Intervention at the Border of Viability

Perspective Over a Decade

Pamela K. Donohue, ScD; Renee D. Boss, MD; Jennifer Shepard, CRNP; Ernest Graham, MD; Marilee C. Allen, MD

Objective: To investigate prenatal management and outcome of infants born at the border of viability during 2 periods, 2001 to 2003 (late epoch) and 1993 to 1995 (early epoch).

Design: Cohort study.

Setting: Single academic, high-risk perinatal referral center.

Participants: All 160 women admitted to labor and delivery with a live fetus who delivered at an estimated gestational age of 220/7 weeks to 246/7 weeks.

Main Outcome Measures: Prenatal management and time between maternal admission and delivery or death of the fetus, infant resuscitation efforts, neonatal intensive care unit interventions, time of death, and morbidities in survivors.

Results: Mothers in both epochs were of similar age, race, and duration of pregnancy at hospital admission. Compared with the early epoch, women during the late epoch were more likely to be transported to a higher level of care (relative risk [RR], 2.01; 95% confidence interval [CI], 1.58-2.57) and receive sonographic surveillance (RR, 1.48; 95% CI, 1.07-2.04), antibiotics (RR, 1.60; 95% CI, 1.10-2.33), and antenatal steroids (RR, 1.61; 95% CI, 1.22-2.12). Life-sustaining interventions were provided for infants admitted to the neonatal intensive care unit more frequently during the late epoch than the early epoch, including high-frequency ventilation (RR, 3.57; 95% CI, 1.93-6.61), chest tubes (RR, 1.44; 95% CI, 1.06-1.94), dopamine administration (RR, 2.49; 95% CI, 1.24-4.97), and steroid administration for blood pressure support (RR, 2.18; 95% CI, 1.60-2.92). Gestational age-specific mortality was the same in the 2 epochs.

Conclusions: More interventions were provided for infants born at 22 to 24 weeks’ gestation in the late epoch than the early epoch. Despite these changes in management, there has been no reduction in mortality in more than a decade.
As part of periodic auditing for performance improvement, medical records for all women admitted to labor and delivery with a live fetus who delivered an infant with an estimated gestational age of 22/7 weeks to 24/7 weeks were reviewed for documentation of counseling, details of interventions, and outcome. Cases were identified from labor and delivery logbooks, the neonatology intensive care unit (NICU) admission database, and pathology records. Gestational age was based on the most recent menstrual period, unless unknown, and then fetal ultrasonography and obstetricians’ best estimate were used. The time between maternal admission and delivery or death of the fetus/infant was measured in days, except when less than 1 completed day, which was calculated as percentage of 24 hours.

Medical records of the infants were reviewed for resuscitation efforts, NICU interventions, time of death, and morbidities in survivors. Duration of hospitalization for survivors is not reported because we began back transporting infants to community hospitals for convalescent care between the 2 study epochs. The study qualified for exemption from institutional review board approval.

Women less than 24 weeks’ pregnant were counseled against cesarean delivery by perinatologists and neonatologists during both epochs because of the implications for future reproductive health. In our hospital, perinatologists ask for neonatology consultation when active obstetrical intervention is contemplated. Antenatal steroid administration for women in preterm labor was not yet routine during the early epoch, but during the late epoch, they were routinely given if there was time and active management was being pursued.

To facilitate antenatal parent counseling, mortality was calculated to include stillbirths who were alive when the mother was admitted to the hospital but who died prior to birth. Likewise, mortality statistics were not limited to neonatal mortality (ie, death within 28 days of birth), but included death before NICU discharge.

For demographic variables, epochs were compared by non-parametric methods (χ², Fisher exact test) for categorical variables and mean or median and 95% confidence intervals (CIs) for continuous variables. Relative risk (RR) and 95% CIs in the late epoch compared with the early epoch were calculated for interventions provided to the pregnant woman or infant and outcome variables. Calculations were performed using SPSS 14.0.9

RESULTS

One hundred sixty women delivered 179 infants, including multiples, at 22 to 24 weeks’ gestation during the 2 study epochs. Ninety women delivered 104 infants during the late epoch, 2001 through 2003, and 70 women delivered 75 infants during the early epoch, 1993 through 1995.

Mothers in the 2 epochs were of similar age, race, and duration of pregnancy at hospital admission (Table 1). Fewer mothers during the late epoch had a history of spontaneous abortion.

There were no differences in reasons for hospital admission during the 2 epochs, and for each epoch, preterm labor was the most frequent admitting diagnosis (Table 2). During the late epoch, significantly more women were transported to our regional perinatal referral center for pregnancy management at the border of viability than during the early epoch. Sonographic surveillance after hospitalization, antibiotics, and antenatal steroids were provided to more women during the late epoch than the early epoch.

Viability of the fetus was discussed with the majority of parents during both epochs (74 [82%] in the late ep-
och vs 50 [72%] in the early epoch). Perinatologists asked for neonatal consultation for a greater percentage of women during the late epoch than the early epoch (65 [72%] vs 35 [50%]; RR, 1.56; 95% CI, 1.12–2.18). Although it did not reach statistical significance, more women in the late epoch had infants delivered by cesarean section than in the early epoch (11 [12%] vs 5 [7%]; RR, 1.44; 95% CI, 0.68–3.05). The reason for operative delivery was not different, with the majority of women in each epoch undergoing cesarean section for fetal indications, malpresentation, or poor fetal heart rate tracing. The time from admission to delivery was not statistically different between the epochs (3.57 days [95% CI, 2.50–4.63 days] for the late epoch vs 2.55 days [95% CI, 1.11–3.99] days for the early epoch).

No resuscitation was planned prior to delivery for 34 fetuses (32%) in the late epoch and 25 (33%) in the early epoch because of a combination of maternal and fetal conditions and extreme prematurity. In all cases, the decision not to resuscitate was made jointly between the family and perinatologist. Despite obstetric interventions short of cesarean section, in each epoch, fetal deaths occurred during labor (4 [4%] during the late epoch and 7 [9%] during the early epoch). Six infants (6%) during the late epoch and 5 (7%) during the early epoch were deemed not viable by a neonatologist’s examination and not resuscitated in the delivery room. In both epochs, infants not resuscitated, for any reason, were significantly more immature than those who were resuscitated (gestational age, 22.51 weeks [95% CI, 22.36–22.67 weeks] vs 23.71 weeks [95% CI, 23.61–23.81 weeks] and birth weight, 498 g [95% CI, 472–524 g] vs 673 g [95% CI, 647–698 g]).

For infants who were resuscitated, 62 (59%) during the late epoch and 38 (51%) during the early epoch, there were no significant differences in gestational age or birth weight (24.12 weeks [95% CI, 23.58–24.58 weeks] vs 24.04 weeks [95% CI, 23.82–24.27 weeks] and 678 g [95% CI, 645–710 g] vs 656 g [95% CI, 621–690 g], respectively). In the delivery room, almost all resuscitated infants had airway management (intubations, 95% during the late epoch vs 92% during the early epoch), while chest compressions were provided more frequently during the late epoch than during the early epoch (32% vs 8%; RR, 1.59; 95% CI, 1.23–2.06). Epinephrine was administered to a similar percentage of infants during the late epoch (7%) and the early epoch (3%). During each epoch, resuscitation was discontinued in the delivery room for a small percentage, after the infant made no response (7 of 62 [11%] in the late epoch vs 3 of 38 [8%] in the early epoch).

In the NICU, immediate life-sustaining interventions were provided to infants more frequently during the late epoch than the early epoch (Table 3). For each epoch, futility of care was discussed with parents, 33% in the late epoch and 38% in the early epoch, and withdrawal of life-sustaining therapy decisions were made for some infants. Do-not-resuscitate orders were written for 13% of infants vs 18% and escalating therapy was withheld from 6% vs 9% in the late epoch compared with the early epoch, respectively. Life-sustaining therapy was withdrawn in 24% of cases in each epoch.

The median survival time was significantly longer during the late epoch than during the early epoch (median, 7 days [95% CI, 4.23–9.77 days] vs 2 days [95% CI, 1.46–2.54 days]). However, mortality remained unchanged (72% vs 69%; RR, 0.93; 95% CI, 0.63–1.36). There were no differences in gestational age–specific mortality over the 2 epochs (Table 4).

For infants who survived to NICU discharge, morbidities were similar between the epochs: only 1 infant in each epoch required shunt placement for posthemorrhagic hydrocephalus, 3 vs 2 infants needed surgical feeding tubes, and 10 vs 5 infants had threshold retinopathy of prematurity, late vs early epochs, respectively.

Our data provide evidence that more interventions were offered for infants born at 22 to 24 weeks’ gestation during 2001 through 2003 than a decade ago. More women are referred to our tertiary care hospital at these early gestational ages and treated with antenatal steroids and antibiotics. More of the infants received chest compres-

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Table 3. Acute Interventions Provided for Infants Admitted to the NICU

<table>
<thead>
<tr>
<th>No./Total No. (%)</th>
<th>EE (1993-1995)</th>
<th>LE (2001-2003)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-frequency ventilation</td>
<td>9 (26)</td>
<td>47 (86)</td>
<td>3.57 (1.93–6.61)</td>
</tr>
<tr>
<td>Chest tube(s)</td>
<td>4 (11)</td>
<td>16 (29)</td>
<td>1.44 (1.06–1.94)</td>
</tr>
<tr>
<td>Dopamine</td>
<td>20 (57)</td>
<td>49 (89)</td>
<td>2.49 (1.24–4.97)</td>
</tr>
<tr>
<td>Hydrocortisone for blood pressure support</td>
<td>2 (6)</td>
<td>30 (55)</td>
<td>2.18 (1.60–2.92)</td>
</tr>
<tr>
<td>Umbilical catheter(s)</td>
<td>30 (86)</td>
<td>55 (100)</td>
<td>1.17 (1.02–1.36)</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>29 (83)</td>
<td>55 (100)</td>
<td>1.21 (1.04–1.40)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>30 (86)</td>
<td>54 (98)</td>
<td>3.86 (1.64–23.25)</td>
</tr>
<tr>
<td>Postnatal steroids for lung disease</td>
<td>16 (46)</td>
<td>34 (62)</td>
<td>1.30 (0.91–1.84)</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation</td>
<td>3 (9)</td>
<td>8 (15)</td>
<td>1.22 (0.82–1.83)</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>3 (9)</td>
<td>6 (11)</td>
<td>1.10 (0.68–1.81)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; EE, early epoch; LE, late epoch; NICU, neonatal intensive care unit; RR, relative risk.

Table 4. Comparison of Mortality at Each Week of Gestation

<table>
<thead>
<tr>
<th>No./Total No. (%)</th>
<th>EE (1993-1995)</th>
<th>LE (2001-2003)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22-wk GA</td>
<td>25 (100)</td>
<td>28 (100)</td>
<td>0.00</td>
</tr>
<tr>
<td>23-wk GA</td>
<td>16/22 (73)</td>
<td>22/26 (85)</td>
<td>1.43 (0.76–2.67)</td>
</tr>
<tr>
<td>24-wk GA</td>
<td>13/28 (46)</td>
<td>24/52 (46)</td>
<td>1.00 (0.73–1.39)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; EE, early epoch; GA, gestational age; LE, late epoch; RR, relative risk.

*aIn the LE compared with the EE.
sions in the delivery room and vasopressors and high-frequency ventilation in the NICU. Despite these changes in management, there has been no reduction in mortality in more than a decade at our institution. In fact, survival is the same as we reported for infants of similar gestational ages born 20 years ago.1

More aggressive perinatal management at the border of viability, however, did increase the duration of infant survival from the time of maternal hospital admission. Although the use of tocolytics and cesarean delivery were not statistically different between epochs, a larger percentage of women during the early epoch than during the late epoch received these interventions. Whether cesarean section improves outcome at the border of viability remains controversial. The contribution of mode of delivery to survival and rates of disability are difficult to calculate because of the “self-selection” of infants delivered by cesarean section. Obstetricians’ willingness to perform an operative delivery is multifactorial and dependent on the perceived health of the mother and fetus. Two studies report a survival advantage without major morbidity after cesarean delivery, but the risk of survival with major disability (cerebral palsy, cognitive and sensory impairment) and/or major health problems (chronic lung disease, necrotizing enterocolitis) is doubled.10,11 In our study, infants delivered by cesarean were older and larger than those delivered vaginally, although cesarean delivery was performed at every gestational age in both epochs.

Our data also suggest that increasingly aggressive obstetric management is not limited to tertiary care centers but practiced in the community. More women during the late epoch were transported from community hospitals to our high-risk perinatal center than during the early epoch, and several women during the late epoch were given antenatal steroids prior to transfer despite their early gestational age. Obstetricians may feel obligated to continue a management strategy started before transfer because of parental wishes and uncertainty of outcome. Despite obstetrical interventions, the time between maternal hospital admission and delivery increased during the late epoch by an average of only 1 day.

US vital statistics show both an improvement in the reporting of fetal deaths among the most immature gestational ages, resulting in an increase in the fetal death rate, and an increase in live births among infants with birth weight less than 750 g.4 Our data illustrate the difficulty of addressing this issue with vital statistics. Among our sample, 4 infants with Apgar scores of zero for more than 5 minutes were actively resuscitated and admitted to the NICU for management; none survived beyond 2 days. In a large data set without individual case review, these infants might be coded either as fetal deaths based on Apgar scores and mortality or as live births with subsequent neonatal death.

It is evident that perinatologists worked to keep parents fully informed during both epochs. Viability was discussed with the majority of mothers. This conversation took place on multiple occasions for women whose medical condition changed over time, such as those admitted with rupture of membranes who later developed signs and symptoms of chorioamnionitis and those with prolonged hospitalization.

Our data should be viewed cautiously. We report the experience of a single perinatal referral center and our conclusions may not generalize to nonteaching hospitals or those serving different populations. Our data do not address whether supportive therapies were withheld across the continuum of perinatal-neonatal care because obstetricians and neonatologists often overestimate mortality and disability rates.12

The notion of a self-fulfilling prophecy has been raised with regard to interventions provided at the border of viability.13 Our data indicate that resuscitation is viewed differently by parents and physicians at 22 weeks’ than 23 weeks’ gestation. Most infants not resuscitated in our study were less than 23 weeks’ gestation and less than 500 g birth weight. Population-based data support this approach, with only 1% survival at 22 weeks’ gestation.14

Would survival increase if cesarean delivery and resuscitation were provided for all infants at 22 to 24 weeks’ gestation? In models of survival for more than 4000 infants born at 22 to 23 weeks’ gestation, operative delivery did not confer an independent survival advantage.15 Our data indicate that aggressive postnatal care among the “fittest” 22- to 24-week infants, as measured by larger birth weight and more mature gestational age, also does not improve survival.

Mortality has not changed in our hospital over the past 10 years despite escalation in care at each gestational age studied. What has changed is the length of time until death. An increase in time to death has also been reported by others, extending from 2 days in 1991 to 10 days in 2001.7 A recent study reports an average time at death of 22 days for infants born at 22 to 25 weeks’ gestation who were provided intensive care.15 Applying all available medical technology to the perinatal care of extremely premature infants prolongs but does not prevent their death.

Do these data help us make decisions about perinatal care at the border of viability? Neither full provision of all possible therapeutics at every gestational age nor withholding of life-sustaining treatment is morally acceptable to all in the face of an uncertain prognosis. There is reported survival at 22 weeks’ gestation, but this raises the question of how many infants need to survive before we offer resuscitation to all parents.

Decision making based on individual characteristics of the fetus/newborn is inherently more appealing. Using large samples, 2 groups of researchers from the National Institute of Child Health and Human Development Neonatal Research Network have proposed decision-making tools for the treatment of extremely preterm infants. The first group suggested that decisions about the provision of supportive therapy be deferred until 5 minutes after birth so that postnatal variables that increase the predictive value of statistical models of mortality (Apgar scores, infant sex, and birth weight) can be considered along with prenatal variables, including race, in decision making.16 How this approach would change outcomes is unknown. The second group proposed counseling parents about the application of neonatal intensive care based on the best likelihood of a favorable outcome calculated using assessment of birth weight, gestational age, sex, exposure to steroids, and singleton...
or multiple births.\textsuperscript{15} Although the researchers acknowledge that the model may overestimate a positive outcome, they believe it will allow for less bias in decision making than the present practice of using gestational age as the primary predictor. How the prospective application of these likelihoods will be used by neonatologists and parents has yet to be studied. Recent work by Boss et al\textsuperscript{17} suggests that statistical information about potential outcome is not meaningful in decision making for most parents. Any decision tool that includes either sex and/or race as a variable has societal implications in excluding large segments of the population and warrants a broader dialog beyond the resuscitation of extremely preterm infants.

Many questions have yet to be answered about the care of these immature infants. The efficacy of many of the interventions routinely provided has never undergone rigorous study and as such should be thought of as experimental and discussed frankly with parents. The study of physician-parent communication around decision making for high-risk newborns is in its infancy and deserves broader attention. What data exist on prenatal counseling indicate only fair agreement between parents and physicians about what was discussed, whether decisions were made, and who made those decisions.\textsuperscript{17-19} The work by Kaempf et al\textsuperscript{19} suggests that scripted prenatal counseling is acceptable to parents, although whether parent comprehension or consensus with staff improved was not evaluated.

The gold standard for decision making is a collaborative one that balances physician, parent, and fetal/incident concerns. Better understanding of the process of this decision making, and its long-term impact on families, is critical to designing further studies with the most clinically relevant outcomes.

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Correspondence: Pamela K. Donohue, ScD, Johns Hopkins Hospital, Nelson 2-133, 600 N Wolfe St, Baltimore, MD 21287-3200 (pdonohu2@jhmi.edu).

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REFERENCES