Annals of Case Reports
Lin J, et al. Ann Case Rep: 9: 101962
www.doi.org/10.29011/2574-7754.101962
www.gavinpublishers.com

OPEN ACCESS

Case Report

GAVIN PUBLISHERS

Neonatal Necrotizing Enterocolitis Totalis in Preterm Infants: A Report of 3 Cases and Literature Review

Jienan Lin, Tiejun Shou*, Gang Wen, Lei Song, Pengjie Zhang

Department of Neonatal Surgery, The Affiliated Women and Children's Hospital of Ningbo University, Ningbo 315012, China

***Corresponding author**: Shou Tiejun, Department of Neonatal Surgery, The Affiliated Women and Children's Hospital of Ningbo University, Ningbo 315012, China

Citation: Lin J, Shou T, Wen G, Song L, Zhang P (2024) Neonatal Necrotizing Enterocolitis Totalis in Preterm Infants: A Report of 3 Cases and Literature Review. Ann Case Report. 9: 1962. DOI:10.29011/2574-7754.101962

Received: 31 August 2024, **Accepted:** 03 September 2024, **Published:** 05 September 2024

Abstract

Objective: To explore the clinical features diagnosis and treatment strategies of neonatal necrotizing enterocolitis totalis (NEC-T) in preterm infants.

Methods: The clinical data of 3 cases of NEC-T were retrospectively analysed and the related literatures were reviewed.

Results: Three cases (2 boys and 1 girl) were all premature infants. Case 1 was a recurrence of NEC. It took only 20 hours from the recurrence of NEC to death. Despite active surgical exploration, the patient died because the lesions involved the intestine extensively. The family members of case 2 gave up treatment considering the prognosis, and the family members of case 3 chose to continue the treatment, but eventually died due to the progression of the disease.

Conclusions: The pathogenesis of NEC-T is still unclear. Early prevention and treatment of NEC-T is both crucial and difficult. The decision-making problems facing NEC-T, such as long-term TPN, intestinal rehabilitation, intestinal transplantation, more treatment measures and more evidence, need to be solved according to scientific guidance in the future.

Keywords: Enterocolitis; Necrotizing; Neonatal; Recurrent; Fulminant; Extensive Necrotizing Neonatal Necrotizing Enterocolitis.

Introduction

Neonatal necrotizing enterocolitis (NEC) is a life-threatening intestinal disease that causes serious complications in the neonatal population, mainly in preterm infants, with an incidence of 5-13% [1] in infants born less than 2500g. It is the most common cause of emergency surgery in the neonatal intensive care unit (NICU) and has a mortality rate of up to 30%. A proportion of infants with NEC show an abrupt clinical onset and a high mortality rate, that is, fulminant neonatal necrotizing enterocolitis (F-NEC) develops and dies within 48 hours after diagnosis; F-NEC often occurs in the early stage, with signs of portal vein gas in imaging, and requires more mechanical ventilation support [2] before and after surgery. Necrotizing enterocolitis totalis (NEC-T) is a rare form of NEC, which is characterized by nearly total intestinal necrosis with a mortality rate of nearly 100% [3]. Among infants who required surgery for NEC, 11% were confirmed to have NEC-T [4] during surgery; In contrast, 33% of infants who died from NEC developed total intestinal necrosis [5]. In this paper, the clinical data and treatment outcome of 3 cases of NEC-T with rapidly progressive disease within 24 hours were retrospectively analysed, and the literature was reviewed.

Case Reports

Case 1

A 57-day-old boy, G6P2, 29+4 weeks of a gestational age and 1050g of birth weight, was born naturally in our hospital due to severe pre-eclampsia, intrahepatic cholestasis of pregnancy, gestational diabetes mellitus, and uterine fibroids. Amniotic

fluid was clear, placenta adhered, umbilical cord normal, and no premature rupture of membranes. The Apgar score was 8 at 1 minute and 9 at 5 minutes after birth. At birth, the baby's face was cyanosis, breathing was still stable, and the limbs were soft, with general reaction. He was transferred to NICU because of shortness of breath and groaning for 13 minutes after preterm birth. The infant was intolerant to feeding for half a month after admission, with repeated milk stagnation and abdominal distension, and the milk volume was about 10ml/kg. Then he was changed to Alfaré milk 10-15ml/kg/d slowly increased milk. On the 31st day of admission, the infant had bulging abdomen and delayed milk intake, and reduced feeding was given. On the 32nd day of admission, the infant developed bloody stool. Routine blood test showed that white blood cell count was 6.9 × 10^9/L, percentage of neutrophils 11%, hemoglobin 9.0g/dl, and high-sensitivity C-reactive protein 16.8mg/L. Biochemical tests showed albumin 30.8g/L, total bilirubin 61.1 μ mol/L, direct bilirubin 25.9 μ mol/L, and indirect bilirubin 35.2 μ mol/L. The prothrombin time was 15.9Sec and activated partial thromboplastin time was 48.6Sec. The 3P test was weakly positive. Abdominal plain X-ray showed dilatation of the intestinal lumen, and the patient was classified as stage IB according to Bell-NEC grading criteria. Then fasting, gastrointestinal decompression for 1 week, and cefoperazone sodium and sulbactam sodium needle anti-infective treatment were given. After that, the fecal occult blood, blood infection index, abdominal radiograph showed no signs of infection, and no signs and symptoms of NEC were continuously monitored. On the 40th day of admission, the infant was continued to be fed with Alfaré milk, and the milk was gradually increased to nearly full amount, without discomfort. On the 57th day of admission, the child developed abdominal distension and progressive aggravation. Physical examination showed that the child had poor mental response, gradually weakened bowel sounds, shortness of breath, and dark red mucus could be aspirated after gastric decompression. Symptomatic treatments such as fasting, gastrointestinal decompression, oxygen inhalation, cefoperazone sodium and sulbactam sodium needle anti-infection, and intravenous nutrition were given immediately, and the relevant examinations were completed. Blood routine examination showed white blood cell count15.3×10^9/L, percentage of neutrophils 38%,hemoglobin 7.9g/dl, and platelet count124x10^9/L. Biochemical tests showed albumin 21.5g/L, total bilirubin 125.6 μmol/L, direct bilirubin 75.9 μmol/L, indirect bilirubin 49.7 μmol/L, blood glucose 1.3mmol/L, potassium 7.9mmol/L, and sodium:132mmol/L, chloride 88mmol/L, calcium 2.18mmol/L; The prothrombin time (PT)was 28.55Sec,activated partial thromboplastin time(APTT) was 115.95Sec, D-dimer was 17340 μg/L. Blood gas analysis showed PH 6.637, lactic acid > 20mmol/L, and actual base excess-29.2mmol/L. Abdominal plain film showed portal vein gas and pneumoperitoneum to be discharged, indicating NEC, which was stage IIIB according to Bell-NEC classification criteria. The patient was treated with mechanical ventilation, meropenem needle combined with vancomycin needle for anti-infection, volume expansion, correction of acid, correction of electrolyte disorder, and blood transfusion. During the operation, extensive segmental black necrosis was found in the abdominal cavity from duodenum to rectum, the intestinal wall was thin and inert, the small intestine and mesocolon were black, and the perforation point was seen in the small intestine 50cm from the ileocecal junction. The patient was returned to the intensive care unit after surgery, and multiple organ failure occurred in the afternoon of the operation day, and the rescue was ineffective and the patient was declared dead.

Case 2

A 26-day-old boy, G5P4, 34 weeks of gestational age, and 2100g of birth weight, was delivered by cesarean section to monochorionic diamniotic twins (one transverse end) due to intrahepatic cholestasis of pregnancy (severe). The twins were delivered in the second order with pale yellow amniotic fluid, no difference between umbilical cord and placenta, and no premature rupture of membranes. The Apgar score was 9 at 1 minute and 10 at 5 minutes after birth. The infant was admitted to the hospital with "abdominal distention and groaning for half a day." The child developed bucking after feeding half a day ago, and appeared to eat less, cry less and move less, drowsiness, abdominal distension, obvious moaning, shortness of breath, slight cyanosis around the mouth, no mouth foam, no convulsions and screams, no fever and other discomfort. On admission, the infant was diagnosed as "abdominal distension of unknown origin, neonatal pneumonia". Physical examination on admission showed poor mental response, sallow complexion, shortness of breath, groaning and suction concave, obvious abdominal distention, exposed abdominal veins, weak bowel sounds, 0-1 times/min, low muscle tension of limbs, and cold endings. Routine blood test showed white blood cell count 6.8 × 10^9/L, percentage of neutrophils 8%,percentage of lymphocytes 87%, hemoglobin 7.8g/dl, platelet count 263 ×10^9/L,andhigh-sensitivityC-reactiveprotein34.88mg/L.

Emergencybiochemistryshowed albumin 39.8g/L, total bilirubin 168.2 μmol/L, direct bilirubin 1.0 μmol/L, indirect bilirubin 167.2 μmol/L, potassium 7.5mmol/L, sodium 132mmol/L, chloride 98mmol/L, and calcium 2.24mmol/L. Routine coagulation test showed that prothrombin time was 27.5Sec, activated partial thromboplastin time was 78.3Sec, thrombin time was 21.6Sec. Blood gas analysis showed that the blood PH value was 6.891, the lactic acid was >12.00mmol/L, and the actual base excess was- 23.1mmol/L. Blood culture and identification of aerobic culture were negative. Abdominal X-ray showed free air under the diaphragm, pneumatosis peritonei, and pneumatosis intestinal is, indicating NEC, which was stage IIIB according to Bell-NEC classification criteria. Chest X-ray showed pneumonia of the new-born. The rest of the examination showed no obvious

abnormalities. After admission, he was given intensive care, fasting, gastrointestinal decompression, electrocardiogram monitoring, endotracheal intubation and ventilator assisted ventilation, meropenemacupuncture for anti-infection, creatine phosphate sodium acupuncture, dopamine acupuncture, volume expansion, and intravenous nutritional support. Surgical abdominal exploration showed a large amount of dark bloody fecal juice like exudate in the abdominal cavity, no vitality, no elasticity, and no vascular pulse in the whole small intestine. There were multiple perforations and dot hemorrhage and necrosis in the whole colon. After informing the family members, the family members considered that the prognosis of the child was very poor and the survival rate was not high. Even though there was a high probability of survival, there were long-term sequelae and there was still the possibility of recurrence, and finally decided to give up treatment.

Case 3

A 38-day-old girl, G3P2, 27+4 weeks of gestational age and 1000g of birth weight, was born spontaneously due to placental abruption and threatened abortion. Her amniotic fluid was bloody, and one third of the placental abruption was observed, and her umbilical cord was normal without premature rupture of membranes. After active rescue, such as respiratory tract cleaning, tracheal intubation, chest compression, and adrenaline needle endotracheal insufflations, the infant was transferred to NICU with a diagnosis of "14 minutes after premature asphyxia resuscitation". After admission, she was given intensive care, electrocardiogram monitoring, endotracheal intubation and ventilator assisted ventilation, intravenous drip of penicillin, ceftazidime, and meropenem for anti-infection, transfusion of plasma to improve coagulation function, symptomatic support with albumin infusion, transfusion of suspended red blood cells without white blood cells to improve anemia, caffeine injection to stimulate respiration, dopamine injection and milrenone injection to improve circulation, and epinephrine to maintain blood pressure. Phenobarbitone sodium needle and levetiracetam oral solution were used to stop spasmopathy, ibuprofen was used to close patent ductus arteriosus, maintain internal environment stability, correct acid-base poisoning and electrolyte disorder, diuretics limited fluid, reasonable feeding combined with partial intravenous nutrition, calciumandphosphorus supplementation, vitamin AD and vitamin D supplementation, phototherapyto relieve jaundice and other symptomatic treatments. On the 38th day of admission, the child developed vomiting. Physical examination showed poor mental response, slightly dark skin colour, slightly lower skin lines, coarse breath sounds in both lungs, no obvious dry rales and moist rales, abdominal distention, high abdominal walltension, pain on palpation of the whole abdomen, suspicious rebound pain, muscle guard, negative moving dullness, no obvious bowel sounds, percussion drum sounds, and weak muscle tension. Routine blood test showed white blood cell count 3.1 × 10^9/L, percentage of neutrophils 45%, percentage of lymphocytes 47%,hemoglobin 9.9g/dl, platelet count 87×10^9/L, and high-sensitivity C-reactive protein 15.8mg/L. Emergency biochemistry showed albumin 22.6g/L, total bilirubin 71.1 μmol/L, direct bilirubin 0.1 μmol/L, indirect bilirubin 71.0 μmol/L, potassium 5.7mmol/L, sodium 137mmol/L, chloride 99mmol/L, and calcium 2.17mmol/L. Routine coagulation test showed prothrombin time 17.7Sec, activated partial thromboplastin time 48.2Sec, fibrinogen 264mg/dL. Blood gas analysis showed blood PH value of 6.963, lactic acid >12.00mmol/L, actual base excess-10.6mmol/Abdominal plain film showed increased bowel inflation, continuous inflation and dilatation, gas in the bowel wall, and unclear abdominal fat lines, indicating NEC. According to Bell-NEC classification criteria, the patient was classified as stage IIIB. Surgical abdominal exploration showed a small amount of light bloody exudation in the abdominal cavity. From the distal duodenum to the middle of the transverse colon, the intestinal wall was thin and no peristalsis, part of the intestinal wall was black, and part of the intestinal wall was gray and transparent. Necrotizing enterocolitis was considered, and all the small intestine was necrotic. The patient was told that the scope of intestinal inflammation was too large, the condition was critical, and it might be life threatening at any time. The follow-up plan was explained to the family members, and the family members showed understanding, chose intestinal decompression and abdominal drainage, continued to observe the changes in the patient's condition, and entered the abdomen again to see if there was a possibility of intestinal condition improvement. Further intestinal decompression was performed, and a Dow's nest rubber drainage tube was placed in the right lower abdomen. After no obvious bleeding was observed, the incision was closed .After surgery, the patient returned to the intensive care unit and continued to receive intensive care. However, the patient's condition continued to deteriorate, and the rescue was ineffective and the patient was declared dead.

Literature review

Using "enterocolitis", "necrotizing", "neonate", "recurrence", "fulminant", "NEC-totalis" as keywords, Cnki, Wanfang database, VIP database, PubMed, Embase, Web of Science, and the Cochrane Library were searched from the establishment of the database to January 1, 2022, and 30 relevant articles were retrieved, 28 of which were in English. Two articles were in Chinese.

Discussion

All the three cases were low birth weight premature infants with rapid onset. Although active surgical exploration was performed, the patients died because the lesions involved the intestine extensively. So far, the author has encountered similar cases many times in clinical work, which has triggered the writer's thinking.

Case 1 had two episodes of NEC after birth. The first episode was cured by conservative treatment, and the second episode progressed rapidly, which was consistent with the clinical characteristics of recurrent neonatal necrotizing enterocolitis (R-NEC). R-NEC occurs in about 10% of infants [6] with successfully treated NEC. Preterm birth, very low birth weight, major congenital anomalies, or persistent cardiovascular injury may be associated4 with R-NEC. In regard to R-NEC, M.D. Stringer [6] and Ricketts [7] stated that the incidence of R-NEC is 6% and 4% of all NEC ones, respectively. Persistent cardiovascular diseases, such as congenital heart disease, recurrent bradycardia or its treatment, and the timing of the resumption of enteral nutrition after NEC may also be relevant. Vollman [8] suggested that the initiation of enteral nutrition within 10 days after the initial onset of NEC may be related to the recurrence of NEC. The issue of enteral nutrition recovery after the initial onset of NEC has attracted the attention of many researchers. According to Bohnhorst's [9] analysis, early enteral feeding initiated within 5 days after diagnosis of NEC was not associated with adverse outcomes (including R-NEC). In addition, the rates of catheter-related sepsis and post-NEC stenosis did not change between the early and delayed post-NEC enteral feeding groups. Brotschim [10] concluded that a shorter duration of fasting after NEC appeared to reduce morbidity after the acute phase of the disease, and in particular, infants with a shorter duration of fasting had significantly fewer catheter-associated septicemia, thus finding no clear benefit of prolonged fasting. There are no standardized guidelines for restarting enteral nutrition after nonsurgical treatment of NEC, such as medications, and in these patients, early re-feeding was not significantly associated [11] with an increase in NEC recurrence, mortality, or stenosis. Patel's [12] NEC early feeding guidelines, based on multidisciplinary consensus, reduced the mean days to start feeding in infants with stage II NEC from 9.4 days to 5.1 days and the mean days to satiety from 24.0 days to 15.7 days, a reduction of 35%.There was no statistically significant difference in recurrence and stricture. Therefore, the time to full enteral feeding was effectively shortened and no adverse events were observed. Early active enteral feeding can stimulate the maturation of intestinal function, increase energy intake, and promote growth and development. Therefore, we believe that the fasting time of NEC children should be reasonably evaluated, the timing of resumption of feeding should be carefully selected, and enteral feeding should be started as early as possible to avoid disease progression.

The three cases had an abrupt onset and an explosive course, and the time from onset to death was less than 24 hours, which was consistent with the characteristics of fulminant neonatal necrotizing enterocolitis (F-NEC). M. Voss a S. W. [13] summarized 128 neonates with NEC who were admitted to the NICU and underwent surgery. Among them, 52 cases developed rapidly into severe cases within 24 hours after the onset of symptoms and required ICU admission and surgical treatment. In addition, surgical exploration found that 19 cases lost the chance of survival after surgical resection of the lesions due to extensive intestinal lesions, but most of them did not have imaging manifestations of extensive intestinal wall gas (more than 1 quadrant on abdominal plain film,3/19) before surgery, and the survival rate within 30 days was 44%. The 30-day survival rate was 44%, which was significantly lower than that of non-fulminant NEC (79%, $P < 0.01$).The positive rate of blood culture in the F-NEC group (23%) was higher than that in the non-F-NEC group (17%), although the difference was not statistically significant. Lambert [14] reviewed 318 cases of Bell stage II NEC diagnosed and treated in 9 years, and found that 35 cases showed explosive progression, and all of them died within 48 hours after onset. The definition of F-NEC was as follows: onset of NEC and death within 48 hours; Anemia, high neutrophil ratio and low lymphocyte count may be related to F-NEC. Parvesh Mohan Garg [2] studied 336 neonates with NEC (35 F-NEC cases, 10%) and found that neonates with F-NEC often had thrombocytopenia, lymphopenia, neutropenia, and leukopenia, and had received red blood cell or platelet transfusions before the onset of NEC. This is partially consistent with the situation of the three children in the article. Due to the lack of typical imaging manifestations and signs, the early diagnosis of F-NEC is difficult, and some serological indicators may be related to the recurrence of NEC. Therefore, it is particularly important to establish a reasonable prediction model to assess the risk of F-NEC, early identification and timely treatment to reduce the mortality of children.

In case 1, extensive segmental black necrosis from duodenum to rectum was found by intraoperative exploration, and case 2, case 3, had total small intestine necrosis with colon involvement. All of the above three cases were classified as necrotizing enterocolitis totalis (NEC-T) [15]. At present, there is no exact definition of NEC-T. Dukleska5 reviewed 32 related articles and found that 52% of them did not provide a clear definition, 30% defined NEC-T as lesions involving the large and small intestine, and 9% defined NEC-T as lesions involving the small intestine. Due to the uncertainty of the definition, the incidence of NEC-T is not uniform, and some studies have suggested that NEC-T may account for 10-15% [13], 16 of all NEC cases. Due to the necrotic bowel involvement of more than 80%, rapid clinical progression and almost 100% mortality [15], NEC-T has been concerned and studied. "Thompson [15] studied data from Yale's Neonatal Intensive Care Unit, pediatric surgery, and pediatric clinical databases from January 1991 to December 2007 and found that NEC-T may be associated with a lower maternal age, near-total enteral feeding, higher feeding volumes, higher caloric supplementation, and fewer interruptions in feeding. "Analysis of risk factors in 157 children with NEC (13 of whom had NEC-T) by Sho [16] found that cases with low platelets, high phosphorus, high creatinine, and older age had a greater risk of NEC-T. Sun

Pengjun et al [15]. Found that abdominal wall erythema, severe sub intestinal gas, hyponatremia, and thrombocytopenia were positively correlated with the risk of NEC-T. The results showed that common laboratory tests and clinical features could be used to predict the occurrence of NEC-T, and the scoring system was highly accurate for diagnosis and prognosis prediction. The scoring system has high accuracy in the diagnosis and prognosis of NEC-T. However, there is still a lack of systematic research on the clinical characteristics, related factors and pathogenesis of NEC-T, and there is no consensus on the timing of surgical intervention, which also becomes a difficulty.

NEC-T is often confirmed by exploratory laparotomy. Dukleska [3] retrospectively reviewed the medical records of 414 children with NEC-T and found that 382 patients (92.3%) underwent non-invasive surgical treatment. The remaining 32 patients (7.7%) underwent active surgical treatment (including bowel resection or enterostomy), and the mortality rate was 68.8%.Therefore, active surgical treatment can effectively reduce the mortality. Although more children survive for a long time, some patients develop short bowel syndrome (SBS) due to too little remaining bowel or insufficient physiological function. Long-term parenteral nutrition is needed to ensure the growth and development of children, and even intestinal transplantation is needed to solve the problem. With the progress of medical treatment and surgical management of NEC children, great progress has been made in the care of children with SBS, including intestinal rehabilitation, the application of new fat emulsions in medium and long-term total parenteral nutrition (TPN), and intestinal transplantation [17-20] with improved immunosuppressive regimens. A multicentre cohort study showed that 272 infants with intestinal failure received long-term TPN treatment. After 2 years, 47% of these infants had intestinal function recovery, 26% underwent intestinal transplantation, and 27% eventually died [21]. Data on the quality of life before and after intestinal transplantation in children are limited due to the small number of cases related to intestinal transplantation. However, from the perspective of patients and their families, most survivors are able to obtain a good quality [22] of life. At present, intestinal transplantation is an important way to effectively solve SBS and intestinal failure, but if a certain period of medium-and long-term TPN can bring about the final recovery of intestinal function in children with SBS, then it may be worth considering that TPN can exchange time for self-recovery of intestinal function. However, there is still a lack of evidence on the long-term prognosis, such as the duration of parenteral nutrition, the progress of small bowel transplantation, and the quality of life, and further research is needed.

In fact, under the active treatment, although the life of the children can be successfully extended, whether it is long-term TPN or intestinal transplantation, it is inevitable to bring many problems to the children and their families, including quality of life, economic cost, and potential pain for parents due to long-term care of the children, heavy psychological burden, etc [23]. In an anonymous survey of members of the American Academy of Pediatrics' Neonatal-Perinatal Medicine and Pediatric Surgery, Pyle [23] found that the following factors often influence the final diagnosis and treatment decisions: The child's quality of life (93%),prognosis for long-term survival (92%),concomitant medical conditions (86%),family burden (75%),the patient's right not to suffer for a poor prognosis (84%), parents' right to choose for their child (69%), and concerns about the lack of promising treatments (77%).Therefore, in the face of NEC-T, how to discuss the patient's condition and the relevant diagnosis and treatment plan with the parents (including long-term TPN, intestinal rehabilitation treatment, and intestinal transplantation, or appeasement, palliative and soothing treatment) has become an unavoidable ethical problem for doctors.

In summary, all the 3 cases in this article were NEC onset and showed explosive progression, extensive gastrointestinal necrosis, and eventually led to the death of the children. R-NEC, F-NEC, and NEC-T are extremely rare in clinical practice, and their pathogenesis is still unclear. How to choose the appropriate feeding time; establish relevant models for disease prediction, and early prevention and treatment are the keys. In the future, TPN, intestinal rehabilitation, intestinal transplantation, more medical progress and more evidence are needed to solve the decision-making problems faced by NEC-T.

Conflicts of interest: All the authors declare no conflicts of interest.

Statement of Author Contributions: Lin Jiannan: case sorting and paper writing; Wen Gang, Song Lei, Zhang Pengjie and Chen Kai: case management, data collation, and paper revision; Shou Tiejun: research guidance, paper revision, and funding support

Fundings:

1.Ningbo medical key supporting discipline(2022-B17)

2.Ningbo Top Medical and Health Research Program (No.2022020405)

References

1. Yee WH, Soraisham AS, Shah VS, Aziz K, Yoon W, et al. (2012) Incidence and timing of presentation of necrotizing enterocolitis in preterm infants. Pediatrics. 2012;129:e298-304.
2. Garg PM, Connor AO, Ansari MA, Vu B, Hobart H, et al. (2021) Hematological predictors of mortality in neonates with fulminant necrotizing enterocolitis. J perinatol. 41: 1110-1121.
3. Dukleska K, Devin CL, Martin AE, Miller JM, Sullivan KM, et al. (2019) Necrotizing enterocolitis totalis: High mortality in the absence of an aggressive surgical approach. Surgery. 165:1176-1181.
4. Houben CH, Davies R, Kiely EM. (2008) Percutaneous transluminal angioplasty in recurrent necrotizing enterocolitis--a case report. J Pediatr Surg. 43:559-561.

5. Jacob J, Kamitsuka M, Clark RH, Kelleher AS, Spitzer AR. (2015) Etiologies of NICU deaths. Pediatrics. 135:e59-65.

6. Stringer R. (1993) recurrent necrotizing enterocolitis. Journal of Pediatric Surgery. 28:979-981.

7. Richard RR, and Matthew LJ (1990) Neonatal Necrotizing Enterocolitis: Experience with 100 Consecutive Surgical Patients. World J. Surg. 14:600-605.

8. Vollman JH, Smith WL, Tsang RC. (1976) Necrotizing enterocolitis with recurrent hepatic portal venous gas. The Journal of pediatrics. 88:486-487.

9. Bohnhorst B, Muller S, Dordelmann M, Peter CS, Petersen C, et al (2003) Early feeding after necrotizing enterocolitis in preterm infants. The Journal of pediatrics. 143:484-487.

10. Brotschi B, Baenziger O, Frey B, Bucher HU, Ersch J. (2009) Early enteral feeding in conservatively managed stage II necrotizing enterocolitis is associated with a reduced risk of catheter-related sepsis. J Perinat Med. 37:701-705.

11. Arbra CA, Oprisan A, Wilson DA, Ryan RM, Lesher AP. (2018) Time to reintroduction of feeding in infants with nonsurgical necrotizing enterocolitis. J Pediatr Surg. 53:1187-1191.

12. Patel EU, Head WT, Rohrer A, Ryan RM, Lesher AP. (2022) A quality improvement initiative to standardize time to initiation of enteral feeds after non-surgical necrotizing enterocolitis using a consensus-based guideline. Journal of perinatology: official journal of the California Perinatal Association. 42:522-527.

13. Voss M MS, van der Merwe I, Pieper C. (1998) Fulminanting necrotising enterocolitis: outcome and prognostic factors. Pediatr Surg Int. 13:576-580.

14. Lambert DK, Christensen RD, Baer VL, Henry BE, Gordon PV, et al. (2012) Fulminant necrotizing enterocolitis in a multihospital healthcare system. Journal of perinatology: official journal of the California Perinatal Association. 32:194-198.

15. Thompson A, Bizzarro M, Yu S, Diefenbach K, Simpson BJ, et al (2011) Risk factors for necrotizing enterocolitis totalis: a case-control study. Journal of perinatology: official journal of the California Perinatal Association. 31:730-738.

16. Sho S, Neal MD, Sperry J, Hackam DJ. (2014) A novel scoring system to predict the development of necrotizing enterocolitis totalis in premature infants. J Pediatr Surg. 49:1053-1056.

17. DeLegge M, Alsolaiman MM, Barbour E, Bassas S, Siddiqi MF, et al (2007) Short bowel syndrome: parenteral nutrition versus intestinal transplantation. Where are we today? Dig Dis Sci. 52:876-892.

18. Hess RA WK, Brown PI, Teitelbaum DH. (2011) Survival Outcomes of Pediatric Intestinal Failure Patients: Analysis of Factors Contributing to Improved Survival Over the Past Two Decades. Journal of Surgical Research. 170:27-31.

19. Bharadwaj S, Tandon P, Gohel TD, Brown J, Steiger E, et al. (2017) Current status of intestinal and multivisceral transplantation. Gastroenterol Rep (Oxf). 5:20-28.

20. Dore M, Junco PT, Moreno AA, Cerezo VN, Munoz MR, et al. (2017) Ultrashort Bowel Syndrome Outcome in Children Treated in a Multidisciplinary Intestinal Rehabilitation Unit. Eur J Pediatr Surg. 27:116-120.

21. Squires RH, Duggan C, Teitelbaum DH, Wales PW, Balint J, et al. (2012) Natural history of pediatric intestinal failure: initial report from the Pediatric Intestinal Failure Consortium. The Journal of pediatrics. 161:723-728 e722.

22. Andres AM, Alameda A, Mayoral O, Hernandez F, Dominguez E, et al. (2014) Health-related quality of life in pediatric intestinal transplantation. Pediatr Transplant. 18:746-756.

23. Pyle AK, Shabanova V, Cleary MA, Ozgediz D, Cummings CL, et al. (2019) Variable management strategies for NEC totalis: a national survey. Journal of perinatology: official journal of the California Perinatal Association. 2019;39:1521-1527.