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Pancreas Graft Drainage in Recipient Duodenum: Preliminary Experience

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Abstract

Pancreas graft survival has continuously improved over the years to become a main treatment option of uncontrolled complicated diabetes. Rejection remains the major challenge as it often goes unnoticed until severe damage of the graft manifests itself by elevatedblood sugar. Pancreas enzymes monitoring in the blood and in the urine is a sensitive marker of rejection but lack of specificity. Biopsy remains the gold standard. Cystoscopy-guided biopsy of bladder-drained pancreas has a good success rate for obtaining tissue but the vesical drainage exposes to metabolic and urologie morbidity. Percutaneous pancreas biopsy can be performed with a low morbidity rate but severe complications can occur. We discuss a technique of pancreas transplantation with the drainage of exocrine secretions of the pancreatic graft in the recipient duodenum, which permits easy monitoring of the graft by upper endoscopy of the duodenum.

Keywords: Pancreas, Transplantation, Monitoring, Rejection.

Pancreas transplantation results have improved dramatically over the recent years through adapted surgical techniques and better immunosuppression. Although 1-year-graft survival of simultaneous kidney pancreas transplantation reaches 85%, the survival of pancreas alone transplant is still challenged by rejection, with 76% survival according to United Network for Organ Sharing and International Pancreas Transplant Registry data (1). Reviewing their experience from 1994 to 2000, Sutherland et al. reported an incidence of rejection episodes at 1 year of 31% for simultaneous kidney pancreas transplantation but of 61% for pancreas alone transplantation (2). Although the risk of rejection might be lower in combined transplantation, early detection of pancreas rejection is facilitated by the monitoring of graft kidney function and percutaneous biopsy of the easily accessible kidney. Rejection of pancreas with normal kidney graft biopsy can however occur. The rate of discordant pancreas rejection with normal kidney biopsy was 23% (kidney only rejection was 23%) in the study ofGruessner in the pig(3) and only 3% (kidney only rejection was 23%) in the dog study from Hawthorne et al. (4). The report of 13.5% discordant pancreas rejection in the clinical series of Bartlett et al. (5) supports those findings but is challenged by the study of Shapiro et al. (6). Simultaneous kidney pancreas recipients with hyperlipasemia, which they showed strongly associated with pancreas rejection, but normal and stable renal function had histological evidence of kidney rejection; this challenges the reality of dyssynchronous allograft rejection. Altogether, these experiences emphasize the need to further study the monitoring of the pancreaticoduodenal graft.

In pancreas transplantation, the physician cannot rely on clinical signs that are absent or too late to be useful. Plasma pancreatic enzymes levels appear sensitive but in 50% of the cases do not correspond to rejection (7). Bladder drainage of the exocrine secretions of the graft permits the monitoring of urine pancreatic enzymes. Benedetti et al. (8) reported a test sensitivity of 100% (stable urinary amylase levels mean no rejection). Defined as a 25% drop below urinary amylase baseline, hypoamylasuria suffered from a lack of specificity for rejection (30%). Predictive value of a positive test was only 53%. Urine amylase monitoring thus needs to be associated with graft biopsy to avoid unnecessary treatment. Cystoscopy-guided biopsy of bladder-drained pancreas has a good success rate for obtaining tissue (87% in the report from Laftavi et al. [9], specimen consisting of pancreas alone [22%], pancreas+duodenum [34%], or duodenum alone [31%]) and a low morbidity (10, 11). These techniques, however, depend on the drainage in the bladder and suffer from its metabolic and urologie complications. Percutaneous pancreas core biopsy also provides a high yield for pancreas tissue (72-83%) (9,12) with low morbidity (13). Severe complications can occur in 1.5-3%, including intra-abdominal hemorrhage

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requiring surgical intervention and graft loss secondary to pancreas ductal leak (5, 9, 14); it appears difficult to propose the technique frequently.

In this paper, we report the feasibility of recipient duodenum drainage of graft exocrine secretions that provides easy access for endoscopic monitoring of the graft. Two candidates for pancreas alone and combined kidney-pancreas transplantation received a pancreas graft whose duodenum was drained in the recipient duodenum.

FIGURE 1. *Retroperitoneal position of pancreas graft with portal venous drainage and drainage of graft duodenum in recipient second duodenum.*

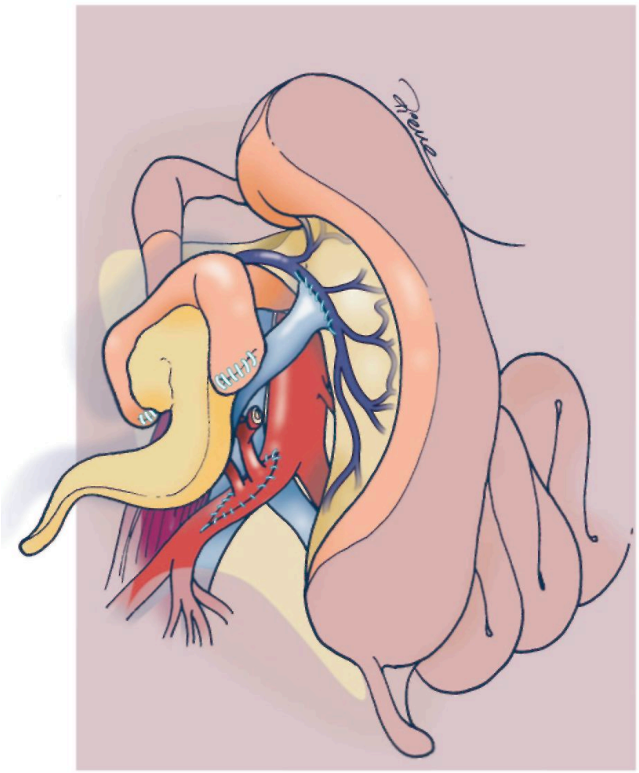
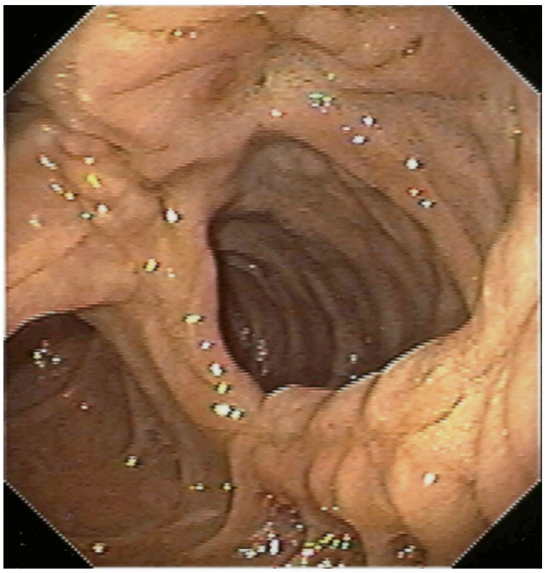


FIGURE 2. *Monitoring of graft duodenum by upper endoscopy. View of the anastomosis between recipient (left) and graft (right) duodenum.*



Total pancreas ischemia times were respectively 368 and 937 min. Graft portal vein was anastomosed retroperitoneally to the infrapancre-atic superior mesenteric vein similarly to the technique described by Boggi (15). An aortic patch carrying celiac trunk and superior mesenteric artery was anastomosed to the right common iliac artery. For the exocrine secretions drainage, we performed a laterolateral duodenoduodenostomy with a first total layer of 4/0 polyglyconate running suture and a second seroserous layer of interrupted 4/0 silk (Fig. 1). To avoid potential food stasis in the duodenal segment of the graft, we avoided keeping it too long and made a large anastomosis at the level of the second portion of the duodenum. Immunosuppression consisted of an induction therapy by 5 days of 1 mg/kg thymoglobulin, oral tacrolimus, and mycophenolate mofetil, and tapering doses of steroids.

A nasogastric tube was left in place for 4 days to avoid tension on the duodenal anastomosis. Both patients resumed oral feeding on postoperative day 5 without complications. Postoperative evolution was uneventful with hospitalization stays of 13 and 14 days, respectively. A contrast x-ray study demonstrated adequate emptying of the duodenal segment without leak. An upper endoscopy with graft duodenum biopsies (endoscope: Olympus GIF-160, Hamburg, Germany; biopsy forceps: RMS 102-23-230, Lennik, Belgium) was performed per protocol 3 and 8 weeks after surgery then every 3 months for the first year while pancreatic enzymes and blood sugar were normal. Macroscopic appearance of graft duodenum was normal (Fig. 2). No signs of rejection were evidenced on the duodenal biopsies with a follow-up of 3 and 9 months for the two patients.

Duodenal drainage of the pancreatic graft was only briefly described in the early experience of portal venous drainage with enteric exocrine diversion (16). However, bladder drainage remained the standard until improved surgical technique, immunosuppression, and percutaneous graft monitoring brought equivalent results in enteric drainage. The incidence of duodenal fistula has drastically diminished in the recently reported experience both in bladder- and enteric-drained pancreas transplantation. This was our experience, and thus prompted us to use this technique of recipient duodenum drainage that added the possibility of graft monitoring. The difficulty of leak management traditionally associated with duodenal anastomosis imposes a meticulous technique. Approximation of both duodenum is restricted to a graft positioned sufficiently high in the abdominal cavity to avoid tension on the anastomosis, and thus adequate for portally drained grafts. The quality of the suture probably also depends on the quality of the duodenal tissue.

Experimentally, we and others have shown that the severity of mucosal injury is directly associated with the length of cold ischemia (17,18) and that adding University of Wisconsin solution in the lumen during the cold preservation decreased the ischemic lesions. Duodenal decontamination using povidone-iodine routinely used in pancreas procurement has been shown to aggravate the intestinal injury (19). Minimizing the length of cold ischemia also decreases the risk of leak in the clinical setting (20). Finally, in pancreas transplantation, we have relied in the immediate postoperative period on early laparotomy if suspicion of a complication arises. This avoids the progression of severe complications and permits their treatment before dense and inflammatory processes develop. If a duodenal leak was evidenced, confection of a new duodenoduodenostomy on healthy tissues would need prolonged decompression of the anastomosis with a nasogastric tube. If this was not indicated (e.g., friable tissue, vascular thrombosis, abscess), a choice between Roux-en-Y conversion of graft drainage or graft removal would have to be done depending on perioperative findings. Recipient duodenum closure possibilities could then include direct repair, plasty with a Roux-en-Y limb, or a laterolateral duodenojejunostomy.

The value of duodenal biopsies for pancreas allograft monitoring was first reported by Carpenter et al. (11). From their report, duodenal findings paralleled those of pancreatic tissue biopsies. The report of Nakhleh et al. (21) supports the validity of duodenal tissue examination for the diagnosis of rejection or other pathological events as cytomegalovirus infection. The advantage of duodenoduodenostomy is that it allows a good macroscopic view of the duodenal mucosa, easily accessed by the endoscope. It helps to avoid discordant results associated to inadequate sampling of the tissue. The mucosa is in contact with its normal environment, whereas the mucosa of the bladder-drained pancreas can be altered or can atrophy in contact with the urine making interpretation of biopsy more difficult. Pancreas tissue can still be obtained percutaneously but could also be obtained through the duo-denostomy guided by echoendoscopy with the advantage of real-time vision without the risk of air interposition between the probe and the graft.

Drainage of the pancreas graft exocrine secretions in the recipient duodenum may be a valuable alternative to intestinal or vesical drainage. It appears technically easy provided that the graft is located sufficiently high in the abdomen. It avoids the urological and metabolic complications associated with bladder drainage while it allows easily visualization of the graft duodenum and obtainment of biopsies without general anesthesia. The main drawback of the technique concerns the potential risk associated with fistula at the duodenal anastomosis. This

risk has to be compared to the known complications of the current techniques and balanced by the potential improvement in pancreas monitoring and survival. This potential value of duodenal monitoring will need to be ascertained by concomitant pancreas and/or kidney biopsy to define to what extent it reflects the entire graft immunological status. Further experience in larger prospective series is thus needed, not only to validate the safety of the technique but also to determine if it can indeed lead to improved graft survival.

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