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Determination of surgical intervention in pre-term infants with necrotizing enterocolitis

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Abstract

Background: Necrotizing enterocolitis (NEC) is the most common surgical disease in the neonatal period with a high mortality rate. To date, there is no consensus on the indications for surgery in the absence of pneumoperitoneum. This study aimed to determine the indications for surgery in pre-term infants with NEC and their mortality. **Methods:** We conducted a descriptive, observational, cross-sectional, and retrospective study including pre-term infants with NEC from two perinatal hospitals in Toluca, Mexico, between 2017 and 2022. Descriptive and inferential statistics and group comparisons were performed using Fisher and Kruskal–Wallis tests. **Results:** Of 236 patients with NEC, 52 (22%) required surgery; we analyzed 42 cases with complete clinical records. The indications for surgery were divided into (a) clinical deterioration (33.3%); (b) radiographic findings (31%); (c) laboratory alterations (19%); and (d) positive paracentesis (16.7%). The group of radiographic findings underwent surgery later, up to 2 days after the other groups. The mortality rate of surgical NEC was 42.9%. **Conclusions:** The most common indication for surgery in pre-term infants with NEC was clinical worsening despite optimal medical management; radiographic findings were the indication associated with the highest mortality. Laboratory abnormalities and positive paracentesis were the indications with the best outcomes but the least used.

Keywords: Necrotizing enterocolitis. Surgery. Newborn. Pediatrics.

Determinación de intervención quirúrgica en pacientes pretérmino con enterocolitis necrosante

Resumen

Introducción: La enterocolitis necrosante (ECN) es la enfermedad quirúrgica más frecuente en la etapa neonatal con una alta mortalidad. A la fecha, no existe consenso en las indicaciones quirúrgicas en ausencia de neumoperitoneo. El objetivo del estudio fue conocer las indicaciones de cirugía en neonatos pretérmino con ECN y la mortalidad. **Métodos:** Se llevó a cabo un estudio descriptivo, observacional, transversal y retrospectivo, incluyendo a neonatos pretérmino con ECN de dos hospitales perinatales de Toluca, México, entre 2017 a 2022. Se realizó estadística descriptiva e inferencial y comparación de grupos con prueba de Fisher y Kruskal - Wallis. **Resultados:** De 236 pacientes con ECN, 52 (22%) requirieron cirugía; se presenta el análisis de 42 casos con su expediente clínico completo. Las indicaciones para intervención se dividieron en los siguientes grupos: a) deterioro clínico (33.3%); b) hallazgos radiográficos (31%); c) alteraciones de laboratorio (19%) y d) paracentesis positiva (16.7%). El grupo de hallazgos radiográficos se operó más tardíamente, hasta dos días después de los

demás grupos. La mortalidad en ECN quirúrgica fue del 42.9%. **Conclusiones:** *La indicación más utilizada para determinar cirugía en neonatos pretérmino con ECN fue el deterioro clínico a pesar de terapéutica médica máxima; los hallazgos radiográficos fueron la indicación que se relacionó con mayor mortalidad. Las alteraciones de laboratorio y paracentesis positiva fueron las de mejores resultados, pero las menos empleadas.*

Palabras clave: *Enterocolitis necrosante. Cirugía. Recién nacido. Pediatría.*

Introduction

Necrotizing enterocolitis (NEC) is the most common acquired inflammatory bowel disease in pre-term and low-birth-weight infants. Although its incidence is 7-12% the exact figure varies depending on the gestational age, the definition used to determine the disease, and whether some other pathologies, such as spontaneous intestinal perforation, are included. NEC has an estimated rate of one newborn per 1000 live births[1-3].

At present, NEC is one of the most common surgical emergencies in the neonatal period, with nearly half of the diagnosed patients requiring surgery. Surgical NEC has worse outcomes compared to the variety that has exclusively medical resolution, with a reported mortality of up to 95% for the total NEC variety[1,4]. Deciding when a patient requires surgical management is still controversial among pediatric surgeons, although it is a determining factor in the patient's prognosis. Pneumoperitoneum remains the only absolute indication for surgery; unfortunately, it is present in < 50% of cases. Relative indications for surgery include the presence of clinical deterioration despite optimal medical management, portal venous gas, ascites, positive paracentesis, fixed bowel loops, abdominal distension with erythema, and thrombocytopenia. Patient survival and quality of life depend not only on the severity of the disease but also on the timing of surgical intervention[5-7].

This study aimed to determine the indications for surgical management in pre-term infants with NEC and their mortality.

Methods

Study design

We conducted an observational, descriptive, retrospective, cross-sectional, and descriptive study.

Setting and participants

Neonates ≤ 36.6 weeks of gestation (WG) with a diagnosis of NEC Stage IIa or greater (according to Bell criteria), admitted to the neonatal intensive care unit (NICU) of two perinatal hospitals in the city of Toluca: Hospital de Ginecología y Obstetricia del Instituto Materno Infantil del Estado de México and Hospital Materno Perinatal Mónica Pretelini Sáenz del Instituto de Salud del Estado de México, between January 2017 and June 2022, were included in the study. Patients with incomplete information in their records were eliminated from the study.

Variables

We analyzed post-natal age, sex, gestational age, weight, primary indication for surgery, procedure performed, radiographic and laboratory findings, Bell staging, time from diagnosis to surgery, days of fasting and parenteral nutrition (TPN), development of short bowel syndrome, and mortality. Data were collected from the medical records of the two participating hospitals.

Definitions

NEC was diagnosed according to modified Bell's clinical, radiographic, and laboratory criteria[8].

Indications for surgery were categorized as (a) clinical worsening despite optimal medical management, (b) radiographic findings, (c) positive paracentesis, and (d) laboratory alterations.

Clinical deterioration was defined as the clinically poor evolution of patients characterized by the presence of hypotension, oliguria, bradycardia, increased abdominal circumference with tension (> 2 cm from the basal circumference), changes in skin color at the abdominal level, and the presence of a palpable abdominal tumor. This clinical picture was present despite the fact that the neonate had maximum intensive management, consisting of fasting, orogastric tube, parenteral feeding, aminergic support, mechanical ventilation, and broad-spectrum antibiotics.

Total NEC was defined when > 80% of the small bowel was ischemic-necrotic.

Paracentesis was considered positive according to Kosloske's criteria if a sample is ≥ 0.5 ml of fluid with a cloudy or clear appearance but with a positive Gram stain was obtained[9].

Extensive pneumatosis was defined as being present in four quadrants on abdominal radiographs.

Statistical analysis

Descriptive statistics were performed using measures of frequency, central tendency, and dispersion. For group comparisons, χ^2 or Fisher's exact test was used for qualitative variables and Kruskal–Wallis for quantitative variables. Data processing was performed using the SPSS V.25 statistical package.

Approval was obtained from the ethics and research committees of the two hospitals.

Results

During the study period, 7550 pre-term infants were born in both hospitals, of whom 236 were diagnosed with NEC Stage IIa or higher according to Bell's staging, with a prevalence of 3%. One hundred and eighty-four neonates (78%) did not require surgery, and the remaining 52 (22%) underwent surgery; of these, 10 were excluded because of incomplete records. Finally, 42 patients with NEC requiring surgery were analyzed.

The median gestational age of the pre-term neonates who underwent surgery was 33 WG, the median age at the time of surgery was 12 days, and the median weight was 1400 g. Of the total number of patients, 17 (40.5%) were treated with vasoactive amines up to 72 h before surgery. Neonates were grouped according to comorbidities into infectious (sepsis was the main one found in 17 neonates, 40.5%), respiratory (respiratory distress syndrome in five, 11.9%), cardiopathies (patent ductus arteriosus in six patients, 14.3%; other cardiopathies including atrial septal defect, ventricular septal defect, and Ebstein's anomaly in four, 9.5%), and others (intrauterine growth retardation and perinatal asphyxia in five, 11.9%). The median of time from the diagnosis of NEC to surgical intervention was 56 h (interquartile range [IQR]: 37.7-86.7).

Once the surgical management was decided, 23 patients (54.8%) underwent exploratory laparotomy (EX LAP), four (9.5%) underwent exclusive peritoneal drainage (PD), and 15 (35.7%) underwent PD followed by EX LAP. The procedures performed during EX LAP were intestinal diversion in 17 neonates (40.5%), intestinal anastomosis in 10 (23.8%), and diversion with intestinal anastomosis in 11 (26.2%) of the cases.

We grouped the indications for surgery according to the main criteria used by the different surgeons as follows: (a) clinical deterioration despite optimal medical management (33.3%); (b) based on radiographic changes (31%); (c) due to changes in laboratory tests (19%); and (d) positive paracentesis (16.7%). The demographic and clinical characteristics of the patients according to each of these groups are shown in table 1.

Radiographic findings were pneumoperitoneum in eight neonates (19%), extensive pneumatosis in three (7.1%), and portal venous gas in two (4.8%) neonates.

Predominant laboratory findings were thrombocytopenia in four neonates (9.5%), hyponatremia in three (7.1%), and neutropenia in one (2.4%) neonate.

Total enetrocolitis was present in 16 cases (38%), of which five patients (31.2%) belonged to the clinical deterioration group, eight (50%) to the radiographic findings group, two (12.5%) to the laboratory changes group, and one neonate (6.3%) to the paracentesis group (p = 0.18). Of these patients, three underwent a second-look surgical reintervention 24-48 h after the initial event, with no improvement in bowel ischemic conditions.

The median number of fasting days in the operated neonates was 13 (IQR: 9.7-19), and the median number of days on TPN was 16 (IQR: 12.7-22).

One of the most frequent and worst prognostic complications of surgical NEC is the development of short bowel syndrome, which occurred in 10 (23.8%) of our patients.

According to Bell's staging, 13 neonates (31%) were in Stage IIa/b at the time of surgery, and 29 (69%) were in Stage IIIa/b; of the latter, 45% belonged to the group with radiographic findings, which were the patients taken to the operating room at the latest. Other significant findings in the neonates who were Bell Stage III were that they accounted for 64% of all those who used amines, 76% of those who required an intestinal diversion, and 100% of those with short bowel syndrome.

The overall mortality of NEC in our study group was 42.9%, corresponding to 18 patients; 12 (66.7%) had total NEC. Of the neonates with Bell Stage III, 72.2% died. There was no difference in mortality between neonates who underwent first-intention intestinal anastomosis and those who underwent intestinal diversion. The analysis between different factors and mortality is shown in table 2.

Discussion

Recent technological advances have allowed more pre-term infants to survive, leading to an increase in the presentation of pre-term conditions, including NEC, whose incidence in most reports is higher than our results[6,10]. This may be secondary to the fact that our study only included patients diagnosed with NEC Bell

Table 1. Demographic and clinical characteristics of patients with surgical NEC according to the indication for surgery

Variable	Clinical deterioration (n = 14)	Radiographic findings (n = 13)	Laboratory alterations (n = 8)	Positive paracentesis (n = 7)	p-value
Females, n (%)	7 (50)	6 (46.2)	3 (37.5)	6 (85.7)	0.26
Gestational age in weeks, median/(IQR)	32.2/(30.3-34.1)	34.1/(31.4-35.3)	34/(32.4-35)	33.5/(31.5-35.2)	0.30
Age in days at the time of surgery, median/(IQR)	9/(7-12)	12/(9-13)	12.5/(8.8-14.5)	12/(10.7-14.3)	0.38
Weight in kilograms, median/(IQR)	1.3/(1.2-1.4)	1.4/(1.4-1.8)	1.3/(1.2-1.6)	1.5/(1.1-1.6)	0.35
Use of amines * n (%)	5/35.7	6/46.2	2/25	4/57.1	0.63
Comorbidities n (%) RDS Sepsis PDA Other cardiopathy Perinatal asphyxia Diaphragmatic hernia IUGR	2 (14.3) 7 (50) 1 (7.1) 2 (14.3) 2 (14.3) 0 0	0 4 (30.8) 3 (23.1) 1 (7.7) 1 (7.7) 2 (15.4) 1 (7.7)	1 (12.5) 3 (37.5) 1 (12.5) 0 0 0 1 (12.5)	2 (28.6) 3 (42.9) 1 (14.3) 1 (14.3) 0 0 0	0.64
Time in hours from diagnosis to surgery, median/(IQR)	61.5 (44-81)	89 (77-96)	43 (45-52)	27 (26-37)	0.01
Bell's stage at the time of surgery, n (%) Bell IIa Bell IIb Bell IIIa Bell IIIb	2 (14.3) 6 (42.9) 6 (42.9) 0	0 0 5 (38.5) 8 (61.5)	0 1 (12.5) 7 (87.5) 0	1 (14.3) 3 (42.9) 3 (42.9) 0	0.01
Surgical intervention, n (%) EX LAP Exclusive peritoneal drainage Peritoneal drainage+EX LAP	7 (50) 2 (14.3) 5 (35.7)	9 (69.2) 0 4 (30.8)	3 (37.5) 0 5 (62.5)	4 (57.1) 2 (28.6) 1 (14.3)	0.25
Procedure, n (%) Intestinal diversion Intestinal anastomosis Diversion + intestinal anastomosis	5 (35.7) 2 (14.3) 5 (35.7)	8 (61.5) 2 (15.4) 3 (23.1)	3 (37.5) 2 (25) 3 (37.5)	1 (14.3) 4 (57.1) 0	0.11
Fasting days, median/(IQR)	16 (10-18)	14 (12-20)	11.5 (8-13)	9 (8-17)	0.13
Days with TPN, median/(IQR)	21 (16-23)	18 (14-29)	14 (11.5-16)	13 (11-20)	0.06
Short bowel syndrome, n (%)	2 (14.3)	7 (53.8)	0	1 (14.3)	0.02
Mortality, n (%)	6 (42.9)	8 (61.5)	2 (25)	2 (28.6)	0.37

*Use of amines up to 72 h before surgery.
p < 0.05: statistical significance.
EX LAP: exploratory laparotomy; IQR: interquartile range; IUGR: intrauterine growth retardation; PDA: persistent ductus arteriosus with hemodynamic repercussions; RDS: respiratory distress syndrome; TPN: parenteral nutrition.

Stage IIa or higher. Similarly, our proportion of patients with NEC requiring surgery was 22%, which is lower than the 25-50% considered internationally[2,11].

At present, there are no definitive guidelines for surgical intervention in patients with NEC without clear evidence of perforation. Thus, surgeons are constantly faced with the difficult situation of choosing between early surgery that benefits the patient or unnecessary late surgery, and in the worst-case scenario, wrongly deciding that a newborn does not need surgery. Therefore, alternatives should be sought to make this decision in a correct and timely manner. Recently, the usefulness of different biomarkers, ultrasound, and technologies such as infrared spectroscopy have been mentioned[1,12,13]. However, they have the disadvantage of not being available in all places, as is the case of the hospitals where this research was conducted. Therefore, it is important to know the indications that are considered when deciding to intervene in a patient since, in most of the world, this decision is made according to the severity of the disease as defined by the modified Bell's criteria[14].

Table 2. Bivariate analysis of mortality in patients with surgical NEC

Variable	Mortality, n (%)	p
Gestational age ≤ 33 WG 34-36.6 WG	 12 (50) 6 (33.3)	0.35
Weight in grams ≤ 1500 ≥ 1501	 13 (46.4) 5 (35.7)	0.37
Use of amines	9 (52.9)	0.22
Comorbidity Sepsis PDA Other cardiopathy Diaphragmatic hernia IUGR	 8 (47.1) 3 (50) 4 (100) 1 (50) 2 (100)	0.01
Bell's stage at the time of surgery: IIa IIb IIIa IIIb	 1 (33.3) 4 (40) 8 (38.1) 5 (62.5)	0.71
Indication for surgery Clinical deterioration Radiographic findings Laboratory alterations Paracentesis	 6 (42.9) 8 (61.5) 2 (25) 2 (28.6)	0.37
Diagnostic time surgery ≤ 36 h 36.1-72 h ≥ 72 h	 3 (33.3) 4 (28.6) 11 (57.9)	0.22
Surgical intervention EX LAP PD PD + EX LAP	 9 (39.1) 1 (25) 8 (53.3)	0.58
Procedure: Intestinal diversion Intestinal anastomosis Diversion and intestinal anastomosis	 7 (41.2) 4 (40) 6 (54.5)	0.76
Radiographic finding Pneumoperitoneum Gas in the portal vein Pneumatosis	 5 (62.5) 2 (100) 1 (33.3)	0.17
Laboratory findings Thrombocytopenia Leukopenia Hyponatremia	 2 (50) 0 0	0.42
Total NEC	12 (75)	0.01
Short bowel syndrome	5 (50)	0.43

p < 0.05: statistical significance.
EX LAP: exploratory laparotomy; IUGR: intrauterine growth retardation;
NEC: necrotizing enterocolitis; PD: peritoneal drainage; PDA: persistent ductus
arteriosus with hemodynamic repercussion; WG: weeks of gestation.

According to our results, the main indication used by surgeons to perform surgery for a premature patient with NEC was having a poor evolution with deterioration of their clinical condition despite optimal medical management. In the report by Bethell et al., this failure of medical management was the second most common indication, the main one being the diagnosis of intestinal perforation[11]. However, radiographic evidence of perforation is rare, being present at best in 50% of cases[15]. Hence, many patients with bowel perforation will not have pneumoperitoneum. Only 19% of our patients had peritoneal free air, and in general, radiographic findings were the second most common criterion for deciding to operate.

In this work, we found that other criteria used for surgery were laboratory findings and paracentesis. Regarding the former, there are reports that support it as an adequate guide for determining surgery, as in the case of the seven indicators of metabolic deterioration described by Tepas et al.[16,17], whose advantage is their easy availability in most hospital units. Accordingly, we found that thrombocytopenia, hyponatremia, and neutropenia were the most common changes in these indicators and were the reason for the surgical decision in 19% of our patients. Regarding paracentesis, it remains a current recommendation in neonates with suspected NEC complicated by necrosis and intestinal perforation; this surgical indicator has the advantage of high sensitivity and specificity (87/100%)[9,18]. However, it was infrequently performed in the NICUs where we conducted this study. It was the least common indication used by surgeons (16.7% of cases), perhaps due to concerns about adverse effects secondary to abdominal puncture.

It is noteworthy that 69% of our surgical population was in Bell Stage III, which is described as a phase of complications of the disease. In our report, we confirmed that these patients presented an advanced stage of NEC, as more than half of them were supported by vasoactive amines before and at the time of surgery. In addition, most of the patients required intestinal diversion for the resolution of the disease, meaning that the patients will require at least one more surgery to restore intestinal transit. This stage showed the highest mortality. We also found that all neonates who developed short bowel syndrome corresponded to Bell's group III. These are undoubtedly important findings that highlight the need for early intervention to improve outcomes in surgical NEC.

Yanowitz et al. reported that EX LAP was the most frequent initial surgical procedure (68% of their cases), followed by PD in 32%[19]; our data also showed a predominance of EX LAP but a lower proportion of PD as the only treatment since although it was used in 45.2% of cases, it was maintained as definitive therapy in only 9.5%.

Therefore, we observed PD as a temporary measure to stabilize the patient with lower weight and gestational age before surgery, which occurred in 36% of our patients.

Patient hemodynamic status, comorbidities, weight, surgical findings, surgeon preference, and available resources, among others, are the main factors that influence the type of surgery performed in neonates[2]. Appropriately designed studies are needed to determine the superiority of primary anastomosis over intestinal diversion in cases of NEC[20]. According to what we reported, we had a 2:1 ratio in the number of neonates with intestinal diversion and anastomosis, with no difference in mortality (41.2% vs. 40%), median fasting days (12 days for both), and median TPN days (16 vs. 17) between the two procedures.

The key to improved survival and quality of life for patients with NEC depends largely on early surgery. Despite technological improvements in neonatal care, including advances in monitoring, medications, parenteral nutrition, and surgical and anesthesia techniques, high morbidity and mortality persist in these neonates[5,21]. In the present study, the median of time from the diagnosis of NEC to the indication for surgery by the surgeon was 56 h. According to the studied groups, we observed that neonates in the group with radiographic findings underwent surgery later, with a difference of > 2 days compared with the neonates who underwent surgery earlier in the paracentesis group (p = 0.01). Similarly, we observed that patients who developed short bowel syndrome had a median of time from diagnosis to surgery of 88.5 h compared to patients who did not develop this complication, with a median of time of 49.5 h (p = 0.02). We suggest that this could be because patients who received earlier surgical care had better bowel conditions—less duration of ischemia and necrosis—which allowed the preservation of a greater amount of viable bowel. Therefore, preventing one of the main complications that alter the quality of life, increase costs for family members and the health system, and put the patient's life at risk, such as short bowel syndrome followed by intestinal insufficiency. Regarding survival, we found no statistical significance in the time between patients who died and those who did not (75 vs. 49.5 h, p = 0.5).

We reported a mortality of 42.9%, higher than the average of 34.5% in international reports[22]. However, our 38% prevalence of total NEC was much higher than the 9.3% reported by Murthy et al.[23]. This high prevalence contributed to the increased mortality we found since this type of NEC is the one with the worst prognosis, with mortality between 68.8-95%[4], consistent with the 75% we reported.

Although no statistically significant differences in demographics and comorbidities were found between the groups, the group with radiographic findings had the highest mortality (61.5%). This may be due to the late presentation of signs, such as pneumatosis and gas in the portal vein, as well as pneumoperitoneum, also absent in most cases of bowel perforation. The frequency of pneumoperitoneum in our results was even lower than that reported in previous literature. In addition, neonates who underwent surgery later likely had a more compromised physiological state, which may have contributed to the poor outcome. Moreover, the groups with lower mortality were those who underwent surgery for clinical NEC and laboratory changes, and those with positive paracentesis. Exploring these surgical indications in prospective studies may lead us to perform timely surgery and improve outcomes.

The main limitation of the study is its retrospective nature, which prevents us from exploring important associations for the evaluation of patients with surgical NEC.

Based on our findings, we conclude that the most common indication for surgery in pre-term neonates with NEC was clinical deterioration despite optimal medical management; radiographic findings were the indication associated with the highest mortality. Laboratory changes and positive paracentesis had the best results but were the least used.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. This study involved a retrospective review of medical records, for which approval was obtained from a formally constituted review board (Institutional Review Board or Institutional Ethics Committee).

Conflicts of interest

The authors declare no conflicts of interest.

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References

1. Robinson JR, Rellinger EJ, Hatch LD, Weitkamp JH, Speck KE, Danko M, et al. Surgical necrotizing enterocolitis. Semin Perinatol. 2017;41:70-9.
2. Hong CR, Han SM, Jaksic T. Surgical considerations for neonates with necrotizing enterocolitis. Semin Fetal Neonatal Med. 2018;23: 420-5.
3. Patel RM, Ferguson J, McElroy SJ, Khashu M, Caplan MS. Defining necrotizing enterocolitis: current difficulties and future opportunities. Pediatr Res. 2020;88:10-5.
4. Dukleska K, Devin CL, Martin AE, Miller JM, Sullivan KM, Levy C, et al. Necrotizing enterocolitis totalis: high mortality in the absence of an aggressive surgical approach. Surgery. 2019;165:1176-81.
5. Bianchi A. Surgical necrotizing enterocolitis: early surgery-the key to live bowel and quality life. In: Neonatal Surgery. New York: Springer, Cham; 2019. pp. 299-309.
6. Kastenberg ZJ, Sylvester KG. The surgical management of necrotizing enterocolitis. Clin Perinatol. 2013;40:135-48.
7. Arul GS, Singh M, Ali AM, Gee OJ. Damage control surgery in neonates: lessons learned from the battlefield. J Pediatr Surg. 2019;54:2069-74.
8. Walsh MC, Kliegman RM. Necrotizing enterocolitis: treatment based on staging criteria. Pediatr Clin North Am. 1986;33:179-201.
9. Kosloske AM. Indications for operation in necrotizing enterocolitis revisited. J Pediatr Surg. 1994;29:663-6.
10. Zozaya C, Avila-Alvarez A, Somoza Argibay I, García-Muñoz Rodrigo F, Oikonomopoulou N, Encinas JL, et al. Prevención, diagnóstico y tratamiento de la enterocolitis necrosante en recién nacidos menores de 32 semanas al nacimiento en España. An Pediatr. 2020;93:161-9.
11. Bethell GS, Knight M, Hall NJ, BAPS-CASS NEC Investigator Group on behalf of BAPS-CASS. Surgical necrotizing enterocolitis: association between surgical indication, timing, and outcomes. J Pediatr Surg. 2021;56:1785-90.
12. Knell J, Han SM, Jaksic T, Modi BP. Current status of necrotizing enterocolitis. Curr Probl Surg. 2019;56:11-38.
13. Prithviraj D, Sandeep B, Suresh A, Balaraju V, Mondal S. Comparison between X-ray and abdominal ultrasound findings of necrotizing enterocolitis, its usefulness in early diagnosis, prognosis, and to assess, is this is the time to change our view of surgeon's intervention according to the Bell's criteria. Int J Sci Study. 2015;3:119-30.
14. Carr BD, Gadepalli SK. Does surgical management alter outcome in necrotizing enterocolitis? Clin Perinatol. 2019;46:89-100.
15. Coursey CA, Hollingsworth CL, Wriston C, Beam C, Rice H, Bisset G 3rd. Radiographic predictors of disease severity in neonates and infants with necrotizing enterocolitis. AJR Am J Roentgenol. 2009;193:1408-13.
16. Tepas JJ 3rd, Sharma R, Leaphart CL, Celso BG, Pieper P, Esquivia-Lee V. Timing of surgical intervention in necrotizing enterocolitis can be determined by trajectory of metabolic derangement. J Pediatr Surg. 2010;45:310-3.
17. 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;210:847-52.
18. Evidence-Based Medicine Group. Clinical guidelines for the diagnosis and treatment of neonatal necrotizing enterocolitis (2020). Zhongguo Dang Dai Er Ke Za Zhi. 2021;23:1-11.
19. Yanowitz TD, Sullivan KM, Piazza AJ, Brozanski B, Zaniletti I, Sharma J, et al. Does the initial surgery for necrotizing enterocolitis matter? Comparative outcomes for laparotomy vs. Peritoneal drain as initial surgery for necrotizing enterocolitis in infants <1000 g birth weight. J Pediatr Surg. 2019;54:712-7.
20. Downard CD, Renaud E, St. Peter SD, Abdullah F, Islam S, Saito JM, et al. Treatment of necrotizing enterocolitis: an American pediatric surgical association outcomes and clinical trials committee systematic review. J Pediatr Surg. 2012;47:2111-22.
21. Rowe MI. Rowe SA. The last fifty years of neonatal surgical management. Am J Surg. 2000;180:345-52.
22. Jones IH, Hall NJ. Contemporary outcomes for infants with necrotizing enterocolitis-a systematic review. J Pediatr. 2020;220:86-92.e3.
23. Murthy K, Yanowitz TD, Digeronimo R, Dykes FD, Zaniletti I, Sharma J, et al. Short-term outcomes for preterm infants with surgical necrotizing enterocolitis. J Perinatol. 2014;34:736-40.