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ORIGINAL PAPER

Short Bowel Syndrome: Parenteral Nutrition Versus Intestinal Transplantation. Where Are We Today?

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Abstract Current management of short bowel syndrome (SBS) revolves around the use of home TPN (HPN). Complications include liver disease, catheter-related infections or occlusions, venous thrombosis, and bone disease. Patient survival with SBS on TPN is 86% and 75% at 2 and 5 years, respectively. Surgical management of SBS includes non-transplant surgeries such as serial transverse enteroplasty and reanastomosis. Small bowel transplant has become increasingly popular for management of SBS and is usually indicated when TPN cannot be continued. Posttransplant complications include graft-versus-host reaction, infections in an immunocompromised patient, vascular and biliary diseases, and recurrence of the original disease. Following intestinal-only transplants, patient and graft survival rate is 77% and 66% after 1 year. After 5 years the survival figures are 49% and 34%, respectively. Future improvements in survival and quality of life will enhance small bowel transplant as a viable treatment option for patients with SBS.

Keywords Parenteral nutrition · Small intestine · Transplantation · Short bowel syndrome

Introduction

Estimating the length of small intestine in an individual patient remains difficult. The average length of the adult human small intestine has been calculated as approximately 600 cm from studies performed on cadavers. According to Lennard-Jones and Weser this figure ranges from 260 to 800 cm [1, 2]. This length may vary depending on whether radiologic, surgical, or autopsy measurements are made [3–7]. Any disease which leaves less than 200 cm of viable small bowel places the patient at risk for developing short bowel syndrome (SBS). This is an approximate length, as most methods of residual intestine measurement (such as radiologic contrast studies, pathology of the resected specimen, and perioperative measurement of unweighted intestine) are not especially accurate [3–7].

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Short bowel syndrome

SBS is a disorder of malabsorption, diarrhea, fluid and electrolyte disturbances, and malnutrition secondary to functional or anatomic loss of extensive segments of small intestine such that the absorptive capacity is severely compromised (Table 1). SBS may be a congenital or acquired condition. Infants born with intestinal atresia constitute the congenital forms. Otherwise, SBS results from surgical resection of bowel. This is usually related to recurrent Crohn's disease, massive enterectomy made because of a catastrophic vascular event such as a mesenteric arterial embolism or venous thrombosis, volvulus, trauma, or tumor resection in adults. In children small bowel resection is often performed for gastroschisis, necrotizing enterocolitis, intestinal atresias, and extensive aganglionosis. Functional SBS may also occur in cases of severe malabsorption where the bowel length is often intact. Such conditions may include chronic intestinal pseudo-obstruction syndrome, refractory sprue, radiation enteritis, and congenital villus atrophy [8–10]. Important cofactors that help to determine whether or not SBS will develop following small bowel resection include the premorbid

Table 1 Etiologies of short bowel syndrome

Congenital
Intestinal atresia
Acquired
Surgical resection of bowel
Recurrent Crohn's disease
Massive enterectomy secondary to a catastrophic vascular event such as a mesenteric arterial embolism or venous thrombosis, volvulus, trauma, or tumor resection
Gastroschisis
Necrotizing enterocolitis
Intestinal atresias
Extensive aganglionosis
Chronic intestinal pseudo-obstruction syndrome
Refractory sprue
Radiation enteritis
Congenital villous atrophy

length of small bowel, the segment of intestine that is lost, the age of the patient at the time of bowel loss, the remaining length of small bowel and colon, and the presence or absence of the ileocecal valve [5, 8, 11, 12].

Estimates of the incidence and prevalence of SBS are difficult to make. One report from the United Kingdom, published by Lennard-Jones in 1990, estimated that the incidence of SBS requiring parenteral nutrition (PN) in the United Kingdom was two patients per million in the population [2, 13]. A European survey, in 1997, indicated the incidence of home PN (HPN), for which SBS was the most prevalent indication, had a prevalence of just over four per million [14]. In comparison, the most recent data for incidence and prevalence of SBS in the United States are from 1992. At that time it was estimated, based on extrapolated data from the Oley Foundation Home Parenteral Nutrition Registry, that approximately 40,000 patients required PN each year [15]. Approximately 26% of the patients in the Oley registry had SBS, although some patients with a primary PN indication of malignancy or radiation enteritis may have had SBS as well. Byrne and her colleagues, in 1995, also have reported that approximately 10,000–20,000 patients are currently receiving HPN for SBS in the United States [11]. These numbers for Europe and the United States do not reflect patients with SBS who never required PN or for whom PN could be initiated successfully. Approximately 50% to 70% of short bowel patients who initially require PN can be weaned off PN successfully in optimal settings [12, 16]. Therefore, the number of patients with SBS may be substantially greater than previously estimated.

The length of remaining small bowel necessary to prevent dependence on PN is approximately 100 cm in the absence of an intact and functional colon or 60 cm in the presence of a completely functional colon [12, 17, 18]. The degree of intestinal adaptation that occurs and the ultimate PN dependence is highly individualized. The intestine adapts to ensure more efficient absorption. Villus diameter and height increase, in addition to some slight lengthening of the small bowel, which effectively increases the absorptive surface [19–22]. This process may evolve over years [12, 17, 23]. A major factor that might affect the absorption and nutrient assimilation in these types of patients is bacterial overgrowth, which is often secondary to ileocecal valve resection and intestinal denervation following surgery [18, 24, 25]. Intestinal motility might also affect a patient's ability to tolerate enteral nutrition after a small bowel resection.

Despite many recent advances, limitations exist in the medical and surgical management of patients with SBS. Most available data on the treatment of SBS are based on retrospective analyses of case series and are few in number [8, 11, 12, 26, 27].

SBS is associated with many short- and long-term complications. Some of these complications are preventable. Other complications may result in life-threatening episodes (Table 2).

Medical therapy of short bowel syndrome

The most important aspects of the medical management of the patient with SBS are to provide adequate nutrition, including both macro- and micronutrients, to provide sufficient fluid, and to correct and prevent acid-based disturbances [28, 29]. Although PN has been a life-sustaining therapy, it is associated with substantial risk.

Home parenteral nutrition and short bowel syndrome

In the 1960s, investigators at the University of Pennsylvania combined central venous access with newly developed nutrient solutions, and the modern era of PN was born [30]. The first patient was discharged on HPN by Shils *et al.* in the late 1960s [31]. The following decade, HPN treatment for severe intestinal failure, mostly secondary to SBS, was available only at a few large medical institutions [32]. Once reports from these institutions showed that HPN produced good rehabilitation with low complication rates [33–39] and once Medicare established a payment mechanism [40], followed by other third-party payers, the use of HPN in the United States expanded rapidly [41].

Table 2 Long-term complications of short bowel syndrome

Liver and biliary complications
Nutrient deficiencies
Fluid and electrolyte disturbances
Bacterial overgrowth
Hyperoxaluria
D-Lactic acidosis

Outcomes studies of patients on HPN are usually retrospective in nature. Therefore, we have an incomplete understanding of 1-year and long-term outcomes of patients on HPN. In cancer patients receiving HPN at 1 year, 70% have expired, almost all (99%) from progression of their malignant disease. In Crohn's disease, the majority of patients at 1 year have returned to full oral nutrition, 25% continue on HPN, and just 4% have died from their primary disease. This picture is similar in both the United States [42] and Europe [14]. Studies in France [10] found that 75% of adults with nonmalignant SBS (<150 cm of small intestine) eventually achieved HPN independence, mostly in their first 2 years. After this time, 94% of adults still on HPN are dependent indefinitely. Children can achieve full bowel adaptation after much longer periods (5–10 years) of HPN dependency [43]. All this indicates that long-term users of HPN are only 15% to 20% of those initially started. This translates to an estimated 6000–8000 truly long-term HPN patients in the United States. Many of these individuals have now lived on HPN for more then 10 years and a few are reaching 30 years on therapy [15]. Studies of these long-term survivors reveal a high percentage of short bowel Crohn's patients (70%) [44]. A long-term user accrues a 10% to 15% yearly chance of dying from a therapy complication both in the United States [45] and in Europe [37, 46, 47]. HPN is life-saving compared to no therapy for patients with irreversible gastrointestinal tract failure and randomized evaluation of its effectiveness would be ethically difficult.

Long-term complications of home parenteral nutrition

The use of HPN is associated with many potential serious medical complications. These complications may affect clinicians' ability to deliver HPN to their patients [28] (Table 3).

Liver complications

Several hepatic abnormalities have been observed in adults receiving PN [48], including biochemical (elevated serum aminotransferases and alkaline phosphatase) and histological (steatosis, steatohepatitis, lipidosis and phospholipidosis, cholestasis, fibrosis, and cirrhosis) alterations. Although these abnormalities are usually benign and transient, a small subset of patients develops more serious and progressive disease. Most of the former complications occur within 4 weeks of starting PN, whereas the more serious complications occur later, usually after 16 weeks of therapy. Hepatic complications occur more frequently and are more severe in infants than in adults [49–54].

Table 3 Long-term complications of home parenteral nutrition

Liver and biliary complications
Catheter-related infections
Catheter occlusion
Other complications
Metabolic bone disease including osteomalacia and osteopenia
Renal dysfunction
Memory deficit
Neurological problems

Patients with the shortest residual small intestine are at greatest risk for development of eventual end-stage liver disease (ESLD), which is a major indication for combined liver/intestine transplantation [49–51]. Liver disease associated with long-term PN is most likely caused by malabsorption or insufficient production of the nutrient required for normal hepatic function, rather than a toxic effect of PN [55–57]. Cholestatic liver disease is more common in patients with SBS than in many other patients on PN, indicating that factors unique to SBS must be important. The degree and severity of the liver disease appear to be related in part to recurrent sepsis including catheter sepsis, bacterial translocation from overgrowth in the small intestine, and cholangitis. Recent data have suggested that choline deficiency may be responsible for the steatohepatitis associated with PN [57].

One paper from the United States reported that 15% of patients receiving PN for more than 1 year will develop ESLD, which is associated with 100% mortality within 2 years of onset [58]. Another recent report from France [54] suggested that more than 50% of adult patients on PN for >5 years will develop complicated liver disease such as severe fibrosis (grade 2), cirrhosis, or one of the following: bilirubin >3.5 mg/dl for more than 1 month, ascites, portal hypertension, hepatic encephalopathy, portal hypertension, or liver failure with a Factor V level <50%. In France, all HPN patients are managed and monitored by government-authorized regional HPN centers. Therefore, these results may be more representative of what occurs in an entire population of HPN patients compared to the fragmented data we have collected in the United States.

Biliary complications

The biliary complications associated with PN are acalculous cholecystitis, gallbladder sludge, and cholelithiasis [59]. Stimulating gallbladder contraction and emptying by either enteral feedings or cholecystokinin injections reduces, or even completely prevents, sludge and gallstone formation [60, 61]. Gallstones which form in patients with significant ileal resections and SBS are usually calcium bilirubinate, and form at a rate three times higher than in patients without previous ileal resection [62, 63]. Some centers recommend prophylactic cholecyctectomy for their long-term HPN patients.

Catheter-related infections

The Oley Foundation registry data indicate that on average, HPN patients were hospitalized for infectious complications approximately once per year [15]. The registry did not identify what percentage of these admissions were for catheter-related infections. Messing *et al*. found that intestinal failure patients on permanent PN have a high mortality rate (>50% with a median follow-up of 64 months), with 31% of overall HPN deaths attributable to sepsis [12]. In this series, the central venous catheter (CVC) was clearly identified as the source of sepsis in 50% of septic deaths.

Mortality from line-related sepsis has decreased since the early years of PN therapy. Some centers have reported that with experience and proper line care technique, the rate of catheter-related infections in patients receiving HPN for gastrointestinal disorders can be as low as 0.8 infection per 1000 catheter days during 1154 patient years of follow-up and 1.4 infections per 1000 catheter days for children in 241 years of patient follow-up [64]. Patients at high risk for morbidity, such as those with mucocutaneous fistulas and skin colonization by multidrug-resistant organisms, metastatic brain abscess, infective endocarditis, or multi-organ failure, should be referred early to an intestinal transplantation center [65].

Catheter occlusion

The need for long-term CVC in intestinal failure patients predisposes to thrombus and/or fibrin formation and, ultimately, occlusion of central veins. Catheter occlusion may also result from PN solution incompatibilities. In many long-term HPN patients, the central veins being utilized for PN infusion will eventually occlude. As new veins are used, multiple central venous occlusions can occur. The incidence of catheter thrombosis is approximately 0.2 episode per 1000 catheter days in 1154 years of patient follow-up [66]. Prior catheter thrombosis is a risk factor for development of superior vena cava (SVC)/inferior vena cava (IVC) syndrome in the future [67]. The Oley Foundation registry did not provide data for all central vein occlusions but did indicate that SVC thrombosis resulted in <0.3 hospital admission per patient year. Moukarzel *et al*. found that in long-term pediatric PN patients, the mean life span of a CVC was 22.4 ± 14.7 months (range, 1.5 to 178 months) and 25% of catheter removals were for thrombotic complications [67]. Other life-threatening complications can be associated with the progressive loss of venous access, including SVC syndrome, pulmonary embolus, and septic thrombi [66, 68–70]. True loss of catheter insertion sites is extremely rare. When all the usual central veins have been exhausted, alternatives include translumbar or transhepatic access to the IVC and thoracotomy with direct placement of an intra-atrial catheter [71–73]. In the 1154 patient years' experience previously described at a single institution, no patient ever lost CVC access and only two required right atrial catheter placement during that time period [66].

Other complications

Metabolic bone disease including osteomalacia and osteopenia have been observed in patients receiving long-term PN for more than a few months [74]. The clinical manifestations of bone disease range from asymptomatic with radiologic evidence of demineralization to severe bone pain and fracture. The cause of metabolic bone disease is not known; mechanisms that have been proposed include aluminum toxicity, vitamin D toxicity, and negative calcium balance [75, 76]. Renal dysfunction [77], memory deficit [78], and neurological problems have also been described in patients who require long-term PN [79].

Quality of life in patients receiving long-term home parenteral nutrition

The quality of life (QOL) of patients on HPN therapy has been sporadically and inadequately addressed. There is limited information about QOL and functional assessment of patients with SBS receiving HPN. In general, QOL parameters are better in younger individuals. One uncontrolled trial suggested that QOL in patients with Crohn's disease improved after this nutritional support was begun. However, patients who are receiving HPN do not perceive their lives as being normal [80].

Different investigators have reached different conclusions regarding QOL in HPN patients [81, 82]. Smith *et al*. found that the overall low QOL was associated with the length of time of HPN, fewer family coping skills, and inability to get along on income, whereas higher QOL was associated with higher self-esteem and quality in the family relationship. Jeppesen *et al*. reported that QOL is reduced in patients on HPN compared with those with anatomical or functional SBS not receiving HPN, and comparable with that reported for patients with chronic renal failure treated by dialysis [28–30, 81, 82].

Survival of home parenteral nutrition patients

In a study by Messing *et al*. survival and PN-dependence probabilities were reported as 86% and 49% at 2 years, and 75% and 45% at 5 years, in a cohort of 124 adults with nonmalignant SBS enrolled in a 13-year period of study. Thirty-two of the 60 patients with permanent intestinal failure (53%) and 8 of the 64 (12.5%) with transient intestinal failure died during follow-up. PN-related complications accounted for 22% of deaths in patients with permanent intestinal failure. Previously published nonactuarial figures show

overall survival rates of 66%–77% in adults [83, 84] and of 54%-94% in children with SBS, respectively [85–87]. In a study by Howard *et al*. the 3-year survival rate of SBS patients was between 65% and 80%. Patients had an average of 2.6 complications requiring hospitalization per year, and 49% experienced complete rehabilitation [12]. Another interesting article was published by Atalay *et al*. In this study, 10 of 42 SBS patients with the shortest remaining small bowel had the poorest survival. Patients with <50 cm of small bowel and no colon had a 100% mortality at 1 year due to multi-organ failure or sepsis [88].

Surgical treatment for short bowel syndrome

In recent years various surgical approaches have been developed to treat patients with SBS either by transplantation or by nontransplant approaches.

Nontransplant approach

The aim of such therapy is to increase nutrient and fluid absorption by either slowing intestinal transit or increasing intestinal surface area. Various surgical procedures have been described in case reports and series only. There are no studies comparing nontransplant surgical and medical approaches for the treatment of SBS.

Restoration of intestinal continuity, such as re-anastomosis of small intestine with colon, should be done whenever possible since it can be performed with a relatively low morbidity and mortality and often with a good probability of discontinuation of PN therapy because of improved fluid absorption. The other forms of surgery for SBS are more technically challenging and should only be considered in select patients. In general, the results are not particularly encouraging, although individual patients with specific criteria may benefit. Operations to slow transit include segmental reversal of the small bowel, colonic interposition, construction of valves, recalculating loops, and electrical pacing of the small intestine [89–98]. Operations for lengthening the small intestine include the Bianchi procedure and the serial transverse enteroplasty procedure (STEP). For the most part, these procedures have been performed in children with a dilated small intestine and SBS. In the Bianchi procedure, the small intestine is essentially split down the middle. The two small bowel pieces are then anastomosed end to end to create a longer small intestinal tract. Twenty percent of these patients develop a postoperative complication such as necrosis of the small intestine, anastamotic leak, fistula, or obstruction. The STEP divides the dilated small bowel into narrower segments with a stapling device, again allowing lengthening of the small intestine. The STEP is technically less difficult than the Bianchi procedure. These procedures are associated with a prolonged postoperative ileus. It appears that 50% of patients receiving these procedures have a sustained benefit of increased small bowel absorption [99]. It must be remembered that studies evaluating bowel lengthening procedures are small in number and reported from only a few insitutions.

Small bowel transplant

Intestinal transplantation was first attempted in dogs in 1959. The evolution of intestinal transplantation has spanned more than 40 years; however, clinical success was achieved only in the last decade. From 1964 through 1970, eight attempts at clinical intestinal transplantation were reported [100–105]. All of the recipients died; only one survived for more than a month [106]. Recipients were treated with intensive conventional immunosuppression, including combinations of prednisone, azathioprine, and antilymphocyte globulin. The discouraging results of these first clinical cases were a consequence of technical complications, sepsis, and the inability of conventional immunosuppression to control rejection, which was attributed to the large quantity of lymphoid tissue and bacterial load of the small intestine. Almost concomitantly, HPN was introduced at this time to sustain life. Consequently, enthusiasm for further development in intestine transplantation declined [100–103, 105–108].

The introduction of cyclosporine (CsA) in 1980 increased survival with kidney, liver, and heart transplantation; however, results with intestine transplantation met with limited success [107]. Nevertheless, extended survival was seen in a few patients [108]. In a series of six intestine transplant recipients treated with CsA, the mean survival rate was 25.7 months [102]. Posttransplantation lymphoproliferative disease (PTLD) secondary to intensive immunosuppression was often the cause of death rather than severe rejection.

The introduction of Tacrolimus (TAC) in 1990 improved actuarial graft and patient survival rates following all types of intestine transplantation [109]. The use of TAC as the primary immunosuppressant in small bowel transplantation as well as improved surgical techniques, the availability of an increased array of potent immunosuppressive medications, infection prophylaxis, and suitable patient selection have contributed to the reality of this procedure for a growing number of patients who are PN dependent and have permanent intestinal failure [100–103, 105–108].

Indications for transplantation

The causes of intestinal failure leading to transplantation in one large series were as follows: SBS, 80%; dysmotility syndrome, 11%; intestinal neoplasm, 6%; and enterocyte dysfunction, 3% [109]. In the pediatric intestinal transplantation experience at Children's Hospital of Pittsburgh, the two most common diagnoses were intestinal volvulus and

gastroschisis, which accounted for nearly 50% of their patients. Other common diagnoses leading to intestinal transplantation include Crohn's disease, eosinophilic enteritis, mesenteric infarction, necrotizing enterocolitis, intestinal atresia, pseudo-obstruction, microvillus inclusion disease, Hirschsprung's disease, intestinal polyposis, and trauma [10, 58, 109, 110].

While clinical experiencewas limited to a few case reports prior to the 1990s, the world experience now includes approximately 1000 intestinal transplants (two-thirds in pediatric patients), with the number performed per year increasing every year [111]. The total number of intestinal transplants performed each year has been >100 since 2001. Most transplants are performed in the United States (75%). The longest short bowel transplant survivor is currently approaching 15 years. So far, intestinal transplants have been performed only in situations where no other therapeutic alternatives were thought to be available. Therefore, there are no randomized controlled studies comparing intestinal transplantation to other therapies. Most available data are based on retrospective analyses of national and international registries, individual center experiences, and individual case reports.

Thus far, intestinal transplants have been performed only in patients who have developed life-threatening complications attributable to their intestinal failure and/or long-term PN therapy. Medicare has approved payment for intestinal transplants in patients who fail PN therapy for one of the following reasons, as stated in Medicare Coverage Policy Decisions—Intestinal and Multivisceral Transplantation (CAG-00036), October 4, 2000.

1. Impending or overt liver disease
2. Thrombosis of major central venous channels (two thromboses in subclavian, jugular, or femoral veins)
3. Frequent central line-related sepsis (two episodes of systemic sepsis secondary to line infection per year, one episode of line-related fungemia, septic shock, or acute respiratory distress syndrome)
4. Frequent severe dehydration [66, 110, 112–115]

Posttransplant complications

Complications of intestinal transplantation are multiple and frequent and can be complex and life-threatening.

Surgical complications

Complications related to the surgical procedure are common, noted in nearly 50% of intestine transplant recipients, but are an infrequent cause of graft failure (Table 4). The most common complications include postoperative hemorrhage, vascular leaks or obstructions, and biliary leaks or obstruction. Other reported surgical-related events include intestinal perforation, wound dehiscence with evisceration, intra-abdominal abscess, and chylous ascites. Morbidity and mortality from the surgical procedure itself and the anesthesia should always be kept in mind [110,115–116].

Table 4 Complications encountered after intestinal transplantation

Postoperative hemorrhage
Biliary complications
Vascular complications
GI complications
Allograft rejection (acute rejection vs chronic rejection)
Graft-vs-host disease
Infection (viral, bacterial, or fungus)
Recurrent disease
Graft loss and retransplantation

Postoperative hemorrhage. Postoperative hemorrhage may be due to coagulopathy or portal hypertension from preexisting liver failure in patients requiring a combined small bowel–liver transplant, from vascularized adhesions due to previous surgeries or technical problems originating from anastomotic leaks, or from bleeding from the peritoneal surfaces. In the setting of normal coagulation, timely surgical re-exploration and repair are necessary [110, 115–119].

Biliary complications. Biliary complications usually occur in the early postoperative period in combined small bowel–liver grafts with the standard Roux-en-Y choledochojejunostomy. Surgical re-exploration is required for repair of dehiscence or revision of the anastomosis. Biliary obstruction is a later complication and is usually secondary to the development of a biliary stricture [110, 115–119].

Vascular complications. Vascular complications are infrequent, but devastating when they occur. Thrombosis of the major arteries results in necrosis of the tissue nourished by that arterial supply which may require graft removal. Venous outflow obstruction may occur in patients receiving an isolated small bowel transplant secondary to obstruction or thrombosis of the anastomosis of the superior mesenteric vein and portal vein axis [110, 115–119].

Gastrointestinal complications. Leaks from the proximal and distal small bowel anastomoses may occur within the first postoperative week due to operative technique and poor wound healing secondary to immunosuppression and malnutrition. Bleeding is the most common GI complication in intestine transplantation and is usually caused by rejection or infection. Bleeding demands immediate attention with evaluation by endoscopy and biopsy. Rejection must be distinguished from an infectious process. Bleeding from ulcerations caused by Epstein–Barr virus or cytomegalovirus can be differentiated from bleeding caused by rejection through

endoscopy. Hypermotility is common in the early posttransplant period. In the absence of rejection or infection, hypermotility is treated with antidiarrheal agents and fiber. Baseline motility of the transplanted bowel is altered, although motility patterns in the denervated allograft are not clearly understood. Acute changes in motility, particularly when occurring in the setting of fever or abdominal distention, are indicative of rejection [110, 115–119].

Allograft rejection

Despite the technical progress made during the last 10 years, the most formidable barrier to successful intestine transplantation is rejection [116, 120–125]. Not only is it frequent and liable to result in graft loss, but rejection can also precipitate opportunistic infection and contribute to graft loss and patient death from other complications [126]. In the largest published series, the incidence of rejection requiring treatment in children and adults was 93% [116–118]. The rates for adults and children were similar [115].

Acute rejection. Acute allograft rejection is commonly seen in small bowel transplantation; the overall incidence is 90% or greater[116,127,128]. For intestine only, intestine/liver, and multivisceral transplants, acute rejection occurred in 79%, 71%, and 56%, respectively, suggesting a protective role of the liver [29, 116, 127, 128]. Although rejection may occur at any time, it is most common in the early postoperative period, with 48% of episodes presenting within 30 days and 66% presenting within the first 100 days posttransplantation [127]. Since there are no serum markers that denote rejection in the transplanted intestine, surveillance endoscopies are usually performed twice weekly through the graft ileostomy for the first 4–6 weeks posttransplantation [129]. Frequency is decreased over the next 6 months from weekly to as clinically indicated, depending on the patient's clinical presentation, history, and risk factors [115].

Chronic rejection. Chronic rejection presents as a consequence of persistent episodes of refractory acute rejection. The incidence of chronic rejection was reported to be 8% in one series, although it was suggested that chronic rejection is underestimated since the diagnosis can only be made through a full-thickness biopsy from an enterectomy sample [109, 115]. There have been reports of successful treatment of late graft rejection with the use of infliximab, a monoclonal antibody to tumor necrosis factor-α [130].

Graft-Versus-Host Disease (GVHD)

Although it was initially believed that intestine transplantation would carry a high risk for GVHD due to the abundant lymphoid tissue in the intestine, the incidence is 0% to 14% at the most active intestine transplant centers [122, 131]. Although GVHD has been fatal in a very few cases, the majority have been self-limiting, with spontaneous resolution [132].

Infection. Infection is the leading cause of morbidity and mortality in the intestine transplant recipient, accounting for up to 70% of deaths [118, 132, 133]. Therefore, a thorough preventive approach to infection control is essential to the care of this patient population. Although preventive strategies are common, specific protocols are center-specific. Fatal septic infections are often polymicrobial and associated with multisystem organ failure. In a postmortem evaluation of 29 intestine transplant recipients, sepsis was the cause of death in 69% [113, 133–135]. However, 94% of patients in this series had a coexisting infection at the time of death. Higher levels of immunosuppression are required in this patient population, which predispose them to infection. Other contributing factors for infection include a prolonged operative time with a technically difficult surgery, the severity of preoperative liver disease, sepsis prior to transplantation, multiple blood transfusions, re-explorations due to surgical complications, inability to close the abdominal wall immediately after surgery, and multiple invasive lines, catheters, and drains that alter skin integrity. Postoperative infections are frequent, with reports of a median of four episodes of infection per patient [128]. Fungal infections may be associated with small bowel wall translocation or develop as a consequence of intravenous line contamination, intense use of immunosuppressants to treat rejection, intestinal leaks, repeated surgical exploration, or extensive use of antibiotics.

Cytomegalovirus (CMV). CMV is the most common viral pathogen following intestinal transplantation, with an overall incidence of 34% [128], and frequently involves the allograft intestine (65%) [117]. Although CMV disease is a common cause of morbidity following intestinal transplantation, it has been successfully managed and treated in up to 90% of cases [116].

Epstein-Barr virus (EBV) and posttransplant lymphoproliferative disorder. Infection with EBV remains one of the most serious consequences of immunosuppressive management in transplantation. EBV-associated PTLD comprises a range of disorders, from nonspecific viral illness or self-limiting mononucleosis to more serious PTLDs with polyclonal or monoclonal disease, and, ultimately, lymphoma. The delicate balance requires the management of rejection with augmented immunosuppression while controlling infection with decreased immunosuppression. PTLD is a significant cause of morbidity and mortality in intestine transplantation, with an overall incidence of about 20%, higher than that observed in other types of solid organ transplantation [136, 137].

Recurrent disease

Recurrent disease is less common in intestinal transplantation than in other types of solid organ transplantation, primarily because SBS as a consequence of trauma, surgical morbidity, or congenital conditions accounts for a significant proportion of the indications for intestinal transplantation, and these disease processes do not usually recur. There has been only one case report of recurrent disease affecting the transplanted intestine [138].

Graft loss and retransplantation

The most common causes of graft loss are infection (43%), rejection (29%), and technical or clinical complications (29%) [118]. However, the cause of death of the graft or the reason for enterectomy is usually multifactorial. Graft enterectomy should be performed if the patient has significant graft dysfunction with severe rejection that is refractory to increased immunosuppression (Table 5). Enterectomy must be completed in a timely manner before gastrointestinal complications and sepsis from perforation occurs, or before infectious systemic complications develop. These complications may persist following graft removal and consequently will affect survival. Isolated intestine transplant patients requiring graft enterectomy will resume PN and will be relisted as transplant candidates if criteria for listing are met and the patient and family desire retransplantation. Survival is significantly decreased in patients who are retransplanted after the development of multiple surgical risk factors or with complications related to liver disease and line sepsis encountered while waiting for an organ.

Follow-up of small bowel transplant

The top three causes of patient deaths following small bowel transplant are sepsis (46%), rejection (11%), and respiratory causes (6.6%). Other causes of death include lymphoma, technical reasons, multi-organ system failure, renal failure, cardiac causes, cerebral causes, thrombosis/ischemia/bleeding, hepatitis C, liver failure, and pancreatitis. In surviving patients, 78% had full graft function, 10% had partial function, and 12% had their grafts removed after 6 months. The most common indication for graft removal was rejection (56.3%), followed by thrombosis/ischemia/bleeding (20.6%), sepsis (8.8%), lymphoma (1.2%), and other (13.1%) [139].

Table 5 Indications for graft removal

Rejection	57%
Ischemia/bleeding	23%
Sepsis	6%
Multi-organ failure	2%
Lymphoma	1%
Other	10%

Note. From Ref. 140.

Outcomes of patients on the small bowel transplant list

A significant percentage of patients referred for intestinal transplantation die while waiting for an organ, especially if more than one organ is needed. In a study by Farmer *et al*. 41% of recipients were intensive care unit-bound prior to transplantation, while another 41% were hospitalized prior to intestinal transplant [115].

Intestinal transplant candidates are placed on the United Network of Organ Sharing (UNOS) waiting list in the Organ Procurement and Transplantation Network (OPTN). Data collected by the OPTN and Scientific Registry of Transplant Recipients (SRTR) reveal that although the waiting list for intestinal transplants is still fairly short, it has continued to grow every year. Median patient waiting time for intestinal transplant is 9.5 months. Of patients on the intestinal transplant waiting list in 2003, 41% waited less than 6 months, 29% between 6 months and 2 years, and 30% longer than 2 years to receive a transplant [140]. While these waiting times compare favorably to those for most other organs [28], the death rate on the waiting list for intestinal transplants is significantly higher than that seen for any other solid organ transplant waiting list [28].

In patients who need a liver and small bowel, it is their status on the liver waiting list rather than their status on the intestine waiting list that determines organ availability. The status, which is primarily determined by the UNOS, depends on the Model for End-stage Liver Disease (MELD) system for determining priority (Table 6). Patients in all UNOS statuses except Status 1, who need both an intestine and a liver, have had higher waiting list mortality than patients listed for a liver only. The higher waiting list mortality applies to all age groups. Despite their higher mortality, liver transplant candidates with coexistent SBS and/or PN failure who also need intestine transplants do not currently receive special priority on the liver waiting list. In 1998 and 1999, the vast majority (85%) of waiting list deaths in candidates needing both intestines and livers occurred in patients who were prioritized as Status 2B or less on the liver waiting list [141]. Although patients should not be considered for transplantation for medically reversible liver dysfunction, early recognition of impending liver failure and timely referral may allow salvage of the native liver and use of a more available intestinal allograft. Given the higher patient survival rates with this single-organ transplant, every effort should be made to identify and consider transplantation for such patients before development of irreversible liver dysfunction [110].

Table 6 UNOS classification for intestinal transplantation

HOST OPO. The Organ Procurement Organization (OPO) responding to an organ donor call from a hospital is the "Host OPO" for that particular donor

INTESTINAL ORGAN ALLOCATION. The following policies apply to intestinal organ allocation which may include the stomach, small and/or large intestine or any portion of the gastro-intestinal tract as determined by the medical needs of individual patients

Degree of Medical Urgency. Each patient shall be assigned one of the following status codes which correspond to the medical condition of the patient

Status 7:	A patient listed as a Status 7 is temporarily inactive; however, the patient continues accruing waiting time up to a maximum of 30 days. Patients who are considered to be temporarily unsuitable transplant candidates are listed as Status 7
Status 1:	A patient listed as a Status 1 has liver function test abnormalities and/or no longer has vascular access through the subclavian, jugular or femoral veins for intravenous feeding, or has other medical indications that warrant intestinal organ transplantation on an urgent basis
Status 2:	All patients awaiting intestinal organ transplantation who do not meet the criteria for Status 1 will be classified as Status 2

Geographic Sequence for Intestinal Organ Allocation. Intestinal organs shall be allocated first to transplant candidates who are size compatible and have a blood type that is identical to that of the organ donor. These patients will be followed by candidates who have a blood type that is compatible to that of the organ donor. Allocation shall be based on length of time waiting and in accordance with the following sequence:

To local Status 1 patients first;
Local Status 2 patients;
Status 1 patients in the Host OPO's region;
Status 2 patients in the Host OPO's region;
Status 1 patients in all other regions; and
Status 2 patients in all other regions

Combined Intestine–Liver Organ Candidates. For patients awaiting a combined intestine–liver transplant, the liver may be allocated by the local OPO to a local or regional intestine recipient based upon priority for receipt of the intestine using the intestine Waiting List unless there is a Status 1 liver patient locally or regionally

Other issues that may delay transplantation in all small bowel transplant candidates include donor/recipient size incompatibility and CMV status. Most candidates for small bowel transplant have had bowel resections, and consequently there is a significant reduction in the capacity of their peritoneal cavity. Therefore, they often require donors who are 50% to 75% smaller, thereby limiting the field of potential donors [142]. In some situations, this issue can be managed by surgical resection of segments of bowel and/or liver from grafts that would otherwise be too large [143]. Also, becuase of the significant problems that CMV enteritis can cause posttransplant, many centers avoid using CMV-positive donors in CMV-negative recipients, which can also exclude many potential donors [144].

Outcomes of patients having small bowel transplantation

Data regarding the results of small bowel transplants are available from three sources: (1) the International Intestinal Transplant Registry (ITR), (2) the OPTN database, and (3) reports from individual centers. The OPNT has collected data for transplants performed since 1986. Based on OPTN data, the number of isolated intestine transplants performed in the United States has increased steadily since 1996. In 2003, there were 52 isolated intestine, 22 intestine/liver, and 29 liver/pancreas/intestine transplants performed. The primary diagnoses in these recipients were SBS in 64%, functional bowel problems in 14%, and other in 22% [140, 145, 146].

The ITR reported in 2003 that a total of 61 centers had performed 989 intestinal transplants in 923 patients in 19 different countries: 433 isolated small bowel transplants, 386 liver–small bowel transplants, and 170 multivisceral procedures (stomach, pancreas, liver, and small bowel) [139]. The majority of transplants have been performed in pediatric patients (61%) [12]. Because intestinal transplants are performed in relatively small numbers at very few academic transplant centers around the world, it is likely that these registry data represent most, if not all, of the intestinal transplants performed worldwide since 1985 [147]. As of September 2005, 257 medical centers were operating organ transplant programs in the United States; 48 had active clinical intestinal transplant programs [148]. The most active programs in the United States are those at the Jackson Memorial Hospital, University of Pittsburgh Medical Center, Nebraska Medical Center, and Children's Hospital of Pittsburgh [148]. Despite this progress, the shortage of cadaveric intestinal grafts continues to result in appreciable morbidity and mortality for patients awaiting transplantation [28, 109, 145, 146].

Patient and graft survival

OPTN/SRTR cohorts (2001–2002, 1999–2000, 1997–1998) evaluated the 1-year patient and graft survivals, which were 77% and 66%, respectively, for intestine-only transplants. With long-term analysis, patient and graft survivals after intestine-only transplants were 63% and 48% at 3 years, and 49% and 34% at 5 years, respectively [140]. These results are improving but still fall short of the results for kidney, heart, lung, and liver. Some individual centers have reported better results than the combined data have shown (Table 7).

Overall patient and graft survivals in patients transplanted after 1995 were 65% and 57% at 1 year, and 50% and 40% at 4 years. These results indicate a statistically significant improvement in graft ($P = 0.02$), but not patient ($P = 0.46$), survival from earlier cohorts. In all cohorts, the highest patient mortality occurs in the first 6 months posttransplant. This high incidence of early mortality was also noted in individual reports from the most experienced centers [109, 121, 122, 149]. Patient ($P = 0.02$), but not graft ($P = 0.32$), survival was significantly better in intestine-only transplants compared with transplants involving additional organs. This likely reflects the higher pretransplant acuity of the patients who also need livers, the greater magnitude of the surgery they undergo, and the inability to remove their transplanted organs as a life-saving maneuver if there is uncontrolled rejection or sepsis posttransplant.

There has been steady improvement in the outcome of intestinal transplantation, particularly during the latter half of the 1990s [109, 116, 119, 121–125, 158–161]. Most of these improvements can be attributed to three factors: (1) technical and clinical learning curves, (2) improvements in the ability to monitor graft function, and (3) newer and more effective immunosuppressive agents. The ITR demonstrated significant differences in graft and patient survival based on the volume of patients transplanted at a center. Those centers that had performed at least 10 intestinal transplants had significantly better graft and patient outcomes than centers that performed fewer than 10 transplants.

In a series of 121 patients receiving 127 transplants at the University of Pittsburgh, actuarial patient survival was reported to be 72% at 1 year and 48% at 5 years [162]. One- and five-year graft survival rates were 64% and 40%, respectively. From 1995 to 1999, a significant improvement in graft survival was seen in this series, with graft survival of 65%, reflecting program modifications, management strategies, immunosuppressive protocols, and refinements in surgical techniques. In a follow-up of 55 pediatric patients who received 58 intestine transplants from 1990 to 1996 at the University of Pittsburgh, 30 patients were alive, with an

Table 7 Patient and graft survival of patients receiving small intestinal and solid organ grafts (adopted from Ref. 184)

Graft type	1-year survival (%)		3-year survival (%)		5-year survival (%)	
	Patient	Graft	Patient	Graft	Patient	Graft
Kidney [150], 1990–1999	94	83	90	73	85	65
Liver [151], 1994–2003[a]	78	73	72	67	67	62
Heart [152], 1990–2002	82	80	72	70	67	66
Lung [153], 1990–2002	75	75	59	59	46	46
Intestine [154]						
1985–2004	72	64	57	42	47	35
1999–2004	78	65	62	50	50[b]	35[b]
Intestine and liver [154]						
1985—2004	58	56	46	44	41	39
1999—2004	60	58	50	45	50[b]	45[b]
Multivisceral [154]						
1985—2004	58	58	50	45	50	40
1999—2004	66	62	62	58	62[b]	50[b]
	1-year survival					
Well-performed individual centers	Patient	Graft				
Sudon et al. [155], *intestine (2000)*	93	71				
Goulet et al. [149], *intestine and liver (1999)*	80	80				
Pinna et al. [122], *multivisceral (2000)*	70	60				
Fishbein et al. [156], *intestinal (2002)*	92	92				
Parenteral nutrition [157], *1990–1996*	90	75				

Note. Data in italics are most appropriate for comparison. Data including during the early development of intestinal transplantation are also given.

[a]Data given for first transplantation only. All other data include a small number of repeat transplantations (heart and lung, 2%; intestine, 7%) which are associated with a poorer income.

[b]Four-year survival values are given.

actuarial survival at 1, 3, and 5 years posttransplantation of 72%, 55%, and 55%, respectively [163].

The impact of different immunosuppressive strategies, patient and graft monitoring, and improvements in surgical techniques was evaluated at the University of Miami in a series of 77 intestine transplants performed in 69 patients during three program phases: 1994–1995, 1995–1997, and 1997–1999 [122]. Two-year graft survival rates for isolated small intestine transplantation for phases 1, 2, and 3 were 0%, 50%, and 80%, respectively. Graft survival rates in combined liver–intestine and multivisceral groups at 2 years during the same phases were 40%, 30%, and 48%, respectively. It was suggested that improvements may have been the result of induction therapy with daclizumab and close surveillance protocols including ileoscopy and biopsy.

From 1990 to 1999, 32 isolated small intestine transplants and 49 combined small bowel–liver transplants were performed in 81 patients at the University of Nebraska [121]. Overall graft survival in the isolated small bowel group was 50%. From 1990 to 1993, six patients received combined small bowel–liver transplants. There is one long-term survivor at 7.5 years posttransplantation. From 1994 to 1999, 43 small bowel–liver transplants were performed, with an overall patient survival rate of 60% ($n = 26$).

Improvements in small bowel transplantation have also resulted in decreased costs. Between 1990 and 1994, the average cost was $203,111 for an isolated intestine transplant, $252,453 for a combined liver–small bowel transplant, and $284,452 for a multivisceral transplant [164]. By 1999, the average costs had decreased appreciably and were $132,285 for an isolated intestine transplant, $214,716 for a combined liver–small bowel transplant, and $219,098 for a multivisceral transplant [164].

Significant progress has been made in small bowel transplantation over the past decade, as it has advanced from an experimental strategy to a feasible alternative for those patients with permanent intestinal failure and complications associated with the underlying disease and/or PN. Further refinements and improvements in immunosuppressive protocols, surgical techniques, infection management, and prophylaxis, as well as early patient referral and appropriate patient selection, are crucial to maximize outcomes.

Living donor transplantation has been pioneered in kidney and liver transplantation and has met with considerable success in terms of patient outcomes, and potentially as a partial solution to the donor shortage. Living-related donor intestinal transplantation (LRDIT) is also being pioneered as a surgical innovation to expand the pool of intestinal graft donors. To date, fewer than 20 living-related segmental transplants have been performed worldwide. Benedetti *et al*. recently reported on three male patients who received LRDIT for trauma-induced SBS [165]. The advantages of living-related segmental intestinal transplantation are the same as those of other living-donor procedures: better matching, the opportunity for preoperative donor optimization, and an increased donor pool. Genton *et al*. reported a LRDIT between monozygotic twins. A 160-cm ileal transplant was used. Both twins did very well, with the transplanted twin requiring no immunosuppressive therapy. The transplanted twin was able to transition from being PN dependent to eating a regular diet within 62 days of the transplantation [166]. However, many questions remain related to donor safety issues, optimum drainage system (portal versus systemic), which segment of intestine (ileum versus jejunum) should be transplanted, and timing and closure of the ostomy. The lack of widespread application of this approach probably reflects ongoing concerns about the ideal circumstances for living-donor intestinal transplantation [167].

The ITR data found no differences in graft survival between recipients of cadaver and recipients of living-donor intestinal grafts. Although early evidence suggests that use of HLA-matched living donors may be associated with less rejection and fewer infectious complications [168], more data are needed before this approach achieves wide acceptance.

Quality of life in small bowel transplant

Despite medical management and/or multiple surgical interventions, patients with intestinal failure often have symptoms leading to a reduced QOL. They are frequently hospitalized for septic, metabolic, and hepatic complications [168–170]. Intestinal transplantation, although a highly successful treatment modality, is not curative. As survival rates increase for intestine transplant recipients, with many patients having an extended survival of >5 years, QOL issues are beginning to be examined. After transplantation, patients and their families face side effects of immunosuppressive drugs, noncompliance, rejection of the transplanted organ, psychosocial stress, and financial burden. For many patients, however, the benefits of transplantation often outweigh the burden or distress associated with these side effects.

Through clinical experience, it is evident that life after intestine transplantation can be challenging. For approximately 6 to 12 months posttransplantation, care routines of pediatric patients may include up to 15 daily medications, tube feedings, intravenous fluids, and maintenance of the gastrostomy tube, jejunostomy tube, ostomy, and central venous catheter, as well as the usual child-care needs [171]. These routines generally decrease over time as a result of ostomy closure, increased oral intake, and removal of appliances. However, a mean of seven daily medications is still required at >3 years posttransplantation, and 17% of patients continue to require enteral feeding due to oral aversion [171]. More than 80% of patients who are school aged are attending school full-time at 3 years posttransplantation [163]or have returned to school at the appropriate level [172].

In a study of parents whose children had received liver and/or intestine transplants, a majority of parents reported elevated psychological symptoms, with fathers showing greater distress than mothers. Although parenting stress was not elevated compared with a normative sample, having a younger child going through transplantation was associated with higher stress. Parents reported better physical function but lower vitality than the normative population [173].

Psychiatric and psychosocial problems affecting QOL following intestine transplantation are a function of the severity of disease, duration of preoperative PN, length of the waiting period, and prolonged postoperative course, and vary inversely with available social support [174]. In the early postoperative period, a high incidence of affective disorders, such as depression and anxiety related to postoperative adjustment, is reported [175].

QOL was assessed in nine adult survivors of intestinal transplantation who reported significant improvements in physical, social, and emotional function compared to their pretransplant status. However, these patients also reported a greater need for medications, decreased mobility, increased pain and discomfort, fewer social supports, and difficulty parenting [176]. QOL improved over time in adult intestinal transplant recipients who were evaluated at a mean time of 2.7 and 5.3 years after transplantation. These patients reported improvements in anxiety, sleep, and impulsiveness/control, which may reflect their successful adjustment and adaptation to chronic care needs.

Assessing QOL in intestine transplant recipients is challenging due to significant patient variability with respect to underlying disease, postoperative course, long-term complications, and psychosocial factors. It is imperative, however, that QOL be evaluated as more patients are offered this therapy to help them make the best decisions for their care and to guide the transplant team in implementing medical management and therapy.

Home parenteral nutrition versus small bowel transplant

Quality of life

There are very few QOL comparisons between intestinal failure patients who remain on PN and those who undergo intestinal transplantation. Retrospective comparisons between small groups of intestinal transplant patients and long-term PN patients matched for age and duration of illness suggest that QOL is the same or slightly better with transplantation [177].

One study compared the QOL of patients with intestinal failure receiving HPN ($n = 10$) to that of patients who underwent intestinal transplantation ($n = 10$) [177]. Longitudinal change in QOL was measured by a self-administered questionnaire, the Quality of Life Inventory. Transplant recipients were evaluated at a mean of 2.7 years after transplantation and after a mean period of 5.3 years of intestinal failure. Patients on HPN were evaluated after a mean of 5.1 years of intestinal failure. Patient-reported QOL was markedly similar between the two groups, with significant differences in only 2 of 25 domains. Transplant recipients reported significant improvement in anxiety ($P = 0.02$), sleep ($P = 0.03$), and impulsiveness/control ($P < 0.001$), reflecting adjustment to their posttranspant status. Substantive research on QOL in intestinal transplantation is lacking, and a systematic study of the issue is necessary.

DiMartini and colleagues [176] conducted a retrospective study to assess and compare the QOL of 2 cohorts of patients: those on HPN versus intestinal transplant recipients. Intestinal transplant recipients reported significant improvement in their functional status and QOL. Transplant recipients also rated their pretransplant (PN-dependent) functional status and QOL worse than before the development of chronic intestinal failure. Similarly, HPN-dependent recipients reported significant worsening of their QOL across most domains when they compared their premorbid period with their HPN-dependent state [176].

Financial concerns

Financial issues must also be considered in managing intestinal failure patients. Today, provision of basic HPN is associated with charges of between $200 and $500 per day for a given patient, although actual costs for PN, including the pharmacist's time for compounding, are of the order of $20 to $30 per day, excluding the additional charges of home care services, monitoring, and management of complications. Therefore, if administered 7 days per week, HPN charges sometimes exceed $150,000/year.. The costs for transplant evaluation, transplant and postoperative care, and posttranspant follow-up are not currently available for comparison.

Data regarding the impact of HPN on resource utilization are limited. A recent cost-utility analysis suggested that 1 year of quality life would be £69,000. The cost of such home care in the United Kingdom was estimated to be £45,000 for the first year and £36,000 for each year thereafter. In 1992, the daily Medicare allowable charge for HPN was $200–$400 (equivalent to $73,000–$146,000 per year) [80]. An economic evaluation of a HPN program measured the incremental costs and health outcomes for a cohort of 73 patients treated from November 1970 to July 1982. Over a 12-year time frame, Detsky *et al*. estimated that HPN resulted in a net savings in health-care cost of $19,232 per patient and an increase in survival, adjusted for QOL, of 3.3 years, compared with the alternative of treating these patients in

hospital with intermittent nutritional support when needed. They also concluded that the cost-utility of HPN compares favorably with that of other health-care programs, when it is used to treat patients with gut failure secondary to conditions such as Crohn's disease and acute volvulus [178].

Four randomized controlled trials used PN delivered at home to assess the utility of longer-term PN in disease states other than irreversible gastrointestinal tract failure (cancer chemotherapy, bone marrow transplantation, AIDS, and cystic fibrosis). Patients presumed to have irreversible gastrointestinal tract failure such as SBS will succumb to starvation unless PN is provided. The use of PN in this scenario is analagous to providing hemodialysis to patients with end-stage renal disease. The decision to use HPN in other patient populations should weigh the risk of complications and economic costs (approximately $100,000 annually) against the expected benefit [29, 179–182].

Patients with SBS can lead a productive, lengthy, happy, and a useful life if educated and managed appropriately. It is possible to reduce or even eliminate PN requirements over time in many of these patients using the evidence-based techniques of dietary and fluid management. Other treatments such as hormonal therapy (growth hormone, GLP-1) may eventually be available to augment the intestinal adaptation process as this becomes better understood. For patients that do require PN, it is essential that the therapy be prescribed appropriately. In addition, PN is associated with several potentially serious complications, many of which can be prevented when both the patient and the caring professional have the appropriate expertise [29]. For many patients a small bowel transplant might be the only option. In these circumstances the benefit of transplant might outweigh the burden and risks associated with the transplant.

Final recommendation

There are limited indications for small intestinal transplantation. Eminent liver failure is currently the most appropriate indication, although as survival of both patient and graft continues to improve, these indications may be broadened. The management of these patients is complex and is undergoing constant evolution. Intestinal transplantation is not yet an alternative for patients who are doing well on PN. Three-year patient survival after isolated intestine transplantation is approximately 70%, which is appreciably better than in earlier eras but not comparable with 3-year survival in at-home, stable, PN-treated patients (90%) [3, 4]. Patients failing PN therapy, however, have a very poor prognosis (<20% 1-year survival). Intestinal transplantation in this select group of patients with PN dependence and life-threatening complications from PN does offer a clear survival advantage. It is essential that patients failing therapy with PN be referred early for evaluation for intestinal transplantation to increase the likelihood of a successful outcome. Timely referral also decreases the likelihood of requiring combined liver–intestine transplantation for PN-induced liver failure. Finally, it is essential that patients with end-stage bowel disease are cared for and managed by a multidisciplinary team at a center that has expertise in all aspects of treatment for intestinal failure including PN, reconstructive surgery of the bowel, and intestinal transplantation [183]. The next few years may bring a significant and dramatic change in the approach to patients with SBS as the surgical and immunological management is improving. This could make transplant the first option if high patient survival and PN-free survival can be achieved after intestinal transplantation, especially in patients who may be at risk of developing liver failure. This is also a valid option for children and those who are looking to live an independent life.

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