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Hospital transfers and patterns of mortality in very low birth weight neonates with surgical necrotizing enterocolitis☆,☆☆

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ABSTRACT

Purpose: The objectives of this study were to evaluate mortality rates in very low birth weight (VLBW) infants with surgical necrotizing enterocolitis (NEC) by level of available surgical resources and to determine the effect of hospital transfer on mortality.
Methods: Mortality among 4328 VLBW neonates with surgical NEC born 2009–2013 was assessed using the Vermont Oxford Network database. NICUs were classified by availability of resources as a marker of overall center capability: type A (restrictions on ventilation or do not routinely perform major neonatal surgery), type B (perform major neonatal surgery but not cardiac bypass), and type C (perform major surgery, including cardiac bypass in infants).
Results: Mortality was higher among those who had surgery at type B centers versus type C centers (44.3% vs 36.4%, adjusted prevalence ratio 1.20 (95% CI: 1.08, 1.33)). Neonates who were not transferred between birth and surgery had a higher mortality compared to those transferred (44.6% vs 31.6%, adjusted prevalence ratio 1.39 (95% CI: 1.25, 1.55)).
Conclusion: Transfer between birth and surgery and a higher level of surgical resources at the operative center were associated with lower mortality. Early transfer of high risk neonates to centers with higher levels of surgical resources may be warranted.

In light of data that show improved outcomes for children treated at centers with specialized pediatric surgical expertise, there has been a push to better match at-risk pediatric surgical patients with appropriate resources [1–3]. However, at the same time, there has been a trend in the United States towards de-regionalization of neonatal intensive care unit (NICU) care [4]. Very low birth weight (VLBW) infants, defined as those with a birth weight less than 1500 g, who require surgery for necrotizing enterocolitis (NEC) are a particularly high-risk group of patients with in-hospital mortality exceeding 30% [5].

It has also been established that the inter-hospital transport of critically ill neonates, especially on an emergent basis, poses a risk of adverse transport related events [6–9]. These adverse events may be attributable to the technical challenges of safely supporting these delicate patients during transport and/or the interruption in continuity of care intrinsic to inter-facility transfer.

The primary aims of this study were to assess the effect of hospital transfer on mortality, and to stratify mortality rates in VLBW neonates with surgical necrotizing enterocolitis by the level of neonatal surgical resources available at the operative center.

1. Methods

1.1. Study design

Vermont Oxford Network (VON) is a nonprofit voluntary collaboration that prospectively collects data on infants of birth weight 401 to 1500 g, who are born at participating institutions or who are transferred to a participating institution within 28 days of birth. Data are collected by local staff using uniform definitions until neonates are discharged

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from the hospital, die, or reach 1 year of age in the hospital. Data are reported to VON by the center where the outcome occurs. Records are subjected to automated checks and returned for correction if needed. Center capabilities, including the availability of specialists, ventilator support resources, types of surgeries performed, American Academy of Pediatrics NICU level, and other characteristics are self-reported by each center in an annual membership survey. Centers are designated as level A, B, or C using these data and each center must confirm agreement with the designated center level in order to be included for analysis. This study was performed as part of an ongoing collaboration between VON and a group of pediatric surgeons. Research using the VON database is approved by the University of Vermont Institutional Review Board (#14–208).

For this cohort study, data were prospectively collected from North American centers on infants born from January 1, 2009 to December 31, 2013 weighing from 401 to 1500 g at birth. Per the VON Manual of Operations definition [10], NEC was diagnosed either by direct observation of the intestine at operation or pathologic exam, or by using a set of strict clinical criteria. A clinical diagnosis of NEC was made based on 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, hepato-biliary gas, or pneumoperitoneum). Discharge home without readmission or hospitalization at 1 year of age was considered survival.

Infants who underwent surgery for NEC were included in this analysis. Patients with length of stay less than 72 hours, who had NEC but did not have surgery, had surgery for NEC performed at multiple hospitals, had a diagnosis of NEC made at multiple hospitals, transferred between more than two hospitals, or had major congenital anomalies as listed in the VON Manual of Operations [10] (e.g. open spinal dysraphism, major cardiac defects, gastroschisis or intestinal atresias, chromosomal anomalies) were excluded. Patients for whom birth, diagnosis, and surgery all occurred at a center other than the reporting center were also excluded because it was not possible to determine whether these events all occurred at a single center, or whether there may have been transfer between multiple centers.

Patient characteristics, type of surgeries performed, mortality, growth, and length of stay were assessed for each infant. Information on whether the location of birth, diagnosis of NEC, and surgery for NEC were at the reporting center (center of infant's final discharge, death, or if still hospitalized, location at 1 year of life), or at a different hospital was available. Infants were categorized based on whether they had been transferred between centers, and if they had, whether transfer occurred between birth and diagnosis, between diagnosis and surgery, or after the time of surgery.

The availability of resources pertinent to neonatal surgical care was used as a marker of overall center capability in order to classify NICUs. Type A centers have restrictions on ventilation or do not routinely perform major neonatal surgery, type B centers perform major neonatal surgery but not cardiac bypass, and type C centers perform major surgery, including cardiac bypass in infants [11]. Infants who were never transferred were compared based on center type. Furthermore, transferred and non-transferred infants were analyzed on the basis of operative center type (i.e. center type at the time of surgery). There was not a sufficient number of infants with surgical NEC who remained entirely at type A centers or underwent surgery at type A centers for statistical analysis, and therefore comparison of outcomes by center type was limited to type B vs type C centers.

The primary outcome was death prior to discharge from the hospital. Secondary outcomes were total length of stay in days by survival status, and among survivors, weight at discharge in grams, <10th percentile for weight at discharge [12], and average growth velocity per day in g/kg/day [13,14].

1.2. Statistical methods

Generalized estimating equation (GEE) regression models were used to assess adjusted associations between NICU type and primary and secondary outcomes controlling for sex, small for gestational age, antenatal steroids, multiple gestation, vaginal delivery, birth weight, APGAR score at 1 minute and clustering of infants within hospitals. GEE models were used to assess adjusted associations between transfer status and primary and secondary outcomes controlling for sex, small for gestational age, multiple gestation, vaginal delivery, birth weight, APGAR score at 1 minute and clustering of infants within hospitals. GEE models stratified by transfer status were used to assess adjusted associations between NICU type and mortality controlling for sex, small for gestational age, antenatal steroids, multiple gestation, vaginal delivery, birth weight, APGAR score at 1 minute and clustering of infants within hospitals. Adjusted prevalence ratios and differences with 95% confidence intervals were generated using the Spiegelman and Hertzmark method [15]. All analyses were produced using SAS version 9.3 (SAS Institute, Cary, NC).

2. Results

There were 10,557 eligible VLBW infants born 2009–2013 who were diagnosed with NEC, 4328 (41%) of whom underwent surgery for NEC and were included in this analysis. Patient characteristics are shown in Table 1, and outcomes are shown in Table 2.

2.1. Outcomes compared by transfer status

There were 1446 (33%) infants with surgical NEC who underwent transfer between the time of birth and time of surgery, and 2882 (67%) who did not. Of the infants who were transferred, 805 (19%) were transferred prior to the diagnosis of NEC. Infants who were not transferred between birth and surgery were more likely to be small

Table 1
Patient Characteristics of Infants With Surgical NEC.

	By transfer status		By NICU type	
	Transferred between birth and surgery (N = 1446)	Not transferred between birth and surgery (N = 2882)	NICU type B (N = 1982)	NICU type C (N = 2247)
Male (%)	58.7	56.3	56.5	57.8
Gestational age in weeks (mean (SD))	26 (2)	26 (2)	26 (2)	26 (2)
Birth weight in grams (mean (SD))	872 (259)	823 (249)	828 (248)	845 (257)
Small for gestational Age (%)	9.8	12.2	11.0	12.0
APGAR, 1 min (mean (SD))	5 (2.5)	5 (2.5)	5 (2.4)	5 (2.5)
Antenatal steroids (%)	63.4	86.5	79.8	78.2
Multiple gestation (%)	20.7	25.9	22.8	25.4
Vaginal delivery (%)	34.2	31.3	33.9	30.8
Type of surgery for NEC				
Surgery only (%)	65.1	67.3	65.3	67.4
PPD and surgery (%)	17.4	17.7	17.7	18.2
PPD only (%)	17.4	14.9	17.1	14.5