First STEPs: Serial transverse enteroplasty as a primary procedure in neonates with congenital short bowel

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Abstract

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Background: Since its introduction as an alternative intestinal lengthening technique, serial transverse enteroplasty (STEP) has been increasingly used as the surgical treatment of choice for patients with refractory short bowel syndrome (SBS). While primary STEP for the treatment of congenital conditions was proposed in the original description of the procedure, emphasis was placed on a delayed or staged approach to these patients. To date, a comprehensive review of the outcomes from this sub-population has not been reported by the International STEP Data Registry.

Methods: A retrospective review of the International STEP Data Registry was performed to identify all patients who underwent STEP as a primary operative procedure for the treatment of congenital SBS. Changes in pre- and post-STEP values were assessed using paired t-tests with significance set at p < 0.05. Data are presented as mean ± standard deviation.

Results: Fifteen patients underwent primary STEP for congenital SBS between September 1, 2004, and April 10, 2012. Thirteen patients had follow-up information available. Causes of congenital SBS included closing gastroschisis, small bowel atresia, and midgut volvulus. Twelve patients had pre- and post-STEP bowel measurements taken. Average pre- and post-STEP bowel lengths were 32 ± 16 cm and 47 ± 22 cm, respectively. Intestinal length was increased by a mean of 15 ± 12 cm for a relative small bowel length increase of 50.4 ± 27.3% (p < 0.001). Only one patient required an ostomy at the time of primary STEP. A second patient required a temporary ostomy at 3 months of age that was later closed. There was one death from intestinal failure associated liver disease (IFALD). Another patient experienced IFALD progression and required liver and intestinal transplantation. The most commonly reported complication following primary STEP was obstruction or bowel re-dilatation requiring additional operative interventions. Nine patients underwent second STEP procedures under these circumstances. Eight patients remain dependent on parenteral nutrition, while three patients achieved enteral autonomy.

Conclusions: Primary STEP is a feasible and safe surgical option for the treatment of congenital conditions resulting in SBS. Primary STEP establishes early bowel continuity, creates intestinal length from congenitally dilated bowel, and appears to obviate the need for interval stomas and their associated loss of bowel length in neonates with congenital SBS. However, with recent changes in SBS management emphasizing intestinal rehabilitation, additional studies are needed to assess the long-term impact on intestinal adaptation of STEP performed in the neonatal period prior to adoption of this technique.

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Short bowel syndrome (SBS) is owing to the anatomic or functional loss of a large segment of small intestine and results in intestinal malabsorption [1]. Although the worldwide incidence has not been reported, a substantial portion of SBS cases are of congenital etiology and culminate in considerable loss of small intestine length [2,3]. Surgical management of congenital SBS focuses on the principles of bowel conservation and restoration of intestinal continuity [3]. However, conservation principles often give way to practical considerations at the time of the initial surgery resulting in resection of dilated intestinal segments or ostomy creation. Primary serial transverse enteroplasty (STEP) is an alternative approach that offers the potential benefits of promptly establishing intestinal continuity and avoiding further loss of intestinal absorptive area [3–5].

The STEP procedure was first described in 2003 as an alternative intestinal lengthening technique for patients with refractory SBS [6].
Similar to other bowel lengthening procedures, STEP lengthens the intestine and narrows bowel diameter with the intent of improving peristalsis and preventing small bowel bacterial overgrowth, malabsorption and sepsis [6,7]. In contrast, STEP has gained favorability as its novel approach is intuitive, relatively easy to perform, poses minimal threat to intestinal blood supply, can be utilized for varying degrees of bowel dilatation, and is repeatable should bowel dilatation recur [1,7]. Accepted STEP indications include intestinal failure and bacterial overgrowth refractory to maximal medical management, as well as neonatal intestinal atresias or obstructions with limited small bowel length and a dilated proximal segment [6,7]. Though neonatal intestinal atresias and other causes of congenital SBS have long been considered indications for STEP, the outcomes for this subgroup have not been formally investigated. This study sought to determine the safety and utility of primary STEP by reviewing the short- and long-term outcomes of this subgroup.

1. Methods

Data were obtained from the International STEP Data Registry. The STEP registry was created in 2004 approximately one year after the procedure’s introduction at Boston Children’s Hospital. Through voluntary reporting, the registry has accrued case data on over 200 patients from more than 45 centers worldwide. Patient variables collected in the registry include patient demographics, primary diagnosis and coexisting medical conditions, operative information, complications, and outcomes.

Study approval was granted by the Kapi’olani Medical Center for Women and Children institutional review board and approval to use the International STEP Data Registry was granted by the registry personnel at Boston Children’s Hospital. The registry was searched to identify all patients who underwent primary STEP for congenital short bowel syndrome (SBS). Data reflect patients treated between September 1, 2004 and April 10, 2012. For patients with incomplete registry data, email and telephone requests with referring surgeons were made. The patient variables used for analysis include gestational age, primary diagnosis, pre- and post-STEP bowel measurements (length and diameter), enteral tolerance, complications, ostomy creation, disease progression with development of intestinal failure associated liver disease (IFALD), need for transplantation, and mortality. Statistical analysis was performed using SPSS software (version 19.0, SPSS Inc./IBM, Chicago, IL). Mean change in bowel length as well as percent change was assessed using paired t-tests with significance set at \( p < 0.05 \). Data are presented as mean \( \pm \) standard deviation.

2. Results

Fifteen patients from 13 medical centers who had undergone primary STEP for congenital SBS were identified. Thirteen patients had follow-up information available. Mean gestational age was 35 weeks. Causes of congenital SBS include intestinal atresias (\( n = 9 \)), closing gastroschisis (\( n = 5 \)), and midgut volvulus (\( n = 1 \)) (Fig. 1). All patients with operative measurements (\( n = 12 \)) experienced intestinal tapering and gained intestinal length with the STEP procedure. Mean intestinal width was tapered from 4.4 \( \pm \) 1.0 cm to 1.7 \( \pm \) 0.3 cm (\( p < 0.001 \)). Pre-STEP bowel length ranged from 10 to 66 cm (mean = 32 \( \pm \) 16 cm). Post-STEP bowel length varied between 15 and 89 cm (mean = 47 \( \pm \) 22 cm). Intestinal length was increased by a mean of 15 \( \pm \) 12 cm translating to a relative increase in small bowel length of 50.4 \( \pm \) 27.3\% (\( p < 0.001 \); Fig. 2).

Few short-term complications and challenges to restoring or maintaining bowel continuity were described. Only 1 patient required ostomy creation at the time of primary STEP. A second patient required a temporary ostomy at 3 months of age that was later closed. No intra-operative complications were reported.

Over time, the most commonly reported long-term complication following primary STEP was obstruction or bowel re-dilatation requiring additional operative interventions. Nine patients underwent second STEP procedures under these circumstances. Late complications were related to the development and progression of intestinal failure associated liver disease (IFALD). One death resulted from IFALD while another patient required liver and intestinal transplantation (Fig. 3).

As all study subjects were neonates, pre-STEP enteral tolerance percentages were not applicable. Eleven patients had post-STEP follow-up data regarding enteral tolerance. Eight patients still require parenteral nutrition (PN) with 5 meeting half their daily caloric needs enterally. Full enteral autonomy was achieved in 3 patients.

3. Discussion

Primary STEP has been described in case reports as a useful tactic for managing the dilated proximal bowel segment in neonatal intestinal atresias. Few intra-operative or technical complications occurred, and the primary intent of preserving bowel length while providing the necessary intestinal tapering for a primary anastomosis was accomplished [4,5,8]. Using data from the International STEP registry, this current report is the first to review the short and long-term outcomes of a cohort of patients undergoing primary STEP.

Short-term outcomes resemble those reported in all-inclusive STEP studies. The STEP procedure was rapidly adopted as early investigations demonstrated its value as a simple technique with easily reproducible results, namely increased bowel length, and few technical drawbacks [7–11]. We found that primary STEP can similarly be performed in neonates with congenital short bowel with few complications in the peri-operative period. While staple

![Fig. 1. Primary diagnosis in 15 patients undergoing primary serial transverse enteroplasty.](image1)

![Fig. 2. Graphic representation of the intestinal lengthening achieved in 12 of 15 patients undergoing primary serial transverse enteroplasty (STEP). Mean intestinal length increased by 15 \( \pm \) 12 cm for a 50.4 \( \pm \) 27.3\% relative increase in small intestine length (\( p < 0.001 \)).](image2)
line leaks are the most commonly reported complication associated with STEP [7,11], no staple line leaks were encountered in our investigation. Previous studies on STEP have also reported significant increases in small intestine length ranging from 45 to 91% [7,9,11,12]. Primary STEP patients similarly experienced a >50% increase in small intestine length.

Surgical strategies for the early treatment of neonatal short bowel syndrome are based on the principles of bowel conservation and prompt establishment of intestinal continuity [3]. Early stoma closure has been associated with more rapid progression to PN independence [13]. Ostomy creation is often required at the time of primary intervention for jejunal-ileal atresias as primary anastomoses are prone to dysfunction. Given the native dysmotility of the bulbous proximal segment along with the large size discrepancy between proximal and distal bowel segments, patients are susceptible to obstruction, feeding intolerance and bacterial overgrowth [5]. Other techniques to deal with the enlarged proximal segment such as resection, longitudinal tapering enteroplasty, and plication either sacrifice absorptive area, or are prone to technical failure [8,14]. In our study, many patients underwent an enterocolic anastomosis in addition to STEP. There were no anastomatic or staple line leaks and most avoided an ostomy. Only 1 patient underwent ostomy creation at the time of primary STEP. A second patient did require ostomy creation at a later time for bowel re-dilatation, though the ostomy was closed 7 months later. As proposed in case reports, our study provides evidence supporting the use of a primary STEP as a feasible approach for promptly establishing bowel continuity, increasing bowel length and conserving residual intestine by avoiding losses associated with stomas or non-functional enteroplasty.

Long-term outcomes of the STEP procedure have been difficult to establish. This is largely because STEP is just one component of the SBS management armamentarium. Moreover, SBS practices are both rapidly evolving and highly variable at an institutional and even care-provider level. Although optimal therapy for SBS remains unknown, current treatment paradigms emphasize a multi-disciplinary team approach with the use of protocol driven strategies to promote intestinal rehabilitation [15]. It has been shown that bowel can rehabilitate with a tremendous increase in absorptive area often times without bowel lengthening procedures [18]. Patients with a little intestine as 35 cm have a 50% chance of achieving full enteral autonomy in the absence of bowel lengthening or tapering procedures [13]. The formation of designated intestinal rehabilitation care teams employing both medical and surgical therapies has dramatically improved the outcomes of SBS afflicted patients [16–19]. An early study following the advent of intestinal care teams showed a survival rate approaching 90% with enteral autonomy achieved in greater than 65% of study patients [16]. A more recent study conducted after the introduction of the STEP procedure as well as the fish oil-based lipid emulsion, Omegaven, demonstrated 100% survival with enteral autonomy achieved in nearly 84% [15]. The impact of each individual component of these intestinal care teams’ practices is unclear. Encouraging outcomes following STEP have been documented with relatively few patients progressing to transplantation or death, and those without progression achieving significant improvements in enteral nutrition tolerance [7–12]. However, it is difficult to determine if the increased enteral tolerance was a direct effect of the STEP procedure or native adaptive mechanisms. In our study, just 3 patients to date (20%) have been able to achieve full enteral autonomy. While two-thirds of our patients had pre-STEP bowel lengths measuring less than 35 cm, a correlation between pre-STEP bowel length and achievement of full enteral autonomy was not demonstrated as the patient
with the shortest and the patients with the two longest pre-STEP bowel lengths met this important milestone.

It is also difficult to extract long-term morbidities and mortality directly related to the STEP procedure. SBS patients with or without having undergone STEP are vulnerable to catheter associated blood stream infection (CABSI), bowel obstruction, IFALD, gastrointestinal bleeding, need for transplantation, and death [3,20]. CABI may prove to be mitigated with proper catheter care and ethanol locks. The deleterious effects of IFALD may similarly be mitigated with lipid-sparing protocols and Omegaven [15,21]. However, there is evidence suggesting that STEP patients may be more prone to gastrointestinal bleeding owing to marginal ulceration and mechanical bowel obstruction related to increased bowel manipulation and adhesion formation [8,12,22]. These risks could potentially be minimized if the intestinal lengthening and tapering achieved with STEP translated into a faster transition to full enteral nutrition. To date, there are no studies to support such a claim.

There are recent studies demonstrating that patients who show radiologic evidence of bowel re-dilatation following STEP are significantly less likely to achieve enteral autonomy [22,23]. Nine patients in our study underwent pre-STEP indicating that a large majority was prone to significant degrees of bowel re-dilatation. Though not reaching statistical significance, one center reported a younger median age at STEP for re-dilated patients compared to non-dilated STEP recipients (11 months vs 36 months respectively, p = 0.63) [22]. Given the high incidence of bowel re-dilation in our study involving only neonates, further studies are needed to determine if a correlation between age at time of STEP and bowel re-dilatation exists.

This study is a useful adjunct to the growing body of literature on the medical and surgical treatment of SBS. The initial report from the Pediatric Intestinal Failure Consortium found most deaths resulting from neonatal intestinal failure occurred within 2 years of study entry suggesting that improvements in early management may be crucial in reducing mortality [20]. Primary STEP thus has the potential to dramatically alter outcomes as an early interventional therapy. The favorable early outcomes of primary STEP demonstrated in this study may bolster surgical confidence to adopt a bowel conservation strategy in neonates that may have otherwise had a dysfunctional enteroplasty or had subsequent bowel loss owing to stoma creation and take-down. That said, answers to the questions posed by the surgical and medical treatment of SBS cannot come without multi-center, multidisciplinary participation in outcome studies or trials in addition to efforts such as the STEP registry. This study has many recognized limitations. First, the study is retrospective with a small sample size. Second, the use of data from the International STEP registry, as with any voluntary data registry, introduces the potential for reporting and selection bias. In addition, large data registries often lack the detailed information required for a sophisticated study. Individual surgeons were contacted to help overcome these last two points, however some patient data remained incomplete. Over 45 institutions and an even larger number of care providers contribute data to the International STEP registry. Our study alone represents 13 institutions and 14 surgeons. In SBS management there is a tremendous amount of clinical variation between and within institutions and the STEP procedure is just one piece of the intricate web supporting SBS patients. Confounding factors such as specific institutional approaches to SBS or indications for surgical intervention were not assessed. Finally, many modern management strategies for SBS had not been developed and hence were not available to a large portion of the patients in our study. It is possible that different outcomes could have been achieved with use of primary STEP in conjunction with other contemporary therapies.

4. Conclusion

Primary STEP is a feasible method of establishing bowel continuity while preserving intestinal length for neonates with congenital causes of SBS and markedly dilated bowel. While short-term outcomes suggest that primary STEP is safe in the peri-operative period, the long-term effect of primary STEP on nutritional outcomes, and hence morbidity and mortality, is difficult to determine owing to multiple confounding factors and requires ongoing evaluation. Use of STEP in the neonatal period should be limited to selected cases of severely short and dilated bowel with the intent of minimizing stoma creation. Outcomes of these cases should be reported so that the long-term impact of STEP on intestinal adaptation and function may be delineated. The guidance of multi-disciplinary, dedicated intestinal rehabilitation care teams should be used to optimize patient selection and long term SBS care.

References

[12] Ching YA, Fitzgibbons S, Valim C, et al. Long-term survival, morbidity and mortality, is difficult to determine owing to multiple confounding factors and requires ongoing evaluation. Use of STEP in the neonatal period should be limited to selected cases of severely short and dilated bowel with the intent of minimizing stoma creation. Outcomes of these cases should be reported so that the long-term impact of STEP on intestinal adaptation and function may be delineated. The guidance of multi-disciplinary, dedicated intestinal rehabilitation care teams should be used to optimize patient selection and long term SBS care.

References

Discussion

Discussant: Mary Brandt (Houston, TX): Thank you very much for presenting this. I think it’s a very important question. At Texas Children’s we have really become concerned that early STEP somehow is interfering with adaptation. It is our impression, and again it’s an impression, I agree it needs to be studied, that they do not do as well, they don’t have as good an outcome as if we wait, and I don’t know if you had the opportunity to compare this group with children that were STEP(ped) later to actually see if you could determine a difference or if you have any suggestions on how we should all study this together.

Response: Dr Gwendolyn Garnett: We didn’t directly compare this to patients that were STEP(ped) later on but I think you can use the previous studies in the STEP registry to make a comparison. There are not very many of the patients that are neonates and most of the patients were STEP(ped) later on. I think that’s a difficult question as far as how to determine how to study its effect on intestinal adaptation. I think that’s probably the main reason we don’t know why if the increase in bowel length is from STEP or if native adaptive mechanisms are making the difference later on.

Discussant: Dr Patricia Donahoe (Boston, MA): I think this is an excellent and very honest presentation of a procedure that seems to have some controversy. First of all, I think it’s a good procedure. Secondly, as we put together small bowel rehabilitation programs, the importance of it is to put it in the context of being part of the rehabilitation, and if we consider, for instance, the previous report with IGF and we know EGF is important in bowel differentiation and development, if we can combine that with other treatments, then I wondered how, for instance, omega-3 affects the subsequent growth of the bowel but I think I would definitely consider this a positive, an honest approach, but it has to be combined for a chronic disease for improvement of the kids.

The other question is, to our previous speaker, how expensive is it to give these growth factors and is that feasible or are we really limited by the economy of getting proteins for treatment?

Discussant: Dr Agostino Pierro (Toronto, Ontario): I really enjoyed your paper. Now obviously the big question here that we don’t know how the patients are doing if you don’t do this at the very beginning and this is an unsolved question. Now I completely agree with your conclusions, particularly the last one that we need to continue to have a multi-institutional effort. Can you share your view? Would there be, continuing obviously the registry but also to do a trial, a randomized trial? Unless you compare the STEP with no STEP you will not know what the real advantage is of this wonderful operation.

Response: Dr Gwendolyn Garnett: I think it is unlikely probably that there will ever been a randomized trial to fully answer our question. We have had so much success with designated intestinal rehabilitation care teams that it might be worthwhile to give kids a chance through those programs and see just what kind of adaptation they can achieve and then save the STEP later for your back pocket if they are just really failing to progress. I think that’s the approach that a lot of people are taking now. It is controversial and I imagine if you asked all the authors on this paper you would get different opinions.