Original article

Predictive scores for mortality in full-term infants with necrotizing enterocolitis: experience of a tertiary hospital in Southwest China

Yu Zhang, Ji-Kun Ma, Hong Wei, Xiao-Wen Li, Lu-Quan Li, Jia-Lin Yu
Chongqing, China

Background: **Although many risk factors for mortality of necrotizing enterocolitis (NEC) were investigated, most of them were obtained from preterm infants, and few works focused on the prognostic risk factors in full-term infants. This study aimed to identify risk factors and develop a prediction score model for mortality in full-term neonates with NEC.**

Methods: **The risk factors were analyzed retrospectively by bivariate and multivariate logistic regression analysis in 153 full-term neonates with NEC, who were hospitalized in Children's Hospital of Chongqing Medical University from 2000 to 2013. A prediction score model was developed according to the regression coefficients of risk factors.**

Results: **The mortality of the infants was 19.6% (30/153). The non-survivors had a younger age of diagnosis and advanced stage of NEC (P<0.05). They had a higher prevalence of respiratory failure, intestinal perforation, peritonitis and other complications, compared with the survivors (P<0.05). On the day of diagnosis, the non-survivors were more likely to have abnormal laboratory indicators than survivors (P<0.05). Age at diagnosis [odds ratio (OR)=0.91, 95% confidence interval (CI)=0.836-0.99], respiratory failure (OR=2.76, 95% CI=1.10-6.92), and peritonitis (OR=26.36, 95% CI=7.52-173.92) had significant independent contributions to death. A score model predicting death was developed, and the area under the receiver operating characteristic curve was 0.869 (95% CI=0.803-0.935). All infants with scores ≥8 died.**

Conclusions: **Younger age at diagnosis, peritonitis, and respiratory failure might be risk factors for the mortality of full-term infants with NEC. Infants with a predictive score of 8 were at high risk for death.**

World J Pediatr 2016;12(2):202-208

Key words: **necrotizing enterocolitis; neonate; predictive score model; prognosis**

Introduction

Necrotizing enterocolitis (NEC) is the most common and frequently dangerous neonatal gastrointestinal emergency. Although modern technology and neonatal care have progressed considerably in the past several years, NEC remains an important cause of neonatal mortality.[1] The reported overall mortality for all patients with NEC is up to 30%, with the greatest mortality among those requiring surgery.[2,3]

The prognostic risk factors of NEC include intrauterine growth retardation,[4] low pH value (<7.3),[5] male gender,[6] low gestational age, low birth weight,[1,4,6,7] and low Apgar score in the first minute.[7] Infants with a high C-reactive protein (CRP) level,[7] congenital heart disease and placement of an umbilical artery catheter,[8] severe thrombocytopenia,[5] multiple organ dysfunction syndrome,[9] requiring ventilation support[10] and surgical intervention[6,10,11] were also found to have poor outcomes.

However, these published risk factors were mainly obtained from preterm infants[3,8] or total neonates including both preterm and term infants.[2,4-6,8-10] Several authors speculated that NEC in full-term neonates is a disorder fundamentally different from that in preterm neonates,[10,12] and full-term neonates develop NEC earlier than preterm neonates.[12,13] Meanwhile,

Author Affiliations: Department of Neonatology, Children's Hospital of Chongqing Medical University, Ministry of Education Key Laboratory of Child Development and Disorders, Key Laboratory of Pediatrics in Chongqing and Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Chongqing, China (Zhang Y, Ma JK, Wei H, Li XW, Li LQ, Yu JL)

Corresponding Author: Lu-Quan Li, MD, Department of Neonatology, Children's Hospital of Chongqing Medical University, Ministry of Education Key Laboratory of Child Development and Disorders, Key Laboratory of Pediatrics in Chongqing and Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Chongqing 400014, China (Tel: +86-23-63635567; Fax: +86-23-6362284; Email: liluquan123@163.com).

doi: 10.1007/s12519-015-0063-x
Online First December 2015

prematurity and low birth weight themselves may have many severe complications which are also associated with high mortality. Thus, the risk factors for mortality in preterm infants may not completely reflect the risk of mortality in full-term infants with NEC.

Although some studies focused on NEC in full-term neonates, risk factors for NEC morality were not further analyzed possibly because of small sample sizes (ranged from 14 to 52 cases).[12-16] In the present study, we reviewed the 13-year medical data of full-term infants with NEC treated at our hospital in attempt to determine the risk factors for in-hospital mortality of full-term infants with NEC and the prognostic risk factors for advanced NEC, and to develop a prediction score model for mortality among full-term neonates with NEC.

Methods

Patients

Medical charts were reviewed for all full-term infants (gestational age ≥37 weeks) with NEC (Bell's stage ≥II)[17] admitted to the Children's Hospital of Chongqing Medical University from January 1, 2000 to August 31, 2013. Infants with stage II were defined as having proven NEC, and those with stage greater than II were defined as having advanced NEC. Infants with congenital gastrointestinal malformations, isolated intestinal perforation, or prior abdominal surgery were excluded from the study. And those with incomplete medical records or discharged against medical advices were also excluded. Physicians' and nurses' notes pertinent to the issue of NEC, laboratory examinations, radiographic reports, and surgical and pathological reports were reviewed. Information abstracted from the medical records included gender, gestational age, birth weight, birth number, the age at onset of NEC (defined as the day of one of the following signs or symptoms appeared: increased pre-feeding gastric residuals, emesis, abdominal distension, or bloody stools), the age of diagnosis with NEC (defined as the day of the abdominal X-ray examination meeting the diagnostic criteria of Bell's stage II), clinical features during hospitalization, etc. Laboratory parameters included complete blood counts, blood cultures, blood electrolytes, and tests of renal and liver function. All the infants underwent the same protocol of treatment, including complete cessation of enteral feeding, total parenteral nutrition, nasogastric suction, triple antibiotics, and, if necessary, intensive care therapy (cardio-respiratory support and blood or blood products transfusion). The need for bowel operation, stoma or peritoneal drainage depended on the judgment of pediatric surgeons. The mortality was examined for all infants from the time of diagnosis during the initial hospitalization; we did not follow up the infants who were initially discharged. The study was approved by the Institutional Review Board of Children's Hospital of Chongqing Medical University.

Statistical analysis

Clinical features and laboratory parameters were compared between dead and survived infants with NEC. Normally distributed continuous data were described with mean and standard deviation and analyzed using independent samples *t* test. Skewed data were described with median and 25th and 75th percentiles [P50 (P25-P75)] and analyzed using the Mann-Whitney *U* test. Proportions were compared with the Chi-square test or Fisher's exact test. The parameters significantly associated with death were tested again using multivariable logistic regression analysis to determine their independent contributions to death. Different score values for variables were developed according to their regression coefficients. Receiver operating characteristic curve (ROC) was constructed, and the cutoff value was determined based on the analysis. The data were processed with SPSS13.0 (SPSS Inc., USA) using descriptive and inferential statistics. Statistical significance was established if $P<0.05$.

Results

Study population

A total of 53 829 infants with gestational age ≥37 weeks were admitted to Children's Hospital of Chongqing Medical University during the study period. Of these infants, 182 (0.34%) were listed in the electronic records as having NEC of Bell's stage II or greater. Twenty-nine patients were excluded from this study due to incomplete data. Among the 153 infants meeting our inclusion criteria, 123 (80.4%) were discharged home, and 30 (19.6%) died. Most of the deaths (25; 83.3%) occurred within 7 days of hospitalization, and 17 (56.7%) died in the first week of life.

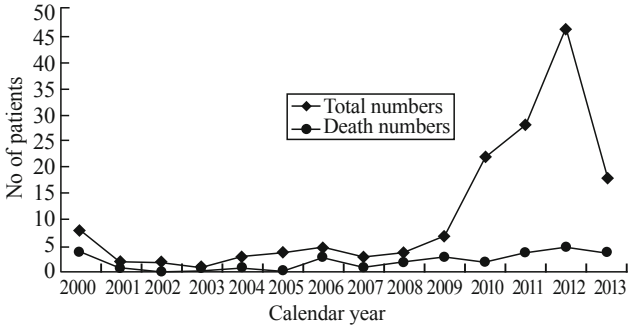

Fig. The total and death number of necrotizing enterocolitis distribution, 2000-2013.

Table 1. The characteristics of the neonates in this study

Variables	Total NEC		Advanced NEC	
	Death group (*n*=30)	Survival group (*n*=123)	Death group (*n*=28)	Survival group (*n*=31)
Gender (male/female)	21/9	76/47	19/9	18/13
Gestational age (wk), mean±SD	39.16±1.25	38.96±1.26	39.04±1.20	38.88±1.42
Birth weight (g), mean±*SD*	3093.17±557.6	3070.39±570.67	3103.75±557.09	3088.06±448.72
Small for gestational age, % (*n*/*N*)	13.3 (4/30)	21.1 (26/123)	10.7 (3/28)	19.4 (6/31)
Multiple gestation, % (*n*/*N*)	6.7 (2/30)	4.9 (6/123)	7.1 (2/28)	6.5 (2/31)
Asphyxia, % (*n*/*N*)	6.7 (2/30)	4.1 (5/123)	7.1 (2/28)	3.2 (1/31)
Congenital heart disease, % (*n*/*N*)	14.3 (3/21)	25.3 (25/99)	11.8 (2/17)	22.2 (6/22)
Age of charge (d), P50 (P25-P75)	3.23 (1.49-6.24)*	4.67 (2.25-13.50)	3.23 (1.22-6.00)*	4.42 (2.83-9.00)
Age of onset (d), P50 (P25-P75)	2.00 (0.75-4.25)*	4.50 (1.00-12.00)	1.59 (0.67-3.75)*	4.00 (1.00-10.00)
Age of diagnosis (d), P50 (P25-P75)	4.50 (2.40-7.53)*	8.00 (5.00-16.00)	3.92 (2.35-6.75)*	6.21 (4.00-11.00)
Time intervals between symptom onset and diagnosis (d), mean±SD	2.40±2.59	3.29±2.93	2.31±2.66	3.56±3.15
Advanced stage of NEC, % (*n*/*N*)	93.3 (28/30)*	25.2 (31/123)	100.0 (28/28)	100.0 (28/28)
Surgery for NEC, % (*n*/*N*)	70.0 (21/30)*	22.8 (28/123)	75.0 (21/28)	90.3 (28/31)

NEC: necrotizing enterocolitis; SD: standard deviation. *: compared with survival group within groups respectively, $P<0.05$.

The tendency of NEC mortality rate from 2000 to 2013 is shown in Fig. Because our ward was expanded in 2009, and new ventilator was introduced in the same year, the respiratory support technology was improved. Therefore, we compared the mortality rate between 2000-2009 (period one) and 2010-2013 (period two), and found that the mortality rate in period one was significantly higher than that in period two [38.5% (15/39) *vs*. 13.2% (15/114), χ^2=11.8, P=0.001, odds ratio=4.13, 95% confidence interval (CI)=1.78-9.59]. First, we analyzed the death distribution in neonates with proven NEC in the two periods, and found that the mortality in period one was higher than that in period two [11.76% (2/17) *vs*. 0% (0/77), Fisher's exact value: 0.031]. Because only two neonates died of proven NEC, we did not explore other causes. We subsequently investigated the death distribution in advanced NEC in the two periods, and found no significant difference in mortality between them [40.5% (15/37) for period one, 59.1% (13/22) for period two, χ^2=1.904, P=0.17]. This result suggested that although the medical technology was improved during the period of 13 years and new ventilator was introduced, the mortality rate for advanced NEC was not changed significantly. Thus, analyzing the relative risk factor for advanced NEC is necessary. This result also suggested that the significant difference in overall mortality between the two periods might be due to the significantly more cases of NEC and greater denominator in period two.

Analysis of risk factors for death

An initial bivariate analysis of the data revealed that the younger age of onset and age of diagnosis were associated with a higher mortality, not only for all infants with NEC, but also for those with advanced NEC (Table 1). Meanwhile, the higher prevalence of advanced stage of NEC and surgery for NEC were also linked with the higher mortality in all patients. Thus, these results suggested that patients with younger age of onset and diagnosis might be more likely to deteriorate, which contributed to their poor prognosis. We further compared the clinical features between survivors and non-survivors, and found that none of the demographics such as gender, gestational age, and birth weight was significantly associated with mortality.

Table 2. Comparison of medical complications after onset of NEC between death and survival group

Variables	Total NEC		Advanced NEC	
	Death group (*n*=30)	Survival group (*n*=123)	Death group (*n*=28)	Survival group (*n*=31)
Sepsis, % (*n*)	53.3 (16)*	22.8 (28)	57.1 (16)	45.2 (14)
Heart failure, % (*n*)	13.3 (4)*	0.8 (1)	14.3 (4)*	0
Respiratory failure, % (*n*)	20.0 (6)*	0.8 (1)	21.4 (6)*	0
Shock, % (*n*)	10.0 (3)	3.3 (4)	10.7 (3)	12.9 (4)
DIC, % (*n*)	6.7 (2)*	0	7.1 (2)	0
Intestinal perforation, % (*n*)	76.7 (23)*	19.5 (24)	82.1 (23)	77.4 (24)
Peritonitis, % (*n*)	93.3 (28)*	25.2 (31)	100.0 (28)	100.0 (31)

NEC: necrotizing enterocolitis; DIC: disseminated intravascular coagulation. *: compared with survival group within group respectively, $P<0.05$.

The dead NEC neonates also had a significantly higher occurrence of intestinal perforation and peritonitis and was more likely to have a higher prevalence of sepsis, organ failure, shock, and disseminated intravascular coagulation after the onset of NEC (Table 2). Furthermore, for infants with advanced NEC, a higher mortality was associated with a higher prevalence of respiratory and heart failure.

For all patients and those with advanced NEC, laboratory evaluations on day of admission are also shown in Table 3. Infants who died were more likely to have higher levels of blood urea nitrogen, creatinine,

Table 3. Comparison of laboratory parameters between the death and survival groups

Variables	Total NEC			Advanced NEC		
	Actual cases	Death group (*n*=30)	Survival group (*n*=123)	Actual cases	Death group (*n*=28)	Survival group (*n*=31)
Laboratory parameters (within 24 h of admission)						
WBC (×10^9/L)	153	9.94±7.48	11.71±6.12	59	9.69±7.68	9.22±6.50
Platelet (×10^9/L)	153	192.24±117.52*	261.69±137.65	59	183.68±113.42	221.77±111.64
CRP (≥8 mg/L), % (*n*/*N*)	136	76.20 (16/21)*	35.20 (37/105)	53	71.40 (20/28)	68.00 (17/25)
BUN (mmol/L)	124	9.44±6.41*	5.08±3.97	50	9.28±6.19	8.49±4.53
Creatinine (μmol/L)	124	75.50±47.34*	50.02±30.32	50	73.48±42.87	65.81±32.69
Uric acid (μmol/L)	124	402.46±237.66*	305.67±188.53	50	411.46±214.39	396.05±209.24
Potassium (mmol/L)	137	4.61±0.60	4.32±1.14	49	4.72±0.27*	3.98±1.18
Sodium (mmol/L)	144	135.96±8.04*	139.18±5.14	54	138.13±9.01	139.00±6.18
Calcium (mmol/L)	144	1.65±0.53*	2.07±0.46	54	1.77±0.41	1.92±0.49
Magnesium (mmol/L)	144	0.89±0.15	0.89±0.17	54	0.96±0.22	0.90±0.13
Albumin (g/L)	136	30.69±7.81*	34.83±6.23	48	32.14±6.93	31.95±7.82
ALT (U/L)	136	24.98±19.32	21.18±16.79	48	25.13±17.68	28.11±22.59
Fibrinogen (g/L)	117	1.59±1.04	2.01±1.05	43	1.29±0.92*	2.44±1.20
pH	121	7.27±0.18*	7.40±0.10	40	7.21±0.15*	7.39±0.10
Laboratory test (within 24 h after diagnosis)						
WBC (×10^9/L)	152	9.21±7.64	10.81±5.29	59	10.21±7.85	9.31±7.09
Platelet (×10^9/L)	152	182.62±110.63*	275.28±147.93	59	173.71±112.51	223.13±99.85
CRP (≥8 mg/L), % (*n*/*N*)	152	72.4 (21/29)*	43.10 (53/123)	59	50.00 (14/28)	61.30 (19/31)
BUN (mmol/L)	151	10.64±6.03*	5.46±4.58	56	9.94±5.63	8.49±4.97
Creatinine (μmol/L)	151	76.96±49.78*	48.52±35.27	56	77.21±44.55	65.71±35.07
Uric acid (μmol/L)	151	419.53±239.08*	287.79±205.02	56	427.72±204.21	355.04±192.29
Potassium (mmol/L)	142	4.49±0.68	4.43±1.08	47	4.29±0.41	4.02±1.22
Sodium (mmol/L)	151	134.62±7.62*	138.65±5.29	54	136.88±5.72	138.25±5.79
Calcium (mmol/L)	151	1.64±0.54*	2.08±0.48	54	1.72±0.78	1.89±0.49
Magnesium (mmol/L)	151	0.88±0.14	0.88±0.19	54	0.75±0.44	0.89±0.14
Albumin (g/L)	131	30.22±8.38*	34.36±6.74	56	33.47±6.31	30.42±8.04
ALT (U/L)	131	26.53±20.33	23.07±15.72	56	22.81±19.76	24.17±14.64
Fibrinogen (g/L)	148	1.63±1.04*	2.31±0.94	54	1.69±0.97*	2.45±1.03
pH	144	7.30±0.20*	7.42±0.10	57	7.24±0.18*	7.40±0.10

WBC: white blood cells; NEC: necrotizing enterocolitis; ALT: alanine aminotransferase; BUN: urea nitrogen; CRP: C-reactive protein. *: compared with the survival group within groups respectively, $P<0.05$.

and uric acid, as well as a significantly lower platelet count, pH, and serum levels of sodium, calcium, and albumin ($P<0.05$). Moreover, significant differences in most of these indicators on day of diagnosis of NEC were found when compared between the two groups. Meanwhile, for advanced NEC, serum fibrinogen and pH in the non-survivor group were lower than those in the survivor group both on day of admission and on day of diagnosis of advanced NEC ($P<0.05$).

Table 4 shows the binary logistic regression analysis of the risk factors for death. Age at diagnosis, respiratory failure, and peritonitis had significant independent contributions to the occurrence of death among full-term infants with NEC.

Table 4. Mortality risk factors by logistic analysis in neonates with NEC and predictive score

Variables	B	*P*	OR	95% CI	Range/grade	Score
Age of diagnosis	-0.09	0.048	0.91	0.84-0.99	≤3.99 d	3
					4-7.99 d	2
					8-14 d	1
					>14 d	0
Peritonitis	3.59	0.000	36.36	7.52-173.92	With intestinal perforation	4
					Without intestinal perforation	2
					No	0
Respiratory failure	1.52	0.030	4.59	1.16-18.21	No	0
					Yes	3
Score maximum						10

NEC: necrotizing enterocolitis; OR: odds ratio; CI: confidence interval.

Score system development

To develop a mortality prediction score for risk factor of NEC, different score values for variables were established according to their regression coefficients (Table 4). The median score was 3.3 (range: 0-10). The area under the receiver operating characteristic curve of the score

Table 5. The predictive scores for mortality of necrotizing enterocolitis

Scores	Mortality, %	Sensitivity, %	Specificity, %	PLR	NLR	AUC (95% CI)
≥3	36.8	93.3	61.0	2.39	0.11	0.772 (0.690-0.853)
≥5	48.1	86.7	77.2	3.80	0.17	0.820 (0.736-0.903)
≥6	50.0	80.0	80.5	4.10	0.25	0.802 (0.710-0.895)
≥7	54.8	56.7	88.6	4.97	0.49	0.726 (0.613-0.840)
≥8	100.0	16.7	100.0	0	0.83	0.583 (0.460-0.707)

PLR: positive likelihood ratio; NLR: negative likelihood ratio. AUC: area under curve; CI: confidence interval.

was 0.869 (95% CI=0.803-0.935) for death from NEC. The sensitivity, specificity, and positive and negative likelihood ratio of different scores for prediction are shown in Table 5. With the increase of predicted scores, the mortality gradually increased. The mortality was 50%, when the patients had more than 6 scores, and all the patients with scores ≥8 died.

Discussion

Although 90% of the infants who develop NEC are born prematurely, full-term infants also develop the disease. Full-term infants with NEC differ from their preterm counterparts in several distinct ways.[10,12,13] Thus, it is important to investigate risk factors for NEC mortality in term infants. In this study, we found that peritonitis, respiratory failure, and younger age at diagnosis were the most likely risk factors for the death of mature infants with NEC.

Peritonitis was a significant independent factor associated with NEC mortality. We found that the non-survivors had a significant higher occurrence of intestinal perforation and peritonitis compared with the survived NEC neonates. Previous studies suggested that gastrointestinal perforation and subsequent peritonitis caused by NEC were associated with high mortality.[6,18] Osifo et al[19] also indicated that peritonitis was an important cause of death in neonates. As an acquired inflammation of the bowel wall, its damage may range from mucosal injury to full thickness necrosis or bowel perforation in NEC infants. Pathophysiological changes in peritonitis can eventually result in systemic inflammatory response syndrome, and excessive inflammatory response itself can damage organs and cause the development of multiple organ dysfunction syndromes, even death.[20] Therefore, peritonitis may be considered a prominent risk factor for NEC mortality.

The other significant independent factor associated with mortality was the presence of respiratory failure. In the current study, we found that respiratory failure was associated with NEC mortality in both bivariate and multivariate analysis. High levels of endotoxin and some proinflammatory cytokines such as interleukin (IL)-1, tumor necrosis factor-α, and IL-6 were found in infants with NEC.[21] Neonatal endotoxemia and the release of proinflammatory cytokines were found to be important contributors of multiple organ failure including respiratory failure.[22] Conversely, the decreased level of oxygen delivery to intestinal tissue because of respiratory failure aggravates this vicious circle. Thus, respiratory failure, a possible result of NEC progression may conversely increase NEC mortality. Our data are consistent with the findings of other investigations.[6]

Another independent factor for NEC mortality was the age of diagnosis. In our study, the non-survivors were usually diagnosed at younger age, and they also had younger age of onset of NEC. Some authors compared the relative factors between early onset NEC and late onset NEC, and found that infants with early onset NEC had older gestational age[23] and received improper enteral feeding too.[24] It was speculated that the seemingly more mature infants were given enteral feeds earlier with more aggressive volume advancement.

In the current study, there was a trend toward increased mortality with some abnormal laboratory parameters, though it was not substantiated on multivariate analysis. Firstly, we found that infants who died were more likely to have severe thrombocytopenia on day of NEC diagnosis, which is similar to the study of Clark et al.[6] A study[25] found that there was a direct correlation between thrombocytopenia and bowel necrosis, mediated probably by cytokines. Severe thrombocytopenia could be an indicator of bowel necrosis,[6] which was associated with high mortality in infants with NEC. Secondly, we found that a significantly higher proportion of the non-survivors had higher CRP levels compared with the survivors in second period. The rise in CRP is presumably a response to tissue inflammation and/or necrosis. Levels of CRP in infants with advanced NEC were significantly higher, and persistence of the high CRP levels might suggest ongoing disease and/or complications in infants with NEC.[7,26] Finally, this study showed that non-survivors were more likely to suffer from metabolic derangement including hyponatremia, hypocalcemia

and acidosis. Thus, sepsis was more common among the non-survivors. In a series of studies, Tepas et al[27] identified seven readily available clinical metrics of metabolic derangement, as indicators of NEC severity and mortality. Thrombocytopenia, hyponatremia, acidosis, and positive blood culture were four of the seven indices.

One way to quantify mortality risk is to develop a predictive model using logistic regression. We established a score mode using logistic regression and validated it by ROC curve. Although the diagnostic value of this mode had a moderate value for prediction according to previous criteria.[28] The high specificity (0.886) for prediction of mortality was the character of this mode. In fact, all the patients with scores ≥8 died in this study, suggesting that neonates with high score should be given priority for treatment and management.

There are limitations of our study, including the inherent errors and bias of retrospective studies. Flaws include factors unknown to us because they were not recorded (some patients were transferred to our center from other hospitals), such as the feeding practices selected and the time that feeds were initiated. Moreover, this study conducted in a level III neonatal intensive care unit of a large tertiary teaching facility in Southwest China, which mainly provides tertiary care for critically ill neonates. Thus, this might not represent a complete picture of full-term neonates with NEC in China. It is suspected that many neonates with severe NEC remain in general wards, given the scarcity of NICU in this country. Unfortunately, we lack data on how many full-term NEC infants are managed in other settings. Further studies on a national basis would be necessary to correctly depict the current status of full-term NEC infants.

In conclusion, we sought risk factors for NEC mortality in full-term infants and observed that neonates diagnosed at younger age, complicated with peritonitis and respiratory failure were more likely to die. The latter two variables can be influenced, to some extent, by the neonatal caregivers. Certainly, any efforts to reduce peritonitis and respiratory failure may actually reduce NEC mortality. Meanwhile, the specific mechanism underlying the early onset of NEC in full-term infants needs further studies.

Funding: This study was supported by the Scientific Research Foundation of Chongqing Municipal Health Bureau (No. 2013-2-051), the National Key Clinical Specialist Construction Programs of China-Neonatology (No. 2011-873), and the Scientific Research Foundation of the science and Technology Commission of Yuzhong District of Chongqing (No. 20140103).

Ethical approval: This study was approved by the Institutional Review Board of Children's Hospital of Chongqing Medical University (ethical approval number: 119/2014).

Competing interest: None.

Contributors: Zhang Y and Ma JK contributed to the acquisition of data and drafting of the manuscript. Li XW contributed to the acquisition of data. Wei H was responsible for the analysis and interpretation of data. Li LQ contributed to the study concept and design, analysis and interpretation, manuscript revision. Yu JL was responsible for study concept and design, manuscript revision.

References

1 Sharma R, Hudak ML. A clinical perspective of necrotizing enterocolitis: past, present, and future. Clin Perinatol 2013;40:27-51.
2 Holman RC, Stoll BJ, Curns AT, Yorita KL, Steiner CA, Schonberger LB. Necrotising enterocolitis hospitalisations among neonates in the United States. Paediatr Perinat Epidemiol 2006;20:498-506.
3 Hull MA, Fisher JG, Gutierrez IM, Jones BA, Kang KH, Kenny M, et al. Mortality and management of surgical necrotizing enterocolitis in very low birth weight neonates: a prospective cohort study. J Am Coll Surg 2014;218:1148-1155.
4 Zampieri N, Zamboni C, Camoglio FS. Necrotizing enterocolitis in multiple gestations: comparison with singletons. Minerva Pediatr 2012;64:1-6.
5 Ji J, Ling XB, Zhao Y, Hu Z, Zheng X, Xu Z, et al. A data-driven algorithm integrating clinical and laboratory features for the diagnosis and prognosis of necrotizing enterocolitis. PLoS One 2014;9:e89860.
6 Clark RH, Gordon P, Walker WM, Laughon M, Smith PB, Spitzer AR. Characteristics of patients who die of necrotizing enterocolitis. J Perinatol 2012;32:199-204.
7 Srinivasjois R, Nathan E, Doherty D, Patole S. Prediction of progression of definite necrotising enterocolitis to need for surgery or death in preterm neonates. J Matern Fetal Neonatal Med 2010;23:695-700.
8 Short SS, Papillon S, Berel D, Ford HR, Frykman PK, Kawaguchi A. Late onset of necrotizing enterocolitis in the full-term infant is associated with increased mortality: results from a two-center analysis. J Pediatr Surg 2014;49:950-953.
9 Thyoka M, de Coppi P, Eaton S, Khoo K, Hall NJ, Curry J, et al. Advanced necrotizing enterocolitis part 1: mortality. Eur J Pediatr Surg 2012;22:8-12.
10 Al Tawil K, Sumaily H, Ahmed IA, Sallam A, Al Zaben A, Al Namshan M, et al. Risk factors, characteristics and outcomes of necrotizing enterocolitis in late preterm and term infants. J Neonatal Perinatal Med 2013;6:125-130.
11 Gane B, Bhat BV, Adhisivam B, Joy R, Prasadkumar P, Femitha P, et al. Risk factors and outcome in neonatal necrotising enterocolitis. Indian J Pediatr 2014;81:425-428.
12 Ostlie DJ, Spilde TL, St Peter SD, Sexton N, Miller KA, Sharp RJ, et al. Necrotizing enterocolitis in full-term infants. J Pediatr Surg 2003;38:1039-1042.
13 Ruangtrakool R, Laohapensang M, Sathornkich C, Talalak P. Necrotizing enterocolitis: a comparison between full-term and pre-term neonates. J Med Assoc Thai 2001;84:323-331.
14 Christensen RD, Lambert DK, Baer VL, Gordon PV. Necrotizing enterocolitis in term infants. Clin Perinatol 2013;40:69-78.
15 Lambert DK, Christensen RD, Henry E, Besner GE, Baer VL,

Wiedmeier SE, et al. Necrotizing enterocolitis in term neonates: data from a multihospital health-care system. J Perinatol 2007;27:437-443.
16 Maayan-Metzger A, Itzchak A, Mazkereth R, Kuint J. Necrotizing enterocolitis in full-term infants: case-control study and review of the literature. J Perinatol 2004;24:494-499.
17 Walsh MC, Kliegman RM. Necrotizing enterocolitis: treatment based on staging criteria. Pediatr Clin North Am 1986;33:179-201.
18 Bălănescu RN, Topor L, Drăgan GC. Clinical and surgical aspects in necrotizing enterocolitis. Chirurgia (Bucur) 2013;108:184-188.
19 Osifo OD, Ogiemwonyi SO. Peritonitis in children: our experience in Benin City, Nigeria. Surg Infect (Larchmt) 2011;12:127-130.
20 Delibegovic S. Pathophysiological changes in peritonitis. Med Arh 2007;61:109-113.
21 Sharma R, Tepas JJ 3rd, Hudak ML, Mollitt DL, Wludyka PS, Teng RJ, et al. Neonatal gut barrier and multiple organ failure: role of endotoxin and proinflammatory cytokines in sepsis and necrotizing enterocolitis. J Pediatr Surg 2007;42:454-461.
22 Woldesenbet M, Rosenfeld CR, Ramilo O, Johnson-Welch S, Perlman JM. Severe neonatal hypoxic respiratory failure correlates with histological chorioamnionitis and raised concentrations of interleukin 6 (IL6), IL8 and C-reactive protein. Arch Dis Child Fetal Neonatal Ed 2008;93:F413-F417.
23 Yee WH, Soraisham AS, Shah VS, Aziz K, Yoon W, Lee SK, et al. Incidence and timing of presentation of necrotizing enterocolitis in preterm infants. Pediatrics 2012;129:e298-e304.
24 Covert RF, Neu J, Elliott MJ, Rea JL, Gimotty PA. Factors associated with age of onset of necrotizing enterocolitis. Am J Perinatol 1989;6:455-460.
25 Song R, Subbarao GC, Maheshwari A. Haematological abnormalities in neonatal necrotizing enterocolitis. J Matern Fetal Neonatal Med 2012;25 Suppl 4:22-25.
26 Pourcyrous M, Korones SB, Yang W, Boulden TF, Bada HS. C-reactive protein in the diagnosis, management, and prognosis of neonatal necrotizing enterocolitis. Pediatrics 2005;116:1064-1069.
27 Tepas JJ 3rd, Leaphart CL, Plumley D, Sharma R, Celso BG, Pieper P, et al. Trajectory of metabolic derangement in infants with necrotizing enterocolitis should drive timing and technique of surgical intervention. J Am Coll Surg 2010;210:847-852, 852-854.
28 Swets JA. Measuring the accuracy of diagnostic systems. Science 1988;240:1285-1293.

Received May 15, 2014
Accepted after revision October 23, 2014