Completion pancreatectomy and islet cell autotransplantation as salvage therapy for patients failing previous operative interventions for chronic pancreatitis

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Purpose. *Traditional decompressive and/or pancreatic resection procedures have been the cornerstone of operative therapy for refractory abdominal pain secondary to chronic pancreatitis. Management of patients that fail these traditional interventions represents a clinical dilemma. Salvage therapy with completion pancreatectomy and islet cell autotransplantation (CPIAT) is an emerging treatment option for this patient population; however, outcomes after this procedure have not been well-studied.*
Methods. *All patients undergoing CPIAT after previous decompressive and/or pancreatic resection for the treatment of chronic pancreatitis at our institution were identified for inclusion in this single-center observational study. Study end points included islet yield, narcotic requirements, glycemic control, and quality of life (QOL). QOL was assessed using the Short Form (SF)-36 health questionnaire.*
Results. *Sixty-four patients underwent CPIAT as salvage therapy. The median age at time of CPIAT was 38 years (interquartile range [IQR], 14.7–65.4). The most common etiology of chronic pancreatitis was idiopathic pancreatitis (66%;* n = *42) followed by genetically linked pancreatitis (9%;* n = *6) and alcoholic pancreatitis (8%;* n = *5). All of these patients had previously undergone prior limited pancreatic resection or decompressive procedure. The majority of patients (50%;* n = *32) underwent prior pancreaticoduodenectomy, whereas the remainder had undergone distal pancreatectomy (17%;* n = *11), Frey (13%;* n = *8), Puestow (13%;* n = *8), or Berne (8%;* n = *5) procedures. Median time from initial surgical intervention to CPIAT was 28.1 months (IQR, 13.6–43.0). All of these patients underwent a successful CPIAT. Mean operative time was 502.2 minutes with average hospital duration of stay of 13 days. Islet cell isolation was feasible despite previous procedures with a mean islet yield of 331,304 islet cell equivalents, which totaled an islet cell autotransplantation of 4,737 ± 492 IEQ/kg body weight. Median patient follow-up was 21.2 months (IQR, 7.9–36.8). Before CPIAT, all patients required a mean of 120.8 morphine equivalent milligrams per day (MEQ/d), which improved to 48.5 MEQ (*P < *.001 compared with preoperative requirements) at most recent follow-up. Of these patients, 44% (*n = *28) achieved narcotic independence. All patients were able to achieve stable glycemic control with a mean insulin requirement of 16 units per day. Of these patients, 20% (*n = *13) were insulin independent after CPIAT. Mean postoperative glycosylated hemoglobin was 7.8% (range, 4.6–12.5). Islet cell viability was confirmed with endocrine testing and mean C-peptide levels 6 months after CPIAT were 0.91 ng/mL (range, 0.1–3.0). The SF-36 QOL survey administered postoperatively demonstrated improvement in all tested modules.*
Conclusion. *This study is the first to examine the results of salvage therapy with CPIAT for patients with refractory chronic pancreatitis. Patients undergoing CPIAT achieved improved postoperative narcotic requirements, stable glycemic control, and improved QOL. (Surgery 2015;158:872-80.)*

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Chronic pancreatitis is a debilitating and progressive disease process that can result in significant morbidity and reduced quality of life (QOL) in afflicted patients. The management of this disease process is variable and ranges from expected medical management to radical operative resection. Advances in technology have increased drastically the endoscopic and image-guided diagnostic/therapeutic modalities available for the management of these patients. Despite these advances, this patient population continues to deal with excessive morbidity and mortality. In fact, almost 50% of these patients will progress to the point of requiring operative intervention.[1] Traditional decompressive and/or pancreatic resection procedures, which include pancreaticoduodenectomy, distal pancreatectomy, duodenal-sparing head resections, and lateral pancreaticojejunostomy, have been the cornerstone of operative therapy for refractory chronic pancreatitis.[2-5]

Over the past decade, total pancreatectomy has emerged as a viable therapeutic option for patients with severe chronic pancreatitis.[6-10] Total excision of the diseased gland removes any nidus for recurrent pain. The emergence of this operative intervention has been made possible by the advancements in islet cell autotransplantation. Successful islet cell autotransplantation abrogates the surgically induced diabetes that had previously plagued these patients. Outcomes of total pancreatectomy and islet cell autotransplantation (TPIAT) in the management of refractory chronic pancreatitis have been quite promising with its ability to achieve pain remission, manageable glycemic control, and return these patients to a normal life. Several centers, including our own, have even been able to demonstrate the long-term durability of this procedure.[6,11,12]

One question that has yet to be addressed is the role that total or completion pancreatectomy and islet cell autotransplantation (CPIAT) has in managing patients with refractory chronic pancreatitis after failed previous pancreatic resection and/or decompression. At our institution, CPIAT is used as salvage therapy for patients with refractory disease after traditional operative intervention. The aim of this study was to review the outcomes of patients undergoing CPIAT as salvage therapy to determine whether this is a viable option for this select patient population.

METHODS

Patient selection. This retrospective, single-center, observational study included all patients undergoing CPIAT for the treatment of refractory or progressive chronic pancreatitis. Each patient included in this study had undergone previous pancreatic resection or decompression for the treatment of chronic pancreatitis. The indication for CPIAT was progression of disease resulting in recurrent refractory pain and worsened QOL. Before CPIAT, a multidisciplinary team evaluation was performed to ensure the appropriateness of CPIAT. This multidisciplinary team consists of gastroenterology, endocrinology, radiology, and pancreatic surgery physicians.

Operative technique and islet cell autotransplantation. Completion pancreatectomy was performed and operative approach varied for each patient depending on previous procedure and intraoperative findings. Care is taken to minimize ischemia time of the pancreatic tissue by dividing vasculature only after the remaining pancreas has been mobilized. In patients with an intact pancreatic duct, the duct was cannulated and infused with collagenase enzymatic solution. For patients with previous ductal drainage, the enzymatic solution is injected directly into the gland. The excised pancreas was then sent to a dedicated laboratory for enzymatic digestion and islet cell isolation, as previously described.[11,13,14] Isolated islet cells were suspended in 5% albumin with heparin (70 U/kg body weight). Suspended cell were then transplanted into the patient's liver via portal venotomy. Operative reconstruction varied based on the patient's previous pancreatic surgery. Where necessary, Roux-en-Y enteral reconstruction was performed with a choledochojejunostomy and gastrojejunostomy.

Postoperative management of these patients was performed under the same guidelines described previously.[11,15] An insulin infusion was initiated immediately after completion pancreatectomy and continued for the first 48 hours after surgery. On postoperative day 3, patients were converted over to a basal bolus insulin regimen. This regimen was adjusted according to blood glucose levels and all patients were kept hospitalized until stable glycemic control was obtained. All patients underwent diabetes education before CPIAT as well as during their hospitalization. All patients were discharged and maintained on insulin for a minimum of 1 month.

Study design and statistical analysis. This study was approved by and conducted in accordance to the University of Cincinnati Medical Center Institutional Review Board. The University of Cincinnati Pancreatic Disease Center patient database was queried to identify all patients undergoing CPIAT after previous pancreatic operative