Isolated Small Bowel Transplant

I. Description

A small bowel transplant may be performed in conjunction with other visceral organs, including the liver, duodenum, jejunum, ileum, pancreas, or colon. When the small bowel and liver are transplanted in conjunction with other gastrointestinal organs, the procedure is referred to as a multivisceral transplant. Small bowel/liver transplants and multivisceral transplants are considered separately.

Background

A small bowel transplant is typically performed in patients with short bowel syndrome. This is a condition in which the absorbing surface of the small intestine is inadequate due to extensive disease or surgical removal of a large portion of small intestine. In adults, etiologies of short bowel syndrome include ischemia, trauma, volvulus, and tumors. In children, gastroschisis, volvulus, necrotizing enterocolitis, and congenital atresias are predominant causes.

The small intestine, particularly the ileum, does have the capacity to adapt to some functions of the diseased or removed portion over a period of 1 to 2 years. Prognosis for recovery depends on the degree and location of small intestine damage. Therapy is focused on achieving adequate macro- and micro-nutrient uptake in the remaining small bowel. Pharmacologic agents have been studied to increase villous proliferation and slow transit times, and surgical techniques have been advocated to optimize remaining small bowel. However, some patients with short bowel syndrome are unable to obtain adequate nutrition from enteral feeding and become chronically dependent on total parenteral nutrition (TPN). Patients with complications from TPN may be considered candidates for small bowel transplant. Complications include catheter-related mechanical problems, infections, hepatobiliary disease, and metabolic bone disease. While cadaveric intestinal transplant is the most commonly performed transplant, there has been recent interest in using living donors.
Intestinal transplants (including multivisceral and bowel/liver) represent a small minority (0.6%) of all solid organ transplants. In 2009, 180 intestinal transplants were performed in the United States, of which all but 2 were from deceased donors. (1) The Centers for Medicare and Medicaid Services (CMS) has approved 8 adult and 6 child intestinal transplant programs.

II. Policy

A small bowel transplant using cadaveric intestine is covered (subject to Administrative Guidelines) in adult and pediatric patients with intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance), who have established long-term dependency on total parenteral nutrition (TPN) and are developing or have developed severe complications due to TPN.

A small bowel transplant using a living donor is covered (subject to Administrative Guidelines) only when a cadaveric intestine is not available for transplantation in a patient who meets the criteria noted above for a cadaveric intestinal transplant.

A small bowel transplant using living donors is not covered in all other situations.

A small bowel transplant is not covered for adults with intestinal failure who are able to tolerate TPN.

III. Policy Guidelines

General

Potential contraindications subject to the judgment of the transplant center:

1. Known current malignancy, including metastatic cancer
2. Recent malignancy with high risk of recurrence
3. Untreated systemic infection making immunosuppression unsafe, including chronic infection
4. Other irreversible end-stage disease not attributed to intestinal failure
5. History of cancer with a moderate risk of recurrence
6. Systemic disease that could be exacerbated by immunosuppression
7. Psychosocial conditions or chemical dependency affecting ability to adhere to therapy

Small Bowel Specific

Intestinal failure results from surgical resection, congenital defect, or disease-associated loss of absorption and is characterized by the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance. (2) Short-bowel syndrome is one case of intestinal failure.

Patients who are developing or have developed severe complications due to TPN include, but are not limited, to the following: multiple and prolonged hospitalizations to treat TPN-related
complications (especially repeated episodes of catheter-related sepsis) or the development of progressive liver failure. In the setting of progressive liver failure, small bowel transplant may be considered a technique to avoid end-stage liver failure related to chronic TPN, thus avoiding the necessity of a multivisceral transplant. In those receiving TPN, liver disease with jaundice (total bilirubin above 3 mg/dL) is often associated with development of irreversible progressive liver disease. The inability to maintain venous access is another reason to consider small bowel transplant in those who are dependent on TPN.

IV. Administrative Guidelines

A. Precertification is required for this service as well as any transplant evaluations. Complete HMSA's Precertification Request and mail or fax the form as indicated.

B. Applicable codes:

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>44132</td>
<td>Donor enterectomy (including cold preservation), open; from cadaver donor</td>
</tr>
<tr>
<td>44133</td>
<td>Donor enterectomy (including cold preservation), open; partial, from living donor</td>
</tr>
<tr>
<td>44135</td>
<td>Intestinal allotransplantation; from cadaver donor</td>
</tr>
<tr>
<td>44136</td>
<td>Intestinal allotransplantation; from living donor</td>
</tr>
<tr>
<td>44715</td>
<td>Backbench standard preparation of cadaver or living donor intestine allograft prior to transplantation, including mobilization and fashioning of the superior mesenteric artery and vein</td>
</tr>
<tr>
<td>44720</td>
<td>Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; venous anastomosis, each</td>
</tr>
<tr>
<td>44721</td>
<td>Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; arterial anastomosis, each</td>
</tr>
</tbody>
</table>

V. Rationale

This policy is based on 1995 and 1999 TEC Assessments. The 1995 Assessment concluded that, in children, small bowel transplant was associated with improved survival compared to TPN. (3) This assessment also concluded that, in adults, the outcomes for small bowel transplant were worse than that associated with total parenteral nutrition (TPN). A 1999 TEC Assessment reevaluated the data on adults. The 1999 Assessment specifically focused on the probability of patient and graft survival with small bowel transplant compared to TPN, and whether successful outcome of small bowel transplant improves health outcomes or reduces adverse outcomes. (4) The Assessment offered the following conclusions:
Small bowel transplants in adults produce patient survival rates from 27%–58% at 4 or 5 years. Graft survival rates (and presumably independence from TPN) range from 13%–30%. It is unknown whether these data represent a net benefit to these patients, since some patients may survive for long periods of time on TPN.

It is possible that some patients with increasingly severe TPN-associated complications may face a high probability of impending mortality such that the risk of continued medical management is higher than the risk of transplantation. However, at this point in time, it is not possible to predict which patients will survive longer on TPN versus small bowel transplant.

This policy has been regularly updated with searches of the MEDLINE database. The most recent literature search was for the period from August 2010 thru July 2011. Much of the published literature consists of case series reported by single centers. These reports, as well as reviews of the reports, observe that while outcomes continue to improve, obstacles to long-term survival remain. Recurrent and chronic rejections and complications of immunosuppression are significant issues in bowel transplantation.

The recent literature emphasizes the importance of timely referral for intestinal transplantation to avoid the necessity of combined liver and intestine transplantation. It has been suggested that improvements in survival over the last 10–15 years may justify removing the restriction of intestinal transplantation to patients who have severe complications of TPN. (5) However, as noted by Vianna and colleagues in their report on the status of intestinal transplantation, no randomized trials compare intestinal transplantation to long-term parenteral nutrition, and optimal timing for earlier transplantation has not been established. (6) This review also notes that the currently reported 1-year graft and patient survival rate for intestinal transplantation is 80%.

A 2010 study retrospectively reported on the incidence of fungal infection after pediatric small bowel transplantation among patients treated between 2003 and 2007 at a single center. (7) The average length of follow-up was not reported. A total of 25 of 98 cases reviewed (25.5%) developed at least one episode of fungal infection; Candida infection was most common. During the study period, the mortality rate did not differ significantly between patients who did and did not develop a fungal infection (32.3% vs. 29.8%, respectively; p=0.46), but the authors stressed the importance of better screening tools to identify and prevent fungal infections.

**Living donors**

Cadaveric intestines have been most commonly used, but recently there has been interest in using a portion of intestine harvested from a living, related donor. Potential advantages of a living donor include the ability to plan the transplantation electively and better antigen matching leading to improved management of rejection. Small case reports have been published of 1 or 2 patients with different lengths of the ileum or jejunum. (8-11) While there appear to be minimal complications to the donors, of the 6 cases reported, 5 recipients remain on TPN for at least part of their nutrition. One patient remains healthy and is off TPN.
Benedetti and colleagues reported outcomes from 4 children and 7 adults who underwent 12 living-related small bowel transplantations between 1998 and 2004. (12) All donors were reported to have had uneventful recovery following removal of up to 40% of the small intestine. The 3-year patient survival was 82%, with graft survival of 75%. Longer follow-up from the earlier cases was not reported. Gangemi and Benedetti published a literature review of living donor small bowel transplantation reports from 2003 to 2006; all of the reports listed Benedetti as author. (13) The authors comment that, “Due to the excellent result in modern series of deceased donor bowel transplantation, widespread use of the procedure [living donor] should not be recommended, in consideration of the potential risks to donor. Furthermore, few centers have acquired the necessary experience with the procedure.”

In June 2010, Sudan published a review of current literature on long-term outcomes after intestinal transplantation. (14) In this paper, the author notes that intestinal transplantation has become standard therapy for patients with life-threatening complications from parenteral nutrition therapy. Data from current single-center series indicates a 1-year patient survival rate of 78-85% and a 5+ year survival rate of 56-61%. With respect to pediatric intestinal transplant patients, the majority achieve normal growth velocity at 2 years post-transplant. However, oral aversion is a common problem; tube feedings are necessary in 45% of children. Sudan also reports on parental surveys of quality of life in pediatric transplant patients in which intestinal transplant patients appear to have modestly improved quality of life compared to patients remaining on TPN and slightly worse than matched school-age controls without intestinal disease.

**HIV+ Transplant Recipients**

This subgroup of recipients has long been controversial, due to the long-term prognosis for HIV positivity, and the impact of immunosuppression on HIV disease. Although HIV-positive transplant recipients may be a research interest of some transplant centers, the minimal data regarding long-term outcome in these patients consist primarily of case reports and abstract presentations of liver and kidney recipients. Nevertheless, some transplant surgeons would argue that HIV positivity is no longer an absolute contraindication to transplant due to the advent of highly active antiretroviral therapy (HAART), which has markedly changed the natural history of the disease.

In March 2009, the United Network for Organ Sharing (UNOS) revised its policies on HIV status in recipients. It reiterates an earlier position that:

“A potential candidate for organ transplantation whose test for HIV is positive but who is in an asymptomatic state should not necessarily be excluded from candidacy for organ transplantation, but should be advised that he or she may be at increased risk of morbidity and mortality because of immunosuppressive therapy.” (15)

In 2006, the British HIV Association and the British Transplantation Society Standards Committee published guidelines for kidney transplantation in patients with HIV disease. (16) As described above, these criteria may be extrapolated to other organs.
The guidelines, which are similar to those cited above, recommend that any patient with end-stage organ disease with a life expectancy of at least 5 years is considered appropriate for transplantation under the following conditions:

- CD4 ≥ 200 cells/micro liter for at least 6 months.
- Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least 6 months
- Demonstrable adherence and a stable HAART regimen for at least 6 months
- Absence of AIDS-defining illness following successful immune reconstitution after HAART.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

In response to requests, input was received through 2 physician specialty societies and 2 academic medical centers while this policy was under review for July 2009. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. The consensus of those providing input was that small bowel transplant should be performed in patients who are developing severe TPN-related complications and that small bowel transplant from living donors may be considered when cadaveric intestinal transplants are not available.

Summary

Based on the evidence review and clinical input, small bowel transplant may be considered medically necessary in patients with intestinal failure who are developing severe TPN-related complications, to obviate the subsequent need for a multivisceral transplant. Small bowel transplantation using a living donor may be considered medically necessary only when a cadaveric intestinal transplant is not available. Routine use of living-donor intestinal transplants is considered not medically necessary because the net health outcome associated with this procedure is reduced (compared to cadaveric transplant) because of donor-related morbidity.

Practice Guidelines, and Position Statements

In 2003, the American Gastroenterological Association produced a medical position statement on short bowel syndrome and intestinal transplantation. It recommends dietary, medical, and surgical solutions. Indications for intestinal transplantation mirror those of CMS. The guidelines acknowledge the limitations of transplant for these patients. (17) As of August 2011, an updated guideline has not been published.

Medicare National Coverage

Effective for services performed on or after April 1, 2001, this procedure is covered only when performed for patients who have TPN and only when performed in centers that meet approval criteria. (18)
1. Failed TPN

The TPN delivers nutrients intravenously, avoiding the need for absorption through the small bowel. TPN failure includes the following:

- Impending or overt liver failure due to TPN induced liver injury. The clinical manifestations include elevated serum bilirubin and/or liver enzymes, splenomegaly, thrombocytopenia, gastroesophageal varices, coagulopathy, stomal bleeding or hepatic fibrosis/cirrhosis.
- Thrombosis of the major central venous channels; jugular, subclavian, and femoral veins. Thrombosis of two or more of these vessels is considered a life threatening complication and failure of TPN therapy. The sequelae of central venous thrombosis are lack of access for TPN infusion, fatal sepsis due to infected thrombi, pulmonary embolism, Superior Vena Cava syndrome, or chronic venous insufficiency.
- Frequent line infection and sepsis. The development of two or more episodes of systemic sepsis secondary to line infection per year that requires hospitalization indicates failure of TPN therapy. A single episode of line related fungemia, septic shock and/or Acute Respiratory Distress Syndrome are considered indicators of TPN failure.
- Frequent episodes of severe dehydration despite intravenous fluid supplement in addition to TPN. Under certain medical conditions such as secretory diarrhea and non-constructable gastrointestinal tract, the loss of the gastrointestinal and pancreatobiliary secretions exceeds the maximum intravenous infusion rates that can be tolerated by the cardiopulmonary system. Frequent episodes of dehydration are deleterious to all body organs particularly kidneys and the central nervous system with the development of multiple kidney stones, renal failure, and permanent brain damage.

2. Approved Transplant Facilities

Intestinal transplantation is covered by Medicare if performed in an approved facility. The criteria for approval of centers will be based on a volume of 10 intestinal transplants per year with a 1-year actuarial survival of 65 percent using the Kaplan-Meier technique.

VI. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4),
generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VII. References