Total Pancreatectomy with Autologous Islet Cell Transplantation

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KEYWORDS

• Chronic pancreatitis • Autologous islet cell transplantation • Type 3c diabetes
• Islet isolation

KEY POINTS

- Total or near-total pancreatectomy is a viable treatment option for patients with end-stage chronic pancreatitis but carries with it the inevitability of insulin-dependent diabetes mellitus.
- The adjunct of autologous islet cell transplantation offers the potential for mitigation or even complete avoidance of insulin use, for a time.
- This highly specialized procedure is performed only in select centers world-wide.
- Both islet isolation and perioperative management require attention to numerous specific details and protocols.
- Further research to optimize islet yield, survival, and function is ongoing, including search for ideal implantation site as well as process tweaks and adjunctive medications.

INTRODUCTION

After decades of research, Najarian and colleagues[1] published the first series of successful autologous human islet cell transplantation for chronic pancreatitis in 1980. Since that time the technique has been sparsely applied due to the complexity of the patient population, surgical techniques, and islet isolation. Yet, despite many nuances and technical considerations, thousands of patients worldwide have successfully undergone this procedure.

Treating severe chronic pancreatitis with total pancreatectomy carries the promise of improved quality of life, with the trade-off of brittle or type 3c diabetes (marked by the paucity or absence of not only insulin but also of the counterregulatory hormone glucagon). Isolation and reimplantation of pancreatic islet cells from the resected specimen offers the hope for relief from diabetes, if not complete then partial, if not

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lifelong then for a period of time. In this treatise the author describes the indications for the procedure, including classic and expanded. Particular surgical considerations as well as details of islet isolation are reviewed. Results for both the primary indication of symptom relief as well as the secondary measure of insulin production are summarized. Finally, current considerations and research as well as future directions are identified.

INDICATIONS

Autologous islet cell transplantation was initially conceived as an adjunct to total pancreatectomy for chronic pancreatitis, which can be an unrelenting, progressive disease, one for which the trade-off of brittle diabetes is worth the cost for patients in the end stages. These patients face significant detriment in quality of life, with chronic or recurrent severe pain and nausea, frequent hospitalizations, inability to work or be an otherwise productive member of society, and often opiate dependence.

In certain circumstances, where maximal medical and endoscopic therapies have become ineffective at symptom control, surgical intervention becomes indicated. Choice of surgery depends on several factors, including anatomic features of the pancreas. For example, a fibrotic pancreas with an enlarged duct may benefit from a surgical drainage procedure, or one with a dominant inflammatory mass may benefit from a partial resection, or some combination of both. Yet not infrequently the gland seems "normal", or diffusely fatty, without the above-mentioned characteristics. Patients with these glands may be particularly helped by a total pancreatectomy.

Causes for chronic pancreatitis vary, with the most frequent being alcohol use and cholelithiasis. Less common causes include hereditary pancreatitis (characterized by specific mutations in the PRSS1, CFTR, SPINK, or CTRC genes), autoimmune pancreatitis, hypertriglyceridemia, congenital ductal anomalies, and medication-related, to name a few; all too often (20%–30%) an identifiable cause is never found, and we are left with the ubiquitous "idiopathic" moniker. Although ultimately any given patient regardless of cause may proceed to total pancreatectomy, cause affects expectations for islet yield and procedural "success."

Sporadic publication of expanded indications is noted in the literature. Because chronic pancreatitis is generally a benign disease (although does carry the harbinger of increased risk of malignant transformation over a patient's lifetime), it is comfortable to reimplant islets with concomitant and unavoidable acinar debris back into the patient. Other conditions of the pancreas may merit consideration of islet autotransplantation, including intraductal papillary mucinous neoplasms and even possibly carcinoma, although currently not enough data are available for the widespread recommendation in these circumstances.

PATIENT SELECTION

TPAIT is a radical, "last-resort" treatment for end-stage chronic pancreatitis. As stated earlier, patients should generally have been through the gamut of symptom management strategies, including dietary management, medications (opiates, nonsteroidal antiinflammatory drugs, neuropathic medications, muscle relaxants), chemical neurolysis, endoscopic retrograde cholangiopancreatography, and regional pain relief therapies (spinal cord stimulator or intrathecal drug delivery devices). Once most of these options have failed, surgery can be considered. Possible leniency of this requirement is applied to cases of hereditary pancreatitis (particularly PRSS1 mutation) where a real risk of malignant transformation exists.