SYSTEMATIC REVIEW

“First STEP” or Nature Deserves a Second Chance! Systematic Literature Review and Meta-analysis

Bashar Aldeiri, Riccardo Coletta, Antonino Morabito*

Department of Paediatric Surgery, Pediatric Autologous Bowel Reconstruction and Rehabilitation Unit, Royal Manchester Children’s Hospital and University of Manchester, Manchester, United Kingdom


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ABSTRACT

Aim: Surgical management of short bowel syndrome (SBS) in children is challenging. Recently, more authors are advocating for the neonatal serial transverse enteroplasty procedure (STEP) in SBS quoting the term “primary STEP” or “first STEP.” This review sought to identify the current published indications for neonatal STEP and to analyze their subsequent outcomes. Methods: We performed an OVID MEDLINE/EMBASE search using the keywords: (Bowel, enteroplasty, intestinal lengthening, STEP, and short bowel) limited to children since the introduction of STEP in 2003. Prospero systematic review registration number (CRD42017076955). Results: Thirteen papers matched our search criteria, and accurate data were available from 10 papers. A total of 26 cases had a STEP procedure at a median age of 2.5 days. The primary diagnosis was Jejunal atresia (62%), gastroschisis (19%), gastroschisis with atresia (15%), and midgut volvulus (4%). Almost a third (7/23) of the cases did not meet the anatomical definition of SBS and had a pre STEP residual small bowel (SB) length of ≥50 cm. Only 6 cases (26%) achieved enteral autonomy after the “first STEP”, interestingly in half the pre STEP SB length was ≥90 cm, 13 (56%) required a second STEP, 9 (40%) are still parenteral nutrition dependant, 4 more cases achieved enteral autonomy following a second STEP, 3 infants died, and one required SB transplantation. Significant post-operative complications were reported in four cases, and bowel redilatation occurred in almost all true SBS cases. Conclusion: Redilatation following “first STEP” is very common, may influence the ability to achieve enteral autonomy and generally necessitates further surgical intervention. The limited current evidence does not support the widespread use of STEP in the neonatal period. STEP can be a method of mucosal-sparing tailoring procedure; however, its outcomes in primary bowel lengthening in the neonatal period are yet to be established, and further studies are required before it is widely adopted.

Key words: Bowel lengthening; Children surgeon; Serial transverse enteroplasty procedure; Short bowel

INTRODUCTION

Advances in medical and surgical techniques coupled with the growing recognition of the importance of a multidisciplinary approach have dramatically improved the management of short bowel syndrome (SBS) in both adults and children over the past four decades [1-3]. Bianchi first described and proposed an effective lengthening procedure, called longitudinal intestinal lengthening and tailoring [4] that led to the concept of autologous intestinal reconstruction (AIR) with the aim of gaining more length from the existing small intestine [5]. Two decades later, the serial transverse enteroplasty procedure (STEP) was introduced and has since gained wide appreciation among surgeons due to its simplicity [6,7]. There is a wide consensus among bowel rehabilitation centers on the medical aspects of bowel rehabilitation programs and the role of bowel conservation and restoration of intestinal continuity in the management of neonatal SBS [8]. However, despite both surgical procedures reporting similar outcomes in achieving bowel lengthening, weaning parenteral nutrition (PN) intake, and overall estimated survival [7,9,10] the technique and perhaps, more importantly, the timing of performing the bowel lengthening procedure remains controversial [7].

Recently, several authors have advocated the role of the STEP in the neonatal period for SBS quoting the term “Primary STEP” or “First STEP” [11]. Single center...
that were subsequently screened and their abstracts.

The initial literature search identified 295 papers on Prospero (Registration number: CRD42017076955, http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017076955).

Inclusion criteria were all papers reporting a lengthening STEP procedure in the first 28 days of life; duplicate data were identified and removed. Every paper meeting the inclusion criteria were retrieved and reviewed in full. Patient variables collected for analysis included: Primary diagnosis of SBS, age at first STEP, pre- and post-STEP SB length, need for re-STEP, short-term complications, length of follow-up and outcome. Pre and post SB length of the 12 cases published in the STEP registry series [11] were extracted from Figure 2. The figure was exported into Corel Draw®, rescaled and data were extracted with ±1 cm error. Statistical analysis was performed using SPSS IBM V22. Mean change in SB length pre- and post-STEP procedure was assessed using Mann–Whitney U-test and \( P < 0.05 \) was set significant. Data presented as the mean ± standard deviation or median and range. The systematic review is registered on Prospero (Registration number: CRD42017076955, http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017076955).

Follow-up data were available for 23/26 cases only. The median follow-up period reported for 23 cases was 16 months (range 1–42), yet even within this relatively short follow-up period 13/23 (56%) underwent a second STEP procedure at a median 6.25 months (range 1–198); however, this did not reach statistical significance (\( P = 0.054 \)) in intestinal length increase achieved post-STEP (Figure 3).

In total, the 10 papers [11,15-23] reported 26 neonates (median gestational age of 36 ± 2.6 weeks) which underwent STEP procedure in the neonatal period (Table 1). Of note, SB atresia accounted for nearly two-thirds of the primary diagnosis, gastrochisis, with or without intestinal atresia, was the diagnosis in almost all of the remaining cases and midgut volvulus was reported in one case only (Figure 2). Median age at STEP was 2.5 days (range 1 and 21). Pre - and post-STEP SB lengths were reported in 23/26 (88.5%) cases, while pre- and post-SB diameter was not reported in any of the studies. Pre-STEP SB length ranged between 10 and 150 cm (median=35). Interestingly, pre-STEP SB length was 50 cm or more in 30% (7/23) of the cases. The mean SB length increase following the STEP procedure was 49 ± 31% and the median SB length achieved was 14 cm (range 4–48). The median post-STEP SB length was 49.5 cm (range 15–198); however, this did not reach statistical significance (\( P = 0.054 \)) in intestinal length increase achieved post-STEP (Figure 3).

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Follow-up data were available for 23/26 cases only. The median follow-up period reported for 23 cases was 16 months (range 1–42), yet even within this relatively short follow-up period 13/23 (56%) underwent a second STEP procedure at a median 6.25 months (range 1–198). The indications were primarily re-dilatation of the SB due to bowel obstruction following the primary STEP and the inability to establish enteral nutrition. Only 6/23 (26%) established full enteral autonomy following the “first STEP;” yet the pre-STEP SB length in 3/6 was ≥90 cm. Another four patients achieved full enteral autonomy after a second lengthening STEP procedure. In total 10/23 patients (43%) achieved enteral autonomy after one or two STEP procedures, yet the pre “first STEP” SB length was ≥50 cm in 6 of them, meaning only 4/23 cases with SB length of < 50 cm achieved enteral autonomy after one or two STEPs. Almost 40% (9/23) still required either partial or full PN support at the time of last follow-up, while one patient required a combined liver and SB transplant due to an
Figure 1: PRISMA flow diagram of study selection

Table 1: Characteristics of included studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Publication year</th>
<th>Location</th>
<th>Study type</th>
<th>&quot;First STEP&quot; cases</th>
<th>Age at STEP* (days)</th>
<th>Pre-STEP SB length^ (cm)</th>
<th>Re-STEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobos et al.</td>
<td>2016</td>
<td>Caba, Argentina</td>
<td>Case report</td>
<td>1</td>
<td>21</td>
<td>90</td>
<td>No</td>
</tr>
<tr>
<td>Garnett et al.</td>
<td>2016</td>
<td>Boston, MA</td>
<td>STEP registry</td>
<td>15</td>
<td>Neonate</td>
<td>32 (10-66)</td>
<td>70%</td>
</tr>
<tr>
<td>Bhalla et al.</td>
<td>2013</td>
<td>Georgia, GA</td>
<td>Case report</td>
<td>1</td>
<td>1</td>
<td>35</td>
<td>Yes</td>
</tr>
<tr>
<td>Roy et al.</td>
<td>2013</td>
<td>Montréal, Quebec</td>
<td>Case report</td>
<td>1</td>
<td>1</td>
<td>35</td>
<td>Yes</td>
</tr>
<tr>
<td>Oh et al.</td>
<td>2013</td>
<td>Seoul, Korea</td>
<td>Case report</td>
<td>1</td>
<td>3</td>
<td>10</td>
<td>Yes</td>
</tr>
<tr>
<td>Ehrlich et al.</td>
<td>2012</td>
<td>Ann Arbor, MI</td>
<td>Case report</td>
<td>1</td>
<td>3</td>
<td>32</td>
<td>Yes</td>
</tr>
<tr>
<td>Wales et al.</td>
<td>2007</td>
<td>Toronto, Canada</td>
<td>Single center series</td>
<td>3</td>
<td>2</td>
<td>106 (90-150)</td>
<td>No</td>
</tr>
<tr>
<td>Cowles et al.</td>
<td>2007</td>
<td>Miami, FL</td>
<td>Case report</td>
<td>1</td>
<td>21</td>
<td>20</td>
<td>No</td>
</tr>
<tr>
<td>Ismail et al.</td>
<td>2007</td>
<td>Doha, Qatar</td>
<td>Case report</td>
<td>1</td>
<td>3</td>
<td>50</td>
<td>No</td>
</tr>
<tr>
<td>Javid et al.</td>
<td>2005</td>
<td>Boston, MA</td>
<td>Single center series</td>
<td>1</td>
<td>1</td>
<td>22</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Age presented as median in series studies. ^SB length presented as median and range in series studies. SB: Small bowel, STEP: Serial transverse enteroplasty procedure
STEP in neonatal short bowel

intestinal failure associated liver disease (IFLAD). Apart from redilatation and need for further surgery, significant short-term complications were reported in four (17%) cases. Two (2/23) patients suffered from stapler line leak; the first had to undergo a repeat laparotomy and eventually died of sepsis at 7 months of age. While the second developed a contained enterocutaneous fistula that was managed conservatively. Another patient developed intestinal obstruction and necrosis 1 month following STEP that required further resection and loss of 20 cm of the bowel. The last case suffered from prolonged dumping, symptom related to SBS and feed intolerance and eventually required a second STEP procedure. Only two cases had stoma formation at the time of the first STEP procedure, while bowel continuity was established in all other cases. Two cases had to undergo stoma formation following the first STEP, one at 1 month of age and required resection and re-STEP, and the second at 3 months due to bowel obstruction. The studies reported a total of three deaths one due to sepsis following stapler line leak, and two died due to progressive IFLAD despite having a re-STEP procedure (Figure 4).

DISCUSSION

Neonatal SBS is associated with high morbidity and mortality in an already fragile patient population. The decision to perform primary bowel lengthening procedure at the time of initial laparotomy as a result of unexpected findings is not straightforward or easy for most pediatric surgeons. The benefit of “First STEP” in the neonatal population has to be fully established before widespread adoption of such an approach in this patient group. Our study provides the first comprehensive analysis of outcomes of neonatal STEP more recently known as “First STEP.”

The most striking outcome of “First STEP” was the requirement for a re-STEP within a relatively short period of time. “First STEP” may allow establishing anatomical bowel continuity, but it does not seem to allow functional use of the bowel in the medium term. Only 13% of the true SBS achieved enteral autonomy following “First STEP” while the rest had a pre-STEP SB length of ≥50 cm raising the question as to whether they should be classified as short bowel at all. Whether the effect on achieving bowel autonomy in the neonatal life is just due to normal bowel adaptive response or a true outcome of STEP remains to be investigated. We show here that bowel redilatation was a frequent outcome following “First STEP.” It has been established that bowel redilatation following AIR is an indicator for poor outcome and generally necessitates further surgical intervention [24]. Moreover, patients developing bowel redilatation following STEP require longer PN support and are less likely to achieve enteral autonomy [25]. Neonates may be at more risk of developing bowel obstruction and redilatation following STEP due to extensive bowel manipulation, multiple use of staplers and adhesion formation.

Bowel dilatation is associated with bacterial overgrowth and poor gut adaptation [26]. Recent reports suggest that bowel dilatation is associated with increased risk of bowel-derived bloodstream infections and liver injury [27]. Furthermore, STEP has been recently flagged to increase the risk of sepsis in children. One study reported nearly 40% perioperative infections with over one-third of patient suffered from catheter-associated bloodstream infection in the immediate post-operative period [28]. Infectious episodes will only further contribute to liver damage and worsen the existing short bowel state.

It has been now long established that the small intestine doubles in length in the last trimester and gains an extra 30% length in the 1st year of life [29]. With the continued growth of the bowel in the 1st year, one needs to carefully consider if major operative intervention provides any additional benefit. Indeed, in two of the cases requiring repeat STEP within 6 months, natural bowel growth between the two procedures
was more than the length achieved in the two STEP procedures combined [18,22]. However, natural bowel growth may still fall short of the length required to gain intestinal autonomy, and the child may continue to suffer from SBS.

We believe that the decision to proceed to AIR and the type of lengthening procedures should be carefully evaluated and offered to short bowel patients in an individualized basis, taking into account each patient’s specific needs, as supported by the literature [2,3]. The choice and timing of lengthening procedure should take into account clinical and anatomical variations in SBS, and hence we find it difficult to believe that one procedure may offer the solution to all the conditions leading to the short bowel state.

This study remains limited by the absence of long-term follow-up. Our data represent findings in only 23 cases that underwent STEP lengthening procedure in the neonatal period, and there is a lack of a matched control group to compare it with. Therefore, the benefit of this approach in this patient cohort remains unclear. More studies are needed to be able to truly evaluate the use of STEP and other lengthening procedures in the neonatal period before it is adopted as a mainstay of treatment. Future studies should look into the effects of such extensive procedures on the short- and long-term adaptive capacity of the bowel. Moreover, how the lengthening procedure affects the general physiology of the neonatal bowel is still to be investigated. A multicenter approach is required to adequately power these studies to evaluate the benefits of performing lengthening procedures in the neonatal period.

**CONCLUSION**

The current evidence demonstrates wide heterogeneity in the use of the STEP procedure in the neonatal period. Of note, bowel redilatation requiring further intervention is the most common result of a “first STEP.” Recent reports of bowel dilatation and STEP-related sepsis dictate the cautious use of STEP procedure in an already high-risk group. The SB continues to grow in the 1st year of life, and the timing of lengthening procedure should take this into consideration. STEP can be a method of mucosal-sparing tailoring procedure; however, its outcomes in primary bowel lengthening in the neonatal period are yet to be established, and further studies are required before it is widely adopted.

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**Author’s contribution**

Mr. Bashar Aldeiri conceptualized and designed the study, performed the literature search, designed the data collection instruments, collected data, carried out data analysis, drafted the initial manuscript, and reviewed and revised the manuscript. Mr. Riccardo Coletta performed a repeat independent literature search, collected data, and reviewed and revised the manuscript. Prof. Antonino Morabito conceptualized and designed the study, coordinated and supervised data collection and critically reviewed and revised the manuscript.

**REFERENCES**


