Proactive Care at the Edge of Viability: Making the Gray Zone Less Gray?

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One of the great success stories in neonatology is the gains made in survival of the smallest and most immature infants over the past 25 years.1,2 However, concerns persist that increased survival may be complicated by increased neurodevelopmental impairment (NDI) for infants born at the edge of viability.3,4 This balance between potential for survival and that of severe NDI weighs heavily on counseling for parents threatened with the birth of an extremely preterm infant.

In this issue of Pediatrics, Serenius and colleagues from the Extremely Preterm Infant Study in Sweden (EXPRESS) team address this concern directly.5 Acknowledging that for some patients the burdens of intensive care (deaths in the NICU but especially long-term morbidity among survivors) may outweigh benefits, they present data to support a proactive approach beginning in utero, aiming to optimize a "trial of life" for infants born at the edge of viability. The EXPRESS investigators recently reported rates of death and NDI at 2.5 years in a cohort of live fetuses at 22 to 26 weeks' gestation.6 In the current study, they delve more deeply into previously reported variation in outcomes between regions in Sweden.7,8 For this purpose, they developed a regional perinatal activity score designed to measure the inclination to provide high-intensity care at 22 to 26 weeks' gestation. This composite score was calculated based on proportions of patients treated with 4 obstetrical interventions (birth at a level III perinatal center, antenatal steroids, Cesarean delivery, tocolysis) and 4 neonatal interventions (surfactant within 2 hours, neonatologist present at birth, intubation after birth, NICU admission). Dividing 7 regions into 2 groups (3 with higher activity scores and 4 with lower scores), they found that the risk for the composite outcome of death or NDI at 2.5 years was lower in regions with higher activity scores. The risk reductions were confined to the 22- to 24-week strata, and the difference in mortality risk was entirely explained by stillbirths and deaths within 12 hours after birth.

These results suggest that with a proactive approach to maternal and newborn care, increased survival may be accomplished without an increase in NDI in 22- to 24-week gestational age infants. However, it may not be that simple. Indeed, in the current study a higher proportion of infants born at 22 to 24 weeks survived in the high-score regions than in the low-score region: 74 of 225 (33%) versus 64 of 231 (28%). However, because gestational age data are presented only in 25- to 26-week and 22- to 24-week strata, the effects of proactive care at 22 and 23 weeks is unclear. In fact, the data suggest that the gestational age for survivors at 2.5 years in the 22- to 24-week strata were similar in the high- and low-score regions. Adjustment for gestational age at birth (in addition to other factors) did not change the odds ratio for NDI at 2.5 years (0.65 unadjusted and 0.63 adjusted), as might be expected if larger numbers of the most immature babies, at highest risk for NDI, survived. This suggests that the beneficial effects associated with the...
proactive approach did not extend far into the 22- to 24-week stratum. Another important factor affecting the generalizability of these results concerns practices involving withdrawal of intensive care. Withdrawal practices vary widely among NICUs, within and between geographic regions. In a previous report, the EXPRESS team reported that 39% of deaths involved a decision to withdraw care due to anticipated poor long-term prognosis. Withdrawal decisions surely affect the mortality-morbidity equation, perhaps as much as decisions to initiate intensive care. So how are we to interpret these results in everyday practice? The good news is that this study supports the conclusion that it is possible to increase survival in extremely premature infants without a "trade-off" of increased NDI. However, it is not clear that this conclusion can be generalized to infants at the lowest gestational age at highest risk. Likewise, NICUs that become more willing to initiate intensive care at the border of viability but do not support withdrawal of care in infants with the worst prognosis might well expect outcomes different from those reported by the EXPRESS team. Among the interventions that contribute to the EXPRESS group’s perinatal activity score, delivery in high-volume perinatal centers and higher rates of treatment with antenatal steroids are the 2 with the strongest evidence base. However, higher perinatal activity scores are likely associated with regional differences in yet undefined aspects of NICU care that could be as or even more important. The road to best outcomes is one with many off-ramps and detours. Understanding the details of those interventions in the perinatal period and in the NICU that result in improved long-term outcomes for infants born at the edge of viability is essential. Parents of these infants deserve nothing less.

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