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REVIEW ARTICLE

Surgical strategies in short bowel syndrome

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Abstract Extensive loss of small bowel in all age groups has significant morbidity and mortality consequences. Despite the astonishing ability of the small bowel to compensate for an extensive loss, long-term parenteral nutrition and enteral nutrition, tailored to the need of the patients in relation to the missing intestinal regions is needed. Organ-preserving surgical intervention becomes necessary in patients with a very short intestinal transit time and in an other group of patients with impaired propulsive peristalsis. Intestinal transplantation is indicated in recurrent septical infections or if nearly all of the small bowel is missing. This review discusses indications and risks of the organ-preserving surgical therapies in children with short bowel syndrome.

Keywords Short bowel syndrome · Intestinal lengthenig procedures · Bianchi's method · Serial transverse enteroplasty (STEP) · Colon interposition · Reversed segments · Intestinal valves · Tapering · Experimental mechanical lengthening · Tissue engineering

Introduction

According to Toulukian and Walker-Smith, the length of the small bowel increases from 150 cm at 23 weeks to 300 cm at 38 weeks of gestational age (GA) [1]. A more recent publication measuring small bowel length in vivo showed that its length is about 100 cm at a GA of 27–29 weeks, 157 cm at 39–40 weeks, and 239 cm between 1 and 6 months of age [2]. Rickham was the first to define a short bowel syndrome (SBS) as a remnant of less than 30% of the total length of the small bowel [3]. That would correspond to a 30 cm remnant in a premature infant with less than 30 weeks' GA, or less than 70 cm in a full-term neonate. However, the intraoperative antimesenteric measurement of intestinal length yielded highly variable results due to the enormous contractility of the bowel even when touched very gently [4]. Regardless of the remaining bowel length, the prolonged requirement of parenteral nutrition remains the best means of balancing the intestinal deficit. The term "short bowel syndrome" is defined by most authors as a state of significant maldigestion and malabsorption requiring a prolonged period of parenteral nutrition to ensure normal growth and development, prevent dehydration, and replace electrolytes, vitamins, and trace elements [5]. The wider term "intestinal failure" (IF) applies to a larger group of patients with a functional loss of absorptive surface area (e.g., due to radiation injury, chronic intestinal pseudo-obstruction, or congenital villus atrophy), and the inability to achieve adequate homeostasis and growth by normal enteral nutrition [6, 7].

The majority of SBS occurs in neonates (Table 1). Around 50% are caused by acquired diseases, such as necrotizing enterocolitis (NEC) or volvulus, resulting in extensive intestinal necrosis and resection. The second largest group consists of neonates with congenital anomalies, resulting from a vascular occlusion of major segments of the mesenteric artery (intestinal atresia), or an intrauterine volvulus of the prolapsed intestine in a baby with gastroschisis, or aganglionosis involving major parts of the small intestine. A rare group consists of patients with

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Table 1 Causes of short bowel in 370 cases collected from the published literature

Necrotizing enterocolitis (NEC)	30%
Volvulus	22%
Intestinal atresia	15%
Gastroschisis and atresia	19%
Extensive intestinal aganglionosis	6.7%
Trauma, mesenterial avulsion	1%
Others	7%

a so-called "congenital short bowel" resulting from a genetic deficiency of the small bowel anlage [8].

The prevalence of SBS has increased over the last decades, since enormous progress in intensive care medicine has improved the initial prognosis of patients who have lost major parts of their small intestines. The actual prevalence is difficult to determine, because the term includes all forms of reduced small bowel length or function associated with maldigestion and malabsorption. Mughal and Irving estimated that patients with severe SBS who remain dependent on long-term parenteral nutritional support amount to two new patients per one million of the population/year [9]. A European survey indicated that the prevalence of total parenteral nutrition at home had increased to four adult patients per one million [10]. According to Wallander, the incidence of extreme SBS in the neonatal age group is around 3–5 new cases per 100,000 births/year [11]. Using Canadian census data and the data of the Canadian Institute of Health, a population-based incidence of 22.1 cases of SBS per 1000 neonatal intensive care admissions and 24.5 per 100,000 live births was calculated, with a greater incidence in preterm infants [12]. A more recent publication showed that the incidence of surgical short bowel syndrome between 2002 and 2005 was 0.7% in very low birth weight infants and 1.1% in extremely low birth weight infants [13]. An Italian multicenter study reported an incidence of 0.1% in all live births and 0.5% among ICU admissions [14].

Extensive loss of small bowel is followed by intestinal adaptation, a process that includes morphological changes in the intestinal remnants, leading to an increase of absorptive surface area with changes at the cellular and functional level.

Enteral nutrition is a principal aspect of SBS. It is a sophisticated means of administering nutritional therapy to optimally stimulate the remaining parts of the intestines. Since each patient is different, nutrition must be tailored to promote intestinal adaptation and achieve complete oral nutrition with normal growth and psychomotor development. In addition to sophisticated nutritional management, pharmacologic therapies may be needed to prevent complications. Recently, growth hormones and trophic factors have been used to promote the adaptation process [15].

Surgical strategies in SBS patients

General aspects

The ileocecal valve (ICV) is considered to benefit from the prolongation of the intestinal transit time. However, the role of the ileocecal valve is controversially discussed. In SBS patients, Coran and Kaufmann registered no difference in outcome between those with the valve and those without [16]. Based on experimental investigation, bacterial translocation in rats with SBS without an ileocecal valve was significantly lower compared to rats with a preserved ileocecal valve [17]. A more recent publication showed that the duration of parenteral nutrition depends significantly on the length of the residual small bowel and the presence of ICV [18]. In a follow-up of 171 pediatric patients at a single institution, 64.3% could be weaned from parenteral nutrition. The presence of $\geq$10% of the anticipated bowel length or an ileocecal valve predicted positive weaning [19, 20]. Patients with an intact ICV benefit additionally from the total colonic length, while patients without ICV will usually have lost some parts of the colon. Furthermore, glucagon-like peptide 2, an enteric hormone for intestinal adaptation, is mainly produced in the terminal ileum and the ascending colon. While definite evidence concerning the role of the ileocecal valve per se in SBS patients is lacking, it should be preserved whenever possible because of its hormonal benefits and prolongation of intestinal transit time.

Enteral nutrients are essential for intestinal adaptation; surgical strategies are used to support this process. The primary goal of operative interventions is to restore bowel continuity as early as possible, thus enabling all intestinal segments to take part in digestion and absorption, and stimulating the adaptation process. The early closure of a stoma—such as after NEC surgery—is an important first step. The majority of SBS patients will eventually be able to tolerate full enteral feeding. No additional surgical procedures may be necessary except for complications due to the underlying disease, such as intestinal obstruction or ileus.

However, surgical procedures may be helpful in three situations:

(a) too fast passage of nutrients as a result of a short bowel remnant with good propulsive peristalsis, not allowing sufficient time for digestion and absorption;

(b) a primary or secondary dilatation of intestinal remnants, causing insufficient to-and-fro peristalsis, bacterial overgrowth, and translocation;
(c) an extremely short bowel remnant with minimal mucosal surface area, not promising any success in long-term enteral nutrition, or recurrent septicemia due to bacterial translocation with loss of venous access sites and IF-associated liver failure. Today, intestinal transplantation procedures are needed for these patients, but future progress in tissue engineering promises to become a valuable alternative.

The following paragraphs discuss indications, advantages, and disadvantages of the conventional surgical strategies in SBS patients as well as recent experimental research. However, intestinal transplantation procedures and results are not included into this review.

Slowing intestinal transit time

A variety of surgical procedures have been developed to reduce the intestinal transit time. The techniques are only indicated in the presence of good propulsion of luminal nutrients; they are contraindicated in cases of dysmotility or stasis of chyme.

Antiperistaltic intestinal segment

The antiperistaltic segment acts as a physiological valve by causing retrograde peristalsis and serving as an effective brake to prolong the contact time of intraluminal nutrients with the intestinal epithelium. The segment must always be located in the most distal part of the small bowel or shortly before the ileocecal valve (ICV). The ideal length is difficult to estimate, but appears to be 10 cm in adults and 3 cm in infants. Excessively, long antiperistaltic segments may cause an ileus. The first publications on the successful use of an antiperistaltic small bowel segment date back to the 1960's and 1970's [20, 21]. Trinkle et al. used reversed colon segments to prolong the passage time [22]. At our clinic, a reversed 3-cm-long jejunal segment was used in a baby after NEC with a 10-cm-long jejunum and a 1-cm-long ileum plus ileocecal valve. The baby was on full or partial parenteral nutrition for 3 years [23]. The patient is now 38 years old and in good health on full oral nutrition, but needs regular replacement of fat-soluble vitamins.

Panis et al. [24] published the results of eight adult patients with bowel remnants between 40 and 70 cm long, in whom segmental reversal had been used. In a more recent report on 38 adult patients permanently dependent on PN, segmental reversal of the small bowel resulted in complete weaning from PN in 17 patients and reduced dependency on PN from 7 to 4 days in a further 7 patients [25]. Energy and macronutrient absorption were investigated in a subsequent study. Seventeen SBS patients who received a reversed segment were compared with 17 matched control patients. The results showed a gain in macronutrient absorption, associated with a lower dependence on home parenteral nutrition (HPN) [26]. A further study in adults revealed that reversed segments may be significantly beneficial in selected patients, but it remained difficult to predict the outcome [27].

Intestinal valves and sphincters

Surgical construction of valves or sphincters is aimed at slowing down the intestinal transit time and delaying the passage of intraluminal nutrients to the colon. The valve must be placed at the distal end of the small bowel [28]. A variety of surgical procedures have been used, mainly in children [29, 30]. The technical challenge is to create a valve that does not result in intestinal obstruction. Valves have also been used to induce adaptation and dilatation of the proximal bowel to perform a lengthening procedure at a later point in time [31].

Isoperistaltic interposition of the colon

The advantage of this surgical technique is that none of the small bowel surface area is used. It is best performed with a 10–15-cm segment introduced into the most proximal part of the small intestine. Experimental evidence exists to show that the isoperistaltic colon prolongs the delivery time of nutrients to the small intestine, and is able to absorb water electrolytes and nutrients by active transport mechanisms [32–36]. In an adult patient, the interposed colon showed adaptive changes to the small intestine [37]. A few clinical cases have been reported in children. About 50% of them experienced a good outcome and no perioperative morbidity or mortality [38–40]. Personal experience in two extreme short bowel infants showed a beneficial effect of a 15-cm-long colon interposed directly beyond the ligament of Treitz allowing finally to wean them from PN.

Intestinal dilatation with stasis and secondary dysmotility

Dilated intestinal loops with inefficient peristalsis and stagnant chyme are common problems in patients with SBS, either as a consequence of the underlying pathology—such as remnants of multiple atresia—but more often after adaptive growth resulting finally in large dilated bowel segments with insufficient motility. Greatly dilated intestinal segments are characterized by to-and-fro peristalsis, stasis of chyme, and consequent bacterial overgrowth and bacterial translocation leading to recurrent

septicemia. Reconstructive surgical methods are aimed at reducing bowel diameter and restoring a normal lumen without sacrificing intestinal length [41]. The appropriate timing for the surgical procedure is determined when maximal adaptation has been achieved or when the rate of progression in enteral calories is slow and hampered by bacterial overgrowth [42]. Patients with primarily severe dysmotility or secondary cholestasis and advanced liver disease should be referred for intestinal transplantation instead, and are not candidates for refashioning or lengthening procedures [15].

Tapering

Tailoring techniques of the antimesenteric site of short dilated bowel segments are only indicated when the remaining bowel is sufficiently long for digestion and the absorption of nutrients. Two options exist: either intestinal refashioning is performed by infolding a short bowel segment at the antimesenteric site and thus not losing any absorptive surface area, or by resection of a triangular antimesenteric part of the bowel wall. The former method has the disadvantage that the plication may unravel after some time. Therefore, it is advisable to take the serosa off at the site where the sutures are placed.

Longitudinal intestinal lengthening technique (LILT)

This technique was first reported by Bianchi [43], based on experimental experience. It is derived from the fact that the mesenteric vessels enter the bowel from either side of the midline, with anterior and posterior branches. In dilated bowel segments, there is a larger avascular space between the two vessel layers. This space can be entered and the dilated bowel divided longitudinally into two halves. The division can be performed with a GIA stapler instrument [44] or by dividing the bowel with scissors and suturing the anastomosis manually [45]. The latter technique consumes less absorptive surface area. We recommend seromuscular stitches for the anastomosis to preserve as much mucosa as possible [28]. The two separated bowel halves are then anastomosed in isoperistaltic fashion. To successfully perform the procedure, the bowel should be clearly dilated to at least double the normal diameter and have a minimum length of 20–40 cm. The disadvantage of the technique is that both segments are suspended from the same part of the mesentery. The lengthening should be performed on a bowel segment no longer than 20 cm to avoid any reduction of mesenteric blood flow to either segment and achieve a safe anastomosis. To induce the bowel dilatation needed for a planned secondary Bianchi's procedure, some authors suggest the introduction of an intermittently clamped tube into the proximal stoma for 20–24 weeks. This controlled obstruction of the proximal bowel segment results in dilatation of the lumen. The effluent fluid of the tube is recycled into the distal stoma [46].

Bianchi published his clinical experience in 1999 [47], reporting a long-term survival rate of 45% in 20 patients. All survivors had >40 cm of residual jejunum, only mild cholestatic jaundice, and most of them had the ileocecal valve as well as a longer colon. It has been suggested that this technique should be reserved for "self-selected survivors" who have come through the neonatal phase with minimal liver injury [48]. However, bowel tailoring and lengthening might be useful even at an earlier stage in a child with appropriate propulsive peristalsis but suffering from stasis and bacterial translocation in dilated bowel segments [47]. Single-center long-term results in 19 consecutive patients who had undergone Bianchi's procedure showed that 7 patients (44%) responded well and came off parenteral nutrition, 9 required transplantation, and 3 were still on the waiting list for transplantation [49]. Patients with inherent motility disorders should not be selected for this procedure [50, 51].

Serial transverse enteroplasty (STEP)

STEP is a relatively new procedure. It has gained significant acceptance throughout the world as an easier method to refashion dilated intestinal loops and thus improve peristalsis and motility [52]. The goal is achieved by serial alternating and opposite transections of one-third or a half of the intestinal lumen, creating a kind of zigzag pattern The remaining lumen for the passage of chyme should not be smaller than 2.5 cm. A further advantage is the absence of any restriction in regard of the length of the bowel segment. A GIA stapler is used for transection. Due to the high rate of bleeding from the central corner of the transection, one or two additional stitches at this location are recommended [15].

STEP has been used successfully to refashion a dilated duodenum in three children with a short bowel (6 months, 5 and 7 years old) [53]. A modification of the STEP procedure was published recently, consisting of spiral intestinal lengthening and tailoring (SILT). Continuous spiral incisions are performed between the mesenteric and antimesenteric border passing between the mesenteric vessels. The bowel is then stretched over an intraluminal catheter and the edges are sutured continuously. The technique requires a rather long distance of suturing to anastomose the stretched bowel. Publications on this technique have been limited to case reports [54].

Long-term results after the STEP procedure show that the majority of children can be weaned from PN, except those with motility problems and/or gastroschisis [55]. The data of an international registry show that 11 of 97 patients died (11%) and 5 progressed to intestinal transplantation; 47% attained full enteral nutrition, and patients with a

primarily longer bowel were significantly more likely to achieve enteral autonomy [56]. A single-center study on 51 patients with 68 STEPs showed a 54 and 20% gain in length after the first and the repeat procedure, respectively. Of 43 non-transplanted children, 2 died, 4 are on HPN, and 13 need some TPN, while the remaining patients are independent of PN [57]. A meta-analysis encompassing 86 children showed that 87% experienced greater enteral tolerance after STEP. Including data from the international registry in the meta-analysis, the overall increase in enteral tolerance was estimated to be 81% [58].

Comparing LILT with STEP

A comparison of 41 LILT and 34 STEP procedures for intestinal lengthening showed that both techniques improved enteral nutrition and overall outcome; 56% could be weaned from parenteral nutrition, and 22% needed transplantation [59]. The most striking differences between the two methods are that STEP is technically easier to perform and can be used in very short segments as well as the duodenum [60]. A recent systematic review showed that the gain of length is approximately identical in both methods, but STEP is associated with significantly fewer severe early complications compared to LILT (Table 2) [61]. Long-term complications are common with both techniques, consisting mainly of bacterial overgrowth, re-dilatation, and adhesive bowel obstruction. Recurrent dilatation occurs more often after STEP than after LILT, but the difference is not significant and STEP can be performed again [62, 63]. However, primary or secondary small bowel dilatation predicts a prolonged need for parenteral nutrition and reduced survival rates [64, 65]. Large bowel diameter correlates negatively with residual bowel length and is a prognostic factor for achieving enteral autonomy [66]. Overall, when comparing the two methods, the weaning rate after LILT is higher (71.5 versus 58.1%); the difference might be due to the much shorter follow-up of patients after STEP. The subsequent need for transplantation is 26% after LILT and 16% after STEP, and the mean mortality rate is 30% after LILT and 14% after STEP [61]. Again, these percentages might be influenced by differences in follow-up time in the two patient groups.

Table 2 Comparison of early complications after LILT and STEP (modified from Frongia et al. [61])

	LILT (mean%)	STEP (mean%)
Bleeding	16.1	22.2
Obstruction	17.7	17.5
Leakage	13.2	12.1
Abscess	6.6	2.6
Intestinal necrosis	10.6	–
Intestinal perforation	10.1	–
Fistula	7.4	–

Experimental approaches in lengthening the short bowel

Inadequate absorptive surface area is a challenge and is the reason for performing experiments to achieve additional bowel length either by mechanically stretching short segments or by tissue engineering.

Mechanical stretching

Printz et al. [67] published their experience with an antimesenteric distractor, achieving nearly 10 cm of additional length in 3 weeks. The distracted segment revealed significant muscle cell hypertrophy and increased villus width [67]. In the following years, several authors used intraluminal devices based on screws [68, 69]. Other groups used nitinol springs [70] or encapsulated polycaprolactone springs [71], achieving a significant lengthening and also greater thickness of smooth muscles. Teitelbaum's group induced osmotically driven intestinal growth with polyethylene glycol. Their results showed significant increases in villus height and crypt depth, as well as intestinal epithelial cell length and numbers [72].

Tissue engineering

In the near future, a tissue-engineered small bowel may become a valuable alternative to some of the above-mentioned surgical techniques. More importantly, it might become a therapy alternative to intestinal transplantation with the potential to avoid lifelong immunosuppression and graft-versus-host disease. In experimental research, acellular biological scaffolds have been used as structural support for native cells and as a basis for the regeneration of intestinal tissue [73]. Another approach employs so-called "organoid units" consisting of the cores of mesenchymal stroma cells with overlying villus structures. Tissue-engineered intestine in these models shows a differentiated epithelium with tight junctions, microvilli, and intact ion transporters/channels [74]. The experimental results are promising, but clinical experience will be needed to determine the value of the tissue-engineered small bowel as a therapeutic option.

Conclusions

Children with a short bowel syndrome are difficult to compare, because the individual situation is dependent on many factors. Congenital forms of short bowel

(gastroschisis, multiple atresias) are very different from postnatally acquired diseases (NEC, volvulus). In addition, not only the length of the remaining bowel but also its location (jejunum, ileum) and its function/motility have a significant effect on the adaptation process and the duration of parenteral nutrition. The multidisciplinary therapy concept is currently the accepted basis for successful therapy. Additional surgical interventions are needed in a small percentage of patients, and the technique must be tailored to the individual needs of the child. They support the adaptation process and result in weaning of parenteral nutrition in about 60% of patients. However, due to individual differences in the short bowel, even identical surgical strategies are not easy to compare unless patients are divided into clear-cut groups. Definitions of such groups have not been provided so far.

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