

Medical Policy Manual

Topic: Small Bowel/Liver and Multivisceral Transplant

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Section: Transplant

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Policy No: 18

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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

Small bowel/liver transplantation is transplantation of an intestinal allograft in combination with a liver allograft, either alone or in combination with one or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, or colon. Small bowel transplants are typically performed in patients with intestinal failure due to functional disorders (e.g., impaired motility) or short bowel syndrome, defined as an inadequate absorbing surface of the small intestine due to extensive disease or surgical removal of a large portion of small intestine. In some instances, short bowel syndrome is associated with liver failure, often due to the long-term complications of total parenteral nutrition (TPN). These patients may be candidates for a small bowel/liver transplant or a multivisceral transplant, which includes the small bowel and liver with one or more of the following organs: stomach, duodenum, jejunum, ileum, pancreas, and/or colon. A multivisceral transplant is indicated when anatomic or other medical problems preclude a small bowel/liver transplant, and the patient requires removal of all of the native gastrointestinal tract and replacement with a multivisceral graft.

Note: Isolated small bowel transplants are considered separately in Transplant Policy No. 9.

MEDICAL POLICY CRITERIA

- I. Candidates for all types of small bowel/liver or multivisceral transplant must meet all of the

following criteria:

- A. Adequate cardiopulmonary status
 - B. Documentation of patient compliance with medical management
- II. A small bowel/liver transplant or multivisceral transplant may be considered **medically necessary** for pediatric and adult patients with intestinal failure (characterized by loss of absorption and the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance), who have been managed with long-term TPN and who have developed evidence of impending end-stage liver failure.

SCIENTIFIC EVIDENCE

Literature Appraisal

Much of the published literature consists of case series reported by single centers. Authors of these reports as well as reviews observe that, while outcomes continue to improve, recurrent and chronic rejection and complications of immunosuppression continue to be obstacles to long term survival.

Technology Assessments

The BlueCross BlueShield Association (BCBSA) Technology Evaluation Center (TEC) published two technology assessments on small bowel transplantation, one in 1994 followed by an update in 1999.^[1,2] The 1999 TEC assessment, which focused on multivisceral transplantation, offered the following conclusion:^[2]

Multivisceral transplantation in patients with small bowel syndrome, liver failure, and/or other gastrointestinal problems such as pancreatic failure, thromboses of the celiac axis and the superior mesenteric artery, or pseudo-obstruction affecting the entire gastrointestinal tract is associated with poor patient survival and graft survival. Pediatric and adult patients have a similar 2- and 5-year survival of 33%-50%. However, without this procedure, it is expected that these patients would face 100% mortality.

Registry Data

The most recent published report from the international Intestinal Transplant Registry reported on 989 transplants in 923 patients from 61 transplant programs in 19 countries.^[3] Participation in this registry was considered to be 100% of all intestinal transplants performed in the world since April 1985. Of the 61 known transplant programs worldwide, 28 had performed a transplant within the past two years. The majority of cases (83%) were performed by ten centers, and 75.5% of these transplants were performed in the United States. Recipients were 61% children or teenagers, and the most common indication for transplantation was short-gut syndrome. The following results were reported:

- One-year graft/patient survival for transplants performed after February 1995 was 65%/77% for small bowel grafts, 59%/60% for small bowel and liver grafts, and 61%/66% for multivisceral grafts.
- There was no significant difference in graft/patient survival rates for cadaveric grafts versus living donor grafts.

- Of the 406 patients alive for more than six months, 328 (81%) were off total parenteral nutrition (TPN), 16 (3.9%) required IV fluids, 26 (6.4%) required partial TPN, and 32 (7.9%) were on TPN.
- The report noted that transplant programs that had performed at least 10 transplants had a significantly higher graft survival rate than those with less experience.
- Other variables that significantly effected survival were transplants performed in patients waiting at home versus waiting in hospital, antibody induction immunosuppression with monoclonal IL- α 2 receptor blockers or polyclonal antilymphocyte agents, and age as a continuous variable when included with age squared.
- Factors that did not reach significance in the survival analyses included primary diagnosis, recipient gender, donor type, transplant type, retransplantation, portal venous drainage, and donor-graft irradiation.

The report concluded that transplantation has become the definitive treatment for patients with chronic intestinal failure who cannot be maintained on total parenteral nutrition, and those who require abdominal evisceration in order to achieve complete removal of locally aggressive tumors.

Non-Randomized Trials

Survival Outcomes

The following studies from investigators at the University of Pittsburg are representative of the current published literature:

- Nayyar and colleagues report improvements in 5-year actuarial patient and graft survival after liver/small bowel transplant since the use of rATG induction began to be used in their pediatric center in 2002 (81% vs. 58% and 76% vs. 52%, respectively).^[4] In addition to innovations in immunosuppressive therapy, the authors cited new approaches to management of short gut syndrome including hypoallergenic formulas and modification of enteral nutrition to prevent total parenteral nutrition-induced cholestasis. The authors noted that better understanding of the protective role of the liver in preventing chronic rejection of the small bowel allograft could improve long-term survival after isolated small bowel transplantation.
- Abu-Elmagd et al., reporting on experience with 500 intestinal and multivisceral transplantations, also found that the best outcomes in their series were in the intestine-liver allografts reporting 1-and 5-year patient survival of 92% and 70%, respectively.^[5]
- Long-term survival data were reported on 227 visceral allograft recipients who survived beyond the 5-year milestone. At a mean follow-up of 10 ± 4 years, 92 adults and 85 children were alive, with 118 (67%) of recipients 18 years or older.^[6] The most significant risk factors were nonfunctional social support and non-inclusion of the liver in the visceral allograft. Nutritional autonomy was achieved in 160 (90%) survivors. Most achieved self-sustained socioeconomic status with reintegration into society despite coexistence or development of neuropsychiatric disorders. Morbidities with potential impact on global health included dysmotility (59%), hypertension (37%), osteoporosis (22%), and diabetes (11%).

Adverse Effects

- A 2011 article focused on complications after small bowel and multivisceral transplantation. Wu and colleagues reported on 241 patients who underwent intestinal transplantation.^[7] Of these, 147 (61%) had multivisceral transplants, 65 (27%) had small bowel transplants and 12% had small bowel/liver transplants. There were 151 children (63%) and 90 adults. A total of 22 patients (9%) developed

graft-versus-host disease (GVHD). Children younger than 5 years-old were more likely to develop GVHD; the incidence in this age group was 16 of 121 (13.2%) compared to 2 of 30 (6.7%) in children between 5 and 18 years and 9 of 90 (4.4%) in adults over 18 years. Among diseases, patients with intestinal atresia were more likely to develop GVHD than those with other conditions (22.2% vs. 2.6%, respectively; $p=0.03$).

- A 2012 retrospective review reported on bloodstream infections among 98 children younger than age 18 years with small bowel/combined organ transplants.^[8] Seventy-seven (79%) patients underwent small bowel transplant in combination with a liver, kidney, or kidney-pancreas, and 21 had an isolated small bowel transplant. After a median follow-up of 52 months, 58 (59%) patients remained alive. The 1-year survival rate was similar in patients with combined small bowel transplant (75%) and those with isolated small bowel transplant (81%). In the first year after transplantation, 68 patients (69.4%) experienced at least one episode of bloodstream infection. The 1-year survival rate for patients with bloodstream infections was 72% compared to 87% in patients without bloodstream infections (p -value= 0.056 for difference in survival in patients with and without bloodstream infections).
- Another 2012 retrospective review focused on the rate of kidney dysfunction, a recognized complication after non-renal solid organ transplantation, in 33 multivisceral and 15 isolated small bowel transplant patients.^[9] A significant decline in kidney function was reported in 46% of patients at one year following transplantation. A significant correlation was found for patient age, pretransplant sCr, estimated GFR (eGFR) at post-transplant day 30, 90, 180, and 270, and tacrolimus live at post-transplant day 7. Lesser decline was found in pediatric patients and patients with multivisceral transplantation compared with adults or isolated small bowel transplantation.

Transplant Recipients with Malignancies

Cruz and colleagues published results from a small case series ($n=10$) of patients with intra-abdominal desmoid tumors secondary to familial adenomatous polyposis who underwent multivisceral transplant.^[10] All patients were able to discontinue home parenteral nutrition by an average 30 days after transplant. Estimated survival was 80% at 5 years and desmoid tumors reoccurred in 1 patient 15 months after transplantation. However, conclusions from this study are limited by the small sample size and the lack of a comparison group, factors which do not allow for the isolation of transplant as a causative factor in patient health outcomes.

HIV Positive Transplant Recipients

The subgroup of HIV positive transplant recipients has been controversial due to the long term prognosis for HIV positivity, the impact of immunosuppression on HIV disease, and the interactions of immunosuppressive therapy 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.”^[11] In 2001, the Clinical Practice Committee of the American Society of Transplantation proposed that the presence of AIDS could be considered a

contraindication to kidney transplant unless the following criteria were present.^[12] These criteria may be extrapolated to other organs:

- CD4 count >200 cells/mm³ for >6 months
- HIV-1 RNA undetectable
- On stable anti-retroviral therapy >3 months
- No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioides mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm)
- Meeting all other criteria for transplantation

Summary

Evidence for small bowel/liver and multivisceral transplant consists of case series and, though infrequently performed, the procedures are demonstrated to provide a survival benefit; therefore the procedure may be considered medically necessary for patients who have been managed with long-term total parenteral nutrition (TPN) and who have developed evidence of impending end-stage liver failure.

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CROSS REFERENCES

[Liver Transplant](#), Transplant, Policy No. 5

[Isolated Small Bowel Transplant](#), Transplant, Policy No. 9

CODES	NUMBER	DESCRIPTION
CPT	43999	Unlisted procedure, stomach
	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
	44799	Unlisted procedure, intestine
	47133	Donor hepatectomy, (including cold preservation) from cadaver donor
	47135	Liver allotransplantation; orthotopic, partial or whole, from cadaver or living donor, any age
	47136	Liver allotransplantation; heterotopic, partial or whole, cadaver or living donor, any age
	47140	Donor hepatectomy (including cold preservation), from living donor; left lateral segment only (segments II and III)

CODES	NUMBER	DESCRIPTION
	47141	total left lobectomy (segments II, III and IV)
	47142	total right lobectomy (segments V, VI, VII and VIII)
	47143	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; without trisegment or lobe split
	47144	with trisegment split of whole liver graft into 2 partial liver grafts (ie, left lateral segment [segments II and III] and right trisegment [segments I and IV through VIII])
	47145	with lobe split of whole liver graft into 2 partial liver grafts (ie, left lobe [segments II, III, and IV] and right lobe [segments I and V through VIII])
	47146	Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; venous anastomosis, each
	47147	Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; arterial anastomosis, each
	48550	Donor pancreatectomy (including cold preservation), with or without duodenal segment for transplantation
	48551	Backbench standard preparation of cadaver donor pancreas allograft prior to transplantation, including dissection of allograft from surrounding soft tissues, splenectomy, duodenotomy, ligation of bile duct, ligation of mesenteric vessels, and Y-graft arterial anastomoses from iliac artery to superior mesenteric artery and to splenic artery
	48552	Backbench reconstruction of cadaver donor pancreas allograft prior to transplantation, venous anastomosis, each
	48554	Transplantation of pancreatic allograft
	48999	Unlisted procedure, pancreas
HCPCS	S2053	Transplantation of small intestine, and liver allografts
	S2054	Transplantation of multivisceral organs
	S2055	Harvesting of donor multivisceral organs, with preparation and maintenance of allografts; from cadaver donor
	S2152	Solid organ(s), complete or segmental, single organ or combination of

CODES	NUMBER	DESCRIPTION
		organs; deceased or living donor(s), procurement, transplantation, and related complications; including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services, and the number of days of pre and posttransplant care in the global definition