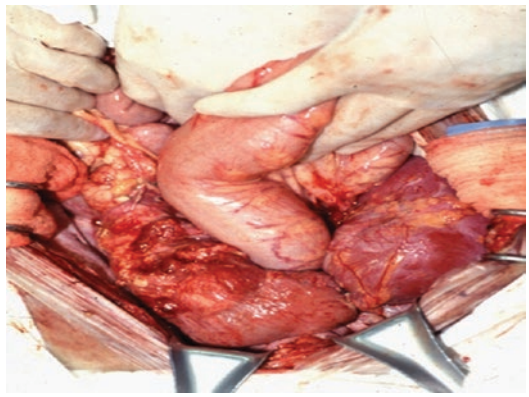


Fig. 10 Simultaneous kidney and pancreas transplantation with bladder drainage (AMC)

Japan

In the case of SPK, it depends on the facility whether to perform a pancreas transplant or a kidney transplant first. The pancreas is transplanted into the right iliac fossa in the abdominal cavity or retroperitoneal space. The external iliac artery and the external iliac vein are sufficiently isolated, and the internal iliac vein is cut if necessary to mobilize the external iliac vein. Venous anastomosis is performed with a running suture between the portal vein of the pancreas graft and the external iliac or common iliac vein of the recipient. The most important point is how to prevent venous thrombosis, and this anastomosis requires the most attention. The points are to secure a sufficient anastomotic opening without any twisting. We usually use 5-0 monofilament nonabsorbable threads for venous anastomosis. Subsequently, an arterial anastomosis between the Carrel patch (or Y-graft) and the external or common iliac artery of the recipient is performed with a running suture using a 5-0 monofilament nonabsorbable thread. In our institution, transposition of iliac artery and vein are frequently performed for the prevention of pressure of graft's artery to graft's vein. After the arteriovenous anastomosis is complete, the blood flow in the pancreas graft is resumed by releasing the vascular clamp. After resuming the blood flow in the pancreas graft, the bleeding from the pancreas graft should be carefully stopped because we use 200 units/h of heparin intraoperatively to prevent venous thrombosis. Also, the pancreas graft is warmed with warm saline. Intestinal drainage or bladder drainage is used for pancreatic juice drainage, but in most recent cases, intestinal drainage is preferred. Overall, 87.7% is intestinal drainage in Japan. The anastomosis between the graft's duodenum and small intestine is performed by the side to side anastomosis or a Roux-Y anastomosis, and we use a 4-0 monofilament absorbent thread (Fig. 11). After confirming hemostasis, two Penrose drains are inserted into the abdominal space near the pancreas graft and connected to J-VAC® closed drainage system. The wound is closed in three layers suture technique.

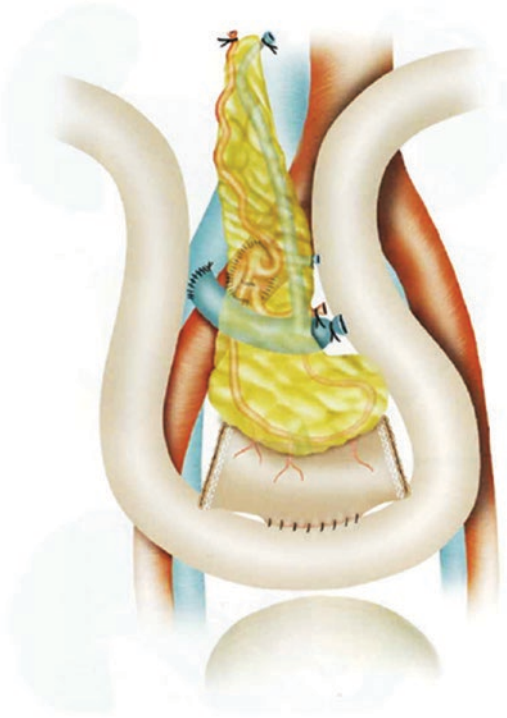


Fig. 11 Technique of pancreas transplantation using enteric drainage (Japan)

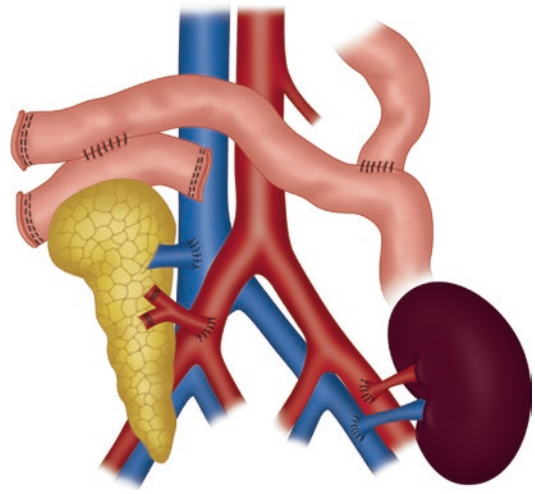


Fig. 12 Pancreas and kidney transplantation for simultaneous pancreas-kidney (SPK) or pancreas-after-kidney (PAK) transplantation. The pancreas graft portal vein is anastomosed to distal inferior vena cava, a systemic venous drainage, and graft duodenum is anastomosed to a roux-y limb of jejunum, an enteric drainage. Retroperitoneally, the pancreas graft is usually placed on the right side. The kidney is placed in the left, opposite, side (Taiwan)

Taiwan

Pancreas transplantation in Taiwan can be categorized mainly into simultaneous pancreas-kidney (SPK) transplantation, pancreas-after-kidney (PAK) transplantation, pancreas-before-kidney (PBK) transplantation (Fig. 4), and pancreas-after-liver (PAL) transplantation (Figs. 12–15). Ideally, a combined kidney and pancreas transplantation should be recommended for patients with severe diabetes and end-stage renal disease. Therefore, SPK is the most common type of pancreas transplantation, accounting for 79% of procedures in the USA in 2016 [2]. Both organs are usually procured from a single deceased organ donor. PAK transplantation is offered to diabetic patients who have already undergone a kidney transplantation. PTA is offered to candidates without end-stage renal disease but with frequent, acute, and potentially life-threatening complications of diabetes such as ketoacidosis, hypoglycemia unawareness, and incapacitating problems with insulin therapy. For this group, pancreas transplantation

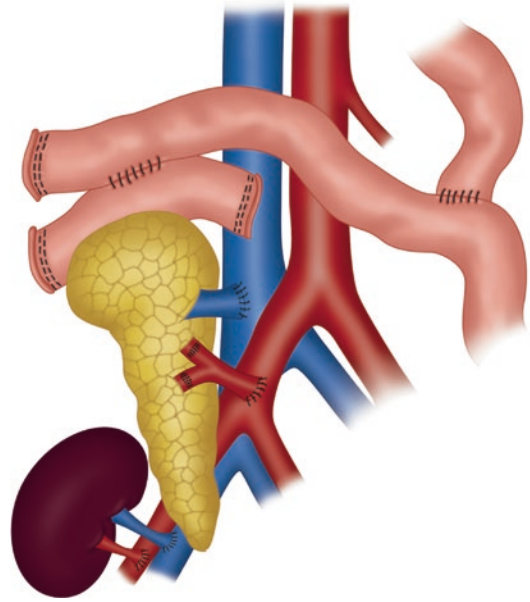


Fig. 13 Ipsilateral placement of pancreas and kidney grafts for simultaneous pancreas-kidney (SPK) or pancreas-after-kidney (PAK) transplantation. The pancreas graft portal vein is anastomosed to distal inferior vena cava, a systemic venous drainage, and graft duodenum is anastomosed to a roux-y limb of jejunum, an enteric drainage. Retroperitoneally, the pancreas graft is usually placed on the right side. The kidney is also placed on the right side (Taiwan)

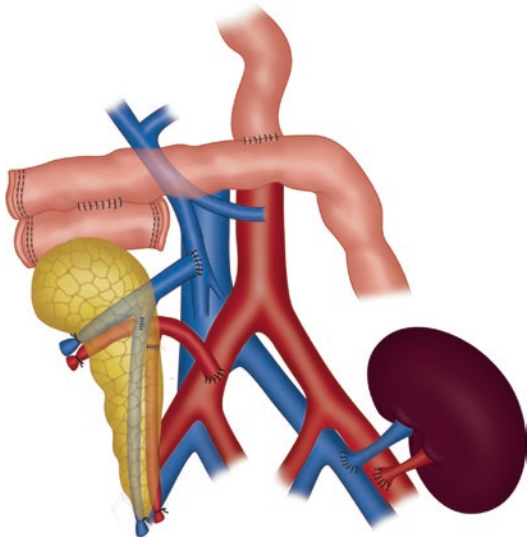


Fig. 14 Pancreas and kidney transplantation for simultaneous pancreas-kidney (SPK) or pancreas-after-kidney (PAK) transplantation. The pancreas graft portal vein is anastomosed to a big tributary of the superior mesenteric vein, a portal venous drainage, and graft duodenum is anastomosed to a roux-y limb of jejunum, an enteric drainage. Retroperitoneally, the pancreas graft is usually placed on the right side. The kidney is placed in the left contralateral, side (Taiwan)

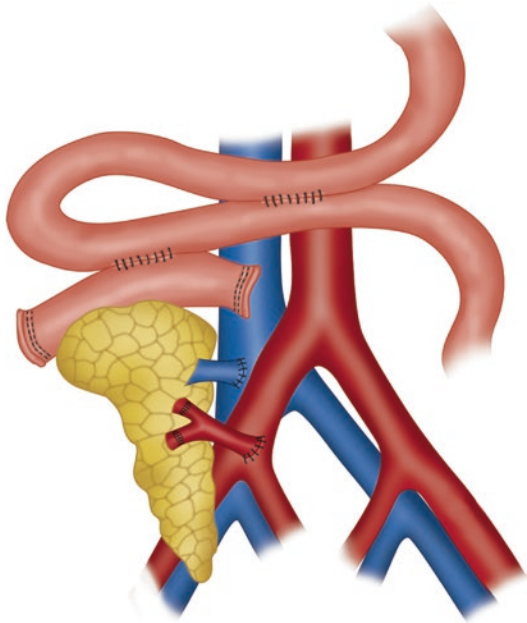


Fig. 15 Solitary pancreas transplantation for pancreas transplant alone (PTA), pancreas-before-kidney (PBK) or pancreas-after-liver (PAL). The pancreas graft portal vein is anastomosed to distal inferior vena cava, a systemic venous drainage, and graft duodenum is anastomosed to a roux-y limb of jejunum, enteric drainage (Taiwan)

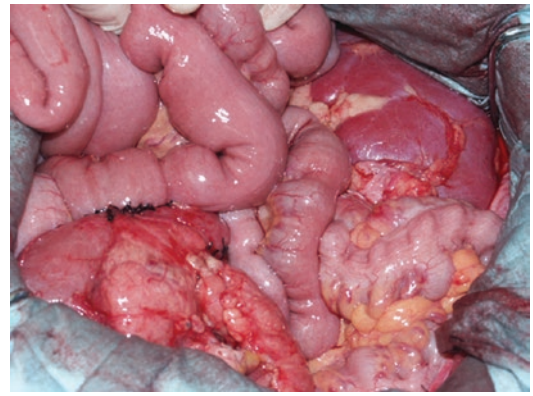


Fig. 16 The first simultaneous pancreas-kidney (SPK) transplantation was performed at Taipei Veterans General Hospital on September 19 of 2003. The pancreas graft was placed in the right side. The kidney was placed on the left, opposite side (Taiwan)

would be life-saving but must be weighed against the untoward risks of life-long immunosuppression [28]. The first simultaneous pancreas-kidney (SPK) transplantation was performed at Taipei Veterans General Hospital on September 19 of 2003 (Fig. 16). In Taiwan, it is very competitive for a uremic patient to have a decreased kidney graft because there are always more than 7000 uremic patients waiting for kidney transplantation [3]. Moreover, the waiting lists for pancreas and kidney transplantation are separate. PTA (48%, 73/151) is the most common type of pancreas transplantation, followed by SPK (24%, 36/151) transplantation, PBK (16%, 24/151), PAK (11%, 17/151), and PAL (1%, 1/151).

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