Early Neonatal Intensive Care Unit Therapy Improves Predictive Power for the Outcomes of Ventilated Extremely Low Birth Weight Infants

Joanne Lagatta, MD,* Bree Andrews, MD, MPH, Leslie Caldarelli, MD, Michael Schreiber, MD, Susan Plesha-Troyke, OT, and William Meadow, MD, PhD

Objective To assess the predictive value of early therapy for ventilated extremely low birth weight (ELBW) infants beyond information available at delivery.

Study design Prospective, single-center cohort analysis of 177 ventilated ELBW infants. We collected information known at delivery (gestational age, birth weight, singleton, sex, antenatal steroids) and additional information while infants were mechanically ventilated (head ultrasound scanning, clinician intuitions of death before discharge). An adverse outcome was defined as mortality or Bayley Mental Developmental Index or Psychomotor Developmental Index <70 at 2 years. We compared the predictive ability of clinical variables separately, in combination, and in addition to information available at delivery.

Results A total of 77% of infants survived to follow-up; 56% of survivors had Bayley Mental Developmental Index and Psychomotor Developmental Index ≥70. A total of 95% of infants with both abnormal head ultrasound scanning results and predicted death before discharge had an adverse outcome, independent of gestational age. Conversely, 40% of infants with normal head ultrasound scanning results and no predicted death before discharge had an adverse outcome, independent of gestational age. After adjusting for variables known at birth, predicted death before discharge and abnormal head ultrasound scanning results added significantly to the ability to predict outcomes.

Conclusion Information gained early in the neonatal intensive care unit improves prediction of mortality or neurodevelopmental impairment in ventilated ELBW infants beyond information available in the delivery room. *(J Pediatr 2011;159:384-91)*.

Advances in perinatal care have increased survival of extremely low birth weight (ELBW) infants.[1,2] However, survivors are at increased risk of neurologic sequelae that place stress on families, schools, and the health care system.[3] Clinicians and parents want to predict which infants are at highest risk for severe impairment, both to prepare families for their follow-up needs and, in the most severe cases, to consider the option of withdrawing intensive care interventions.

The most common predictors of neonatal mortality and morbidity, gestational age and birth weight, are available at birth.[4,5] Recently, other predictors available before delivery have been shown to add prognostic power: sex, antenatal steroids, and singleton status.[6] This prognostic information is commonly used to counsel families in deciding whether to initiate resuscitation of an extremely preterm infant.

However, for some families, and some doctors, information available before birth remains insufficient for them to decide whether to initiate neonatal intensive care unit (NICU) intervention. For those who wish to attempt a trial of resuscitation and neonatal intensive care, it is important to understand what, if any, added prognostic power can be gained during the first days and weeks of life.

Because conversations on withdrawal of intensive care intervention are generally precipitated by a clinician's assessment of either an infant's likely non-survival or poor neurologic prognosis if the infant does survive, we chose to study these two outcomes directly. Earlier work at our institution has shown that when clinicians predict that an infant will die before discharge from the NICU, those predictions are correct only 50% of the time, but that 80% of infants predicted to die will either die or survive with a Bayley Mental Developmental Index (MDI) or Psychomotor Developmental Index (PDI) score <70 at 2 years of age.[7,8] This predictive power remained unsatisfactory for many of our physicians and families.

ELBW	Extremely low birth weight
IVH	Intraventricular hemorrhage
MDI	Mental Developmental Index
NICU	Neonatal intensive care unit
NPV	Negative predictive value
PDI	Psychomotor Developmental Index
PPV	Positive predictive value
PVL	Periventricular leukomalacia

From the Department of Pediatrics, University of Chicago, Chicago, IL

*Currently at Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI.

The authors declare no conflicts of interest.

0022-3476/$ - see front matter. 10.1016/j.jpeds.2011.02.014

Head ultrasound scanning is one of the most widely used predictors of neurologic outcome for ELBW infants.[9] Increasingly abnormal head ultrasound scanning results are associated with increasing neurologic morbidity. Unfortunately, the correlation between abnormal head ultrasound scanning results and death or neurologic impairment remains imperfect.[10-12]

The primary goal of this study was to assess the prognostic value of combining intuitions of non-survival with head ultrasound scanning to predict an adverse outcome, defined as either death in the NICU or survival with neurologic impairment (Bayley MDI or PDI <70 at 2 years of age). Specifically, we tested a two-part hypothesis : (1) combining these two predictors while an infant remains on a mechanical ventilator (and, consequently, while the opportunity to withdraw intervention was available) would predict death or severe neurologic morbidity significantly better than either factor alone; (2) combining clinical intuitions of death before discharge with head ultrasound scanning would predict death or neurologic morbidity better than gestational age, birth weight, or any combination of information available at delivery.

Methods

We identified ELBW infants who were ventilator dependent, were admitted to our hospital's NICU from 1999 to 2004, and were enrolled in one of two clinical studies with coordinated post-discharge monitoring.[13,14] To focus our study specifically on the ethical dilemma of predicting outcomes for ventilated ELBW infants in the NICU, we excluded infants with lethal congenital malformations, infants <23 weeks gestational age, delivery room deaths (although such instances are extremely rare in our institution), and infants who died in <24 hours.[15,16]

Clinical Intuition Protocol

For each infant, on every day of mechanical ventilation in the NICU, we asked medical caregivers including attending physicians, fellows, residents, nurses, and nurse practitioners whether they believed the infant would die in the NICU or survive to discharge. Caregivers were polled privately to minimize the potential influence of co-workers on their responses. We collected caregiver intuitions on all days that patients received mechanical ventilation, independent of illness severity. Infants requiring nasal continuous positive airway pressure but not mechanical ventilation were excluded. For infants who were re-intubated after initial extubation, assessments were resumed on the day of re-intubation. Each infant contributed only once to an outcome. "Predicted death before discharge" was defined as at least 1 day when two or more clinicians answered that the infant would die before discharge.

Head Ultrasound Scanning Scoring

Infants underwent ultrasound scanning at least twice within the first 2 weeks of life and another by 36 weeks corrected gestational age; additional head ultrasound scanning was performed at the discretion of the clinical service, and usually occurred weekly when abnormalities were noted. Imaging was performed and interpreted by the pediatric radiology service. Severely abnormal head ultrasound scanning results were defined as grade III to IV intraventricular hemorrhage (IVH), isolated ventriculomegaly, cystic lesions (other than subependymal), echodensities, echolucencies, or periventricular leukomalacia (PVL). Because the purpose of this study was to assess the usefulness of head ultrasound scanning and clinical intuition in making decisions about intensive care interventions, we included only the most severe head ultrasound scanning results reported while the infant remained intubated. Consequently, infants with late-onset intracranial injury that became apparent only after extubation were not categorized in this study as having an abnormal head ultrasound scanning results.

Follow-Up Neurologic Assessment

Surviving infants were assessed at 24 months corrected age, with the Bayley Scales of Infant Development II MDI and PDI.[17] The evaluator was blinded to clinical intuitions and head ultrasound scanning reports. An adverse outcome was defined as mortality or Bayley MDI or PDI <70. Additional analyses were performed for secondary outcomes of mortality alone and Bayley MDI or PDI <70 in surviving infants.

Statistical Analysis

For each risk factor known at the time of delivery (gestational age, birth weight, singleton status, sex, antenatal steroids) or gathered in time in the NICU (head ultrasound scanning results, predicted death before discharge), we calculated the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), RR, and positive LR of adverse outcomes. We then calculated the RR of adverse outcome for infants by gestational age and birth weight, stratifying on abnormal head ultrasound scanning results and clinical intuition; Mantel-Haenszel methods were used to test for statistical significance. We used multiple logistic regression to evaluate the significance of abnormal head ultrasound scanning results and clinical intuitions of death after controlling for risk factors present at birth. Finally, we calculated predicted outcome for infants serially in the first 3 weeks in the NICU, evaluating the prognostic impact of clinical intuitions and head ultrasound scanning results as they occurred day by day. Statistical significance was accepted at a P value <.05.

This study was approved by the institutional review board of the University of Chicago.

Results

Of 232 eligible ELBW infants admitted during the study period, we enrolled 191 ELBW infants who were ventilated (82% of eligible); follow-up data were available on 177 of 191 infants (93% of enrolled). The 41 infants who were not enrolled had no statistically significant differences in mortality rate compared with the study population (24% versus 23%, two-sample test of proportion P = .8913). **Table I** presents demographic data for the 177 infants. The median gestational age was 25 weeks; the median birth weight was