#### ORIGINAL ARTICLE

# Risk factors for early readmission after total pancreatectomy and islet auto transplantation

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#### **Abstract**

**Background:** Little published data exist examining causes of hospital readmission following total pancreatectomy with islet autotransplantation (TPIAT).

**Methods:** A retrospective analysis was performed of a prospectively collected institutional TPIAT database. Primary outcome was unplanned readmission to the hospital within 30 days from discharge. Reasons and risk factors for readmission as well as islet function were evaluated and compared by univariate and multivariate analysis.

**Results:** 83 patients underwent TPIAT from 2006 to 2014. 21 patients (25.3%) were readmitted within 30 days. Gastrointestinal problems (52.4%) and surgical site infection (42.8%) were the most common reasons for readmission. Initial LOS and reoperation were risk factors for early readmission. Patients with delayed gastric emptying (DGE) were three times more likely to get readmitted. In multivariate analysis, patients undergoing pylorus preservation surgery were nine times more likely to be readmitted than the antrectomy group.

**Conclusion:** Early readmission after TPIAT is common (one in four patients), underscoring the complexity of this procedure. Early readmission is not detrimental to islet graft function. Patients undergoing pylorus preservation are more likely to get readmitted, perhaps due to increased incidence of delayed gastric emptying. Decision for antrectomy vs. pylorus preservation needs to be individualized.

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#### Introduction

Chronic pancreatitis (CP) is characterized by irreversible inflammatory damage to the pancreas and is associated with varying degrees of loss of exocrine and endocrine functions.<sup>1</sup> Severe, intractable pain is the hallmark of chronic pancreatitis.<sup>2,3</sup> Debilitating chronic pain gradually degrades the health-related quality of life (QOL) and patients seek medical treatment.<sup>4,5</sup> Most patients are dependent on chronic opioid analgesics to help control pain. The initial management is with narcotic and non-narcotic pain medications, endoscopic procedures and celiac ganglion blocks.<sup>6–8</sup> However, in late stages of the disease, surgical interventions (surgical drainage procedures, partial and total pancreatic resections) remain the mainstay of treatment.<sup>9</sup>

Total pancreatectomy with islet autotransplantation (TPIAT) is a surgical alternative for patients with unrelenting intractable pain from CP. It improves the QOL of patients by alleviating pain, while preventing or minimizing post-surgical brittle diabetes by preserving the beta cell function. Il, It is nonetheless a major procedure with its associated morbidity and readmissions.

Currently, hospital readmissions are one of the central topics in the setting of health care policy and reform. <sup>14</sup> It is considered a measure of health care quality and some health care services reduce reimbursements to hospitals with high rate of readmissions. <sup>15</sup> A problem that occurs with reimbursement based on readmission rates is that readmission may not always correlate with quality of care. This is particularly true following a surgical procedure like TPIAT for which the follow-up is inherently complex. <sup>16</sup> Patient related factors, admission diagnosis, indicated

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procedures, and disease-specific prognosis have a role in determining whether a patient is at risk for early readmission. Many studies have been performed in TPIAT patients, but an accurate baseline measure of readmissions has not been done.

The aim of this study was to evaluate the rate of readmission following total pancreatectomy at our hospital and to identify patient and procedure related factors predictive of those readmissions.

#### **Materials and methods**

#### **Patient selection**

This study was approved by and performed according to the guidelines of the Baylor University Medical Center institutional review board. All patients undergoing TPIAT from 2006 to 2014, with at least 1-year of follow-up, were identified from a transplant database. Patient clinical, demographic, laboratory and event data (such as graft failure, insulin independence) are prospectively collected and locked in the islet cell transplant research database. All patients with previously diagnosed chronic pancreatitis who are considered for TPIAT are evaluated by a multidisciplinary team, including gastroenterologists, endocrinologists, and transplant surgeons. The diagnosis of CP is based on the patient's history, laboratory results, computed tomographic scans, endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography, magnetic resonance imaging, and pathologic diagnosis. The indications for surgery are intractable pain despite previous medical and surgical interventions. Our primary outcome of interest was early readmission, defined as unplanned admission to the hospital within 30 days of discharge from the hospital. None of the patients died in this period. For the purpose of this study, data were gathered about patient demographics, cause of CP, pre-op patient comorbidities like hypertension, diabetes mellitus, ischemic heart disease, obesity (BMI > 30), smoking, alcohol consumption, prior biliary/pancreatic stent placement and previous pancreatic or other abdominal surgeries.

#### Operative procedure and islet cell transplantation

In all the patients, the pancreas is removed as a whole, along with the spleen and the C-loop of duodenum. During the surgery, pancreatic blood supply is preserved as long as possible to minimize islet cell ischemia. Pancreas and attached tissue is then removed and dissected free from spleen and duodenum on backtable. University of Wisconsin solution is used to flush the gastroduodenal and splenic arteries in the back-table, pancreas duct cannulated and organ placed in the organ retrieval bag and then transferred to the islet isolation facility. Liberase HI (Roche, Indianapolis, IN), Collagenase NB with neutral proteases (SERVA Electrophoresis GMbH, Heidelberg, Germany) or Liberase MTF (Roche) is infused into the main pancreatic duct for pancreas digestion. Islets are isolated by modified Ricordi method.<sup>17</sup> When the tissue volume exceeds 15–20 mL, islets are

purified with a COBE 2991 cell processor (Caridian BCT, Inc., Lakewood, CO) using a density-adjusted iodixanol-based continuous density gradient. Endotoxin, Gram staining, and bacterial and fungal cultures are taken from the final products as product release testing criteria. Isolated islets are infused along with heparin (70 U/kg body weight) into the portal vein via a branch of the superior mesenteric vein. Portal pressures are routinely monitored during the islet infusion. When the portal pressure exceeds 22 mmHg, the infusion is halted and rest of the islets infused intraperitoneally.

The post-pancreatectomy reconstruction is undertaken with a retrocolic Roux-en-Y choledochojejunostomy and a retrocolic gastrojejunostomy (GJ), either as a standard GJ with antrectomy or a pylorus preserving procedure. The decision to preserve the pylorus is patient-dependent. Generally, diabetic patients receive antrectomy in an attempt to minimize post-op gastroparesis. Non-diabetic patients may have their pylorus preserved if the first portion of the duodenum appears well vascularized and free of substantial inflammation. Early in the series (for the first 20 cases), jejunostomy tubes were placed in all patients. As the experience grew, it was noted that the jejunostomy tubes were infrequently used after discharge. Therefore, a decision was made to switch to naso-jejunal tubes which are used for early post-op enteral feeding and are mostly removed before discharge.

Data were compared on operative time, type of operation (pylorus preserving or antrectomy), blood loss, transfusion requirements, islet yield, intraoperative portal pressures during islet infusion and postoperative complications.

### Postoperative care and assessment of clinical outcome

Patients were monitored in the intensive care unit after surgery for 1–2 days for pain control, sedation, and insulin infusion. They were converted to a basal bolus insulin regimen on post-op day (POD) 3. Blood glucose level was maintained within normal limits (80–120 mg/dL) during the hospital stay. All patients were discharged with an individualized insulin regimen and weaned off insulin as outpatients, as appropriate. Enteral feeds via jejunostomy tube (early in the series) or naso-jejunal tubes (later in the series) were started 24 h post-op and gradually advanced. By hospital discharge, the vast majority of patients (>95%) were on oral feeds only. Patients were started on a rate of heparin at 500 U/h, 4–6 h after surgery. After 36 h of heparin, they were transitioned to prophylactic low molecular weight heparin (LMWH) for 14 days. The patients were thereafter converted to aspirin 81 mg daily indefinitely.

Adverse events were recorded retrospectively and graded using the Common Terminology Criteria for Adverse Events (AE) in total pancreatectomy and Islet autotransplantation. All patients had their portal vein assessed by duplex imaging before and after the surgical intervention. Postoperative care was provided and improvement in clinical symptoms assessed by the transplant surgery and endocrinology specialists.

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