



The New Paradigm for the Treatment of Chronic Pancreatitis

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Effective treatment of chronic pancreatitis remains one of the greatest surgical challenges to date. The incidence of chronic pancreatitis ranges from 3 to 10 cases per 100,000 populations per year worldwide. In the United States alone, more than 50,000 hospitalizations per year are caused by this disease. Chronic pancreatitis is an inflammatory process, progressive and irreversible in nature that eventually leads to complete destruction of pancreatic parenchyma and ductal structures. The result of pancreatic fibrosis and atrophy is initially exocrine, and later endocrine, deficiency.

Chronic pancreatitis frequently develops in patients between the ages of 30 and 40, and is more common in men than women. While symptoms and the time interval between diagnosis and development of end-stage pancreatic disease differs greatly, chronic, and often intractable, pain is the predominant symptom. Because of the chronic pain syndrome, patients with chronic pancreatitis are frequently completely disabled with an extremely low quality of life and depend on chronic use of narcotic drugs. Most therapeutic efforts are directed toward pain control. But medical and endoscopic management usually fails over time; as a result, surgical options are eventually explored.

For decades, no single surgical procedure was considered the treatment of choice for patients with chronic pancreatitis. The large variety of organ-sparing, resective or drainage procedures illustrates the lack of consensus. In fact, the focus on organ-sparing operations has been part of the problem: partial pancreatic resections, drainage procedures, and combinations thereof leave diseased tissue behind, are frequently prone to major complications due to their complexity, and, above all, usually do not improve the patients' intractable pain. Total pancreatic resections are considered to be the last resort but they inevitably cause brittle diabetes mellitus, low quality of life, and significant morbidity and mortality due to associated hypoglycemia. The annual mortality rate due to hypoglycemia is substantial, ranging from 4% to 10%.

Most surgeons consider a total pancreatectomy for patients with chronic pancreatitis to be a radical therapy for a "benign" disease. For endocrinologists and diabetologists alike, apancreatic patients are particularly challenging: because they are prone to hypoglycemic episodes or hypoglycemic unawareness and because of their postoperative lack of glucagon and other glucose regulatory hormone production, they are frequently more difficult to manage than type 1 diabetic patients. On the positive side, a total pancreatectomy usually achieves better pain relief than a partial pancreatectomy or a drainage procedure.

But there is already an efficient and satisfactory, yet little-known, solution available to patients that undergo a total pancreatectomy: beta-cell preservation in nondiabetic patients through islet auto transplantation into the native liver via the portal vein offers the opportunity to either maintain insulin independence or at least better manage the surgery-induced diabetes mellitus.

To achieve insulin independence, usually an islet yield of at least 300,000 islet equivalents per kilogram is required. Even though lower islet yields usually do not lead to insulin independence, such transplants can still prevent the development of brittle diabetes mellitus with its wide fluctuations in blood sugar levels and therefore can still improve the recipient's physical and mental health.

Given the strict technical requirements for islet processing facilities (and the high costs associated with facility construction), only a handful of medical centers in the country offer a total pancreatectomy combined with a simultaneous islet autotransplant (TP-IAT). The prospect of either insulin independence or development of only a mild form of diabetes after a TP-IAT should be a major incentive for physicians to refer their patients with chronic pancreatitis to the few centers that offer the combined operation, rather than settling for the imperfect solution of a total pancreatectomy alone.

The key to a successful metabolic outcome after a TP-IAT lies in early referral. Yet all too often, patients with chronic pancreatitis are still subjected to inadequate endoscopic and surgical procedures that do not relieve their chronic pain but do cause further deterioration of their endocrine function and their overall quality of life. Early referral of patients with normal hemoglobin A_{1c} levels, and with normal or slightly abnormal continuous glucose monitoring results, provides the best outcomes after a TP-IAT, as shown in our own experience and based on our novel technological innovations [1-4].

Of note, not only for adults, but also for children with chronic pancreatitis, outcomes after a TP-IAT have been very satisfactory. Delaying surgery until early adulthood needlessly erodes quality of life during childhood and adolescence, causing psychosocial and learning issues not only for the patient but also for the entire family.

When it comes to the treatment of patients with chronic pancreatitis, surgeons and gastroenterologists must become bolder: yes, a TP-IAT is a radical therapy — but the disease is not benign and not reversible. To date, a TP-IAT must be considered the only definitive treatment option early in the disease process, i.e., before the patient develops abnormal glucose metabolism and becomes

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dependent on pain medications. Once the diagnosis of chronic pancreatitis is established, the numerous endoscopic and inadequate surgical procedures that patients typically undergo are unnecessary and totally ignore the irreversibility of their disease. Only an early referral to a TP-IAT center will decrease chronic dependence on pain medications and improve metabolic outcome as well as quality of life. The time has come that surgeons, gastroenterologists and endocrinologists acknowledge that, with chronic pancreatitis, the most radical surgical option provides the best results and is, therefore, in the best interest of our patients.

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