



Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedisurg

Severe neurodevelopmental disability and healthcare needs among survivors of medical and surgical necrotizing enterocolitis: A prospective cohort study[☆]

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ARTICLE INFO

Article history:

Received 12 September 2017

Accepted 5 October 2017

Available online xxx

Key words:

Necrotizing enterocolitis

Long term outcomes

Disability

Tube feeding

Neurodevelopmental outcomes

Extremely low birth weight

ABSTRACT

Purpose: This study characterizes neurodevelopmental outcomes and healthcare needs of extremely low birth weight (ELBW) survivors of necrotizing enterocolitis (NEC) compared to ELBW infants without NEC.

Methods: Data were collected prospectively on neonates born 22–27 weeks' gestation or 401–1000 g at 47 Vermont Oxford Network member centers from 1999 to 2012. Detailed neurodevelopmental evaluations were conducted at 18–24 months corrected age. Information regarding rehospitalizations, postdischarge surgeries, and feeding was also collected. "Severe neurodevelopmental disability" was defined as: bilateral blindness, hearing impairment requiring amplification, inability to walk 10 steps with support, cerebral palsy, and/or Bayley Mental or Psychomotor Developmental Index < 70. Diagnosis of NEC required both clinical and radiographic findings.

Results: There were 9063 children without NEC, 417 with medical NEC, and 449 with surgical NEC evaluated. Significantly higher rates of morbidity were observed among infants with a history of NEC. Those with surgical NEC were more frequently affected across all outcome measures at 18–24 months corrected age: 38% demonstrated severe neurodevelopmental disability, nearly half underwent postdischarge operations, and a quarter required tube feeding at home.

Conclusion: At 18–24 months, extremely low birth weight survivors of necrotizing enterocolitis were at markedly increased risk ($p < 0.001$) for severe neurodevelopmental disability, postdischarge surgery, and tube feeding.

Level of evidence: II (prospective cohort study with <80% follow-up rate).

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Necrotizing enterocolitis (NEC) and spontaneous intestinal perforations (SIP) commonly affect extremely low birth weight (ELBW) neonates and are associated with significant mortality or prolonged and complicated hospital courses [1,2]. In addition, ELBW neonates are known to be at increased risk for long-term developmental disabilities [3,4]. To better characterize morbidity among survivors of NEC, we evaluated neurodevelopmental outcomes and healthcare needs among survivors of medical and surgical NEC, compared to those without a history of NEC, at two year follow-up.

1. Methods

1.1. Study design

This study is a retrospective review of prospectively collected data from the Vermont Oxford Network (VON), a nonprofit voluntary clinical

collaborative dedicated to improving the safety and quality of care provided to neonates and their families. VON members prospectively collect data on infants with birth weights 401–1500 g, or gestational age at birth of 22 to 29 completed weeks, who are admitted to a participating center neonatal intensive care unit (NICU) within 28 days of birth. Data are collected by local staff using uniform definitions until neonates are discharged from the hospital, die, or reach one year of age in the hospital. Records are subjected to automated checks and returned for correction if incomplete. Of the 731 North American centers participating in VON, 47 centers participate in the VON ELBW follow-up project and contributed data for this study, on infants born 1999–2012 (Appendix 1, online only). These centers conduct follow-up evaluations with detailed neurodevelopmental assessment on ELBW infants (birth weight 401–1000 g or gestational age at birth 22 to 27 completed weeks) between 18 and 24 months corrected age. For this study, infants with a major congenital anomaly or initial hospital length of stay < 72 h were excluded. A clinical diagnosis of NEC required at least one physical finding (bilious gastric aspirate or emesis, abdominal distention, or occult/gross blood in the stool in the absence of anal fissures) and at least one radiographic finding (pneumatosis intestinalis, hepatobiliary gas, or pneumoperitoneum), i.e. minimum Bell's Stage II. Bowel perforation or NEC could also be diagnosed at laparotomy or at postmortem examination [5]. Detailed definition of all data points is as specified in the

[☆] Financial Disclosure: Dr. Horbar, Dr. Soll, Ms. Morrow and Ms. Ferrelli are employees of the Vermont Oxford Network. Dr. Edwards is supported by a grant from the Vermont Oxford Network to the University of Vermont. Dr. Fullerton is supported by the Boston Children's Hospital Department of Surgery Chair's Research Fellowship

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Vermont Oxford Network Manual of Operations [5]. Surgical NEC was defined as that subset of patients who received laparotomy or primary peritoneal drainage.

Follow-up was coordinated by participating institutions, and informed consent for inclusion in the ELBW follow-up project was obtained according to the specifications of each institution's IRB; attempts were made to schedule follow-up with the families/caregivers of all infants who were alive at hospital discharge. Infant status was reported as dead, alive, or unknown. Outcome measures for infants who completed follow-up at 18 to 24 months corrected age included assessment of the home living situation, healthcare needs, and developmental status of the children. Measures were reported using standardized data collection tools; each data item was defined in the ELBW Infant Follow-Up Manual of Operations [6].

The assessment of the home living situation included information regarding with whom the child resided, the type of social support at home, and primary caregiver educational attainment. For infants born after 2005 maternal age at birth was assessed for all infants, and primary language of the caregiver and household income in relation to federal poverty guidelines were collected at US centers. The assessment of healthcare needs included: medical support after hospital discharge (tracheostomy, ventilator, oxygen, gastrostomy, nasogastric feeds, apnea or cardiorespiratory monitor), surgical procedures since discharge, and any medical rehospitalizations requiring an overnight stay. Rehospitalization data do not include rehospitalizations for surgery. Reasons for rehospitalization were categorized as respiratory illness (including apnea), nutrition or failure to thrive, seizure disorder, shunt complications, infections, or other. Infections requiring rehospitalization were further categorized as meningitis, urinary tract infection, gastrointestinal infection, or other. All rehospitalization and surgery write-in codes were reviewed by surgeons at Boston Children's Hospital and appropriately categorized.

The assessment of the developmental outcomes included information from the neurological and developmental evaluations, with definition of severe disability based on the work of Schmidt et al. [4]. The neurological evaluation included assessment of vision (blindness in one or both eyes), hearing (corrective hearing aids for one or both ears), and muscle tone (hypotonia, hypertonia). Whether the infant could walk 10 steps independently or with support was assessed.

Cerebral palsy (quadriplegia, hemiplegia, diplegia) was defined as a nonprogressive, nontransient central nervous system disorder characterized by abnormal control of movement and/or posture not owing to mental retardation. The developmental evaluation included Bayley Scales of Infant and Toddler Development (BSID-II or BSID-III); participating centers were given the option to use BSID-III starting in 2004. A score of less than 70 (more than two standard deviations below the mean), using age adjusted for prematurity, was interpreted to represent significantly delayed performance. Severe disability was defined by the presence of one or more of the following: bilateral blindness, hearing impairment requiring amplification, inability to walk 10 steps with support, cerebral palsy, or a BSID Mental Development Index (MDI) or Psychomotor Development Index (PDI) of less than 70.

This study was performed as part of an ongoing collaboration between VON and pediatric surgeons at Boston Children's Hospital. The Committee on Human Research at the University of Vermont approved the use of the VON Research Repository for this analysis (#15-143).

1.2. Statistical methods

Risk ratios are adjusted for gestational age and clustering of infants within hospitals. All analyses were produced using SAS version 9.4 (SAS Institute, Cary, NC).

2. Results

After the exclusion of 2265 infants for congenital anomalies and/or length of stay less than 72 h, and 19 infants for missing data on survival status at hospital discharge, there were 24,018 eligible ELBW infants; 20,762 of these infants survived until hospital discharge. Survival to follow-up was 88% among those without NEC, 74% among those diagnosed with medical NEC, and 62% for those with a history of surgical NEC or bowel perforation. Of 20,565 infants eligible for follow-up, 48% were evaluated: 9063 without NEC, 417 with medical NEC, and 449 with surgical NEC (Fig. 1). The 9929 evaluated infants had a mean gestational age of 26 weeks (± 2 weeks) and a mean birth weight of 803 g (SD ± 169 g). Characteristics associated with risk of disability [3] were similar between survivors with and without follow-up

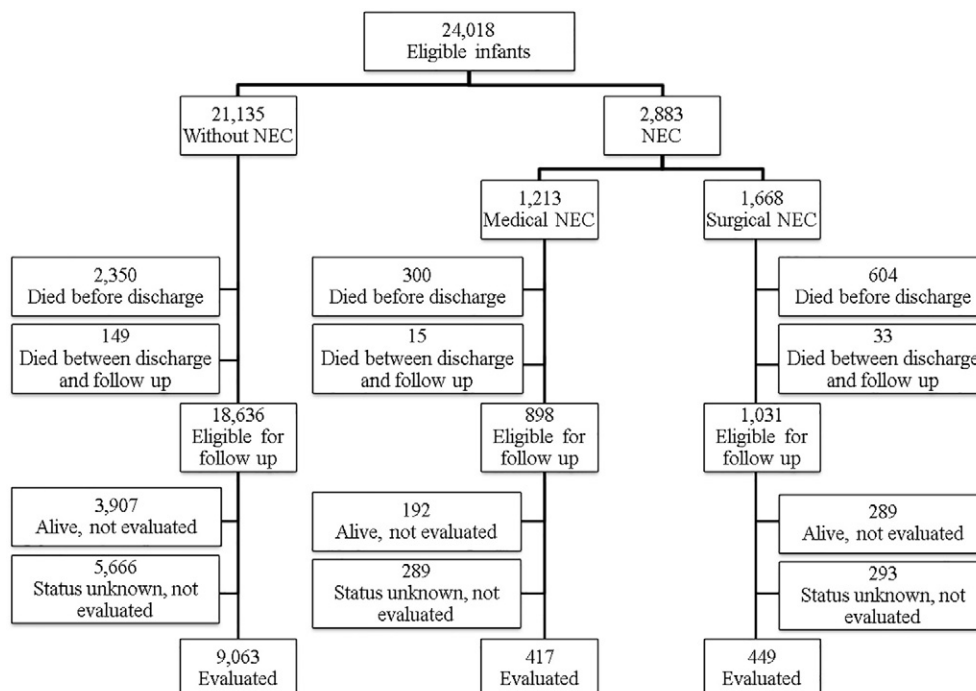


Fig. 1. Infant survival and follow-up.

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