Islet Transplantation

Description

Autologous islet transplantation, performed in conjunction with pancreatectomy for chronic pancreatitis is proposed to reduce the likelihood of insulin-dependent diabetes following pancreatectomy.

Background

In autologous islet transplantation, during the pancreatectomy procedure, islet cells are isolated from the resected pancreas using enzymes, and a suspension of the cells is injected into the portal vein of the patient’s liver. Once implanted, the beta cells in these islets begin to make and release insulin.

Chronic Pancreatitis

Primary risk factors for chronic pancreatitis include toxic-metabolic, idiopathic, genetic, autoimmune, recurrent and severe acute pancreatitis, or obstructive (the TIGAR-O classification system). Patients with chronic pancreatitis may experience intractable pain that can only be relieved with a total or near total pancreatectomy. However, the pain relief must be balanced against the certainty that the patient will be rendered an insulin-dependent diabetic. Autologous islet transplantation has been investigated as a technique to prevent this serious morbidity.

Related Policies

2.01.43 Chronic Intermittent Intravenous Insulin Therapy (CIILT)
7.03.02 Allogeneic Pancreas Transplant

Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Autologous pancreas islet transplantation may be considered **medically necessary** as an adjunct to a total or near total pancreatectomy in patients with chronic pancreatitis.

Islet transplantation is considered **investigational** in all other situations.
Rationale

Chronic Pancreatitis

In 2012, Bramis and colleagues published a systematic review of studies on islet transplantation after total pancreatectomy in patients with chronic pancreatitis. (1) The investigators searched for studies reporting on patients who had been treated with total, subtotal or completion pancreatectomy followed by islet autotransplantation. Case series were included if they included more than 5 patients and reported outcomes for consecutive patients. A total of 72 full-text articles were reviewed, and 5 studies were found to meet inclusion criteria. The postoperative insulin independence rate in the 5 studies ranged from 10% (mean follow-up, 8 years) to 46% (mean follow-up, 5 years). In the study with the longest follow-up, the insulin independence rate was 28% at 10 years. Two studies reported postoperative morphine use. In 1 study, patients reported a mean postoperative decrease in morphine use of 116 mg and in the other, a mean decrease of 55 mg of morphine was reported.

An earlier systematic review of studies on islet transplantation after pancreatectomy was published in 2011 by Dong et al. (2) Studies were included regardless of design or sample size. After reviewing 84 studies, 15 observational studies were found to meet eligibility criteria. There were 11 studies of total pancreatectomy, 2 studies of partial pancreatectomy, and 2 studies that included both types of surgery. Sample sizes in individual studies ranged from 3 to 173 patients. Thirteen studies included patients with chronic pancreatitis, and 2 included patients with benign pancreatic tumors. The pooled 30-day mortality was 5% (95% confidence interval [CI]: 2% to 10%), and the cumulative mortality at 1 year (reported by 10 studies) was 4.9% (95% CI, 2.6% to 7.3%) In a pooled analysis of data from 14 studies, the rate of insulin dependence at last follow-up was 4.6 per 100 person years (95% CI: 1.53 to 7.62). The pooled rate of insulin independence at 1 year (5 studies) was 27% (95% CI: 21% to 33%) and at 2 years (3 studies) was 21% (95% CI: 16-27%).

Representative studies in the systematic reviews or published studies are described next:

A large single center series was reported by Sutherland et al in 2012. (3) The study included 409 patients with chronic pancreatitis who underwent total pancreatectomy and islet transplantation between February 1977 and September 2011. Fifty-three of 409 patients (13%) were children between the ages of 5 and 18 years. Actuarial survival post-surgery was 96% in adults and 98% in children after 1 year and 89% in adults and 98% in children after 5 years. A total of 15.9% of patients experienced surgical complications requiring reoperation during the initial admission. The most common reason for reoperation was bleeding, occurring in 9.5% of patients. At 3 years, 30% of patients were insulin-independent (25% of adults and 55% of children). A survey of quality-of-life outcomes was initiated in October 2008; responses were available for 102 patients. At baseline, all 102 patients reported using narcotics for pain. At 12 months, the proportion of patients on narcotics decreased to 56% (n=32), and at 24 months, 41% of respondents (n=21) reported using narcotics.

A 2014 study by Chinnakotla et al included 484 patients with chronic pancreatitis. (4) Patients underwent total pancreatectomy and immediate islet auto transplantation. Using a Kaplan-Meier analysis method, 10-year survival was 84%. Patient survival at 5 years was 90.3% in the 80 patients with hereditary/genetic pancreatitis and 89.7% in the 404 patients with nonhereditary pancreatitis; the
difference between groups was not statistically significant. Pancreatitis pain decreased significantly after the procedures, and there was no statistically significant difference in the rate of pancreatitis pain between the groups with and without genetic/hereditary disease.

In 2008, Webb et al reported on 46 patients who had total pancreatectomy with immediate islet auto transplant. Twelve had periods of insulin independence for a median of 16.5 months (range, 2–63 months), and 5 remain insulin-independent. (5) Insulin requirements increased over the 10-year follow-up, as have HgA1c levels; however, all patients tested were C-peptide positive at their most recent assessment, and high fasting and stimulated C-peptide positive values recorded at 10 years after transplantation suggest significant graft function in the long term.

Type 1 Diabetes

In April 2004, TEC completed an evidence report on islet cell transplantation in type 1 diabetes in its capacity as an Evidence-based Practice Center for the Agency for Healthcare Research and Quality (AHRQ). (6) The evidence report found that published data on clinical outcomes of islet-alone transplantation were limited by small patient numbers; few transplant centers, short duration of follow-up, and lack of standardized methods of reporting clinical outcomes.

Practice Guidelines and Position Statements

Guidance from the National Institute for Clinical Excellence (NICE), a 2008 update of guidance on autologous islet cell transplantation for improved glycemic control after pancreatectomy states that studies show some short-term efficacy, although most patients require insulin therapy in the long term. Complications mainly result from the major surgery involved in pancreatectomy rather than from the islet cell transplantation. (7)

Summary

Autologous islet transplantation is proposed in conjunction with pancreatectomy for patients with chronic pancreatitis. Although the published experience with autologous islet cell transplantation is limited, the procedure appears to significantly decrease the incidence of diabetes after total or near total pancreatectomy in patients with chronic pancreatitis. In addition, this procedure is not associated with serious complications itself and is performed as an adjunct to the pancreatectomy procedure. Thus, this may be considered medically necessary.

Medicare National Coverage

Effective October 1, 2004, Medicare (Manual Section 260.3.1) will cover pancreatic islet transplantation in patients with type 1 diabetes participating in the context of a clinical trial sponsored by the National Institutes of Health. (8) Partial pancreatic tissue transplantation or islet transplantation performed outside the context of a clinical trial will continue to not be covered.
References


Policy History

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<tr>
<th>Date</th>
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<th>Reason</th>
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<tbody>
<tr>
<td>September 2012</td>
<td>New Policy</td>
<td>Policy updated with literature review; policy statement unchanged.</td>
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<tr>
<td>March 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review; references added; policy statements unchanged.</td>
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<tr>
<td>September 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review. Reference 4 added. No change in policy statement.</td>
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Keywords

Autologous Transplantation, Islet
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 12, 2014 and is effective October 15, 2014.

Signature on File
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