Original Article

Risk Factors of Surgical Necrotizing Enterocolitis: A Cohort Study

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Objective: To find risk factors of surgical necrotizing enterocolitis (NEC) and early detection.

Materials and Methods: The present study was a retrospective cohort study that reviewed all patients with NEC in Chiang Mai University Hospital between January 2009 and December 2016. Major gastrointestinal anomalies were excluded. Associated factors for surgical NEC were reviewed and analyzed.

Results: One hundred seventy-two NEC patients were identified. Seven patients were excluded due to an indefinite diagnosis of NEC and major gastrointestinal (GI) anomalies. One hundred sixty-five patients were included in the present study. Thirty-nine patients (23.6%) were in the surgical NEC group, and 126 (76.4%) patients in the non-surgical NEC group. In the multivariable analyses, significant factors associated with surgical NEC were plain abdominal X-ray findings of intraperitoneal fluid (RR 3.36, p=0.001, 95% CI 1.68 to 6.73), and pneumatosis intestinalis (RR 2.69, p=0.007, 95% CI 1.30 to 5.41). The overall mortality rate of NEC was 13.9%, whereas surgical NEC had a higher mortality rate of 28.2%.

Conclusion: Intraperitoneal fluid and pneumatosis intestinalis were the significant factors for prediction of perforation of NEC. Therefore, close clinical monitoring and prompt management in these patients are recommended.

Keywords: Surgical necrotizing enterocolitis, Risk factors, Perforation, NEC

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Necrotizing enterocolitis (NEC) is the most common cause of morbidity and mortality in neonates, especially in the cases requiring surgical intervention. The incidence varies geographically. In a large prospective cohort study in the United State of America (USA), nine percent of NEC in very low birth weight (VLBW) patients was found. The mortality rate of this group was 28%, which divided in 21% in non-operated NEC and 35% in operated NEC(1). In Thailand(2), 2.8 cases per 1,000 live births occurred with a mortality rate of 27.3%, which is similar to many previous studies(3,4). Mortality and complication rates depend on the severity, systemic involvement, abdominal sign, and radiologic signs, which are classified by the Modified Bell staging criteria. The goals of surgery are to remove any gangrenous bowel and preserve the intestinal length. The optimal time for surgery is important. Surgery should not be performed before gangrene is present and should not be delayed until perforation has occurred. Signs or symptoms to detect the presence of gangrenous bowel in NEC patients are difficult to find. Consequently, the current precise indications for surgery are perforation or presentation of pneumoperitoneum. The relative indications are abdominal wall cellulitis, palpable abdominal mass, portal vein gas, and evidence of a fixed intestinal bowel loop from abdominal X-ray, positive paracentesis, which is greater than 0.5 mL of brown fluid or yellow fluid containing bacteria from Gram staining, and clinical deterioration despite maximal medical therapy(5). Therefore, advanced NEC, classified as Modified Bell Stages IIIa and IIIb with severe illness are managed by surgical intervention and known as surgical NEC.

To date, there are no definite causes or pathogenesis of NEC. Previous studies have revealed various risk factors including maternal health and environment such as maternal age, antenatal antibiotics, and steroid administration(6). The prenatal, perinatal, and postnatal conditions of the patient such as prematurity, low birth weight, neonatal

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resuscitation, enteral feeding in prematurity, neonatal sepsis, umbilical catheter insertion, indomethacin or surfactant usage, and blood transfusion are the risk factors of NEC[7]. More than 90% of NEC patients are premature babies who were fed inappropriately. High levels of serum amyloid A and plasma platelets showing a correlation with perforation of NEC might be found[8]. However, in clinical practice, serum amyloid A and plasma platelet testing are unavailable. Radiologic findings are the most important assessment tools for newborns suspected of NEC. Findings associated with NEC range from dilated bowel loops to pneumatosis intestinalis, portal venous gas and pneumoperitoneum. Correlations between clinical and radiologic findings are reported in some studies but are still controversial[9].

Hull et al found that low birth weight is a risk factor of surgical NEC, but it is an unpreventable risk of perforation[1]. Although some factors might predict the severity of NEC, no factor could precisely predict the risk of perforation or surgical NEC.

The main objective of the present study was to evaluate and identify risk factors of surgical NEC. If preventable risk factors were identified, the morbidity and mortality of NEC patients will be likely to decrease. The present study also identified the incidence, morbidity and mortality rates, complications, and treatment outcomes of NEC, and described surgical outcomes for each operative choice at Chiang Mai University Hospital.

Materials and Methods

The present study was an observational, retrospective cohort study that enrolled all patients diagnosed with NEC by pediatricians and pediatric surgeons in Chiang Mai University Hospital between January 2009 and December 2016. The electronic database using International Classification of Diseases, Tenth revision (ICD-10) code P77 for infants with NEC was reviewed to accrue all relevant data.

Exclusion criteria included any major gastrointestinal anomaly such as intestinal atresia, and patients that underwent a laparotomy due to other causes such as idiopathic intestinal perforation. The patients were divided into two groups, surgical NEC, and non-surgical NEC. Surgical NEC was defined as a patient diagnosed with NEC requiring surgical intervention or met indications for surgery. Non-surgical NEC was defined as a patient diagnosed with NEC not requiring surgical intervention.

Baseline characteristics including gender, route of delivery, time to diagnosis from birth, Modified Bell's staging at diagnosis including operative procedure, time to operate from diagnostic date, operative findings, outcomes, complications, and other data with suspected factors mentioned in the literature review were collected.

Antenatal and perinatal factors were recorded. The antenatal were the maternal age, antibiotic usage, and glucocorticoid usage, while the perinatal factors were the gestational age, birth weight, APGAR score at one minute, and perinatal resuscitation or perinatal endotracheal tube insertion.

Postnatal factors were also collected. These included enteral feeding, age of feeding, amount and concentration of initial feeding, amount, and concentration of feeding at NEC diagnosis, surfactant administration, indomethacin administration, blood transfusion, umbilical catheterization, cardiac surgery, congenital pneumonia, neonatal sepsis and antibiotic administration, and radiologic findings at the first diagnosis of NEC[1,2,6,9,10].

Factors associated with surgical treatment of NEC were the primary endpoint. Secondary outcomes were the incidence of surgical NEC, mortality rate, complication rates, operative findings, hospital stay, and periods of total parenteral nutrition (TPN). Overall mortality was defined as mortality that might not be specifically associated with NEC. Neonatal mortality was defined as mortality within 28 days of life.

Statistical analysis

All statistical analyses were performed using Stata, version 11 (StataCorp LP, College Station, TX, USA). Sample size was estimated to give 80% power at the 5% significance level (two-sided) to detect the difference between surgical and non-surgical NEC. The difference between independent mean formula was used with ratio between group was 3 according to the incidence of the surgical NEC. The authors estimated that sample size of 60 patients in surgical NEC and 180 patients in non-surgical NEC calculated from the gestational age parameter in study of Hull et al[1]. As in the study the actual sample size was 39 in surgical NEC group and 126 in non-surgical NEC group.

Descriptive data in normally distributed continuous variables were reported as mean and standard deviation (SD) and analyzed using a Student's t-test. The non-normally distributed variables were reported as median and interquartile range (IQR) and analyzed using Mann-Whitney

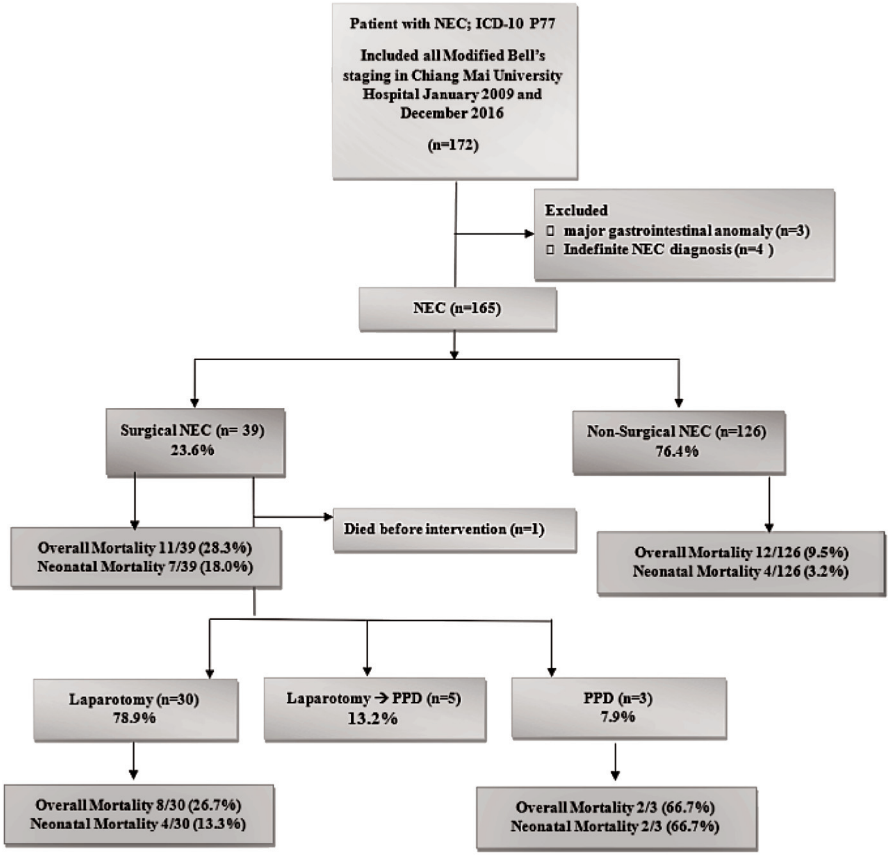

Figure 1. Results.

U test. Fischer's exact test was used to analyze categorical data (number and percentage). In the final comparative data, univariable analysis and multivariable analysis were used to identify the potential variables associated with surgical treatment of NEC. Analysis by log risk regression was reported by risk ratio (RR) with a p-value of less than 0.05 considered as being statistically significant.

Ethical approval

The present study was approved by the Ethics Committee of Chiang Mai University Hospital, Research ID: 3312/ Study Code: SUR-2558-03312.

Results

One hundred seventy-two patients diagnosed with NEC and identified from the electronic data base were admitted to Chiang Mai University Hospital between January 2009 and December 2016. Seven patients were excluded from the study due to an indefinite diagnosis of NEC (n=4), or major gastrointestinal anomalies which were gastroschisis, intestinal atresia, and Hirschsprung disease (n=3). One hundred sixty-five patients were included in the present study. Thirty-nine patients (23.6%) were surgical NEC group, and 126 (76.4%) patients were non-surgical NEC group as shown in Figure 1. Demographic characteristics are listed in Table 1. There were no significant differences in characteristic data such as gender, gestational age, twins, and mode of delivery between the groups. The mean birth weight in the surgical NEC was higher than the non-surgical NEC (1,260 gram versus 1,105 gram). The difference was not statistically different. Antenatal and perinatal risk factors, including antenatal antibiotic usage, antenatal glucocorticoid usage, APGAR score, perinatal resuscitation, and perinatal endotracheal tube insertion did not differ between the two groups either. The percentage of surgical NEC patients was significantly higher as regards to referred cases than in the cohort of hospital cases (66.7% versus 33.3%, $p<0.001$).

The median age at diagnosis was six days in the surgical NEC group and four days in the non-surgical

Table 1. Data in surgical and non-surgical NEC group

Parameter	Surgical NEC (n=39); n (%)	Non-surgical NEC (n=126); n (%)	p-value
Demographic data			
Sex			
• Male	23 (61.5)	66 (524.2)	0.36
• Female	15 (38.5)	60 (47.6)	
Twin	7 (17.9)	15 (11.9)	0.42
Average maternal age (years); mean±SD	27.1±8.2	27.2±6.8	0.92
Antenatal antibiotics used	27 (79.4)	83 (72.8)	0.51
Antenatal glucocorticoid	11 (33.3)	51 (45.9)	0.23
Mode of delivery			
• Vaginal delivery	23 (59.0)	64 (50.8)	0.46
• Cesarean section	16 (41.0)	62 (49.2)	
Route			
• CMU	13 (33.3)	84 (66.7)	<0.001
• Referred	26 (66.7)	42 (33.3)	
Gestational age (weeks); mean±SD	31.3±4.6	30.2±4.3	0.18
Birth weight (g); median (IQR)	1,260.0 (780.0 to 2,100.0)	1,105.0 (880.0 to 1,840.0)	0.62
Average APGAR (score); median (IQR)	6.5 (5.0 to 8.0)	7.0 (4.0 to 9.0)	0.89
ETT insertion or CPR after delivery	35 (89.7)	98 (77.8)	0.11
Comorbidities	33 (84.6)	107 (84.9)	1.00
• ARDS	26 (66.7)	79 (62.7)	0.71
• PDA	27 (69.2)	91 (72.2)	0.84
• Other congenital heart diseases	6 (15.4)	24 (19.0)	0.81
• Congenital pneumonia	1 (2.6)	11 (8.7)	0.30
Average age at diagnosis of NEC (days); median (IQR)	6.0 (3 to 10)	4 (2 to 10)	0.29
Modified Bell stage at diagnosis			
• Stage I	3 (7.7)	83 (65.9)	<0.001
• Stage II	3 (7.7)	42 (33.3)	
• Stage III	33 (84.6)	1* (0.8)	
Enteric feeding data			
Enteral feeding before NEC diagnosis			
• Yes	31 (81.6)	114 (90.5)	0.15
• No	7 (18.4)	12 (9.5)	
Type of enteral feeding			
• Formula	14 (51.9)	63 (57.3)	0.57
• Breastmilk	7 (25.9)	20 (18.2)	
• Both	5 (18.5)	25 (22.7)	
Average interval of starting enteral feeding (days); median (IQR)	1.0 (1.0 to 3.0)	1.0 (0.5 to 3.0)	0.74
Average initial dose of enteral feeding (mL/kg/day); median (IQR)	7.1 (2.6 to 11.4)	9.5 (4.5 to 20.0)	0.21
Initial concentration of enteral feeding (mL/kg/day); median (IQR)	20.0 (0.0 to 20.0)	20.0 (20.0 to 20.0)	0.19
Average dose of incremental enteral feeding (mL/kg/day); median (IQR)	0.0 (0.0 to 10.0)	10.0 (0.0 to 27.0)	0.023
Concentration of step enteral feeding (mL/kg/day); median (IQR)	0.0 (0.0 to 20.0)	20.0 (0.0 to 20.0)	0.058
Average NPO days (days); median (IQR)	14.0 (11.0 to 30.0)	12.0 (5.0 to 18.0)	0.088
Postnatal risk factors			
Surfactant Used in ARDS	10 (27.0)	39 (31.2)	0.69
Indomethacin used in PDA	12 (30.8)	45 (35.7)	0.70
Blood transfusion	25 (69.4)	61 (51.3)	0.059
Average blood transfusion volume (units); median (IQR)	1.0 (0.0 to 2.0)	0.0 (0.0 to 1.0)	0.097
Umbilical catheter	18 (56.3)	74 (63.8)	0.54
Average duration of umbilical catheter insertion (days); median (IQR)	0.0 (0.0 to 5.0)	2.0 (0.0 to 5.0)	0.72
Cardiac surgery	1 (2.6)	24 (19.0)	0.010
Pre-diagnostic antibiotic usage by patient	37 (94.9)	111 (88.8)	0.36
Duration of antibiotic usage (days); median (IQR)	5.0 (2.5 to 8.5)	3.0 (2.0 to 7.0)	0.087
Multiple episodes of NEC	10 (25.6)	12 (9.5)	0.015
Radiologic finding at first diagnosis			
Bowel dilation	35 (94.6)	104 (85.2)	0.17
Persistent dilated loops	21 (56.8)	51 (41.8)	0.13
Intraperitoneal fluid	20 (54.1)	11 (9.1)	<0.001
Portal venous gas	1 (2.9)	0 (0.0)	0.22
Pneumatosis intestinalis	23 (62.2)	24 (19.7)	<0.001

NEC=necrotizing enterocolitis; CMU=Chiang Mai University; ETT=endotracheal tube; CPR=cardiopulmonary resuscitation; ARDS=acute respiratory distress syndrome; PDA=patent ductus arteriosus; NPO=nil per os; SD=standard deviation; IQR=interquartile range

* 1 NEC patient, Modified Bell stage IIIa required no surgical intervention

Table 2. Multivariable risk ratio of surgical NEC

Characteristics	Univariable risk ratio	95% CI	p-value	Multivariable risk ratio	95% CI	p-value
Pneumatosis intestinalis	3.91	2.01 to 7.60	<0.001	2.69	1.30 to 5.41	0.007
Intraperitoneal fluid	4.82	2.52 to 9.20	<0.001	3.36	1.68 to 6.73	0.001

NEC=necrotizing enterocolitis; CI=confidence interval

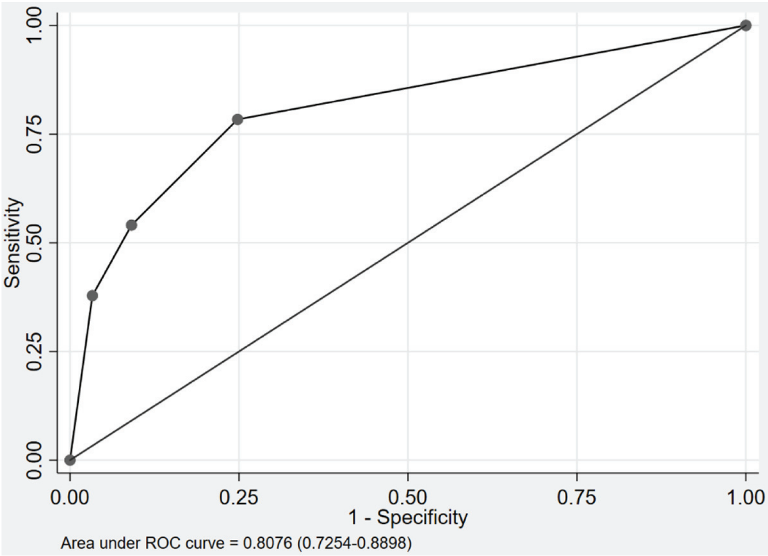

Figure 2. Receiver operating characteristic curve of intraperitoneal fluid and pneumatosis intestinalis for surgical NEC prediction.

NEC group. Most of the non-surgical group were first diagnosed as Modified Bell criteria Stage I or II while the surgical group was diagnosed as Modified Bell criteria Stage III.

There were no significant differences in enteral feeding data between the surgical and non-surgical NEC groups, except the amount of increase in enteral feeding was higher in non-surgical NEC group (0 versus 10 mL/kg/day, p=0.023). Multivariable analysis indicated no significant differences between the two groups. The average NPO time was longer in the surgical group, but this did not reach statistical significance.

There were no significant differences in postnatal risk factors between surgical and non-surgical NEC, except cardiac surgery and multiple episodes of NEC as shown in Table 1. Surgical NEC had significantly higher episodes of previously diagnosed NEC, however in the non-surgical NEC group, patients frequently underwent cardiac surgery.

Radiologic findings at first diagnosis revealed intraperitoneal fluid (54.1%), pneumatosis intestinalis (62.2%), and pneumoperitoneum (76.3%) were found significantly more frequently in surgical NEC cases, p<0.001 (Table 1).

The multivariate logistic regression analysis using the significant parameters from the univariate analysis showed that the two parameters significant in the surgical NEC group were radiologic findings for intraperitoneal fluid (RR 3.36, p=0.001, 95% CI 1.68 to 6.73), and pneumatosis intestinalis (RR 2.69, p=0.007, 95% CI 1.30 to 5.41). No clinical parameters were found to be significant. Using the receiver operating characteristic (ROC) curve, which determined the discriminating power of intraperitoneal fluid and pneumatosis intestinalis for predicting surgical NEC, the area under the curve reached 80.76% and 95% CI was 72.54 to 88.98 (Table 2, Figure 2).

The comparison of outcomes between the surgical and the non-surgical NEC are shown in Table 3. The overall mortality rate of NEC in the present study was 13.9% (23 out of 165 cases). Neonatal mortality was 6.7% (11 out of 165 cases). The rate of mortality occurred in the surgical NEC group was significantly higher than in the non-surgical NEC group at 28.2% versus 9.5% for overall mortality and 18.0% versus 3.2% for neonatal mortality. Complication rates were

Table 3. Outcomes of patients with surgical NEC and non-surgical NEC

Parameters	Surgical NEC (n=39); n (%)	Non-surgical NEC (n=126); n (%)	p-value
Overall mortality	11 (28.2)	12 (9.5)	0.007
Neonatal mortality	7 (18.0)	4 (3.2)	0.004
Hospital stay (days); median (IQR)	65.0 (15.0 to 123.0)	66.5 (35.0 to 104.0)	0.83
Duration on TPN (days); median (IQR)	32.0 (14.0 to 71.0)	18.0 (11.0 to 24.0)	<0.001
Complications	21 (53.8)	21 (16.7)	<0.001
Short bowel syndrome	10 (25.6)	0 (0.0)	<0.001
Intestinal stricture	5 (12.8)	1(0.8)	0.003
Cholestasis liver disease	12 (30.8)	10 (7.9)	<0.001
Body weight at discharge or death (g); median (IQR)	2,910.0 (1,660.0 to 3,525.0)	2,715.0 (2,300.0 to 3,450.0)	0.46

NEC=necrotizing enterocolitis; TPN=total parenteral nutrition; IQR=Interquartile range

Table 4. Operative findings and outcomes in each operative choices

Parameters	Laparotomy (n=30); n (%)	PPD→Laparotomy (n=5); n (%)	PPD (n=3); n (%)
Operative findings			
Focal disease	12 (40.0)	1 (20.0)	-
Multisegmental disease (>50% viable)	16 (53.3)	3 (60.0)	-
NEC totalis (<25% viable)	2 (6.7)	1 (20.0)	-
Overall mortality	8 (26.7)	0 (0.0)	2 (66.7)
Neonatal mortality	4 (13.3)	0 (0.0)	2 (66.7)
Complications	17 (56.7)	4 (80.0)	0 (0.0)
Average time from diagnosis to surgery (days); median (min-max)	1 (0 to 8)	1 (0 to 16)	1 (0 to 3)

NEC=necrotizing enterocolitis; PPD=primary peritoneal drainage

higher in surgical cases at 53.8% in surgical NEC and 16.7% in the non-surgical NEC group. The duration of TPN administration was also longer in the surgical NEC group at 32 days (14 to 71), (p<0.001). Duration of hospital stay, body weight at discharge, and death rate of the two groups did not show significant differences.

Thirty patients in the surgical NEC group (76.9%) underwent laparotomy, three patients (7.7%) underwent primary peritoneal drainage (PPD), and five patients (12.8%) underwent PPD followed by laparotomy. One patient in the surgical group died before surgery or PPD. Focal disease was identified in 13 laparotomy cases, multi-segmental disease in 19 cases, and NEC totalis in three cases. The interval between diagnosis to operation was one day in all operative choices. Eight patients died in the laparotomy group and two patients in the primary peritoneal drainage group as shown in Table 4.

Discussion

One of the major emergency conditions and poor outcomes of treatment in newborn and infants remains NEC in particular surgical NEC. As described in Hull et al studies[1], the present study showed a higher mortality rate (28.2%) and complication rate (53.8%) in surgical NEC patients compared with non-surgical NEC. The surgical NEC group included the referral cases, because Chiang Mai University Hospital is the pediatric surgical center in this area. At present, there are no known causes or detailed pathogenesis of surgical NEC. Many studies showed many risk factors of NEC but the risk factors for perforated NEC were rarely mentioned. In the present study, premature and low birth weight infants were the major groups diagnosed with NEC. The more severe stages at the first diagnosis had greater risks of perforation. However, 15.4% of patients diagnosed as Modified Bell Stage I or II, had clinical progression to perforation later in the present study. Therefore, the severity at the first diagnosis was not always a predictor of perforation.

The previous studies showed many significant risk factors[2,6,10] for the development of NEC. These included low birth weight, prematurity, comorbidity, indomethacin usage, or umbilical catheterization, but in the present study, there were no significant differences among these characteristics in the surgical NEC and non-surgical NEC groups. The widely acknowledged risk factors for developing NEC were not always the risks of perforation.

In 2008, Moss et al reviewed the risk factors of NEC progression(11). The authors included some of these factors in the present study and the results showed similarities and differences. The similar risk factor was pneumatosis intestinalis, which significantly increased in the surgical NEC group according to the multivariable analysis. In 2014, Markel et al mentioned radiographic predictors for the severity of NEC. Sensitivity and specificity for pneumatosis intestinalis was 44% and 100%, respectively. Sensitivity and specificity for portal venous gas was 13% and 100%. Sensitivity and specificity for pneumoperitoneum was 52% and 92%(12). In the present study, radiologic findings at the first diagnosis were found to be significant in surgical NEC cases, revealing intraperitoneal fluid (54.1%) and pneumatosis intestinalis (62.2%) ($p<0.001$). In the multivariate logistic regression analysis, significant radiologic findings in the surgical NEC group were intraperitoneal fluid (RR 3.36, $p=0.001$, 95% CI 1.68 to 6.73), and pneumatosis intestinalis (RR 2.69, $p=0.007$, 95% CI 1.30 to 5.41); the area under the curve reached 80.76% and 95% CI 72.54 to 88.98. In general practice, pneumatosis intestinalis was a definite sign for a diagnosis of NEC and implied a greater severity of disease. However, not all cases with pneumatosis intestinalis required surgery. Plain abdomen films showed intraperitoneal fluid had no specificity to indicate NEC severity. Ascites could be found in other conditions such as heart failure. If it was found in patients diagnosed with NEC, the disease had more severe intra-abdominal pathology. From the results of the present study, pneumatosis intestinalis and intraperitoneal fluid found in the first plain abdominal film could predict a higher risk of perforation, indicating the need for close professional monitoring of the patient's clinical status.

Other significant reported factors(6,13) such as portal vein gas, neonatal resuscitation, low birth weight of less than 1,000 gm and maternal age did not demonstrate any statistical differences in the present study. These findings may be due to the small number of cases.

Many studies mentioned enteral feeding factors associated with NEC(12). One report showed that formula feeding had twice the incidence of NEC. A Thai study by Na Pathalung et al found a significant risk of NEC in high concentrated formula feeding of 24 kcal/oz, adjusted OR 6.9, 95% CI 2.6 to 17.9(2). In the present study, there were no significant differences in the types of feeding between the surgical and non-surgical group as well as amount and concentration of initial enteral feeding. The independent significant enteral factor in the present study was the amount of progressive enteral feedings before diagnosis of NEC, $p=0.023$. Non-surgical NEC also had a high level of progressive feeding, whereas most surgical NEC patients did not receive enteral feeding before diagnosis due to the severity of the disease. Both surgical and non-surgical NEC patients received similar small amounts and minimal concentrations of enteral feeding due to severity of the disease.

The independent factor found in the present study, which has never been cited in any previous literature, was "multiple episodes of NEC". Multiple episodes of NEC were defined as NEC diagnosed at any stage before enrollment in this period. There was a significantly higher rate of multiple episodes of NEC in the surgical NEC, but there was no significant difference shown by the multivariable analysis. "Multiple episodes of NEC" is an interesting factor that warrants further study in the future. If this is a significant risk factor of perforation, clinicians must be aware of perforation in cases of recurrent NEC episodes.

The present study is a single institute study that included both surgical and non-surgical NEC cases. Patients with spontaneous intestinal perforation, focal, and pan-NEC were all included. The results could be used in predicting the course of disease whether the requirement for surgical intervention includes the need for both surgery and drainage. Limitations of the present study were the retrospective nature, which meant the study data could not be verified and standardized, and the small sample size could limit the statistical power of the study results.

The authors recommended close monitoring of the clinical condition in NEC patients with pneumatosis intestinalis and/or intraperitoneal fluid as these might assist in early detection of surgical NEC.

Conclusion

There were no significant differences in practical risks or protective factors against surgical NEC. The present study showed the intraperitoneal fluid and the pneumatosis intestinalis were the significant predictors of NEC perforation. Close regular monitoring for clinical signs of surgical NEC in patients who had related radiologic signs is recommended.

What is already known in this topic?

Many risk factors of NEC have been reported. Some factors were associated with diagnosis while some factors were used to predict the severity of the disease. Serial clinical monitoring and plain abdominal films help detecting perforation earlier and improving outcome of treatment. Some factors may predict the severity of NEC, but no factor could precisely predict the risk of perforation or surgical NEC.

What this study adds?

The risk factors predicting the severity are not the same as risk factors of perforation. An early stage of diagnosis may still result in surgery. Close observation is essential in patients who showed pneumatosis intestinalis and intraperitoneal fluid or ascites in plain abdominal films. Prompt diagnosis of perforation and recommendation for surgery are more likely to result in a good outcome.

Funding disclosure

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Informed consent

Due to the retrospective nature of the present study, using medical records data, informed consent was not required. This is in accordance with the Ethics Committee of Chiang Mai University Hospital.

Conflicts of interest

The authors declare no conflict of interest.

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