“The more things change...”: The challenges ahead

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Central Message

Cognitive and performance outcomes after newborn heart surgery seem to be the same regardless of the surgical era or country in which they are measured.

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We have known for some time now that the most common long-term morbidities of newborn heart surgery are related not to the heart, but instead to the cognitive challenges experienced by this population. The first and most comprehensive study to describe the neurodevelopmental challenges was the Boston Circulatory Arrest Trial (BCAT), which followed participants from birth to the recently reported 16-year outcomes.¹ The BCAT results show that compared to national normative data, teens with congenital heart defects (CHD) were twice as likely to have a full-scale IQ <1 SD from the mean (31% vs 16% in normative data) and 3 times as likely to have a full scale IQ <2 SD from the mean (6% vs 2%).

In this issue of the *Journal*, Dr Kalfa and colleagues² report long-term cognitive outcomes in young adults (average age, 23 years) from Ile-de-France who had undergone the arterial switch operation as newborns. Here, as in the BCAT, the proportion of survivors with test scores <1 SD was double and that of survivors with test scores <2 SD was triple of the expected values based on normative data. The patients in this study are only marginally older (7 years) than those in the BCAT, but the findings provide independent confirmation of the results in a cohort operated on in a different country. This is reminiscent of Gaynor and colleagues' study of pooled 1-year Bayley Scales of Infant Development (BSID) data from 22 institutions,³ which reported strikingly similar short-term neurodevelopmental outcomes across institutions, which were not significantly improved over the 2 decades of the study.

So where does that leave us? If scores are not different across centers or surgical strategy, and have not improved over time, does that mean we are helpless to improve neurodevelopmental outcomes in this population? The lack of change across time and place of surgery suggest that prenatal and presurgical factors weigh heavily on outcomes and can help us be more directed in our quest for interventions. Two very plausible lines of attack exist and are currently being pursued: maternal/fetal interventions and the prevention of white matter injury.

Maternal/fetal intervention studies are a brave new path for improving outcomes, and some studies are already underway, including studies of maternal hyperoxia and maternal supplemental progesterone, and others are in the planning stage. There are major roadblocks ahead, given that standard assessments of drug bioavailability and safety are inadequate or not feasible in the fetus. In some states, laws that were enacted to protect the fetus now broadly prohibit/inhibit fetal research. Furthermore, institutional review boards do not have precedent and may feel poorly prepared to adjudicate regarding the safety of fetal drug trials.

Currently, all research on white matter injury in severe CHD⁴⁻⁶ has pointed to maturational vulnerability^{7,8} as a leading risk factor. However, there is recent evidence implicating the timing of surgery as a major modifiable risk factor.^{9,10} Dr Kalfa and colleagues² give us hope, given their identification of time to surgery as a significant risk factor for poor long-term outcomes in their study.

In summary, for this challenging but deserving patient population, poor long-term neurodevelopmental outcomes remain heartbreaking; however, there are glimmers of hope that need to be aggressively pursued.

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