



Surgery for Chronic Pancreatitis: What is the Future?

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Abstract

Chronic pancreatitis can lead to chronic pain resulting in disability and poor quality of life in many patients. Currently, management centers on adequate pain control, however some patients continue to suffer from pain despite multimodal efforts. Resection and drainage procedures are often attempted; however pain may persist due to remnant pancreas. Total pancreatectomy with auto islet transplantation, once considered to be a radical therapy, and has been increasingly employed as a strategy to treat this disease. Outcomes are promising with some patients achieving both narcotic and insulin independence. Total pancreatectomy and auto islet transplantation should be considered as an early treatment strategy in select patients.

Introduction

Chronic pancreatitis is a progressive and irreversible process resulting in fibrosis and atrophy of the pancreas and subsequent endocrine and exocrine dysfunction. The etiology of chronic pancreatitis is multifactorial with causes ranging from alcohol and smoking to genetic, autoimmune and idiopathic cases. In the US, it accounts for 125,000 outpatient visits, and 25,000 hospitalizations yearly [1]. Patients suffer from abdominal pain, nutritional deficits, and weight loss [2]. Pain can be characterized as intermittent or persistent. Patients with persistent chronic pain syndrome have poor quality of life, require disability, have frequent hospitalizations, and rely on pain medication to function [3]. In addition to these challenges, pancreatic exocrine insufficiency has been identified as a risk factor for mortality in patients with chronic pancreatitis [4]. Currently, effective management of chronic pancreatitis continues to present a tremendous challenge with multimodal modalities for pain control often failing.

Chronic Pancreatitis Guidelines

Current guidelines for management of pain related to chronic pancreatitis centers on analgesic therapy. Suggested stepwise pain control includes paracetamol, pregabalin, and opioids. Additional unconventional modalities such as ketamine and somatostatin analogues have also been described. Endoscopic therapies include relieving obstruction of the main pancreatic duct with sphincterotomy, stent placement for ductal strictures and Extracorporeal Shock Wave Lithotripsy (ESWL) for pancreatic stones. Celiac plexus blocks and splanchnic nerve ablation are considered when medical treatment fails [5]. New non-surgical modalities such as radiotherapy, which can have anti-inflammatory and antalgic effects, have been described but further research is warranted [6]. When medical management fails, surgical management is the next step; however the type of surgery to pursue is controversial. Historically, partial pancreatic resections as well drainage procedures were considered the treatment options of choice. The Whipple procedure has been more often employed in patients with chronic pancreatitis than the distal pancreatectomy due to the fact that the head of the pancreas is the 'pacemaker' of the disease and most commonly the cause of ensuing chronic pain syndrome. Over time, combined drainage and resection procedures have been described including the Frey and Beger procedures and the Berne and Hamburg modifications. While the Beger and Frey procedures have demonstrated similar efficacy compared to the Whipple operation, there remains a group of patients that continue to have recalcitrant pain [7]. This comes to no surprise because even small remnants of diseased pancreatic tissues will cause chronic pain. Factors associated with poor pain outcome after the Frey procedure include decreased volume of pancreatic head resected and small pancreatic duct diameter. Pain with small duct disease is attributed to nerve inflammation, and ischemia [8]. In general, drainage and partial resection are most commonly inadequate as they leave diseased tissue behind and do not relieve patients' intractable pain.

Pancreatectomy Procedures

When partial pancreatectomy and drainage procedures fail to control pain, Total Pancreatectomy

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(TP) is the next step. Considered by many surgeons as a last resort, concerns stem from morbidities associated with post-operative brittle diabetes mellitus including hypoglycemic unawareness, hypoglycemic episodes and development of secondary diabetic complications. Due to lack of glucagon and other glucose regulating hormones, glucose management is extremely challenging. Thus, post-pancreatectomy patients are prone to emergency room visits and hospitalizations due to hypoglycemia, ketoacidosis and failure to thrive. Prevention of brittle diabetes is an important adjunct to total pancreatectomy. Currently, only Islet Auto Transplantation (IAT) provides a mechanism for beta cell preservation in post-pancreatectomy patients. The concept of beta-cell preservation has evolved since its conception in the 1970s from auto transplanted segmental pancreas to the sophisticated isolation of beta cells auto transplanted into the liver via the portal vein. At least 3,000 islet equivalents per kilogram are required for insulin-independence following total pancreatectomy. Lower islet yields may not result in insulin-independence but however, prevent the development of brittle diabetes [9]. Patients with previous partial pancreatic resections are also amenable to completion pancreatectomy with IAT. For best outcomes, the key is early referral in patients with normal hemoglobin A1C levels and mild glucose abnormalities. Children with chronic hereditary pancreatitis are also candidates for this procedure which has been performed in patients as young as 5 years of age. In pediatric patient's younger age, no prior Puestow procedure, and higher islet yield were associated with higher rates of insulin-independence [10]. Early identification of these patients and avoiding delays into early adulthood can prevent psychosocial and learning issues that result from coping with the burden of this illness [11]. Although many consider TP to be an aggressive approach recent outcomes in TP-IAT have demonstrated low post-operative morbidity and mortality in addition to dramatically improved pain relief and increased quality of life. In-hospital post-operative mortality has declined from 1% to 2% in early reports to none in more recent series [12]. Within one month, patients report improvements in general health, increased energy, improved mental health, and social functioning [13]. Long terms, about one-third of patients are insulin-independent, one third has partial islet function, and one third is insulin-dependent at 3 years. In more recent studies, insulin-independence is up to 50% at 3 years and 73% at 5 years [14-16]. Lower rates of insulin-independence are usually be related to an advanced disease stage at the time of the operation. Opioid independence can be achieved in 46% to 59% [15,17]. Predictors for persistent narcotic use and persistent pain after TP-IAT include history of previous and multiple stent placements, sphincterotomy, and previous Whipple procedure [18]. This further highlights the importance of early referral. While promising, TP-IAT is not ideal for all patients. The post-operative care requires commitment from the patient involving strict monitoring of glucose, adherence to post-operative medication regimen, possible management of jejunal feeding, diet monitoring as well as ongoing follow-up with surgeons and endocrinologists. Patient non-compliance and continued alcohol abuse are contraindications to the procedure. Further advances in TP-IAT are forthcoming. Laparoscopic and robotic approaches to TP-IAT have been performed with early reports of reduced length of stay and reduced time to opioid independence [19-21].

Conclusion

In the treatment of chronic pancreatitis, TP-IAT has demonstrated excellent outcomes in selected patients. It has become the treatment of choice for pain and glucose control. Attempts at endoscopic,

drainage and partial pancreatectomy are inadequate and usually delay a patient's steps toward pain relief and an improved quality of life. Even worse, delay results in impaired glucose metabolism or even insulin-dependence. Early referral to TP-IAT centers is pivotal and must be incorporated into the strategy of managing this destructive disease.

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