Protocol

Isolated Small Bowel Transplant

(70304)

Medical Benefit		**Effective Date**: 01/01/15	**Next Review Date**: 03/21
Preauthorization	Yes	**Review Dates**: 01/10, 01/11, 01/12, 01/13, 01/14, 11/14, 11/15, 11/16, 03/17, 03/18, 03/19, 03/20	

Preauthorization is required and must be obtained through Case Management.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With intestinal failure	Interventions of interest are: • Small bowel transplant	Comparators of interest are: • Medical management • Parenteral nutrition	Relevant outcomes include: • Overall survival • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With failed small bowel transplant without contraindication(s) for retransplant	Interventions of interest are: • Small bowel retransplant	Comparators of interest are: • Medical management • Parenteral nutrition	Relevant outcomes include: • Overall survival • Morbid events • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

A small bowel transplant may be performed as an isolated procedure or in conjunction with other visceral organs, including the liver, duodenum, jejunum, ileum, pancreas, or colon. Isolated small bowel transplant is commonly performed in patients with short bowel syndrome. Small bowel/liver transplants and multivisceral transplants are considered in the Small Bowel/Liver and Multivisceral Transplant Protocol.

SUMMARY OF EVIDENCE

For individuals who have intestinal failure who receive a small bowel transplant, the evidence includes case series. Relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. Small bowel transplant is infrequently performed, and only relatively small case series, generally single-center, are available. Risks after small bowel transplant are high, particularly related to infection, but may be balanced against the need to avoid the long-term complications of total parenteral nutrition dependence. In addition, early small bowel transplant may obviate the need for a later combined liver/small bowel transplant. Transplantation is contraindicated in patients in whom the procedure is expected to be futile due to comorbid disease or in whom posttransplantation care is expected to worsen comorbid conditions significantly. Guidelines and U.S. federal policy no longer view HIV infection as an absolute contraindication for solid organ transplantation. The

evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have failed small bowel transplant without contraindication(s) for retransplant who receive a small bowel retransplant, the evidence includes case series. Relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. Data from a small number of patients undergoing re-transplantation are available. Although limited in quantity, the available data have suggested a reasonably high survival rate after small bowel retransplantation in patients who continue to meet criteria for transplantation. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Based on clinical input, obtained in 2009, 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 with a cadaveric transplant) due to donor-related morbidity.

POLICY

A small bowel transplant using cadaveric intestine may be considered **medically necessary** 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 dependence on total parenteral nutrition (TPN) and are developing or have developed severe complications due to TPN.

A small bowel transplant using a living donor may be considered **medically necessary** 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 retransplant may be considered **medically necessary** after a failed primary small bowel transplant.

A small bowel transplant using living donors is considered **not medically necessary** in all other situations.

A small bowel transplant is considered **investigational** for adult and pediatric patients with intestinal failure who can tolerate TPN.

POLICY GUIDELINES

GENERAL CRITERIA

Individual transplant facilities may have their own additional requirements or protocols that must be met in order for the patient to be eligible for a transplant at their facility.

Potential contraindications for solid organ transplant are subject to the judgment of the transplant center include the following:

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 CRITERIA

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. 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 greater than three 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.

MEDICARE ADVANTAGE

If a transplant is needed, we arrange to have the Medicare-approved transplant center review and decide whether the patient is an appropriate candidate for the transplant.

BACKGROUND

SMALL BOWEL SYNDROME

Short bowel syndrome 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 the small intestine. In adults, etiologies of short bowel syndrome include ischemia, trauma, volvulus, and tumors. In children, gastroschisis, volvulus, necrotizing enterocolitis, and congenital atresia are predominant causes.

Treatment

The small intestine, particularly the ileum, can adapt to some functions of the diseased or removed portion over a period of one to two years. Prognosis for recovery depends on the degree and location of small intestine damage. Therapy focuses on achieving adequate macro- and micronutrient 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. Patients with complications from total parenteral nutrition may be considered candidates for a 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 a recent interest in using living donors.

Intestinal transplants (including multivisceral and bowel/liver) represent a small minority of all solid organ transplants. In 2016, 147 intestinal transplants were performed in the U.S.; all were from cadaver donors.[1]

REGULATORY STATUS

Small bowel transplantation is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration.

The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation Title 21, parts 1270 and 1271. Small bowel transplants are included in these regulations.

RELATED PROTOCOL

Small Bowel/Liver and Multivisceral Transplant

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. U.S. Department of Health and Human Services (DHHS). Organ Procurement and Transplantation Network National Data. 2018; https://optn.transplant.hrsa.gov/data/. Accessed August 29, 2019.
2. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Small bowel transplant. TEC Assessments. 1995;Volume 10:Tab 27.
3. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Small bowel transplants in adults and multivisceral transplants. TEC Assessments. 1999;Volume 14:Tab 9.
4. Ueno T, Wada M, Hoshino K, et al. Impact of intestinal transplantation for intestinal failure in Japan. Transplant Proc. Jul-Aug 2014;46(6):2122-2124. PMID 25131121.
5. Benedetti E, Holterman M, Asolati M, et al. Living related segmental bowel transplantation: from experimental to standardized procedure. Ann Surg. Nov 2006;244(5):694-699. PMID 17060761.
6. Sudan D. Long-term outcomes and quality of life after intestine transplantation. Curr Opin Organ Transplant. Jun 2010;15(3):357-360. PMID 20445450.
7. Lacaille F, Irtan S, Dupic L, et al. Twenty-eight years of intestinal transplantation in Paris: experience of the oldest European center. Transpl Int. Feb 2017;30(2):178-186. PMID 27889929.
8. Dore M, Junco PT, Andres AM, et al. Surgical rehabilitation techniques in children with poor prognosis short bowel syndrome. Eur J Pediatr Surg. Feb 2016;26(1):112-116. PMID 26535775.
9. Rutter CS, Amin I, Russell NK, et al. Adult intestinal and multivisceral transplantation: experience from a single center in the United Kingdom. Transplant Proc. Mar 2016;48(2):468-472. PMID 27109980.
10. Lauro A, Zanfi C, Dazzi A, et al. Disease-related intestinal transplant in adults: results from a single center. Transplant Proc. Jan-Feb 2014;46(1):245-248. PMID 24507060.

11. Garcia Aroz S, Tzvetanov I, Hetterman EA, et al. Long-term outcomes of living-related small intestinal transplantation in children: A single-center experience. Pediatr Transplant. Jun 2017;21(4). PMID 28295952.
12. Matarese LE, Costa G, Bond G, et al. Therapeutic efficacy of intestinal and multivisceral transplantation: survival and nutrition outcome. Nutr Clin Pract. Oct 2007;22(5):474-481. PMID 17906271.
13. Vianna RM, Mangus RS, Tector AJ. Current status of small bowel and multivisceral transplantation. Adv Surg. Oct 2008;42:129-150. PMID 18953814.
14. Wu GS, Cruz RJ, Jr., Cai JC. Acute antibody-mediated rejection after intestinal transplantation. World J Transplant. Dec 24 2016;6(4):719-728. PMID 28058223.
15. Florescu DF, Qiu F, Langnas AN, et al. Bloodstream infections during the first year after pediatric small bowel transplantation. Pediatr Infect Dis J. Jul 2012;31(7):700-704. PMID 22466325.
16. Florescu DF, Langnas AN, Grant W, et al. Incidence, risk factors, and outcomes associated with cytomegalovirus disease in small bowel transplant recipients. Pediatr Transplant. May 2012;16(3):294-301. PMID 22212495.
17. Florescu DF, Islam KM, Grant W, et al. Incidence and outcome of fungal infections in pediatric small bowel transplant recipients. Transpl Infect Dis. Dec 2010;12(6):497-504. PMID 20626710.
18. Calvo Pulido J, Jimenez Romero C, Morales Ruiz E, et al. Renal failure associated with intestinal transplantation: our experience in Spain. Transplant Proc. Jul-Aug 2014;46(6):2140-2142. PMID 25131125.
19. Boyer O, Noto C, De Serre NP, et al. Renal function and histology in children after small bowel transplantation. Pediatr Transplant. Feb 2013;17(1):65-72. PMID 22882667.
20. Fujimoto Y, Uemoto S, Inomata Y, et al. Living-related small bowel transplant: management of rejection and infection. Transplant Proc. Feb 1998;30(1):149. PMID 9474986.
21. Gruessner RW, Sharp HL. Living-related intestinal transplantation: first report of a standardized surgical technique. Transplantation. Dec 15 1997;64(11):1605-1607. PMID 9415566.
22. Jaffe BM, Beck R, Flint L, et al. Living-related small bowel transplantation in adults: a report of two patients. Transplant Proc. May 1997;29(3):1851-1852. PMID 9142299.
23. Tesi R, Beck R, Lambiase L, et al. Living-related small-bowel transplantation: donor evaluation and outcome. Transplant Proc. Feb-Mar 1997;29(1-2):686-687. PMID 9123480.
24. Colfax G. HIV Organ Policy Equity (HOPE) Act Is Now Law. 2013; https://obamawhitehouse.archives.gov/blog/2013/11/21/hiv-organ-policy-equity-hope-act-now-law. Accessed August 29, 2019.
25. United Network for Organ Sharing (UNOS). OPTN policies, procedures implemented to support HOPE Act. 2015; http://www.unos.org/optn-policies-procedures-implemented-to-support-hope-act/. Accessed August 29, 2019.
26. Organ Procurement and Transplantation Network (OPTN). Organ Procurement and Transplantation Network Policies. 2018; https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf. Accessed August 29, 2019.
27. Working Party of the British Transplantation Society. Kidney and Pancreas Transplantation in Patients with HIV. Second Edition (Revised). British Transplantation Society Guidelines Macclesfield, UK: British Transplantation Society; 2017.
28. Desai CS, Khan KM, Gruessner AC, et al. Intestinal retransplantation: analysis of Organ Procurement and Transplantation Network database. Transplantation. Jan 15 2012;93(1):120-125. PMID 22113492.
29. Abu-Elmagd KM, Costa G, Bond GJ, et al. Five hundred intestinal and multivisceral transplantations at a single center: major advances with new challenges. Ann Surg. Oct 2009;250(4):567-581. PMID 19730240.
30. American Gastroenterological Association. American Gastroenterological Association medical position statement: short bowel syndrome and intestinal transplantation. Gastroenterology. Apr 2003;124(4):1105-1110. PMID 12671903.
31. Kaufman SS, Atkinson JB, Bianchi A, et al. Indications for pediatric intestinal transplantation: a position paper of the American Society of Transplantation. Pediatr Transplant. Apr 2001;5(2):80-87. PMID 11328544.

32. Centers for Medicare and Medicaid Services. National Coverage Determination for Intestinal and Multi-visceral Transplantation (260.5). 2006; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=280&ncdver=2&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=intestinal+transplantation&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAACAAAAAAAA%3d %3d&. Accessed August 29, 2019.