

Early postoperative outcomes of surgery for intestinal perforation in NEC based on intestinal location of disease

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Abstract

Current surgical strategies for necrotizing enterocolitis (NEC) include primary drainage, resection with enterostomies, and primary anastomosis. There is considerable controversy regarding the preferable surgical management of NEC. We sought to investigate whether the surgical outcomes of newborns with NEC undergoing exploratory laparotomy differed according to the location of the disease site.

A total of 204 patients with NEC following laparotomy between July 2007 and May 2017 were retrospectively reviewed. Clinical outcomes, including mortality, neonatal intensive care unit (NICU) length of stay and complications, were evaluated based on the type of surgical operation.

Enterostomy creation or primary anastomosis was performed in 98 patients, and 106 cases underwent laparotomy and simple drainage because of panintestinal involvement with near total intestinal compromise or no perforation. The ileum was the most commonly affected location ($n = 170$, 83.3%). Patients who had undergone a simple drainage procedure experienced less blood loss ($P = .023$) and a shorter procedure time ($P = .061$), although no statistical significance was attained. Infants with bowel anastomosis or ostomy had significantly shorter times to beginning enteral feeds ($P = .023$) and times on mechanical ventilation ($P = .011$) compared with infants who had undergone drainage (Student's t test). The mean NICU length of stay ($P = .088$) was longer for the patients with drainage, although the difference did not attain significant. No difference in the overall mortality rate was detected between the 2 groups ($P = .10$).

The postoperative outcomes in newborns undergoing laparotomy were associated with the surgical type, which was determined by disease location in the bowel.

Abbreviations: NEC = necrotizing enterocolitis, NICU = neonatal intensive care unit, PD = peritoneal drainage.

Keywords: laparotomy, mortality, necrotizing enterocolitis (NEC), NICU length of stay, postoperative complications

1. Introduction

Necrotizing enterocolitis (NEC) is a major cause of gastrointestinal-associated morbidity frequently affecting premature infants. In China, this condition affects approximately 25% of preterm (gestational age <37 weeks) infants among 16 million live

newborns per year.^[1,2] Currently, more than 30% of infants with NEC may receive require surgery, which poses substantial risks, especially in the critically ill premature infant.^[4,5] The common surgical approach is the involved bowel resection following intestinal stomas creation or direct anastomosis; the complication rate is as high as 60%, including local infection, intestinal stenosis, obstruction, incisional hernia, and so on.^[3]

For patients who are unstable to undergo a laparotomy, primary peritoneal drainage (PD) is preferred by some surgeons with a subsequent operation performed after clinical improvement.^[6,7]

Surgical management depends mostly on the individual surgeon, based on their clinical experience.^[8,9] There is a considerably controversial aspect to this surgical intervention, including the distribution of bowel most commonly affected and patient outcomes (Table 1).

In this research, we aim to evaluate the results of preterm infants with surgical NEC in terms of lesion location who underwent resection/enterostomy or a drainage placement procedure at a single tertiary pediatric center. We have enrolled a sizeable number of infants for better comparison of the surgical treatment of patients and their clinical outcome.

2. Materials and methods

2.1. Patients

We conducted this retrospective study of a hospital-based cohort drawn from 4 neonatal intensive care units (NICUs) at Yongchuan Hospital, Children's Hospital of Chongqing Medical

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The raw/processed data required to reproduce these findings cannot be shared at this time due to technical or time limitations.

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Table 1
Baseline demographics of eligible patient and preoperative variables (χ^2 test & Student *t* test).

	Anastomosis or ostomy (98)	Drainage (106)	<i>P</i> Values
Male: female	29:69	35:71	.35
Gestational age, wk	30.4±2.1	25.8±1.9	.057
Birth weight, g	1994.8±588.5	1794.6±611.2	.13
Weight at diagnosis, g	2122.7±605.4	2011.6±588.5	.22
History of enteral feeding, n (%)	61 (66.7)	69 (68.1)	.39
Probiotics, n (%)	36 (2.8)	48 (11.0)	.14
APGAR scores at 5 minutes	8.4±1.1	8.3±1.0	.34
Cesarean delivery, n (%)	62 (81.0)	68 (67.5)	.51
Maternal age, years	29.1±3.3	29.6±3.7	.36
SGA infant, n (%)	8 (13.3)	11 (9.6)	.38
Postnatal age at operation, days	17.2±10.2	15.7±8.5	.39
Congenital anomalies, n (%)	56 (52.4)	48 (45.8)	.060
Transfusion preoperation, n (%)	15 (9.5)	9 (7.5)	.098
Vasopressor use at enrollment, n (%)	46 (23.8)	38 (39.6)	.071
Respiratory support, n (%)	31 (17.1%)	26 (27.7)	.17
First platelet count (onset of symptoms) (109/L)	286.9±91.6	294.5±85.1	.28
Hemoglobin, g/L	133.4±42.6	128.6±39.7	.25
First WBC (onset of symptoms) (109/L)	18.4±3.3	17.8±3.6	.16
First procalcitonin (onset of symptoms) (ng/ml, normal value: 0–0.5)	6.2±1.7	5.9±1.2	.34
First CRP (onset of symptoms)(mg/L, normal value: 0–10)	23.1±9.3	21.6±8.6	.28
Albumin (g/L, normal range, 35–50)	30.8±5.4	31.2±4.9	.19

APGAR=Appearance, Pulse, Grimace, Activity, and Respiration, CRP=C-reactive protein, SGA=small-for-gestational-age, WBC=white blood cell.

University, Sanxia Hospital, and Jinan Maternity and Child Care Hospital. Approval was provided by the institutional review board at each site. The protocol was approved by the Institutional Review Board of the Chongqing Medical University (IRB, No: CHMU2016–086). Infants with a diagnosis of NEC who had undergone a related surgical procedure during the study period were eligible for inclusion. The electronic medical records of patients who had undergone such a surgical procedure from July 2007 to May 2017 were reviewed, including demographic information, diagnosis and procedure information, clinical management, laboratory data, mortality, length of stay (LOS), and discharge summaries. Exclusion criteria included infants from in vitro fertilization (IVF) and those with acute pulmonary bacterial infection or gastrointestinal anomalies (aprotia, intestinal atresia, or Hirschsprung disease) or who died in the early stage without the based information of outcome measures. All infants with NEC were followed up in the hospital's outpatient clinic until at least 3 months of corrected age.

The primary outcome was 30-day mortality following the initial operation. The surgical and postoperative outcomes were defined as secondary outcomes, including total parenteral nutrition 90 days postoperatively, ventilator rates, short-term postoperative complications (e.g., burst abdomen), and the NICU length of stay for patients surviving over 90 days.

2.2. Statistical analysis

The data from the results were subjected to statistical comparisons using the SPSS 17.0 software package (SPSS Inc., Chicago, IL). Continuous data are presented as mean±standard deviation or median (minimum, maximum or 25th and 75th interquartile range (IQR), as indicated) unless otherwise indicated. Categorical data are reported as percentages. For univariate comparisons, the Student's *t* test, Shapiro–Wilk test or Wilcoxon rank sum (Mann–Whitney *U* test) were used to compare continuous variables, whereas χ^2 tests or Fisher exact tests were used to compare categorical variables. The statistical significance was evaluated

using a 2-tailed 95% confidence interval (CI), and a *P* value less than .05 was considered statistically significant.

3. Results

3.1. Demographic data

Between July 2007 and May 2017, there were 204 preterm infants with an NEC diagnosis who were eligible for analysis. We recorded type of the surgical intervention for all the patients. Abdominal exploration was performed to resect the necrotic intestine and intestinal stomas or end-to-end intestinal anastomoses were created in the location; otherwise, only drainage was placed. Patients were followed daily throughout their hospitalization. All patients received the same postoperative program, including fluid resuscitation, parenteral nutrition support, and perioperative broad-spectrum antibiotics, if necessary. Complications and readmissions were recorded by the surgical team.

A total of 106 patients were identified who underwent laparotomy with simple drainage for NEC and 98 patients who underwent laparotomy for bowel resection and subsequent intestinal anastomosis or ostomy. There were no significant differences with respect to sex (0.35), Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) scores (at 5 minutes) (*P*=.34), weight at diagnosis (*P*=.22), postnatal age at operation (*P*=.39), history of enteral feeding (.39), and other disease severity in the perforated NEC. Infants who received bowel resection or ostomy procedures were not more likely to have a low average gestational age (*P*=.057) and birth weight (*P*=.13), as the *P* values are not significant. With respect to some maternal features, such as maternal age (*P*=.36) and delivery mode (cesarean or vaginal) (*P*=.26), there was no difference among the 2 groups. Additionally, the difference between the number of diagnoses of congenital anomalies recorded during each inpatient stay was not significant (*P*=.060). No differences were found between the 2 groups regarding other clinical characteristics of the patients, such as basic laboratory measures,

Table 2
Surgical features of patients who undergone surgery (χ^2 test & Student *t* test).

	Laparotomy for ostomy (98)	drainage (106)	P
Pneumoperitoneum, n (%)	43 (43.9)	49 (46.2)	.42
Portal venous gas, n (%)	26 (26.5)	31 (29.2)	.39
Positive paracentesis, n (%)	32 (32.7)	28 (26.4)	.21
Progressive clinical deterioration, n (%)	29 (29.6)	22 (20.8)	.098
Operative time, mins	136.3±36.5	120.2±24.6	.061
Operative blood loss, mL	16.8±6.7	10.1±4.3	.023
Transfused patients, n (%)	69 (70.4)	77 (72.6)	.42
Bowel involvement, n (%)			
Distal ileum	44 (44.9)	35 (33.0)	.055
Distal ileum and colon	32 (32.7)	59 (55.7)	.001
Ascending colon	13 (13.3)	12 (11.3)	.43
Descending colon	9 (9.2)	0 (0)	.001
Extent of disease, n (%)			
Multifocal NEC	49 (50.0)	40 (37.7)	.052
Localized NEC	38 (38.8)	15 (14.2)	.000
Panintestinal NEC	11 (11.2)	51 (48.1)	.000

NEC=necrotizing enterocolitis.

probiotics use ($P=.14$), vasopressor use at onset of NEC ($P=.071$), or respiratory support before or at the time of referral ($P=.17$).

3.2. Surgical features

The choice of procedure often depended upon the extent of disease, as shown in Table 2. For the surgical approaches, enterostomy creation with or without necrotic bowel resection was performed in 91 patients (jejunostomy, ileostomies, and transverse colostomies). Seven infants required resection and primary anastomosis. There were 106 cases that involved laparotomy and simple drainage because of panintestinal involvement, whereas for the 98 cases with ostomy, most of them were involved in localized NEC ($P<.001$) (Table 2). The commonly affected sites were the distal ileum, ascending colon, and descending colon. The ileum was the most commonly affected location ($n=170$, 83.3%). Laparotomy with stoma formation was performed in most localized and multifocal cases. However, simple drainage was used in 88.5% of panintestinal patients. Not surprisingly, patients who had undergone a simple drainage procedure were more likely to have experienced less blood loss ($P=.023$) and a shorter procedure time ($P=.061$), although no statistical significance was attained.

Table 3
Patient outcomes based on the surgical strategy (multivariate logistic regression).

	Laparotomy for ostomy (98)	Drainage (106)	P Values	Odds ratio (95% CI)
Days to enteral feeds (median)	19.5±11.3	23.6±12.7	.043	0.42 (0.28–1.00)
90 ds parenteral nutrition depend, n (%)	5 (5.1)	8 (7.5)	.34	
NICU length of stay, days, Mean±SD	24.9±13.2	29.8±11.8	.088	0.32 (0.18–1.09)
Albumin minimum (g/L, normal range, 35–50)	32.8±6.5	31.6±5.4	.125	
Mortality, n (%)	26 (26.5)	38 (35.8)	.10	
Mechanical ventilation, days	14.2±6.8	15.6±7.9	.011	0.19 (0.08–0.93)
No. of patients with complications, n (%)	24 (24.5)	27 (25.5)	.50	
Bacterial sepsis, n (%)	14 (14.3)	16 (15.1)	.52	
weight gain				
Short bowel syndrome	3 (3.1)	6 (5.7)	.29	

CI=confidence interval, NICU=neonatal intensive care unit, SD=standard deviation.

3.3. Outcomes

According to established criteria, a comparison of the outcomes between the 2 groups is summarized in Table 3. Infants with bowel anastomosis or ostomy had significantly shorter times to beginning enteral feeds (23.9 ± 12.1) compared with infants who had undergone simple drainage (18.6 ± 8.8) ($P=.023$, Student *t* test). There were no significant differences for dependence on parenteral nutrition for the 71 surviving patients ($P=.34$). The NICU length of stay ($P=.088$) was longer for the patients with drainage, although no significant was found. Durations of mechanical ventilation were significantly different between the 2 groups ($P=.011$). The overall mortality rate was not different between the 2 groups ($P=.10$). The cause of death was primarily attributed to panintestinal NEC in 45 infants. The remaining deaths resulted from sepsis ($n=11$) and severe short bowel syndrome ($n=8$). There were no deaths after stoma closure. There were no differences in respect to postoperative complications between the 2 groups ($P=.50$, Table 3). The most common complications were sepsis, short bowel syndrome, and intestinal stricture.

4. Discussion

This study demonstrates that based on the clinical information relating to the location of bowel affected by NEC, clinical outcomes were varied. Although any surgical intervention should be of beneficial once NEC was proven perforation, the NEC mortality was still high, ranging from 20% to 50%, which might be determined by the location of lesion.^[10] Currently, surgical management varies from resection with ostomy and/or anastomosis to primary PD.^[11] In smaller babies and those in an unstable condition to tolerate laparotomy, PD was used as a temporizing procedure. Multiple studies examining the outcomes for primary PD have indicated its advantage compared with laparotomy.^[12,13] The babies usually improve slowly following PD, and in some cases, it should be taken laparotomy in the following days. Our mortality rate in this group of patients was high (35.8%) than that among patients with laparotomy followed by either ostomy or anastomosis, reflecting the severity of the intestinal damage. The critical issues for intestinal resection are the length of the retained small bowel.^[7,14] Our findings indicated the remarkable adaptive capacity of the bowel, even with long small bowel resection. It is likely that in the course of treatment, patients treated with drainage suffer high rates of early mortality. Prematurity could be a factor for worse outcomes because the admission age of 6.32 days is the period when the gastrointestinal tract is not yet well colonized; the very low-birth-

weight infants have not yet reached even half of enteral feeding nutrition. Although we did control the variables of birth weight and gestational age in the current analysis, there may be other prematurity variables, which would be not involved in this research.

The radiographic findings play an important role in indicating the perforated NEC for operation. The site of pneumatosis may imply extensive intestinal involvement, which should be beneficial for bowel resection and ostomy or drainage.^[15,16] Free intraperitoneal air represents isolated intestinal perforation, usually treated with anastomosis. Our analysis also shows a trend toward drainage with pneumatosis (i.e., more extensive disease) compared with free intraperitoneal air (i.e., with more limited disease). The resection and anastomosis are not advisable because invariably they will result in short bowel syndrome.^[17,18,19]

The extent of bowel involvement is the most important factor to decide the surgery selection the, for which there are limited reports regarding the association with the outcomes of NEC. In our study, diffuse bowel involvement of the small bowel was associated with surgical selection, such as ostomy or drainage, which should result in different rates of mortality. When the disease was limited, the outcome seemed more favorable.^[20,21] The lower survival was observed for infants with pan-intestinal involvement compared with limited disease of NEC.^[22,23] In the present study, when the rectum, jejunum, and ileum were involved for the disease, which means greater extent, there were more patients who died. Furthermore, for the panintestinal involvement patients, the presentation age was lower, which suggested that worse outcomes do not result from the delay in diagnosis. NEC with panintestinal involvement was also observed necrosis of the distal ileum and proximal colon, which contributed to the widespread inflammatory process. Previous reports have also suggested that a significantly better survival rate was observed for the colonic involvement than those with small bowel involvement.^[24] The current data indicated that survival was better in patients with the terminal ileum involved than in patients with disease associated with colonic lesions, including the ascending colon.

Among the weaknesses of our study is that the data were collected retrospectively for a very long span of time; over the years, there were many changes in care practices leading to different clinical treatment algorithms and an inherent risk of selection bias between study patients. Another point is that surgical decision making cannot be controlled in terms of variability, which directly affects the intraoperative and postoperative care of the patients. For example, some infants who had extensive severe involvement might undergo an exploratory laparotomy with no further surgical intervention as well as bowel resection and ostomy by different surgeons. Another weakness is that it is probable that survival was more dependent on the medical problems of prematurity than the type of operation, which was not controlled for sufficiently. Furthermore, there were a number of instances of infant withdrawal of support, making it difficult to interpret the survival data.

In summary, our analysis suggests that patients who undergo drainage for NEC and small gestational age suffer a higher mortality rate and incur a longer length of stay and dependence on total parenteral nutrition. Further study in the design of clinical trials of new therapies to optimize the treatment of NEC is needed to better elucidate the factors influenced the clinical outcomes for infants who undergo surgical procedures.

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Author contributions

Qiankun Geng, Yongming Wang, Lei Li designed, analyzed the data, and evaluate the manuscript. Chunbao Guo performed the statistic measurement and analyzed the data. Chunbao Guo analyzed the data, and wrote the paper.

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