

Surgical Options in Necrotizing Enterocolitis

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Abstract

Necrotizing enterocolitis (NEC) is a devastating neonatal disease primarily seen in premature infants with an incidence rate around 1 - 5% in intensive care unit. Despite the advancement in neonatal care, NEC is still associated with high morbidity and mortality. Many cases of NEC are managed medically, but up to 40 - 50% of the patients refractory to medical management and all patients with perforated NEC require surgery. The most appropriate timing for surgery and the optimum surgical management in advanced stages of NEC remains controversial. Typically, the surgical options is influenced not only by the patient's clinical status and the extent of the disease but also by surgeon's preference. The surgical options at laparotomy include resection with stoma fashioning, resection with primary anastomosis, "clip and drop" or "Patch-drain-wait" technique. In Extremely Low-Birth Weight Infant, Peritoneal drainage placement has been taken in consideration. As NEC is still an emerging rare disease, network such as ERNICA (European Reference Network on Rare Inherited and Congenital Anomalies) can help to pool together disease-specific expertise in order to provide high-quality care for patients and improve a cross-border healthcare.

Keywords: Necrotizing Enterocolitis; Prematurity; Newborns; Surgery; Bowel Sparing

Abbreviations

NEC: Necrotizing Enterocolitis; NICUs: Neonatal Intensive Care Units; SBS: Short Bowel Syndrome; VLBWI: Very Low Birth Weight Infants; NIRS: Near-Infrared Spectroscopy; ER: Enteral Refeeding; RCT: Randomized Controlled Trial; TPN: Parenteral Nutrition; PD: Peritoneal Drainage; NEC-T: Nec Totalis; ERNICA: European Reference Network on Rare Inherited and Congenital Anomalies

Introduction

Necrotizing Enterocolitis (NEC) is a devastating neonatal disease with an incidence rate around 1-5% among newborns in neonatal intensive care units (NICUs) [1]. Up to 40 - 50% of the patients refractory to medical management (progressive clinical deterioration, multi organ failure) and all patients with perforated NEC require surgery [2]. In spite of ongoing research and advancement in neonatal care, NEC remains a significant source of morbidity and mortality in preterm infants. In particular, Short Bowel Syndrome (SBS) may develop in around 42% of patients undergone surgery [3-5] and mortality remains high, approximately 30 - 50% in very low birth weight infants (VLBWI) [6]. The most appropriate timing for surgery and the optimum surgical management in advanced stages of NEC in order to limit mortality and complications is still controversial. As a result, NEC still represents an enlarging burden for families and the society. In this paper we aim to discuss the current surgical options for this dramatic disease.

Surgery indications and goals

Clear indications for surgery include:

- Free intraperitoneal air on X-ray.
- Multi-organ failure despite maximal medical treatment (fasting and total parenteral nutrition, Broad spectrum of antibiotics, fluid resuscitation, correction of metabolic and coagulation derangement).
- Persistent NEC Bell stage IIB > 12 - 24h.

Many other criteria are cited in literature as relative indication for surgery, such as abdominal mass severe gastrointestinal hemorrhage, thrombocytopenia, a persistent dilated loop and/or portal vein on X-ray [7-11]. Nevertheless, these criteria are not specific enough to be considered as strict indicators for surgery.

As demonstrated by an UK survey, there is a lack of consensus on the optimal timing for surgical intervention [12]. As such, individual treatment should be guided by a multidisciplinary team of neonatologists, surgeons and anesthesiologists. To avoid unnecessary laparotomy, some centers have proposed gasless laparoscopy, an approach that might help to identify intestinal viability and evaluate the extent of NEC lesions, assisting the decision making on the need for laparotomy [13,14]. However, there is limited published evidence on diagnostic laparoscopy in neonates affected by NEC, due to possible false-negative laparoscopies, under-estimating intestinal lesions. Currently, non-invasive tools, including abdominal ultrasound, neonatal splanchnic oxygenation measured with abdominal near-infrared Spectroscopy (NIRS) and Doppler ultrasound of the superior mesenteric artery can be considered as additional prediction surrogates to continually monitor premature neonates and early detect predictive change.

Surgery aims are:

- Reduce the inflammatory cascade and progression of coagulations disorders with the resection of frankly necrotic bowel.
- Avoid the bacterial translocation by diverting feces.
- Limit the risk of SBS minimizing the intestinal resection.
- Short operative time in order to reduce surgical stress in very unstable patients.

All of these aims help to prevent multiorgan failure.

Surgical options

The surgical approach is largely determined by the extent of the disease and the patient's clinical status in addition to surgeons' experience. A variety of operative techniques have been used in the management of NEC, from placing peritoneal drainage to exploratory laparotomy with resection of the necrotic or perforated bowel and either primary anastomosis or stoma creation. The wide range of different surgical approaches is due to the lack of multicenter randomized prospective studies. In addition, the majority of studies published to date comparing different treatments are retrospective, so with a higher risk of bias.

Laparotomy: Stoma fashioning vs primary anastomosis

The ideal surgical intervention for the management of NEC remains a controversial issue. Exploratory laparotomy and stoma fashioning has been historically performed as first line of treatment since it allows adequate healing and rest of the downstream bowel prior to restore bowel continuity [15]. In addition, it may require shorter surgical time compared to primary anastomosis, essential in unstable newborns (increase need of ventilatory support and/or fluid resuscitation). However, it is known that stoma fashioning is frequently associated to metabolic disturbances and poor growth, mainly due to electrolyte depletion. Refeeding the proximal stoma through the distal mucous fistula to stimulate mucosal growth and minimize fluid and electrolyte losses are used in some center even though little data support the safety and efficacy of this practice. Koike, *et al.* showed that neonates undergone the enteral refeeding (ER) procedure had a better gain in body weight than those without ER, regardless of gestational age. In addition, Low-birth-weight neonates may receive additional benefits from ER, such as accelerated growth, compared to those with normal birth weight [16]. Conversely, Haddock, *et al.* demonstrated a significant increase of complication in ER patients, such as intestinal perforation caused by the insertion of an ER tube and leakage between the skin and the bowel ends [17]. Timing for ER initiation and protocols for management of enteric fluids remains an issue.

In patients with ileostomies, the timing of stoma closure is matter of discussion as well. Early re-establishment of bowel continuity, within 3 weeks, has been proposed to avoid problems related to high volume ileostomy output and to prevent strictures in unused intestinal tracts [18-20]. However, most common practice is to wait for at least 6 - 8 weeks after first surgery to reach an increased body weight and for bowel inflammation to be settled.

A recent systematic review demonstrated no significant postoperative complications between early and late stoma reversal [21]. Limitations of this review are the retrospective nature of the majority of included studies and the small number of patients. A Randomized Controlled Trial (RCT) should be proposed to show the superiority of late versus early stoma reversal. The incidence of complications in patients with enterostomies is up to 65% including prolapse or retraction of stoma, excessive fluids losses and poor growth; this led different centers to consider primary anastomosis as the first option to treat severe NEC [22,23]. Guelfand, *et al.* reported primary anastomosis as a safe procedure in the treatment of complicated NEC, independently from the extension or the localization of the inflammatory disease with low morbidity and mortality (11.6%) [24].

Although it is common thought that preserving the ileocecal valve is important to reduce the parenteral nutrition (TPN) dependance, some studies did not find any differences in terms of duration of the TPN, length of postoperative stay and growth between neonates with or without ileocecal valve [25,26]. These data suggest that the length of the residual intestine is more significant than maintaining the ileocecal valve in influencing post-operative outcomes. Indeed, neonates seem to have a notable adaptive capacity in response to the loss of the ileocecal valve. A recent systematic review comparing stoma fashioning and primary anastomosis did not show any significant difference in terms of complications in these two groups, potentially due to selection bias for treatment options and heterogeneity of included studies [27]. An European survey reported that the majority of surgeons (67%) opted for bowel resection and primary anastomosis in the case of focal NEC, while the 75% would perform a stoma in case of multi-focal disease [28]. Therefore, bowel condition, as well as patient's hemodynamics and comorbidities, should be considered when deciding upon stoma creation versus primary anastomosis.

Peritoneal drainage

As the peritoneal drainage (PD) placement is usually a bedside procedure, performed under local anesthesia, it is often advocated in Very Low Birth Weight Infants (VLBWI), with free air at X-ray, who are too unstable to tolerate exploratory laparotomy. Over the years, PD has not only been proposed as a temporizing measure but also as a definitive treatment. Two randomized control trials have been conducted to clarify the treatment of choice in VLBW affected by NEC: the North American trial (NECSTEPS trial) and the European Trial (NET Trial) [29,30]. Both these studies as well as a Cochrane meta-analysis of these randomized control trials did not show differences between infants undergoing PD and those undergoing laparotomy in terms of survival rate [31].

Nec totalis

Nec totalis (NEC-T) refers to a pan-intestinal involvement, even though no univocal definition is reported in the literature. Some authors define NEC-T when the entire small bowel is involved, while others in case of necrosis affecting both the small and the large bowel [32]. This scenario poses greater surgical challenge as in these cases, defining the bowel vitality might be difficult and it can lead to unnecessary intestinal resection. Therefore, the retrievability of intestine has promoted the practice of “doing less”, avoiding bowel resection of doubtful vitality, during the explorative laparotomy. Many different techniques have been proposed. In “Patch-drain-wait” technique all perforations are repaired (Patch), drainages are placed in the abdominal cavity (drain) delaying further laparotomy for at least 14 days (wait) [33]. In this way no bowel is resected at the first laparotomy but necrotic bowel persistence might permit continued bacterial translocation. For this reason, this approach is not commonly used in current clinical practice. “Clip and drop technique has been described for the first time in 1996 by Vaughan, *et al.* to maximize bowel preservation and avoid stoma fashioning in infants with diffuse NEC [34]. This technique consists in necrotic bowel resection and tying the ends of the remaining bowel during the first exploratory laparotomy. The second-look performed around 48 - 72 hours later, involves the restoration of bowel continuity, when it is feasible. If necrotic bowel is identified also during the second-look, a further laparotomy is planned, in order to preserve as much as intestine possible. This surgical option may be useful for clinically unstable patients with multifocal disease. In absence of healthy small bowel at the exploratory laparotomy, proximal diverting jejunostomy or tube duodenostomy can be used as a temporizing maneuver in these neonates [35]. The critical aspects of this type of treatment is the incapacity to remove necrotic tissue that might lead to bacterial translocation and consequently sepsis.

Author’s point of view

Our institution policy consists in performing surgery in case of persistent NEC Bell stage IIB for more than 12 - 24h, free intraperitoneal air detected on radiological examination, and worsening of multi organ failure. When laparotomy is performed, minimal bowel handling is recommended as well as avoiding resection. In particular, the abdominal cavity is entered via a transverse supraumbilical incision to provide adequate exposure. If patients stability allows, only frankly nonviable bowel is resected, while segments with some chances of recovering viability is left in situ. As neonatal liver is very delicate, its manipulation should be minimized to avoid subcapsular hematoma and hemorrhage, which is associated with a high mortality rate. The stoma are brought out through the skin ideally far from the transverse incision and a short fascial and skin bridge separates them. Our policy is to reverse stoma in 6 weeks (if the management of ostomy’s losses allows it), and best when the patient weight is over 2 kilograms. Residual bowel length should always be measured during this operation. This will guide future management and maneuvers, included the placement of a central line tunneled if parenteral nutrition is supposed to be needed for longer than 6 weeks.

PD is advocated in ELBWI with unstable conditions (need for inotrope or maximal ventilator support) when perforation is suspected or when free intraperitoneal air is detected on X-ray without previous clinical or radiographic signs of NEC. This latter condition is highly suspicious for isolated bowel perforation. PD involves the placement of a drain in the abdominal cavity through the lower quadrants, under local anesthesia at the bedside of patients. Absence of improved condition and enteral output from PD after 24 h are indications for

delayed laparotomy. As previously described, this policy based on a “sparing surgery” is safe and it seems to be associated with a lower mortality rate than the one reported in the literature (6.4%) [36,37]. In newborns with pan-NEC the Clip and drop technique is preferred to attempt to rescue as much intestine as possible avoiding short bowel syndrome.

As Necrotizing enterocolitis is still an emerging rare disease, network such as ERNICA (European Reference Network on Rare Inherited and Congenital Anomalies) aims to pool together disease-specific expertise and knowledge from across different countries in order to provide high-quality care for patients and improve a cross-border healthcare.

Conclusion

The most appropriate timing for surgery and the optimum surgical management in advanced stages of NEC remains controversial. Therefore, individual treatment should be guided by a multidisciplinary team of neonatologists, surgeons and anaesthesiologists. Minimizing demolitive surgery should guide surgeons in first instance. Network of expert-multidisciplinary healthcare professionals might be useful to reduce health inequality and standardize practices, especially in case of rare disease, such as NEC.

Conflict of Interest

The authors declare no conflict of interest.

Bibliography

1. Hall Nigel J., *et al.* “Necrotizing enterocolitis: Prevention, treatment, and outcome”. *Journal of Pediatric Surgery* 48.12 (2013): 2359-2367.
2. Papillon Stephanie., *et al.* “Necrotizing enterocolitis: contemporary management and outcomes”. *Advances in Pediatrics* 60.1 (2013): 263-279.
3. Duro Debora., *et al.* “Risk factors for intestinal failure in infants with necrotizing enterocolitis: a Glaser Pediatric Research Network study”. *The Journal of Pediatrics* 157.2 (2010): 203-208.
4. Bazacliu Catalina and Josef Neu. “Necrotizing enterocolitis: long term complications”. *Current Pediatric Reviews* 15.2 (2019): 115-124.
5. Federici Silvana and Lorenzo De Biagi. “Long term outcome of infants with NEC”. *Current Pediatric Reviews* 15.2 (2019): 111-114.
6. Blakely Martin L., *et al.* “Laparotomy versus peritoneal drainage for necrotizing enterocolitis or isolated intestinal perforation in extremely low birth weight infants: outcomes through 18 months adjusted age”. *Pediatrics* 117.4 (2006): e680-e687.
7. Kosloske Ann M. “Indications for operation in necrotizing enterocolitis revisited”. *Journal of Pediatric Surgery* 29.5 (1994): 663-666.
8. Hutter Jr., *et al.* “Hematologic abnormalities in severe neonatal necrotizing enterocolitis”. *The Journal of Pediatrics* 88.6 (1976): 1026-1031.
9. Ververidis M., *et al.* “The clinical significance of thrombocytopenia in neonates with necrotizing enterocolitis”. *Journal of Pediatric Surgery* 36.5 (2001): 799-803.
10. Coursey Courtney A., *et al.* “Radiographic predictors of disease severity in neonates and infants with necrotizing enterocolitis”. *American Journal of Roentgenology* 193.5 (2009): 1408-1413.
11. Tam Alda L., *et al.* “Surgical decision making in necrotizing enterocolitis and focal intestinal perforation: predictive value of radiologic findings”. *Journal of Pediatric Surgery* 37.12 (2002): 1688-1691.

12. Rees CM, *et al.* "Surgical strategies for necrotising enterocolitis: a survey of practice in the United Kingdom". *Archives of Disease in Childhood-Fetal and Neonatal Edition* 90.2 (2005): F152-F155.
13. Pierro A, *et al.* "Laparoscopy assists surgical decision making in infants with necrotizing enterocolitis". *Journal of Pediatric Surgery* 39.6 (2004): 902-906.
14. Leva Ernesto, *et al.* "The role of laparoscopy in newborns affected by NEC". *Journal of Laparoendoscopic and Advanced Surgical Techniques* 20.2 (2010): 187-189.
15. Kosloske Ann M. "Surgery of necrotizing enterocolitis". *World Journal of Surgery* 9.2 (1985): 277-284.
16. Koike Yuhki, *et al.* "Enteral refeeding is useful for promoting growth in neonates with enterostomy before stoma closure". *Journal of Pediatric Surgery* 51.3 (2016): 390-394.
17. Haddock Candace A, *et al.* "Mucous fistula refeeding in neonates with enterostomies". *Journal of Pediatric Surgery* 50.5 (2015): 779-782.
18. Struijs Marie-Chantal, *et al.* "Late vs early ostomy closure for necrotizing enterocolitis: analysis of adhesion formation, resource consumption, and costs". *Journal of Pediatric Surgery* 47.4 (2012): 658-664.
19. Gertler Jonathan P, *et al.* "Early ileostomy closure in necrotizing enterocolitis". *Journal of Pediatric Surgery* 22.2 (1987): 140-143.
20. Musemeche CA, *et al.* "Enterostomy in necrotizing enterocolitis: an analysis of techniques and timing of closure". *Journal of Pediatric Surgery* 22.6 (1987): 479-483.
21. Zani Augusto, *et al.* "The timing of stoma closure in infants with necrotizing enterocolitis: a systematic review and meta-analysis". *European Journal of Pediatric Surgery* 27.01 (2017): 007-011.
22. Pierro Agostino. "The surgical management of necrotising enterocolitis". *Early Human Development* 81.1 (2005): 79-85.
23. Hall Nigel J, *et al.* "The evidence base for neonatal surgery". *Early Human Development* 85.11 (2009): 713-718.
24. Guelfand Miguel, *et al.* "Primary anastomosis in necrotizing enterocolitis: the first option to consider". *Pediatric Surgery International* 28.7 (2012): 673-676.
25. Fasoli Lorella, *et al.* "Necrotizing enterocolitis: extent of disease and surgical treatment". *Journal of Pediatric Surgery* 34.7 (1999): 1096-1099.
26. Ladd AP, *et al.* "Long-term follow-up after bowel resection for necrotizing enterocolitis: factors affecting outcome". *Journal of Pediatric Surgery* 33.7 (1998): 967-972.
27. Haricharan Ramanathapura N, *et al.* "Primary anastomosis or ostomy in necrotizing enterocolitis?". *Pediatric Surgery International* 33.11 (2017): 1139-1145.
28. Zani Augusto, *et al.* "International survey on the management of necrotizing enterocolitis". *European Journal of Pediatric Surgery* 25.01 (2015): 27-33.
29. Moss R Lawrence, *et al.* "Laparotomy versus peritoneal drainage for necrotizing enterocolitis and perforation". *New England Journal of Medicine* 354.21 (2006): 2225-2234.
30. Rees Clare M, *et al.* "Peritoneal drainage or laparotomy for neonatal bowel perforation?: A randomized controlled trial". *Annals of Surgery* 248.1 (2008): 44-51.

31. Rao Shripada C., *et al.* "Peritoneal drainage versus laparotomy as initial surgical treatment for perforated necrotizing enterocolitis or spontaneous intestinal perforation in preterm low birth weight infants". *Cochrane Database of Systematic Reviews* 6 (2011).
32. Dukleska Katerina., *et al.* "Necrotizing enterocolitis totalis: high mortality in the absence of an aggressive surgical approach". *Surgery* 165.6 (2019): 1176-1181.
33. Moore Thomas C. "The management of necrotizing enterocolitis by "patch, drain, and wait". *Pediatric Surgery International* 4.2 (1989): 110-113.
34. Vaughan W Glaze., *et al.* "Avoidance of stomas and delayed anastomosis for bowel necrosis: the 'clip and drop-back' technique". *Journal of Pediatric Surgery* 31.4 (1996): 542-545.
35. Martin Lester W and Wallace W Neblett. "Early operation with intestinal diversion for necrotizing enterocolitis". *Journal of Pediatric Surgery* 16.3 (1981): 252-255.
36. Duci Miriam., *et al.* "Neonatal independent predictors of severe NEC". *Pediatric Surgery International* 34.6 (2018): 663-669.
37. Moschino Laura., *et al.* "Optimizing Nutritional Strategies to Prevent Necrotizing Enterocolitis and Growth Failure after Bowel Resection". *Nutrients* 13.2 (2021): 340.

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