Neurodevelopmental Outcomes in Early Childhood

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KEYWORDS

• Preterm • Neurodevelopment • Early childhood • Developmental outcomes

KEY POINTS

- Survival of preterm infants is improving, but high risk for neurodevelopmental deficits remains.
- Guidelines exist for earlier assessment and diagnosis of cerebral palsy before 6 months of age.
- High-prevalence/low severity dysfunctions are increasing.
- A longer duration of follow-up is needed.

INTRODUCTION

Technological advances in neonatal-perinatal medicine have led to a steady increase in the survival of preterm infants (**Table 1**). Indeed, survival of children at the very lowest gestations (22–24 weeks) has increased from 30% in 2000 to 2003% to 36% in 2008 to 2011.[1] Although the increase in survival is a remarkable success, children born preterm remain at high risk for brain injury and long-term neurodevelopmental deficits. As survival rates have improved over the past decades, there is an increased focus on long-term morbidity associated with preterm birth. Recently, the fact that rates of extremely preterm (<28 weeks of gestation) infant survival without neurodevelopmental impairment (NDI) have increased from 16% to 20% between the years 2000 and 2011 has been celebrated.[2] Despite this, the rate of moderate to severe NDI at 2 years of age remains exceptionally high among children at the lowest gestational ages (GAs). Of infants born at 22 weeks GA, 85% to 90% have severe NDI, with a similar outcome reported at 23 weeks GA.[3] In infants born less than 25 weeks GA, there has not been a significant improvement in neurodevelopmental outcomes in recent studies.[3,4] However, longer follow-up of these infants is needed to understand the full impact of preterm birth at the limits of viability. Additionally, even though more

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Table 1
Survival of children born extremely preterm

Year	Survival Rate, %
1943–1945	0
1980–1985	10
2006–2011	65

Data from Gong A, Johnson YR, Livingston J, et al. Newborn intensive care survivors: a review and a plan for collaboration in Texas. Matern Health Neonatol Perinatol 2015;1:24.

infants at extremely low GAs are surviving, most preterm births occur in the moderate preterm (32–33 weeks' gestation) to the late preterm (34–36 weeks' gestation) range.[5,6] Although the survival rate in this cohort is greater than 99%, there is an increased risk for NDI in this group.[5,7–9]

Because of the high risk of neurodevelopmental deficits, survival without NDI at 2 years of age has become a common benchmark for success. The Eunice Kennedy Shriver National Institute of Child Health and Development Neonatal Research Network defines NDI as having one or more of the following at 2 years: moderate to severe cerebral palsy (CP), profound hearing loss requiring amplification in both ears, profound visual impairment with visual acuity less than 20/200 in both eyes, moderate to profound cognitive delay on the Bayley Scales of Infant Development 3rd edition (Bayley-III) assessment (Cognitive Composite score of <54–84), and/or a Gross Motor Function Classification System (GMFCS) level of greater than 2 on a 5-point scale.[1] A GMFCS score of 2 or greater translates functionally to a child who cannot walk or pull to stand and may or may not have head control or the ability to sit unsupported. Infant-related factors associated with survival without NDI in early childhood include female sex, higher birth weight or gestation, larger head size, and absence of neonatal morbidities and interventions.[10] Although these early benchmarks, such as NDI, are extremely important, particularly for research purposes, it must be remembered that most neurodevelopmental deficits suffered by preterm children are mild to moderate. These deficits result in a significant functional burden. In addition, preterm children are more likely to have language deficits, and far more likely to have behavioral deficits than their term-born counterparts, which may adversely impact motor, cognition, language development, and testing.[11,12] Such deficits may not be considered in research outcomes using common definitions of NDI, although they must be considered clinically. Furthermore, many developmental deficits in cognition, emotional and behavioral development, and social adaptive functioning may emerge at older ages in the absence of NDI in toddlerhood.[12,13] These "high-prevalence/low severity dysfunctions" occur in 50% to 70% of very low birth weight infants (<1500 g) and are increasing-especially in children born most premature-and include attention-deficit/hyperactivity disorder, executive function deficits, visuomotor problems, learning disabilities, and behavior problems.[12]

This demonstrates a need for longer follow-up of all infants born preterm. This article reviews neurodevelopmental outcomes for children born preterm, with a focus on early childhood.

FACTORS IMPACTING NEURODEVELOPMENTAL OUTCOMES

The factors that influence neurodevelopment in infants born preterm are multifactorial, contributing to the complexity of follow-up research and variations in reported outcomes (**Box 1**). Certain perinatal and postnatal factors confer a higher risk for long-term neurodevelopmental deficits. These include severe intraventricular hemorrhage,