

Medical Policy Manual

Topic: Isolated Small Bowel Transplant

Date of Origin: January 1996

Section: Transplant

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Policy No: 9

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Intestinal failure is a serious medical condition which 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.^[1] Short bowel syndrome, one type of intestinal failure, 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. Etiologies of short bowel syndrome include: volvulus, atresias, necrotizing enterocolitis, gastroschisis, desmoid tumors, and trauma. Patients with short bowel syndrome are unable to obtain adequate nutrition from enteral feeding and become dependent upon total parenteral nutrition (TPN). Patients with complications from TPN, such as catheter-related mechanical problems, infections, hepatobiliary disease, and metabolic bone disease, may be considered candidates for small bowel transplant.

Intestinal transplants, including multivisceral and bowel/liver, represent a small minority of all solid organ transplants. In 2011 and 2012, 129 and 106 intestinal transplants, respectively, were performed in the United States, of which all but one was from deceased donors.^[2] While cadaveric intestinal

transplant is the most commonly performed transplant, there has been more recent interest in using living related donors. Potential advantages of a living donor include the ability to plan the transplant electively and better antigen matching, leading to improved management of rejection.

Note: 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 (see cross-reference list below).

POLICY/CRITERIA

I. Candidates for all types of small bowel transplant must meet all of the following criteria:

- A. Adequate cardiopulmonary status
- B. Documentation of patient compliance with medical management

II. Cadaveric Donor

A small bowel transplant using a 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 dependency on total parenteral nutrition (TPN) and are developing or have developed one or more of the following severe complications due to TPN:

- A. TPN intolerance to the point that multiple and prolonged hospitalizations are required to treat TPN-related complications
- B. The development of progressive but reversible liver failure
- C. Inability to maintain venous access

III. Living Donor

- A. 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 transplant (I-II).
- B. A small bowel transplant using living donors is considered **not medically necessary** in all other situations.

IV. A small bowel transplant is considered **not medically necessary** for adults with intestinal failure who are able to tolerate TPN.

SCIENTIFIC EVIDENCE

Ideally, for intestinal transplant to be considered as a replacement for total parenteral nutrition (TPN),

head-to-head comparisons of transplantation versus TPN are needed, preferably in well-designed randomized controlled trials (RCTs). Further, for chronic conditions such as intestinal failure, comparative trials with long-term follow-up are necessary in order to determine the durability of any beneficial treatment effects, and to establish guidelines regarding the timing of intestinal transplant. In order to establish the net benefit of using living donors versus cadaveric intestinal transplant for treatment of intestinal failure, clinical trials that compare these therapies are needed, and the impacts on health outcomes for both the donors and recipients must be considered.

Literature Appraisal

The current literature on small bowel transplantation included the following general observations:

- The importance of timely referral for intestinal transplantation was emphasized to avoid the necessity of combined liver and intestine transplantation.
- 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.
- 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.^[3] 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.^[4]

Technology Assessments and Systematic Reviews

This policy was initially based on 1995 and 1999 BlueCross BlueShield Association Technology Evaluation Center (TEC) assessments.^[5,6]

- The 1995 assessment concluded that in children, small bowel transplant was associated with improved survival compared to TPN. This assessment also concluded that in adults, the outcomes for small bowel transplant were worse than those associated with TPN.
- The 1999 TEC assessment reevaluated the data on adults, specifically focusing on the probability of adult 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.^[6] 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 this represents 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.
- In 2010, Sudan published a review of current literature on long-term outcomes after intestinal transplantation.^[7] The author noted that intestinal transplantation has become standard therapy for patients with life-threatening complications from parenteral nutrition therapy. Data from current single-center series indicate 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 noted that parental surveys of quality of life in pediatric transplant patients have shown that 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.

Randomized Controlled Trials (RCTs)

No RCTs were identified that compared intestinal transplantation with ongoing parenteral nutrition with or without subsequent small bowel/liver or multivisceral transplantation.

Non-randomized Trials

Despite the lack of RCTs, isolated small bowel transplantation has become an accepted alternative to continued total parenteral nutrition (TPN) to avoid the need for multivisceral transplantation in carefully selected patients with intestinal failure who are developing severe complications related to total parenteral nutrition (TPN).

The following is a summary of non-randomized trials that are representative of the available data on small bowel transplantation from living donors and post-transplantation complications.

Living Donor

- The literature related to living-related intestinal transplant consists of small case reports of 1 to 11 patients in which different lengths of the ileum or jejunum were used.^[8-15] While there appeared to be minimal complications to the donors, of the cases reported, a significant number of recipients remained on TPN for at least part of their nutrition while others remain healthy and off TPN.
- Benedetti et al reported outcomes from 4 children and 7 adults who underwent 12 living-related small bowel transplantations between 1998 and 2004.^[16] 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.^[17] The authors commented 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.”

Complications

- Florescu and colleagues have published the following articles retrospectively reviewing complications in a cohort of 98 pediatric patients. Twenty-one of these children (21.4%) had an isolated small bowel transplant; the remainder had combined transplants.
 - 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.^[18] The average length of follow-up was not reported. A total of 25 of 98 cases reviewed (26%) 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), but the authors stressed the importance of better screening tools to identify and prevent fungal infections.

- A 2012 study reported that 68 of the 98 patients (69%) developed at least one episode of bloodstream infection.^[19] Among the patients with an isolated small bowel transplant, the median time to infection for those who became infected was 4.5 months (95% confidence interval [CI]: 2.4 to 6.7 months).
- Also in 2012, the researchers reported that 7 of 98 patients (7%) developed cytomegalovirus (CMV) disease; only one of these had an isolated small bowel transplant.^[20]
- As noted previously, Sudan reported oral aversion to be a common problem in pediatric patients with tube feedings necessary in 45% of children following small bowel transplantation.^[7]
- In 2013, Boyer et al. reported that 7 of 12 children who had an isolated small bowel transplant had renal function complications at some point after surgery.^[21] Prior to treatment, all of the patients had normal renal functioning.

HIV Positive 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 outcomes 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.

The most recent recommendations from the United Network for Organ Sharing (UNOS) agree that HIV status is no longer an absolute contraindication, stating, “A potential candidate for organ transplantation whose test for HIV is positive should not be excluded from candidacy for organ transplantation unless there is a documented contraindication to transplantation based on local policy.”^[22]

Clinical Practice Guidelines

American Gastroenterological Association (AGA)

The AGA issued a medical position statement on short bowel syndrome and intestinal transplantation citing that intestinal transplants have only been performed in patients with life-threatening complications attributable to their intestinal failure and long-term TPN therapy and that standards of care for this type of transplantation are still evolving.^[23]

Summary

- There is sufficient evidence to determine that small bowel transplant may be considered medically necessary to avoid the need for multivisceral (i.e., small bowel combined with liver and/or other gastrointestinal organ) transplantation in select patients with intestinal failure who are developing severe complications related to total parenteral nutrition (TPN).

- Small bowel transplantation using a living donor may be considered medically necessary only when a cadaver 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 due to donor-related morbidity.
- A small bowel transplant is considered not medically necessary for adults with intestinal failure who are able to tolerate intravenous total parenteral nutrition (TPN). Transplantation has a significantly higher risk for severe adverse events compared with TPN, including but not limited to surgery-related risks, possible organ rejection, and the need for life-long immune system suppression.

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CROSS REFERENCES

[Small Bowel/Liver and Multivisceral Transplant](#), Transplant, Policy No. 18

CODES	NUMBER	DESCRIPTION
CPT	44132	Donor enterectomy (including cold preservation), open; from cadaver donor
	44133	Donor enterectomy (including cold preservation), open partial, from living donor
	44135	Intestinal allotransplantation; from cadaver donor
	44136	Intestinal allotransplantation; from living donor
	44715	Backbench standard preparation of cadaver or living donor intestine allograft prior to transplantation, including mobilization and fashioning of the superior mesenteric artery and vein
	44720	Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; venous anastomosis, each
	44721	Backbench reconstruction of cadaver or living donor intestine allograft prior to

		transplantation; arterial anastomosis, each
HCPCS	None	