The American Journal of Surgery 217 (2019) 772–782

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Review

Retracing our STEPs: Four decades of progress in intestinal lengthening procedures for short bowel syndrome

Chasen J. Greig [a], Pilyung S. Oh [b], Erica R. Gross [c], Robert A. Cowles [a, *]

[a] Section of Pediatric Surgery, Department of Surgery, Yale School of Medicine, New Haven, CT, 06520, USA
[b] Division of Pediatric Surgery, Department of Surgery, Weill Cornell Medicine, New York, NY, 10021, USA
[c] Division of Pediatric Surgery, Department of Surgery, Stony Brook Medicine, Stony Brook, NY, 11794, USA

ARTICLE INFO

Article history:
Received 10 August 2018
Received in revised form
7 November 2018
Accepted 19 November 2018

ABSTRACT

The surgical management of intestinal failure secondary to short bowel syndrome has undergone tremendous evolution in the last several decades. From the landmark description of an intestinal lengthening procedure by Bianchi in 1980 to the multidisciplinary modern care paradigm known as intestinal rehabilitation, innovative new treatments in this field have vastly improved patient outcomes. Initial attempts to treat short bowel syndrome surgically saw the birth of reversed intestinal segments, artificial valves and colonic transposition, all aimed at decreasing transit time and thus increasing absorption. In the long term, a common pitfall of these approaches, and intestinal adaptation itself, is bowel dilation and the associated poor motility, dysfunction and propensity for bacterial overgrowth. The development of techniques to mitigate these unfavorable conditions was a prelude to the birth of modern day operations aimed at increasing bowel length and improving function. This review examines the relevant historical approaches to short bowel syndrome and how they provided the foundation for the development of current intestinal lengthening surgery, followed by an in-depth discussion of surgical techniques and their outcomes.

Introduction

Intestinal failure (IF) is a disease affecting both adults and children and can be defined as a reduction in gastrointestinal absorptive function below what is required for adequate growth or homeostasis.[1] While the majority of adult IF cases are due to acquired conditions, childhood IF most commonly results from a congenital abnormality or a major intestinal catastrophe occurring early in life (Table 1). One can postulate that the small intestine of a growing child must function more efficiently than in the adult since it not only supports normal homeostasis but, in addition, absorbs additional protein and calories necessary for somatic growth. A combination of effective motility, unimpaired enterocyte function, and sufficient intestinal surface area facilitates absorption of these necessary calories and nutrients.

Although the terms IF and short bowel syndrome (SBS) are often used interchangeably, they are not truly synonymous as there are causes of IF where the bowel length is either minimally shortened or normal. The common causes of IF in neonates, infants and children are shown in Table 2. When a large segment of the intestine is lost, the remaining intestine undergoes compensatory changes collectively known as intestinal adaptation. The adaptive response of the intestine has been reviewed elsewhere[2,3] but can be summarized as alterations in mucosal morphometric parameters and bowel length and diameter which result in an overall increase in surface area for absorption within the remaining intestine. Intestinal adaptation in the pediatric population differs from the adult population in that enteral autonomy can be seen after many years of parenteral nutrition (PN) dependence, in contrast to adults in which autonomy is rarely achieved beyond 2 years. Unfortunately, reported autonomy rates vary widely, ranging from ~40 to 80%, and it should be noted that these data come from leading IF centers across the world.[4,5] Moreover, liberation from supplemental PN does not eliminate the possibility of regression back to dependence, highlighting the importance of understanding the factors involved in the ability of the intestine to adapt and eventually absorb sufficient nutrients for growth and survival. For those who continue to rely on supplemental PN, most will undergo intervention at some

* Corresponding author. Division of Pediatric Surgery, Yale School of Medicine, 333 Cedar Street, FMB 131, New Haven, CT, 06520-8062, USA.
E-mail address: robert.cowles@yale.edu (R.A. Cowles).

https://doi.org/10.1016/j.amjsurg.2018.11.025
0002-9610/

Table 1
Causes of pediatric intestinal failure.

- *Short Bowel Syndrome (See Table 2)*
- *Mucosal Enteropathies*o Microvillus Inclusion Disease
  - o Tufting Enteropathy
  - o Autoimmune Enteropathy
  - o IPEX Syndrome
  - o Transport Defects
  - o Enzyme/Micronutrient Defeciencies
  - o Lymphangiectasia
- *Motility Disorders*o Chronic Intestinal Pseudo-Obstruction
  - o Long-segment Hirschsprung Disease
  - o Neuromuscular Disorders of the Intestine/Colon

point in the form of surgical lengthening procedures or transplantation in an effort to achieve enteral autonomy or due to complications of prolonged PN exposure.

While the intestinal adaptive response aims to increase function, the associated dilation which occurs has the potential to be counterproductive by preventing effective peristalsis. The result in patients whom have undergone massive resection is short and dilated bowel which has poor motility, a prime environment for bacterial overgrowth and poor absorption. This observation prompted surgeons interested in SBS to design surgical methods aimed at mitigating these maladaptive changes, and represents a paradigm shift in the strategy of surgical management.

Rather than merely review techniques and outcomes for surgery in short bowel syndrome, this review will discuss the initial early observations and procedures which provided the foundation for development of modern-day techniques. Particularly, the rationale leading to the procedures at the time of their development will be discussed and the role of those techniques in the progression toward the currently performed procedures will be highlighted. Along with these historical perspectives, the available outcomes data for these techniques will be reviewed, which were arguably the most important aspect of the success or failure of the various techniques. One of the aims of this review is to highlight the value of persistent innovation through research, which was critical in the development of surgical lengthening procedures resulting in the significant improvement in patient outcomes and ultimately the chance for enteral autonomy for patients with short bowel syndrome.

History of early surgical treatment of short bowel syndrome

Surgical therapy for SBS dates as far back as the late 19th century. Early techniques were developed in animal models and aimed to increase the contact time between the intestinal mucosa and ingested food to allow for more complete intestinal digestion and absorption. Interposed segments, valve construction, and intestinal pacing all originated with the intent of slowing antegrade flow and increasing transit time.

Mall and Halsted first investigated the use of a reversed segment of bowel in dogs near the turn of the century, which was successful in creating a functional obstruction and slowing transit.[6,7] The use of this reversed segment proved to be fatal, however, and further investigations over the next several decades failed to change prevailing opinion that reversed intestinal segments were incompatible with survival. It was a half century before Hammer et al. performed the procedure as a means to develop an animal model for gastric ulcers and provided some of the first evidence of feasibility of the operation, which would later be supported by Singleton et al.[8,9] In 1957 Poth performed segmental reversal in dogs to combat dumping syndrome after gastric resection, setting the stage for subsequent investigators to utilize these techniques for further study of post-gastrectomy sequela in animal models.[10] Gibson was the first to apply the procedure to humans in 1962.[11] An elderly patient presented with peritonitis and was found to have necrosis of a large portion of her small bowel and colon which was resected and reconstructed with a reversed segment of distal jejunum with jejunocolic anastomosis (Fig. 1). The patient did remarkably well given the presenting pathology, and went on to demonstrate weight gain, normalization of metabolic derangements, and normal bowel function in the postoperative period. Encouraging results over the next several years stimulated the adoption of reversed segments as a treatment option for patients with post-resection gastric hypersecretion, post-vagotomy diarrhea and high output ileostomies.[12,13]

In addition to reversed segments, this time period also saw the rise of partially obstructive intestinal valves as a technique to treat SBS. These valves were initially developed for hepatobiliary surgery to prevent the grave complications seen with regurgitation of intestinal contents into the biliary system,[14] but Stahlgren applied the technique for the management of malnutrition following massive intestinal resection.[15] Using partial thickness sutures to create a pleated valve in the jejunum of dogs following major small bowel resection, the authors successfully improved nitrogen and fat absorption while avoiding intestinal obstruction and contractile dysfunction (Supplementary Fig. 1). Success in animal models resulted in the first attempts at valve creation in humans by Ackroyd et al., in 1969 and Waddell et al., in 1970.[16,17] However, subsequent data were inconsistent in both human and animal models[18–20] which contributed to the decline in the popularity of the procedure, although it is currently felt to be useful as an adjunct procedure in select patients.[21,22]

Together, these techniques provided the foundation for the concept of altering intestinal transit time as a treatment modality of SBS. In the pursuit of improved outcomes, proponents of colon transposition hypothesized that the infrequent contractions intrinsic to the colon might improve the inconsistent results seen when using the small bowel. Hutcher et al. first investigated the transposition of colonic segments in dogs following extensive loss of small intestine,[23] resulting in dramatically improved mortality rate and growth. This group also demonstrated the utility of colonic transposition irrespective of the location of remaining bowel, i.e. ileum vs jejunum.[24] One of the earliest reports in humans involved colonic transposition of a 24 cm isoperistaltic segment of colon in a five month-old boy with SBS.[25] The child had 15 cm of small bowel after resection for volvulus, and suffered from diarrhea and difficulty maintaining weight. Following colonic transposition, transit time improved and he was maintained on an enteral diet with resolution of diarrhea. Three years later, a series of six infants treated with colonic transposition was published by Glick et al.[26] which saw the treated infants go on to meet growth and developmental milestones while tolerating an oral diet during the follow-up period.

Despite short term success with targeting transit time, a new hurdle in the successful surgical management of these patients

Table 2
Causes of pediatric short bowel syndrome by age group.

Neonatal	Infant	Childhood
Abdominal Wall Defects	Necrotizing Enterocolitis	Intussusception
Intestinal Atresias	Trauma	Inflammatory Bowel Disease
Necrotizing Enterocolitis	Vascular Accidents	Trauma
Neuromuscular Disorders	Volvulus	Tumor
Vascular Accidents		Vascular Accidents
Volvulus		Volvulus

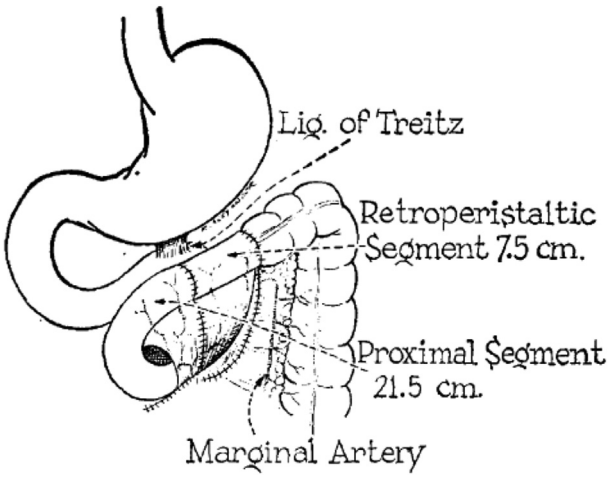

Fig. 1. Original figure from Gibson et al.[11] depicting the use of a reversed distal jejunal segment following massive bowel resection for necrosis.

emerged in the form of bowel dilation. With its associated detriments, dilation was increasingly appreciated as a common outcome and contributing factor to late complications in nearly all of the available procedures at the time. Initially, the techniques developed to combat dilation were intended to treat patients with intestinal atresia. One of the earliest reports from Thomas[27] describes a tapering jejunoplasty to allow for anastomosis between the dilated bowel proximal to the atresia and the smaller caliber bowel distal to the atresia. Howard and Otherson[28] later described three cases in which the tapering jejunoplasty was used to facilitate anastomosis between the two segments of bowel with significantly different diameters. Grosfeld et al. later used staplers to facilitate the operation[29] and a subsequent technique developed by de Lorimier et al.[30] allowed for the preservation of mucosa despite tapering needed to complete the anastomosis (Fig. 2 and Supplementary Fig. 2). The optimal surgical management of dilated bowel would thus become one of the most critical elements in the field of intestinal rehabilitation, and many of the core principles were developed in this era and provided the foundation for the development of the modern techniques to treat short bowel syndrome.

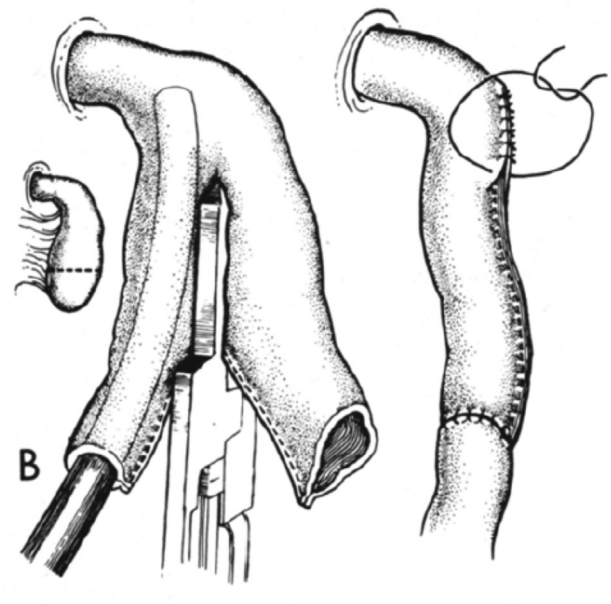

Fig. 2. Portion of the original figure taken from Grosfeld et al.[29] depicting the use of a stapler to resect the antimesenteric portion of dilated bowel, with subsequent creation of the anastomosis with the smaller caliber distal segment.

The birth of intestinal lengthening procedures

The bianchi procedure: longitudinal intestinal lengthening and tailoring (LILT)

Adrian Bianchi is considered one of the pioneers in intestinal lengthening surgery. In his landmark paper in 1980, he described blunt division of the peritoneal leaves of the small bowel mesentery, which supply distinct halves of the bowel, and division of the small intestine longitudinally along the mesenteric and antimesenteric walls.[31] Each of these halves were subsequently tubularized to create two parallel, vascularized loops of bowel with half the original diameter which were then anastomosed end-to-end in an isoperistaltic fashion (Fig. 3). In the initial animal model, six of eight pigs survived and the neo-intestine was examined 21 weeks postoperatively, revealing peristalsis with stimulation and increased diameter.

Within a year of Bianchi's publication, Boeckman and Traylor described the first human case of a four year old with history of gastroschisis and intestinal ischemia at birth.[32] At a seven month follow up, the patient had gained weight, was tolerating a regular diet and was having formed stools. Shortly after, another group of surgeons successfully performed the procedure with remarkable results: all four patients were weaned from PN within months of the surgery.[33]

In 1995, Bianchi reviewed eleven subsequent case reports with the aim of developing specific indications for the lengthening procedure. By then the technique was known as longitudinal intestinal lengthening and tailoring, or LILT, and was one of the most popular options in a limited surgical armamentarium of lengthening procedures referred to as autologous gastrointestinal reconstruction (AGIR).[34] In his review, Bianchi found the most commonly reported complications were loss of hemiloop and anastomotic stricture while anastomotic leak and fistula formation were surprisingly rare occurrences. Although all survivors were able to tolerate enteral nutrition postoperatively, only four of 11 patients survived (36%). Five of the seven deaths were attributed to hepatic failure, one to sepsis, and one as a result of a failed intestinal transplant. In a subsequent report in 1997, Bianchi reviewed the surgical outcomes of LILT in 20 patients since 1995. These data again showed a clear association between survival and the severity of the underlying liver disease.[35] Nine of 20 patients survived, and strikingly ten of 11 (90%) deaths were attributed to hepatic failure. Along with mild or no hepatic dysfunction, greater than 40 cm of dilated residual bowel was associated with survival, while presence of the ileocecal valve, length of colon, and age at time of LILT did not appear to impact outcomes. Bianchi acknowledged that one could argue against early intervention as a means of self-selection of those patients in whom bowel adaptation has reached a plateau and have made it through the initial neonatal phase. However, he believed these data were compelling for early surgery as a means to help prevent hepatic injury and subsequent failure, especially in high risk infants (i.e. those with <40 cm residual bowel). Surgery at a time when the infant is in good physical condition and prior to the onset of liver injury would result in less dysmotility, dilatation and stasis and promote adaptation. Limiting these risk factors for bacterial translocation and subsequent septic insults would help prevent hepatic injury, while also theoretically increasing the amount of enterocyte-derived “hepatoprotective factors”.

Skeptics of the long-term benefits, including Thompson et al. stressed the importance of patient selection in determining

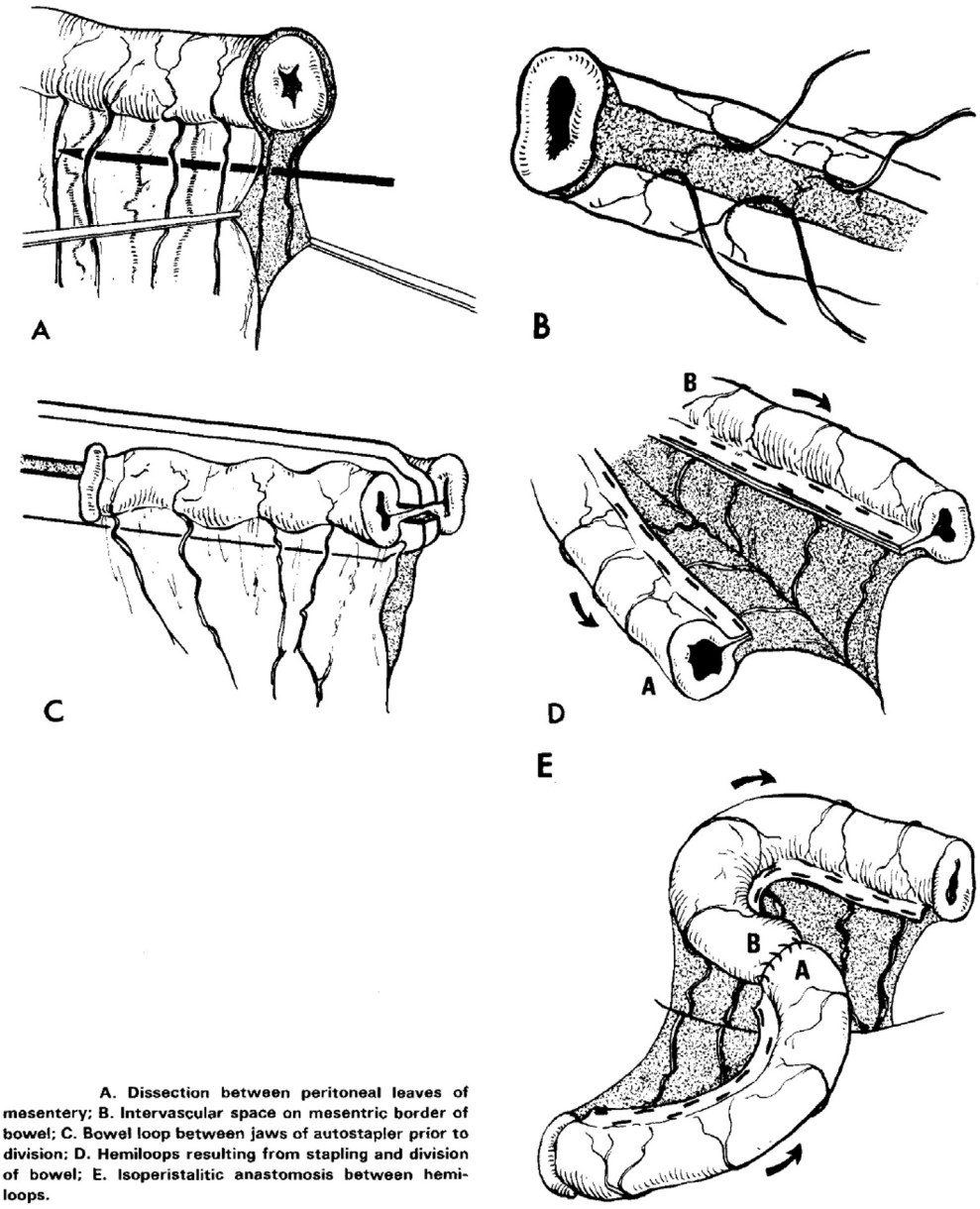

Fig. 3. Original figure from the landmark paper by Bianchi,[31] depicting the procedure that was the foundation for the longitudinal instestinal lenghtening and tailoring (LILT) technique.

whether LILT is appropriate, citing their experience that long-term benefits were realized in only about half of the patients receiving LILT.[36] Bueno et al. published a review of patients from their institution whom had undergone LILT and subsequently were referred for evaluation for transplantation.[37] Based on their data, these authors felt that while LILT was certainly beneficial in select patients, there should be particular attention paid to the status of the liver when considering patients for surgery early in life. They argued that with the complication rate associated with the procedure from their series, especially when performed within days of birth, the procedure should be deferred in the neonatal period until hepatic evaluation and involvement of multidisciplinary teams could take place.

In 2006, more than 25 years after Bianchi's initial description, two reviews were published updating the outcomes of the procedure. The first of these came from Walker and colleagues who discussed their experience with 19 patients over the course of 20 years.[38] The second was published by Bianchi summarizing his experience with AGIR.[39] In it he supported intestinal lengthening paired with maximal medical therapy as the primary management of SBS, with intestinal transplantation reserved for those unable to receive or following failed AGIR and medical management. Bianchi stressed the importance of an individualized and multidisciplinary approach to management of these patients, which he felt was best accomplished at dedicated intestinal failure centers.

Staged management for non-dilated bowel

As the benefits of LILT were becoming apparent, the requirement for dilated bowel meant a certain subset of patients who did not develop dilation were not candidates for lengthening surgery. Georgeson attempted to solve this issue and published a series describing a staged approach for non-dilated SBS in 1994.[40] Using artificial “nipple valves” created at an initial operation the authors

caused proximal dilatation and subsequently performed lengthening (LILT) procedures in a staged fashion. Six of the nine patients in this report underwent the staged approach, and results were modest with 4 of 6 patients able to tolerate at least 50% of their calories from enteral nutrition, compared to only two preoperatively.

Bianchi also developed a method for staged management of non-dilated SBS. As detailed in his review,[39] he developed a dual tube enterostomy approach which he termed the "controllable expansion-recycle model". In this technique, large bore enterostomy tubes are inserted into the proximal and distal bowel and brought out of the abdominal wall as tube enterostomies. Absorption and adaptation are stimulated by regulated delivery of the proximal contents to the distal bowel via the distal tube. The proximal intestine is induced to dilate through intermittent clamping of the proximal tube. This model fosters both proximal dilation and adaptation throughout the bowel, setting the stage for intestinal lengthening.

Alternatives to LILT

The kimura technique

The technical difficulty of performing the LILT procedure and the extensive handling of the mesentery prompted Kimura et al. developed a staged approach for isoperistaltic bowel elongation through the creation of an isolated bowel segment via myoenteropexy, which they had described previously.[41,42] To adapt this model to intestinal lengthening, they developed a staged procedure in which the dilated small bowel undergoes seromyotomy to expose the mucosa and then fixed to a "donor" organ such as the liver or abdominal wall. Following an interval of 8–10 weeks during which collaterals are formed, the patient returns to the OR where the dilated and now dual-perfused intestine is split longitudinally, and subsequently re-anastomosed end-to-end in an isoperistaltic manner (Fig. 4).

The technique was first performed in a clinical setting on a 1-day old infant born with an intrauterine midgut volvulus with the remaining small intestine limited to the duodenum, precluding the application of the Bianchi procedure but allowing for Kimura's staged approach.[43] Total small bowel length was increased from 34 to 90 cm and the patient went on to tolerate 50%–60% of calories enterally at 18 months of age. The major benefit of the Kimura technique, later adapted to what is now known as the isolated bowel segment or Iowa model, was the ability to offer a lengthening procedure to patients in which the anatomy of the remaining bowel made LILT prohibitive, such as in patients with only duodenum and colon remaining or in patients with inadequate mesentery.

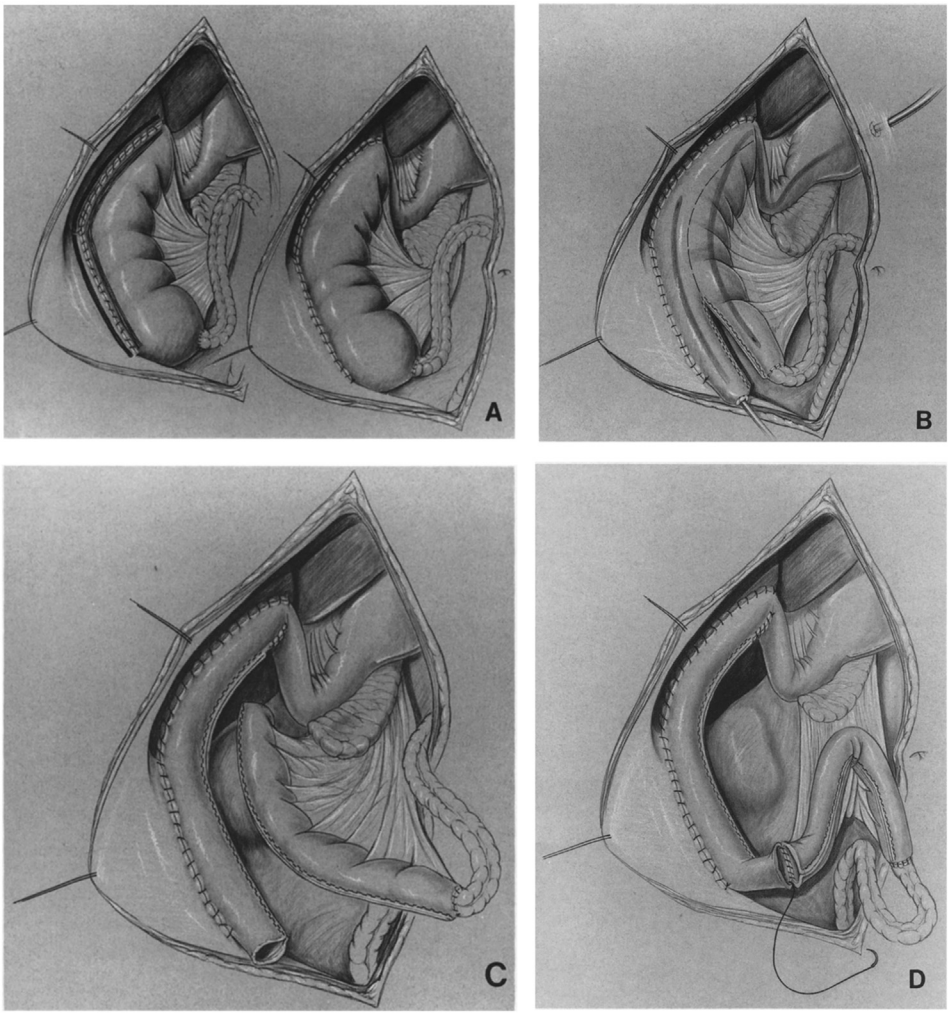

Fig. 4. Original diagrams of the Kimura Technique.[43] A – Seromyotomy and coaptation of dilated small bowel to the liver. B – Longitudinal division of the dilated small bowel following collateral formation. C – Completion of division and mobilization of mesenteric portion. D – Anastomosis.

Serial transverse enteroplasty

Another promising alternative to LILT which was developed in the early 2000's was the serial transverse enteroplasty, or STEP, which is now one of the most commonly performed lengthening procedures alongside LILT. Kim et al. described the technical principles of the procedure in a pig model in 2003.[44] Six young pigs underwent laparotomy and interposition of a 55 cm reversed jejunal segment creating partial intestinal obstruction and intestinal dilation. A stapler was then applied from alternating directions perpendicular to the long axis of the intestine with partial overlap to form a zig-zag-like channel (Fig. 5). In this manner, all applications of the stapler were placed parallel to the direction of the mesenteric blood supply, avoiding compromise of intestinal blood flow. This initial description demonstrated both the feasibility, with all animals surviving to study endpoint, and advantages of the procedure, as all animals remained obstruction-free and had an increased linear length of bowel both immediately post-procedure and at the conclusion of the study six weeks later. This group subsequently published follow-up data demonstrating an increase in intestinal function following STEP in this animal model.[45]

The first clinical application of the STEP procedure was performed by this group in a two year old boy in 2003.[46] The infant suffered from gastroschisis with necrosis of the majority of the bowel, leaving only a portion of proximal jejunum and distal colon. The initial management of the child included an end jejunostomy and Hartmann's procedure, and commencement of parenteral nutrition. Bowel continuity was restored at three months of age, but he was still TPN-dependent and suffered from poor motility with bacterial overgrowth in the dilated jejunal segment. The patient underwent a Bianchi (LILT) procedure at 11 months of age, which produced an additional 58 cm of intestinal length (from 72 cm to 130 cm), but remained TPN-dependent and developed recurrent dilation. Thus, at 23 months of age the STEP procedure was performed and an 83 cm segment of dilated distal jejunum was lengthened to 147 cm. He had a very successful course with oral nutrition restarted within the first two weeks and radiographic studies demonstrating good tapering effect without obstruction or leak. Six months after surgery he was taking 50% of his calories enterally and weaning from PN.

Javid et al. provided the first aggregate analysis of outcomes in patients who underwent STEP.[47] Four out of five patients received the STEP procedure as the primary lengthening modality, with an 82% average increase in small bowel length and no perioperative complications. While follow-up nutrition information was only available for three of the five patients, the mean percentage of enteral nutrition was significantly increased in these patients from time of STEP (49%) to post-STEP (80%) and one patient was able to be fully weaned off parenteral nutrition. Around this time, another group of investigators applied STEP as the initial surgery for a newborn with severe short bowel secondary to a type IIIa jejunal atresia.[48] The patient had severely dilated jejunum proximal to the defect and a large discrepancy in caliber with distal colon such that anastomosis following tapering would have resulted in a substantial loss in mucosal absorptive area. The STEP procedure was performed and within 2 weeks, the child began having bowel function and was tolerating full enteric feeds without radiographic evidence of leak or obstruction.

As the STEP procedure gained popularity, new reports documented the feasibility of repeat STEP following re-dilation after initial lengthening procedures.[49,50] The first report of long-term nutritional outcomes was later published by Duggan et al.[51] Four children with SBS treated with STEP were analyzed after a mean postoperative follow-up period of approximately one year (range: 252–493 days). The mean enteral nutrition intake rose significantly from 48% preoperatively to 62% postoperatively and the procedure was associated with improved growth and body composition in all four subjects.

The continued rise in number of patients treated with a STEP led to the formation of the International STEP Data Registry allowing for larger, multicenter patient enrollment and follow-up. Initial data were compiled and analyzed for 38 patients from 19 centers across 3 countries in 2006.[52] Indications for STEP included SBS, bacterial overgrowth, and neonatal atresia and mean intestinal length was significantly increased in all groups (68 cm ± 44 cm to 115 ± 87 cm) while the SBS cohort also had a significant increase in

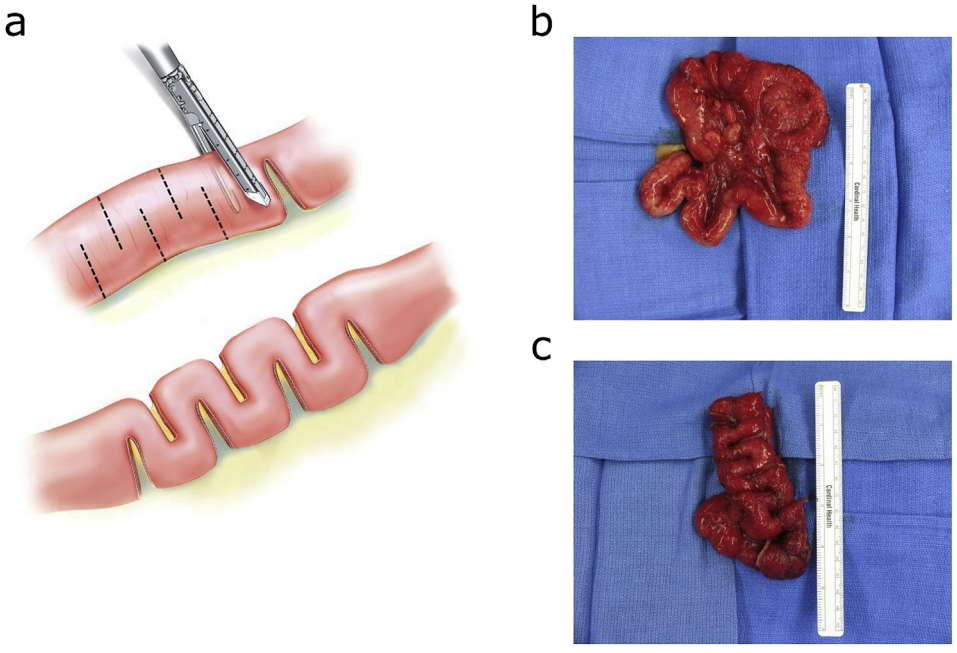

Fig. 5. (a) Artist rendition of the serial transverse enteroplasty (STEP) procedure. Intraoperative photos of the STEP procedure prior to staple firings (b), and after staple firings (c).

enteral tolerance (31% ± 31%–67% ± 37%). Minor complications included bowel obstruction, abscess, and staple line leak and occurred in a total of seven patients. In long-term follow up, three patients progressed to transplantation and another three patients died. Since then, the international STEP registry has released a follow-up report updating the outcomes of all patients entered into the registry.[53] Although the increase in intestinal length in this follow-up report wasn't as large as in the initial report (median increase from 49 to 75 cm), mortality did not significantly change (9.9% vs 7.9%), and the number of patients requiring transplantation actually decreased by nearly half (4.5% vs 7.9%). Table 3 summarizes patient data and outcomes from these two reports.

The original STEP investigators also released long-term follow up data not long after the reports from the registry.[54] This report included 16 patients whom received the STEP procedure with a median postoperative observation period of 23 months. The most common indication for STEP was failure to advance on enteral nutrition. At five years, 6/16 (38%) had been weaned from PN and remained on enteral nutrition, but an increase in enteral tolerance of 1.4% per month overall was observed. Two of the patients ultimately received transplantation and another five went on to develop re-dilation, with one of these patients requiring repeat STEP operation. Reported complications included catheter-related bacteremia (31%), GI bleeding (13%) and obstruction requiring operative intervention (7%), but no deaths. The relative frequency of re-dilation observed following STEP prompted Kang to evaluate the factors associated with re-dilation and its effect on outcomes.[55] The authors found longer PN use following STEP increases the probability of bowel re-dilation and, not surprisingly, that re-dilation was associated with lower rates of enteral autonomy. The phenomenon triggered investigation into using LILT to manage dilation after STEP, analogous to the circumstances in which STEP was initially employed.[56]

With the rise of STEP came one of the first systematic reviews of the literature comparing the two predominant lengthening techniques of the time: STEP and LILT.[57] This report found the two procedures to be very similar in terms of increased intestinal length, successful weaning from PN and subsequent progression to transplantation. Postoperative complications including bleeding, stricture, leakage and redilation were not significantly different, although bleeding and redilation trended toward occurring more frequently with STEP. Arguably the most significant conclusion drawn from this report was that outcomes did not differ significantly, but STEP offers several technical advantages. For example, the STEP can be performed in the duodenum and proximal jejunum as well as in short and asymmetric bowel segments in which LILT is not feasible. In addition, the STEP can be repeated while LILT cannot.

As is often the case, the predominantly positive early data following the development of STEP were tempered as more follow-up data were published. These included reports of staple line ulcers resulting in GI bleeding following STEP and an analysis of infectious complications following STEP.[58,59] Overall these data did not suggest complications occurred at an unacceptably high rate, however, and the STEP procedure continues to be paramount in the surgical management of SBS.

Emerging techniques: mechanical distraction, spiral intestinal lengthening and tailoring and tissue engineering

The trophic effect of mechanical stress on tissues was initially recognized in the orthopedic arena as it related to limb-lengthening.[60] By the end of the century, investigators began to experiment with the tension-stress principle to induce intestinal growth. Chen et al. in China and Printz et al. in Germany both experimented with the use of mechanical distraction of the intestine as a means to increase length.[61,62] Over the next several years, investigators demonstrated the feasibility of mechanical distraction to induce "enterogenesis" in various animal models, including early reports of preserved function in the lengthened segments.[63,64] More recent work in this area has focused on novel polymers and materials used to develop distraction devices which are easier to place and result in reliable lengthening.[65–67] These reports have investigated both extraluminal and intraluminal devices, and some have begun to address one of the known limitations of mechanical distraction: the need for surgical isolation of the bowel segment being lengthened (Supplementary Fig. 3). While still in its infancy, the role of distraction enterogenesis in the future management of SBS appears promising.

The development of spiral intestinal lengthening and tailoring, or SILT, represents the evolution of the LILT procedure. An investigative group including Bianchi sought to develop a method to lengthen bowel without the technically difficult and potentially morbid dissection of the mesentery (Fig. 6). The initial report described the procedure in simulated and porcine bowel to demonstrate technical feasibility, with encouraging results for lengthening and tapering of diameter. In the initial *in vivo* study using pigs, investigators successfully increased length and decreased diameter, and importantly demonstrated normal orientation of muscle fibers. To proponents of SILT, the orientation of the muscle fibers is a key advantage over STEP, as it theoretically provides for improved motility and thus diminished stasis and

Table 3
Comparison of reports from the International STEP Data Registry.

	2007 (*Modi* et al.) n = 38	2013 (*Jones* et al.) n = 111
Sex		
Male	20 (52.6%)	55 (49.5%)
Female	18 (47.4%)	56 (50.5%)
Median Age at STEP (months)	15.6	6.6
Primary Diagnosis		
Intestinal Atresia	13 (34.2%)	38 (34.2%)
Gastroschisis ± Volvulus	11 (29.0%)	50 (45.1%)
Necrotizing Enterocolitis	7 (18.4%)	9 (8.1%)
Other	7 (18.4%)	14 (12.6%)
Operative Data		
Preoperative Bowel Length	68 cm (mean)	49 cm (median)
Postoperative Bowel Length	115 cm (mean)	75 cm (median)
Outcomes		
Mortality	3 (7.9%)	11 (9.9%)
Transplant	3 (7.9%)	5 (4.5%)
Enteral Autonomy	*Not reported*	51 (45.9%)

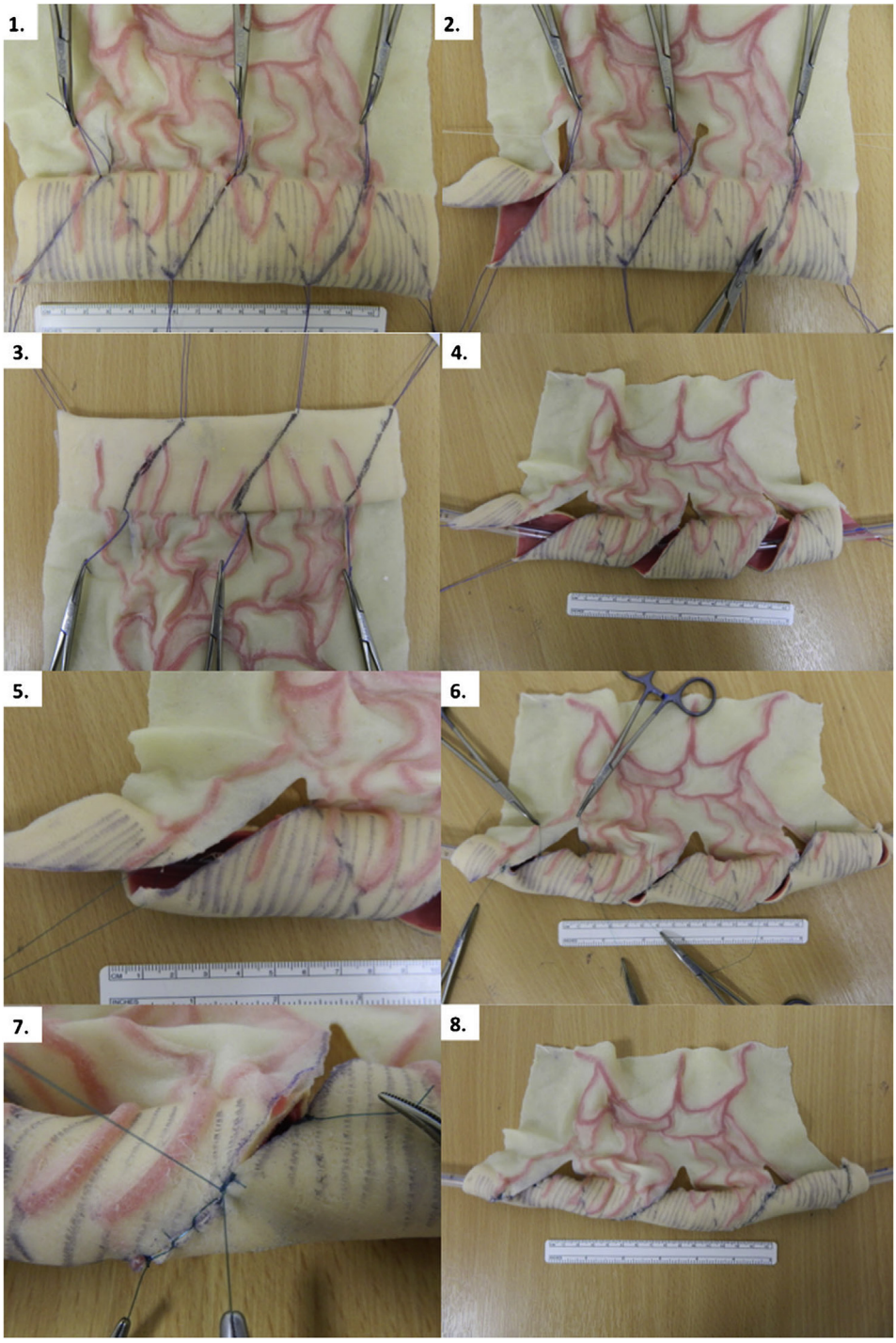

Fig. 6. Image from Cserni et al.[68] demonstrating the spiral intestinal lengthening and tailoring (SILT) technique on simulated bowel.

bacterial overgrowth compared to the drastically altered muscular architecture seen with STEP. The first clinical application of SILT was published in 2014 and involved a child who underwent massive small bowel resection at birth for midgut volvulus, leaving her proximal jejunum and a small segment of proximal colon.[68] The child had initially undergone a jejuno-colic anastomosis following resection, but developed a leak which prompted evaluation for SILT. Preparation for SILT included placement of tube jejunostomy and colostomy, and feeding gastrostomy. Nutrition was provided by a combination of PN, oral and tube feedings. Over the next 12 months, the proximal bowel was expanded as described previously [39] inpreparation for SILT. Following the SILT procedure the child had been weaned off PN and at six months follow up she had gained 1.8 kg, was having regular bowel movements, and was tolerating oral feedings in addition to overnight tube feedings. Soon after this initial report, a second case was reported involving a child whom also required massive resection for midgut volvulus.[69] One year following SILT, the child was gaining weight, taking over 80% of his calories enterally, and was having 2–3 semisolid bowel movements per day. Given its recent development, long term follow-up for SILT

Table 4
Summary and comparison of major surgical lengthening techniques.

	Rationale	Benefits	Complications	Key Lessons
Bianchi/LILT	Utilize dual mesenteric blood supply to bowel to lengthen and correct dilatation	Isoperistaltic and minimal disruption of muscle fibers	Ischemia/necrosis of hemiloop and anastsamotic strictures	Critical component of long term survival is severity of hepatic disease
STEP	Transverse staple firings parallel to the blood supply creates both tapering and linear length	Less technically difficult; high rates of enteral autonomy; less anatomic limitation compared to LILT	Disruption of muscle fibers; bacterial overgrowth; staple line ulcers; re-dilation after STEP	Surgeon controls the amount of lengthening and tapering depending on degree of dilation
Kimura Technique/Iowa Model	Use coaptation to induce a dual blood supply, allowing surgical lengthening	Can be performed on bowel with anatomic restrictions to other lengthening procedures	Failure of myenteropexy to result in adequate perfusion; multiple operations	Problematic anatomy does not prohibit surgical lengthening
Staged Procedures for Non-Dilated Bowel	Create dilatation in normal caliber short bowel to allow surgical lengthening	Can be performed on normal caliber bowel	Increased morbidity of multiple surgeries	Manipulation of inherent anatomy can allow for subsequent lengthening

is lacking and is required to better understand the potential benefits and complications. Despite this, the developers of the procedure have recently devised a modification to the procedure in an animal model which aims to improve on potential complications. The modified SILT consists of limited spiral incision of the seromuscular layers only, leaving the mucosa intact. This technique offers the theoretical advantage of an intact mucosa which could limit complications including leakage and abdominal abscess.[70]

The field of tissue engineering has the potential to revolutionize organ replacement in the future. While this review will not specifically address the current state of intestinal tissue engineering, it too may be a therapy that will positively impact patients with massive intestinal loss. Intestinal tissue engineering is currently under active study in the basic sciences and the concept has been the subject of several recent reviews.[71–73]

Conclusion

James C. Thompson once remarked “If we fail to vigorously pursue research, the medicine and surgery of tomorrow will be the medicine and surgery of today”.[74] The preceding review demonstrates the significance of translational research in the progress of surgical techniques to improve care for those with short bowel syndrome. While a major improvement in the mortality of these patients came with the development and eventual refinement of PN and the adoption of a multi-disciplinary management approach, non-transplant surgical procedures have had a substantial contribution to the care of SBS patients. Prior to the 1980's and introduction of PN, mortality rates were reported as high as 60%.[75] At the end of the following decade, two reviews of SBS patients revealed improved, but still unacceptably high, mortality rates of greater than 20%.[76,77] More recently, a review by Merras-Salmio reported a mortality rate of 5% for patients at a single institution from 2009 to 2014 who were treated according to a multidisciplinary modern protocol-based approach.[78] While these improvements in mortality cannot be solely attributed to the progress seen in the field of surgical lengthening, it is no doubt a significant contributor. Moreover, the improvements in morbidity associated with decreased time requiring PN, decreased central venous catheter-associated infections and avoiding intestinal transplant are not insignificant.

Table 4 summarizes and compares the most commonly applied procedures discussed in this review, reviewing the rationale, major benefits, complications and lessons learned from outcomes of each approach. As highlighted by the recent reviews above, contemporary surgical approaches such as STEP or LILT/SILT procedures allow for the best chances at achieving enteral autonomy, and are indicated in surgical management of intestinal failure due to short bowel syndrome. However, a critical aspect of these surgical approaches is that they are implemented in the setting of a multidisciplinary plan of care. Comparison of surgical lengthening procedures will continue, especially as technology improves and new techniques are developed, but the available data suggest that success of any given procedure requires that it be one facet of multimodal therapy. For this reason, most experts recommend management of these patients take place at intestinal failure/intestinal rehabilitation centers with the necessary expertise and comprehensive subspecialty support.

From the animal experiments of Mall and Halsted to clinical application of STEP and LILT/SILT, surgical procedures to treat SBS have undergone substantial progression through dedicated research. This commitment to improving clinical management through scientific innovation will continue to promote progress and enable innovations from the laboratory to change the surgical treatments of today into the surgical treatments of tomorrow.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2018.11.025.

References

1. Bines JE. Intestinal failure: a new era in clinical management. *J Gastroenterol Hepatol*. 2009 Oct;24(Suppl 3):S86–S92. PubMed PMID: 19799705.
2. Bharadwaj S, Tandon P, Meka K, et al. Intestinal failure: adaptation, rehabilitation, and transplantation. *J Clin Gastroenterol*. 2016 May-Jun;50(5):366–372. PubMed PMID: 26974760. Epub 2016/03/15. eng.
3. Tappenden KA. Intestinal adaptation following resection. *JPEN - J Parenter Enter Nutr*. 2014 May;38(1 Suppl):23S–31S. PubMed PMID: 24586019.
4. Squires RH, Duggan C, Teitelbaum DH, et al. Natural history of pediatric intestinal failure: initial report from the Pediatric Intestinal Failure Consortium. *J Pediatr*. 2012 Oct;161(4):723–728 e2. PubMed PMID: 22578586. Pubmed Central PMCID: PMC3419777.
5. Khan FA, Squires RH, Litman HJ, et al. Predictors of enteral autonomy in children with intestinal failure: a multicenter cohort study. *J Pediatr*. 2015;167(1):29–34.e1, 7//.
6. Corman ML. Classic articles in colonic and rectal surgery. William Stewart Halsted 1852-1922. Circular suture of the intestine–an experimental study. Part 3. *Dis Colon Rectum*. 1984 Nov;27(11):755–757. PubMed PMID: 6389048.
7. Mall FP. Reversal of the intestine. *Johns Hopkins Hospital Reports*. 1896;1:93–110.
8. Hammer JM, Visscher F, Hill EJ. EXperimental gastrojejunal ulcers produced by reversing the duodenum. *AMA Arch Surg*. 1953;67(1):23–28.
9. Singleton Jr AO, Rowe EB. Peristalsis in reversed loops of bowel. *Ann Surg*. 1954 Jun;139(6):853–857. PubMed PMID: 13159136. Pubmed Central PMCID: PMC1609499.
10. Poth EJ, Smith LB. Digestion and absorption following gastrectomy using reversed jejunal segments: follow up of 50 cases. *Ann Surg*. 1966 Jun;163(6):957–960. PubMed PMID: 5933810. Pubmed Central PMCID: PMC1477039. Epub 1966/06/01. eng.

11. Gibson LD, Carter R, Hinshaw DB. Segmental reversal of small intestine after massive bowel resection. Successful case with follow-up examination. *J Am Med Assoc*. 1962 Dec 1;182:952–954. PubMed PMID: 13947733.
12. Herrington Jr JL, Edwards WH, Carter JH, Sawyers JL. Treatment of severe postvagotomy diarrhea by reversed jejunal segment. *Ann Surg*. 1968 Sep;168(3):522–541. PubMed PMID: 5675938. Pubmed Central PMCID: 1387360.
13. Kimura S, Dragstedt 2nd LR. Reversed jejunal segments and gastric hypersecretion. *Arch Surg*. 1969 Jun;98(6):713–715. PubMed PMID: 5768066. Epub 1969/06/01. eng.
14. Basso DE. The efficacy and applicability of an intussuscepted conical valve in preventing regurgitation and leakage of intestinal contents. *Ann Surg*. 1951 Apr;133(4):477–485. PubMed PMID: 14819984. Pubmed Central PMCID: PMC1616856. Epub 1951/04/01. eng.
15. Stahlgren LH, Roy RH, Umana G. A mechanical impediment to intestinal flow; physiological effects on intestinal absorption. *J Am Med Assoc*. 1964 Jan 4;187:41–44. PubMed PMID: 14067968.
16. Waddell WR, Kern Jr F, Halgrimson CG, Woodbury JJ. A simple jejunocolic "valve". For relief of rapid transit and the short bowel syndrome. *Arch Surg*. 1970 Apr;100(4):438–444. PubMed PMID: 4906822.
17. Ackroyd FW, Giles G, McDermott Jr WV. Ileal mucosal valve to prevent reflux at the ileorectal anastomosis in the colon exclusion operation for hepatic encephalopathy. *Surg Forum*. 1969;20:356–357. PubMed PMID: 5383086.
18. Ricotta J, Zuidema GD, Gadacz TR, Sadri D. Construction of an ileocecal valve and its role in massive resection of the small intestine. *Surg Gynecol Obstet*. 1981 Mar;152(3):310–314. PubMed PMID: 7466579.
19. Grieco GA, Reyes HM, Ostrovsky E. The role of a modified intussusception jejunocolic valve in short-bowel syndrome. *J Pediatr Surg*. 1983 Aug;18(4):354–358. PubMed PMID: 6620073. Epub 1983/08/01. eng.
20. Careskey J, Weber TR, Grosfeld JL. Ileocecal valve replacement. Its effect on transit time, survival, and weight change after massive intestinal resection. *Arch Surg*. 1981 May;116(5):618–622. PubMed PMID: 7235955.
21. Beyer-Berjot L, Joly F, Maggiori L, et al. Segmental reversal of the small bowel can end permanent parenteral nutrition dependency: an experience of 38 adults with short bowel syndrome. *Ann Surg*. 2012 Nov;256(5):739–744. discussion 44-5. PubMed PMID: 23095617.
22. Sommovilla J, Warner BW. Surgical options to enhance intestinal function in patients with short bowel syndrome. *Curr Opin Pediatr*. 2014 Jun;26(3):350–355. PubMed PMID: 24759225. Epub 2014/04/25. eng.
23. Hutcher NE, Salzberg AM. Pre-ileal transposition of colon to prevent the development of short bowel syndrome in puppied with 90 percent small intestinal resection. *Surgery*. 1971 Aug;70(2):189–197. PubMed PMID: 5560180. Epub 1971/08/01. eng.
24. Hutcher NE, Mendez-Picon G, Salzberg AM. Prejejunal transposition of colon to prevent the development of short bowel syndrome in puppies with 90 per cent small intestine resection. *J Pediatr Surg*. 1973 Oct;8(5):771–777. PubMed PMID: 4753012. Epub 1973/10/01. eng.
25. Garcia VF, Templeton JM, Eichelberger MR, et al. Colon interposition for the short bowel syndrome. *J Pediatr Surg*. 1981 Dec;16(6):994–995. PubMed PMID: 7338785. Epub 1981/12/01. eng.
26. Glick PL, de Lorimier AA, Adzick NS, Harrison MR. Colon interposition: an adjuvant operation for short-gut syndrome. *J Pediatr Surg*. 1984 Dec;19(6):719–725. PubMed PMID: 6440966.
27. Thomas Jr CG. Jejunoplasty for the correction of jejunal atresia. *Surg Gynecol Obstet*. 1969 Sep;129(3):545–546. PubMed PMID: 5820936. Epub 1969/09/01. eng.
28. Howard ER, Othersen Jr HB. Proximal jejunoplasty in the treatment of jejunal atresia. *J Pediatr Surg*. 1973 Oct;8(5):685–690. PubMed PMID: 4753004. Epub 1973/10/01. eng.
29. Grosfeld JL, Ballantine TV, Shoemaker R. Operative mangement of intestinal atresia and stenosis based on pathologic findings. *J Pediatr Surg*. 1979 Jun;14(3):368–375. PubMed PMID: 480102. Epub 1979/06/01. eng.
30. de Lorimier AA, Harrison MR. Intestinal plication in the treatment of atresia. *J Pediatr Surg*. 1983;18(6):734–737, 1983/12/01.
31. Bianchi A. Intestinal loop lengthening—a technique for increasing small intestinal length. *J Pediatr Surg*. 1980;15(2):145–151, 1980/04/01.
32. Boeckman CR, Traylor R. Bowel lengthening for short gut syndrome. *J Pediatr Surg*. 1981 Dec;16(6):996–997. PubMed PMID: 7338786. Epub 1981/12/01. eng.
33. Bianchi A. Intestinal lengthening: an experimental and clinical review. *J R Soc Med*. 1984;77(Suppl 3):35–41. PubMed PMID: 6471060. Pubmed Central PMCID: PMC1440516.
34. Bianchi A. Autologous gastrointestinal reconstruction. *Semin Pediatr Surg*. 1995 Feb;4(1):54–59. PubMed PMID: 7728509.
35. Bianchi A. Longitudinal intestinal lengthening and tailoring: results in 20 children. *J R Soc Med*. 1997 Aug;90(8):429–432. PubMed PMID: 9306995. Pubmed Central PMCID: PMC1296456.
36. Thompson JS, Pinch LW, Young R, Vanderhoof JA. Long-term outcome of intestinal lengthening. *Transplant Proc*. 2000 Sep;32(6):1242–1243. PubMed PMID: 10995930.
37. Bueno J, Guiterrez J, Mazariegos GV, et al. Analysis of patients with longitudinal intestinal lengthening procedure referred for intestinal transplantation. *J Pediatr Surg*. 2001 Jan;36(1):178–183. PubMed PMID: 11150461.
38. Walker SR, Nucci A, Yaworski JA, Barksdale Jr EM. The Bianchi procedure: a 20-year single institution experience. *J Pediatr Surg*. 2006 Jan;41(1):113–119. discussion -9. PubMed PMID: 16410119.
39. Bianchi A. From the cradle to enteral autonomy: the role of autologous gastrointestinal reconstruction. *Gastroenterology*. 2006 Feb;130(2 Suppl 1):S138–S146. PubMed PMID: 16473062.
40. Georgeson K, Halpin D, Figueroa R, et al. Sequential intestinal lengthening procedures for refractory short bowel syndrome. *J Pediatr Surg*. 1994 Feb;29(2):316–320. discussion 20-1. PubMed PMID: 8176611. Epub 1994/02/01. eng.
41. Kimura K, Soper RT. Isolated bowel segment (model 1): creation by myoenteropexy. *J Pediatr Surg*. 1990 May;25(5):512–513. PubMed PMID: 2141072.
42. Yamazato M, Kimura K, Yoshino H, et al. The isolated bowel segment (Iowa model II): motility across the anastomosis with or without mesenteric division. *J Pediatr Surg*. 1992 Jun;27(6):691–695. PubMed PMID: 1501024.
43. Kimura K, Soper RT. A new bowel elongation technique for the short-bowel syndrome using the isolated bowel segment Iowa models. *J Pediatr Surg*. 1993 Jun;28(6):792–794. PubMed PMID: 8331504.
44. Kim HB, Fauza D, Garza J, et al. Serial transverse enteroplasty (STEP): a novel bowel lengthening procedure. *J Pediatr Surg*. 2003 Mar;38(3):425–429. PubMed PMID: 12632361.
45. Chang RW, Javid PJ, Oh JT, et al. Serial transverse enteroplasty enhances intestinal function in a model of short bowel syndrome. *Ann Surg*. 2006 Feb;243(2):223–228. PubMed PMID: 16432355. Pubmed Central PMCID: PMC1448911.
46. Kim HB, Lee PW, Garza J, et al. Serial transverse enteroplasty for short bowel syndrome: a case report. *J Pediatr Surg*. 2003 Jun;38(6):881–885. PubMed PMID: 12778385. Epub 2003/06/05. eng.
47. Javid PJ, Kim HB, Duggan CP, Jaksic T. Serial transverse enteroplasty is associated with successful short-term outcomes in infants with short bowel syndrome. *J Pediatr Surg*. 2005 Jun;40(6):1019–1023. discussion 23-4. PubMed PMID: 15991189. Epub 2005/07/02. eng.
48. Wales PW, Dutta S. Serial transverse enteroplasty as primary therapy for neonates with proximal jejunal atresia. *J Pediatr Surg*. 2005 Mar;40(3):E31–E34. PubMed PMID: 15793710. Epub 2005/03/29. eng.
49. Piper H, Modi BP, Kim HB, et al. The second STEP: the feasibility of repeat serial transverse enteroplasty. *J Pediatr Surg*. 2006 Dec;41(12):1951–1956. PubMed PMID: 17161180.
50. Ehrlich PF, Mychaliska GB, Teitelbaum DH. The 2 STEP: an approach to repeating a serial transverse enteroplasty. *J Pediatr Surg*. 2007 May;42(5):819–822. PubMed PMID: 17502191.
51. Duggan C, Piper H, Javid PJ, et al. Growth and nutritional status in infants with short-bowel syndrome after the serial transverse enteroplasty procedure. *Clin Gastroenterol Hepatol*. 2006 Oct;4(10):1237–1241. PubMed PMID: 16904948.
52. Modi BP, Javid PJ, Jaksic T, et al. First report of the international serial transverse enteroplasty data registry: indications, efficacy, and complications. *J Am Coll Surg*. 2007 Mar;204(3):365–371. PubMed PMID: 17324769. Pubmed Central PMCID: PMC3217837. Epub 2007/02/28. eng.
53. Jones BA, Hull MA, Potanos KM, et al. Report of 111 consecutive patients enrolled in the international serial transverse enteroplasty (STEP) data registry: a retrospective observational study. *J Am Coll Surg*. 2013 Mar;216(3):438–446. PubMed PMID: 23357726. Epub 2013/01/30. eng.
54. Ching YA, Fitzgibbons S, Valim C, et al. Long-term nutritional and clinical outcomes after serial transverse enteroplasty at a single institution. *J Pediatr Surg*. 2009 May;44(5):939–943. PubMed PMID: 19433174. Pubmed Central PMCID: PMC3217836.
55. Kang KH, Gutierrez IM, Zurakowski D, et al. Bowel re-dilation following serial transverse enteroplasty (STEP). *Pediatr Surg Int*. 2012 Dec;28(12):1189–1193. PubMed PMID: 23160903. Epub 2012/11/20. eng.
56. Fusaro F, Hermans D, Wanty C, et al. Post-serial transverse enteroplasty bowel redilatation treated by longitudinal intestinal lengthening and tailoring procedure. *J Pediatr Surg*. 2012 Oct;47(10):e19–e22. PubMed PMID: 23084225. Epub 2012/10/23. eng.
57. Frongia G, Kessler M, Weih S, et al. Comparison of LILT and STEP procedures in children with short bowel syndrome – a systematic review of the literature. *J Pediatr Surg*. 2013 Aug;48(8):1794–1805. PubMed PMID: 23932625. Epub 2013/08/13. eng.
58. Gibbons TE, Casteel HB, Vaughan JF, Dassinger MS. Staple line ulcers: a cause of chronic GI bleeding following STEP procedure. *J Pediatr Surg*. 2013 Jun;48(6):E1–E3. PubMed PMID: 23845650. Epub 2013/07/13. eng.
59. Fujioka WK, Cowles RA. Infectious complications following serial transverse enteroplasty in infants and children with short bowel syndrome. *J Pediatr Surg*. 2015 Mar;50(3):428–430. PubMed PMID: 25746702. Epub 2015/03/10. eng.
60. Ilizarov GA. Clinical application of the tension-stress effect for limb lengthening. *Clin Orthop Relat Res*. 1990 Jan;(250):8–26. PubMed PMID: 2403497.
61. Chen Y, Zhang J, Qu R, et al. An animal experiment on short gut lengthening. *Chin Med J (Engl)*. 1997 May;110(5):354–357. PubMed PMID: 9594302.
62. Printz H, Schlenzka R, Requadt P, et al. Small bowel lengthening by mechanical distraction. *Digestion*. 1997;58(3):240–248. PubMed PMID: 9243119.
63. Park J, Puapong DP, Wu BM, et al. Enterogenesis by mechanical lengthening: morphology and function of the lengthened small intestine. *J Pediatr Surg*. 2004 Dec;39(12):1823–1827. PubMed PMID: 15616941.
64. Safford SD, Freemerman AJ, Safford KM, et al. Longitudinal mechanical tension induces growth in the small bowel of juvenile rats. *Gut*. 2005 Aug;54(8):1085–1090. PubMed PMID: 15840689. Pubmed Central PMCID: PMC1774906.
65. Sullins VF, Scott A, Wagner JP, et al. Intestinal lengthening in an innovative rodent surgical model. *J Pediatr Surg*. 2014 Dec;49(12):1791–1794. PubMed PMID: 25487485. Epub 2014/12/10. eng.

66. Fisher JG, Sparks EA, Khan FA, et al. Extraluminal distraction enterogenesis using shape-memory polymer. *J Pediatr Surg*. 2015 Jun;50(6):938–942. PubMed PMID: 25812443. Epub 2015/03/31. eng.
67. Scott A, Sullins VF, Steinberger D, et al. Repeated mechanical lengthening of intestinal segments in a novel model. *J Pediatr Surg*. 2015 Jun;50(6):954–957. PubMed PMID: 25818320. Epub 2015/03/31. eng.
68. Cserni T, Biszku B, Guthy I, et al. The first clinical application of the spiral intestinal lengthening and tailoring (silt) in extreme short bowel syndrome. *J Gastrointest Surg*. 2014 Oct;18(10):1852–1857. PubMed PMID: 24957255.
69. Alberti D, Boroni G, Giannotti G, et al. Spiral intestinal lenghtening and tailoring (SILT)" for a child with severely short bowel. *Pediatr Surg Int*. 2014 Nov;30(11):1169–1172. PubMed PMID: 25119303.
70. Mehrabi V, Mehrabi A, Jamshidi SH, et al. Modified spiral intestinal lengthening and tailoring for short bowel syndrome. *Surg Innovat*. 2016 Feb;23(1):30–35. PubMed PMID: 26220675. Epub 2015/07/30. eng.
71. Martin LY, Ladd MR, Werts A, et al. Tissue engineering for the treatment of short bowel syndrome in children. *Pediatr Res*. 2018 Jan;83(1-2):249–257. PubMed PMID: 28937976. Pubmed Central PMCID: PMC6002962.
72. Nakamura T, Sato T. Advancing intestinal organoid technology toward regenerative medicine. *Cell Mol Gastroenterol Hepatol*. 2018;5(1):51–60. PubMed PMID: 29204508. Pubmed Central PMCID: PMC5704126.
73. Hussey GS, Cramer MC, Badylak SF. Extracellular matrix bioscaffolds for building gastrointestinal tissue. *Cell Mol Gastroenterol Hepatol*. 2018;5(1):1–13. PubMed PMID: 29276748. Pubmed Central PMCID: PMC5736871.
74. Thompson JC. Presidential address. The role of research in the surgery of tomorrow. *Am J Surg*. 1984 Jan;147(1):2–8. PubMed PMID: 6691546.
75. Booth IW, Lander AD. Short bowel syndrome. *Bailliere Clin Gastroenterol*. 1998;12(4):739–773, 12//.
76. Mayr JM, Schober PH, Weissensteiner U, Hollwarth ME. Morbidity and mortality of the short-bowel syndrome. *Eur J Pediatr Surg*. 1999 Aug;9(4):231–235. PubMed PMID: 10532264. Epub 1999/10/26. eng.
77. Coran AG, Spivak D, Teitelbaum DH. An analysis of the morbidity and mortality of short-bowel syndrome in the pediatric age group. *Eur J Pediatr Surg*. 1999 Aug;9(4):228–230. PubMed PMID: 10532263. Epub 1999/10/26. eng.
78. Merras-Salmio L, Pakarinen MP. Refined multidisciplinary protocol-based approach to short bowel syndrome improves outcomes. *J Pediatr Gastroenterol Nutr*. 2015 Jul;61(1):24–29. PubMed PMID: 25729889. Epub 2015/03/03. eng.