

The Timing of Stoma Closure in Infants with Necrotizing Enterocolitis: A Systematic Review and Meta-Analysis

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Abstract

Aim Some infants with necrotizing enterocolitis (NEC) undergoing surgery require the formation of a stoma. The timing of stoma closure in these patients remains controversial. Our aim was to determine whether the different timing of closure had an impact on patient outcome.

Methods Using a defined search strategy (PubMed, Embase, and Web of Science), two investigators (Q.L. and G.L.) independently identified studies comparing early stoma closure (ESC, before 8 weeks from stoma formation) versus late stoma closure (LSC, after 8 weeks) in infants with NEC. Outcome measures included the duration of parenteral nutrition, the length of hospital stay, and complications. Meta-analysis was performed using RevMan 5.3 (The Cochrane Collaboration, Copenhagen, Denmark). Data are expressed as mean ± standard deviation.

Results Of the 505 articles screened, 6 articles met the inclusion criteria (280 infants). All studies but one were retrospective. The total duration on parenteral nutrition was similar in infants with ESC versus LSC, and the total length of hospital stay (pre- plus poststoma closure) was not influenced by the timing of stoma closure. Three studies (79 infants) reported similar complication rates after stoma closure between ESC (5/16, 31%) and LSC infants (13/63, 19%; $p = 0.5$).

Conclusions This systematic review demonstrates that there is no difference between different timings for stoma closure in post-NEC infants. With the current supporting evidence, ESC seems to be as safe and feasible as LSC. Studies with a higher level of evidence are needed to confirm these conclusions.

Keywords

- ▶ ostomy
- ▶ ileostomy
- ▶ jejunostomy
- ▶ colostomy

Introduction

Necrotizing enterocolitis (NEC) is a devastating disease of newborn infants characterized by a severe intestinal inflammatory process.¹ A proportion of infants with NEC require acute surgical intervention, due to intestinal perforation or clinical deterioration and unresponsiveness to medical management.¹ The universal principles of surgery in NEC are to remove necrotic

intestine and control intraabdominal sepsis while preserving as much intestinal length as possible.² The classical approach to NEC has been to resect all areas of the necrotic intestine and fashion a stoma to allow adequate time for healing and growth before restoring intestinal continuity at a later stage. However, stomas, and in particular jejunostomies, are poorly tolerated by preterm infants as they predispose to nutritional and metabolic disturbances and poor growth as a consequence of fluid and

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electrolyte depletion.² Therefore, some surgeons would resect necrotic bowel and perform a primary anastomosis even in neonates weighing less than 1,000 g.³

Another way of reducing stoma complications is the early reestablishment of bowel continuity. Traditionally, stomas are not closed before 6 weeks from the initial laparotomy to avoid (1) bowel friability and persistent intraperitoneal inflammation, and (2) the lack of diagnosis of developing intestinal strictures.^{4,5} The time limit of 6 weeks comes from a seminal article by Kosloske et al who reported the death of an infant due to late diagnosis of post-NEC strictures and recommended a barium enema for all infants who had NEC about 6 weeks after the acute episode.⁴ However, there are no recommendations on how long to keep the stoma safely. Several authors have investigated the best timing of stoma closure in infants with NEC, but reached different conclusions. As the optimal timing for stoma closure remains controversial, we aimed to determine whether the different timing of closure had an impact on patient outcome.

Methods

To investigate the best timing for stoma closure in infants with NEC, a systematic review of the literature was made. Two investigators (Q. L. and G. L.) independently searched scientific databases (PubMed, Medline, Cochrane Collaboration, Embase, and Web of Science) using a combination of keywords (–Table 1). Only studies comparing early stoma closure (ESC) versus late stoma closure (LSC) were included in our analysis. Outcome measures included the type of stoma, duration of parenteral nutrition, the length of hospital stay, and complications after stoma closure. Meta-analysis was

performed using RevMan 5.3 (The Cochrane Collaboration, Copenhagen, Denmark) and included only studies that had the same cutoff for stoma closure: ESC was considered when bowel continuity was reestablished before 8 weeks from stoma formation and LSC after 8 weeks. Data are expressed as mean \pm standard deviation.

Results

Of 505 abstracts screened, 22 articles were analyzed in detail. Of these, 6 papers for a total of 280 infants met our inclusion criteria (–Table 2). All studies except one were retrospective.

Ileostomy was the commonest type of stoma created for infants with NEC in the six studies analyzed (–Table 3). The total duration on parenteral nutrition was similar in infants with ESC versus LSC (–Table 4). Likewise, the total length of hospital stay (pre- plus the poststoma closure) was not influenced by the timing of stoma closure (–Table 5). Three studies (79 infants) reported similar complication rates after stoma closure between ESC (5/16, 31%) and LSC infants (13/63, 19%; $p = 0.5$; –Fig. 1). This was confirmed when we analyzed the poststoma closure complication in infants who had an ileostomy (–Fig. 2).

Discussion

The present study demonstrates that different timings for stoma closure in infants who underwent surgery for NEC have no influence on postoperative outcomes and complications.

Several aspects of NEC surgical treatment are still controversial, as reported in a recent international survey of practice on NEC management.⁶ According to this study, there was no consensus on the type of stoma to fashion and where to locate it with regards to the surgical wound. The literature on stoma closure in infants who had surgery for NEC dates back to the 1980s, when the overall mortality for preterm babies had started to decrease, a larger population of preterm infants was alive, and younger and smaller infants with NEC were eventually considered good candidates to receive a stoma. In 1982, Rothstein et al suggested that the bowel maximal adaptation is obtained in the first few weeks after stoma closure, thus advocating early ileostomy closure to prevent chronic salt and water losses.⁷ In 1985, Cogbill and Millikan were the first to report in detail the outcome of infants with NEC who underwent stoma formation and reestablishment of intestinal continuity.⁸ In this study, 69% of the infants with ileostomy and 100% of the infants with jejunostomy experienced severe dehydration, electrolyte imbalance, and acidosis that required stoma closure.⁸ The authors had not made a comparison between ESC and LSC, but provided all the details of their patients, so that we could analyze their results with the selected cutoff of 8 weeks. In 1987, Gertler et al were the first to conduct a prospective study on early closure of ileostomy following NEC as a way to reduce salt and water imbalance and long-term parenteral nutrition dependence.⁹ No other types of stomas were included in this study. The authors concluded that early ileostomy closure was feasible and safe in infants weighing

Table 1 Inclusion criteria of systematic review

Publication	
Language	Any
Date	After 1950
Subject	Human studies
Study type	Retrospective
	Prospective
	Case control
	Cohort
Excluded	Case reports
	Letters
	Editorials
Keywords	Necrotizing enterocolitis
	Stoma
	Ostomy
	Enterostomy
	Jejunostomy
	Ileostomy
Colostomy	

Table 2 Studies comparing ESC versus LSC in infants who had surgery for necrotizing enterocolitis

Author	Year	Stoma closure cut-off	ESC n	Complications ESC n (%)	LSC n	Complications LSC n (%)	Conclusions
Cogbill and Millikan ⁸	1985	8 wk	6	4 (66.7)	19	10 (52.3)	No differences
Gertler et al ⁹	1987	8 wk	3	0 (0)	7	0 (0)	No differences
Musemeche et al ¹⁰	1987	3 mo	39	9 (23.1)	50	9 (18.0)	No differences
Al-Hudhaif et al ¹¹	2009	10 wk	13	n.r.	24	n.r.	Longer hospital stay, longer parenteral nutrition, and longer ventilation in ESC
Struijs et al ¹²	2012	6 wk	13	4 (30.8)	62	14 (22.6)	No differences
Veenstra et al ¹³	2015	8 wk	7	1 (14.3)	37	3 (8.1)	Shorter admission in ESC

Abbreviations: ESC, early stoma closure; LSC, late stoma closure; n.r., not reported.

Table 3 Type of stoma created in infants who had surgery for necrotizing enterocolitis

Author	Year	Type of stoma n (%)		
		Jejunostomy	Ileostomy	Colostomy
Cogbill and Millikan ⁸	1985	3 (12)	16 (64)	6 (24)
Gertler et al ⁹	1987	–	10 (100)	–
Musemeche et al ¹⁰	1987	10 (10)	75 (75)	15 (15)
Al-Hudhaif et al ¹¹	2009	4 (10.8)	28 (75.7)	5 (13.5)
Struijs et al ¹²	2012	6 (8)	62 (82.7)	7 (9.3)
Veenstra et al ¹³	2015	14 (32)	28 (64)	2 (4.5)

Table 4 Total days on parenteral nutrition in infants who underwent ESC versus LSC

Author	Year	Total PN (d)		Conclusions
		ESC	LSC	
Al-Hudhaif et al ¹¹	2009	Mean: 107.8 (SEM: 25.6)	Mean: 63.1 (SEM: 15.1)	No differences
Veenstra et al ¹³	2015	Mean: 60 (SD: 22)	Mean: 97.5 (SD: 31.8)	No differences

Abbreviations: ESC, early stoma closure; LSC, late stoma closure; PN, parenteral nutrition; SD, standard deviation; SEM, standard error of the mean.

Table 5 Total length of hospital stay for infants who underwent surgery for necrotizing enterocolitis followed by ESC versus LSC

Author	Year	Total length of hospital stay (d)		Conclusions
		ESC	LSC	
Al-Hudhaif et al ¹¹	2009	Mean: 169.7 (SEM: 47.0)	Mean: 86.3 (SEM: 20.6)	No differences
Struijs et al ¹²	2012	Median: 100 (IQR: 83–119)	Median: 96 (IQR: 73–141)	No differences
Veenstra et al ¹³	2015	Mean: 93 (SD: 56)	Mean: 117 (SD: 33.9)	No differences

Abbreviations: ESC, early stoma closure; IQR, interquartile range; LSC, late stoma closure; SD, standard deviation; SEM, standard error of the mean.

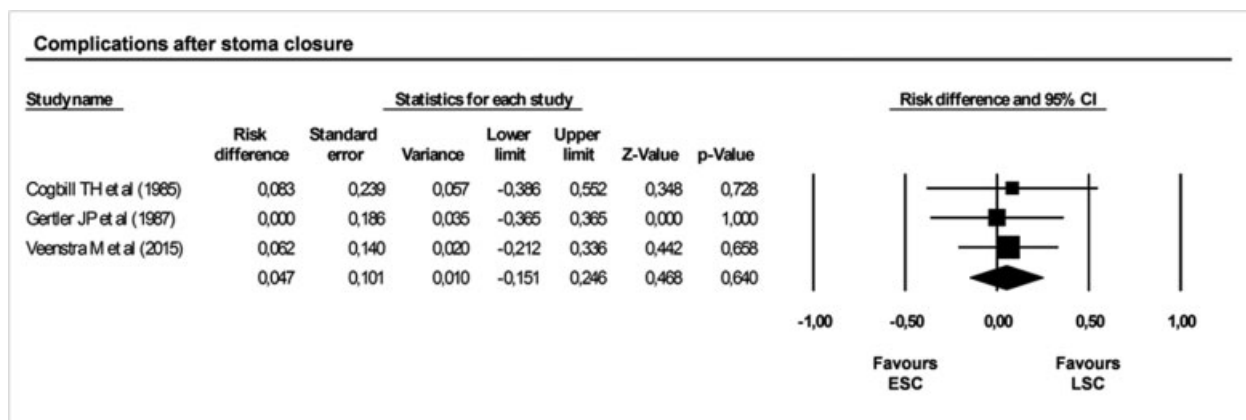


Fig. 1 Forest plot comparison of postoperative complications in infants who underwent early (< 8 weeks) versus late (> 8 weeks) stoma closure. This analysis considers all types of stomas.

as low as 1.9 kg, and that normal bowel function and accelerated growth were readily achieved following restoration of intestinal continuity, thus minimizing potential metabolic and nutritional complications. In 1987, Musesmeche et al reached similar conclusions when they compared the complication rate between early (before 3 months or under 2.5 kg) and LSC.¹⁰ The authors also reported that morbidity following stoma closure was unrelated to the type of enterostomy (jejunostomy, ileostomy, or colostomy), stoma formation through a separate incision, or age or weight of the infant at closure.¹⁰

For about two decades, there were no studies on stoma closure in post-NEC infants, until 2009 when an article from two institutions in Canada addressed the timing of enterostomy closure after NEC.¹¹ In this retrospective study, infants who had the stoma closed within 10 weeks were compared with infants who had a stoma closed more than 10 weeks after stoma formation. Babies who had had earlier stoma closure had a longer postoperative duration of mechanical ventilation, a longer need for parenteral nutrition, and a longer hospital stay. Conversely, no differences were observed in survival rates or anastomotic complications. Al-Hudhaif et al concluded that the timing of stoma closure significantly impacted the postoperative

course after NEC and that unless indicated, stoma closure should be deferred until at least 10 weeks after its creation. The opposite results were reported in 2012 by a retrospective Dutch study comparing stoma closure before or after 6 weeks from its creation.¹² Struijs et al reported no differences between the two approaches in terms of postoperative adhesion formation, costs of hospital stay, surgical interventions, and outpatient clinic visits. The authors concluded that, after stabilization of the patient, the stoma closure could be considered within 6 weeks during the same admission of the initial laparotomy. In 2015, a North American study comparing stoma closure before or after 8 weeks of its creation reported no differences in parenteral nutrition duration and associated cholestasis, duration of mechanical ventilation, the incidence of bowel adhesive obstruction, morbidity and mortality after closure.¹³ Veenstra et al reported that the duration of hospital admission was shorter in infants who had the stoma closed earlier.

A systematic review of the literature had already been conducted by Struijs et al in 2012, but it included noncomparative studies and did not comprise two recently published studies.¹⁴ Nonetheless, the authors reached similar conclusions in the present study: complication rates were not different between ESC versus LSC.

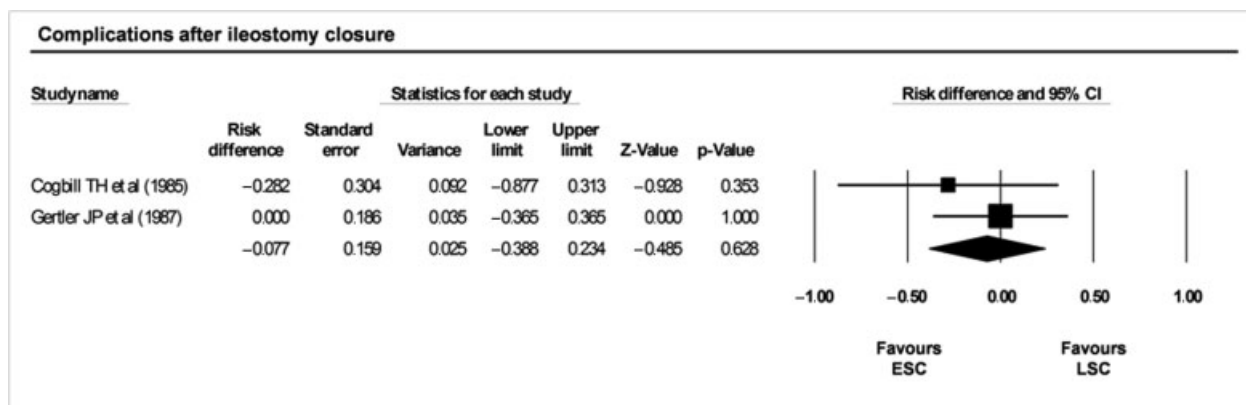


Fig. 2 Forest plot comparison of postoperative complications in infants who underwent early (< 8 weeks) versus late (> 8 weeks) stoma closure. This analysis considers only ileostomies.

When we compared all six studies, we encountered difficulties due to the fact that they had different cutoff values for stoma closure. Therefore, we conducted a meta-analysis considering only those studies with a similar cutoff, that is, 8 weeks. The forest plot comparison of three studies showed that the postoperative complication rates after stoma reversal were similar between ESC and LSC. This result was confirmed also when we restricted the comparison to just postileostomy closure complications. Unfortunately, it was not possible to conduct a more extensive meta-analysis comparison of the other variables as the data were not available or were incomparable. As any meta-analysis, also the present one relies on the quality of the studies and data that are available in the literature and as previously reported a meta-analysis of several small studies does not predict the results of a single large study.¹⁵ Moreover, other limitations of the present study are due to the retrospective nature of most studies included, the small number of participants in those studies and the differences in NEC and stoma management between the 1980s and 2000s. A multicentre randomized controlled trial would be essential to demonstrate whether ESC is superior to LSC. In such a study, criteria such as weight, prematurity, type of stoma, should be considered, to stratify patients and avoid imbalance in group allocation.

In conclusion, using the evidence currently available, in infants operated for NEC early stoma closure seems to be as safe as LSC. As this conclusion is based on mainly retrospective studies, higher level of evidence is needed to confirm these observations.

Conflict of Interest

None.

Acknowledgments

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