ORIGINAL ARTICLE

Total pancreatectomy with islet cell autotransplantation as the initial treatment for minimal-change chronic pancreatitis

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Abstract

Objectives: Patients with minimal-change chronic pancreatitis (MCCP) are traditionally managed medically with poor results. This study was conducted to review outcomes following total pancreatectomy with islet cell autotransplantation (TP/IAT) as the initial surgical procedure in the treatment of MCCP.

Methods: All patients submitted to TP/IAT for MCCP were identified for inclusion in a single-centre observational study. A retrospective chart review was performed to identify pertinent preoperative, perioperative and postoperative data.

Results: A total of 84 patients with a mean age of 36.5 years (range: 15–60 years) underwent TP/IAT as the initial treatment for MCCP. The most common aetiology of chronic pancreatitis in this cohort was idiopathic (69.0%, $n = 58$), followed by aetiologies associated with genetic mutations (16.7%, $n = 14$), pancreatic divisum (9.5%, $n = 8$), and alcohol (4.8%, $n = 4$). The most common genetic mutations pertained to *CFTR* ($n = 9$), *SPINK1* ($n = 3$) and *PRSS1* ($n = 2$). Mean ± standard error of the mean preoperative narcotic requirements were 129.3 ± 18.7 morphine-equivalent milligrams (MEQ)/day. Overall, 58.3% ($n = 49$) of patients achieved narcotic independence and the remaining patients required 59.4 ± 10.6 MEQ/day ($P < 0.05$). Postoperative insulin independence was achieved by 36.9% ($n = 31$) of patients. The Short-Form 36-Item Health Survey administered postoperatively demonstrated improvement in all tested quality of life subscales.

Conclusions: The present report represents one of the largest series demonstrating the benefits of TP/IAT in the subset of patients with MCCP.

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Introduction

Minimal-change chronic pancreatitis (MCCP) is characterized by chronic inflammatory destruction of the gland with subsequent exocrine/endocrine dysfunction and persistent abdominal pain without main duct dilation.[1] In a subset of these patients, findings are so subtle that classical imaging modalities often do not detect the findings of chronic pancreatitis (CP). These patients usually present with debilitating abdominal pain or recurrent acute pancreatitis. When present, the disease usually involves the entire gland. Traditional management strategies have historically focused on medical therapy for the control of symptoms. Exocrine dysfunction has been abated through the administration of replacement enzymes. Endocrine dysfunction and the resulting diabetes have been managed with oral hypoglycaemic medications and/or exogenous insulin administration. Attempts at pain management are made by escalating analgesic and narcotic regimens.[2]

It was commonly accepted that CP would progress to the point of organ failure or burnout, at which point the patient's abdominal pain would subside.[3] Therefore, medical management was

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considered the standard of care and narcotic medications represented an ideal bridging therapy until organ burnout occurred. Additional studies have since questioned this burnout phenomenon and demonstrated that abdominal pain persisted in the majority of patients with CP over a 10-year follow-up period.[4] In MCCP, not only does pain persist, but almost 80% of patients experience worsening functional status despite optimal medical management.[5] Given the inadequacies of medical management in MCCP, surgical intervention has been advocated for patients with refractory disease. Lateral pancreaticojejunostomy with or without limited gland resection has been widely accepted for the treatment of large duct CP,[6–9] but it does not address the underlying pathophysiology in MCCP.[10] The development of surgical interventions for the treatment of MCCP has focused on varying degrees of gland resection. Classical and pylorus-preserving pancreaticoduodenectomy (PD) have been shown to provide benefit in head-dominant disease, but the remnant gland provides a source of persistent disease.[1,11] Izbicki *et al.* and Yekebas *et al.* reported on the benefits of longitudinal excision of the ventral pancreas for small duct disease and demonstrated pain reduction in the majority of patients.[12,13] Near-total or total pancreatectomy (TP) was largely reserved for the worst cases because of its associated morbidity, but its use in the treatment of CP has been rejuvenated with advances in islet cell autotransplantation (IAT).[14–16]

At the study institution, practitioners have advocated for TP/IAT as the initial procedure for patients with MCCP. This paper reports on outcomes in a series of patients submitted to TP/IAT as the initial surgical intervention for the treatment of MCCP with an emphasis on islet yields, postoperative insulin and narcotic requirements, and standardized quality of life (QoL) assessments.

Materials and methods

Patient selection

Patients referred to the University of Cincinnati Pancreatic Disease Center were submitted to a thorough multidisciplinary team evaluation conducted by practitioners in gastroenterology, endocrinology, radiology and pancreatic surgery. Minimal-change CP was diagnosed according to the results of imaging and functional testing, and patient symptomatology that was consistent with CP but in the absence of pancreatic duct dilation. Imaging modalities included computed tomography (CT), endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP). Functional testing included the measurement of fecal fat and elastase levels in conjunction with pancreatic bicarbonate levels. In most patients, diagnosis was based on clinical symptoms and confirmed with EUS, ERCP and CT findings. Confirmation with EUS required the presence of four or more of the nine conventional criteria: parenchymal findings included hyperechoic foci, hyperechoic stranding, hyperechoic lobularity and cysts, and ductal findings included irregular duct contour, hyperechoic ductal margin, visible side branches, and ductal calculi.[17] If a patient had fewer than four (Rosemont or conventional) findings but a concomitant major finding (stones or honeycomb lobularity), that patient was diagnosed with MCCP. The confirmation of a diagnosis by ERCP was based on the Cambridge classification.[18] Patients with Cambridge II and III disease were designated as having MCCP. Patients with debilitating pain and/or a disturbed QoL despite maximal medical and endoscopic management were considered as surgical candidates. At the study institution, TP/IAT was offered to patients with MCCP as the initial surgical intervention, but was only considered in patients with type 2 diabetes mellitus if they were insulin-independent or required <0.5 units of insulin per kilogram body weight per day.

Operative procedure and islet cell transplantation

Total pancreatectomy was performed in all patients and included splenectomy and resection of the duodenum and distal common bile duct. The body and tail of the pancreas were mobilized first and the pancreatic blood supply was preserved as long as possible to minimize islet cell ischaemia. The distal pancreas was divided at the level of the superior mesenteric vein and infused with enzymatic solution through the pancreatic duct. Islet cell isolation was performed by enzymatic degradation of the pancreatic tissue as previously described.[19,20] Cell viability was confirmed with acridine orange and propidium iodine staining and alamar blue staining. Islet cells were suspended in 5% albumin solution containing heparin at 70 units per kilogram of body weight and transplanted via portal vein infusion. Roux-en-Y surgical reconstruction consisted of choledochojejunostomy and gastrojejunostomy.

Postoperative care

All patients were monitored in the surgical intensive care unit following TP/IAT for insulin infusion and strict blood glucose control (serum levels of <120 mg/dl). Patients were converted to a basal bolus insulin regimen starting on postoperative day 3. Strict glycaemic control was maintained throughout the hospitalization and all patients were discharged to home with an insulin regimen. All patients were counselled on the management of diabetes prior to hospital discharge. Insulin regimens were adjusted and weaned based on a review of patient blood glucose journals and haemoglobin A1c levels by the patient's endocrinologist.

Data collection and statistical analysis

This study was approved by the University of Cincinnati Institutional Review Board and informed consent was obtained from all study participants. The University of Cincinnati Pancreatic Disease Center patient database was reviewed to identify all patients submitted to TP/IAT for MCCP between 2002 and 2012. A retrospective chart review identified pertinent preoperative, intraoperative and postoperative details. The overall mean ± standard error of the mean (SEM) follow-up time for the patient cohort was 32.0 ± 3.4 months after TP/IAT. All medication