Magnetic Resonance Imaging in Congenital Heart Disease
What to Do With What We See and Don’t See?

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Magnetic resonance imaging (MRI) is increasingly being applied to critically ill newborns with congenital heart disease (CHD) with the hope of understanding mechanisms accounting for adverse neurodevelopmental outcome. This powerful technique has opened an unprecedented window into normal development and pathogenesis during fetal life and surrounding surgery. Much as the technological advances of cardiopulmonary bypass, cardiac intensive care, and transcatheter and surgical techniques have translated into improved survival for neonates with complex congenital heart lesions, MRI promises to elucidate mechanisms and measure outcomes in a way that will inform treatment and establish neurointensive care to lessen neurologic morbidity. Many agree that improving neurodevelopmental outcome in CHD is the preeminent challenge to the field. MRI studies in CHD have made the important and surprising observations that (1) brain injury is present before surgery,2 (2) injury is most commonly focal affecting the white matter,3 and (3) brain development is delayed in term infants with CHD.4 Despite its promise as a sensitive early outcome variable that could be used to structure interventional studies with novel trial design,5 success to date has largely been descriptive, identifying clinical risk factors in limited case series. A particular challenge applying these findings to clinical practice is that the incidence of injury and associated risk factors are often unique to each form of CHD.6 For this reason, the approach has not substantially altered clinical care to date. However, several themes have emerged from multiple studies, providing confidence that the identified risk factors are valid and potent. These include the significance of postoperative hypotension,3,6 hypoxemia3 and diminished regional cerebral oxygen saturation.6,7 Although multiple studies have noted the high frequency of preoperative brain injury, particularly in neonates with transposition of the great arteries (TGA),2,6,8 few risk factors have been identified for preoperative injury. The notable exception is a link between balloon atrial septostomy (BAS) and preoperative stroke.9 No risk factors have been identified to date for preoperative white matter injury (WMI) in neonates with TGA.

In this issue of Circulation, Petit and colleagues report an important analysis of preoperative MRI in a series of 26 neonates with TGA drawn from 2 separate prior research studies of preoperative brain injury.10 Of the 26 neonates with TGA enrolled, 10 (38%) were found to have WMI, which is by far the highest incidence reported for any group of neonates with CHD, with prior studies putting the rate between 16% and 18%.2,6 Although 14 neonates required BAS, no strokes were identified. In agreement with prior studies, BAS was not a risk factor for WMI. WMI was identified in 6 of 14 patients (43%) who had undergone BAS and in 4 of 12 patients (25%) not receiving the procedure. Analysis of clinical variables identified lower preoperative arterial partial pressure of oxygen (PaO2) >40 mm Hg. The interval from birth to surgery was also longer in neonates that developed WMI (5.6 versus 3.9 days).

To date, 2 studies address the risk of injury with BAS, the present study by Petit and colleagues and a prior study by McQuillen et al. Whereas important differences can be found between these 2 studies, a striking similarity exists in the overall rate of preoperative injury, with the major difference being a preponderance of stroke over WMI in the study of McQuillen et al, a finding confirmed when analyzed in a larger cohort.6 Despite this difference, conclusions that can be drawn from these studies that impact clinical care are largely the same. In a Clinical Perspective that accompanies the McQuillen study, the authors note the “safety profile and clear benefits of BAS” and caution that any attempts to “avoid BAS” or modify the procedure would need to be prospectively evaluated because “these strategies may be associated with independent risks,” including “prolonged hypoxia.” The present results are consistent with the idea that BAS should be used selectively for patients with significant hypoxemia, hemodynamic instability, or both at presentation. The present work provides new insight into the definition of “significant” hypoxia and illustrates that simply performing BAS is insufficient to prevent WMI. Moreover, the data call attention to the risk of WMI in patients who fail to improve oxygenation after BAS and those who do not achieve a PaO2 of at least 40 mm Hg by day of life 3. Finally, the work by Petit and colleagues identifies a risk to delaying the surgery that will restore normal circulation. Despite these important conclusions, neither study provides the necessary information to determine whether altering BAS frequency or timing of surgery will improve subsequent neurodevelopmental outcome. Furthermore, neither study answers the important

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question of the natural history of preoperative lesions and the risk of injury extension, hemorrhagic conversion, or associated development of new injury with surgery, cardiopulmonary bypass, and postoperative hemodynamic instability.

With similar overall injury rates but an apparent trade-off of increased WMI in place of stroke, the 2 studies may provide clues that could prove useful for improving outcome of newborns with TGA through the differences in clinical care that they exhibit. These differences include (1) a rate of septostomy of 53% (14/26) in the present study versus 66% (19/29) in the prior study; (2) location where BAS was performed: the catheterization laboratory with fluoroscopy was used more frequently in the present study (9/14) whereas the bedside with ultrasound guidance was used more frequently (17/19) in the prior study; (3) predominant use of the umbilical vein for access at BAS in the present study (10/14) versus femoral (15/19) in the prior; and (4) continued use of prostaglandin E1 after septostomy: 5/14 in the present study versus 8/12 in the prior. A final important difference relates to in-hospital care that they exhibit. These differences include (1) a rate of newborns with TGA through the differences in clinical care as they relate to outcome is an opportunity to identify existing beneficial approaches that should not be missed.

Finally, to realize the ultimate promise of this approach, imaging must be connected with outcome. Experience with advanced MRI is more extensive in the premature infant and term infant with birth asphyxia where MRI has been shown to be the most sensitive study for detection of acquired injuries, but MRI can also be used for quantitative measurement of brain macro- and microstructural development and metabolic development and function. Neurodevelopmental outcome after premature birth or asphyxia at term has been predicted by WMI on early and later MRI, spectroscopy, morphometry, and cortical folding. Studies establishing the association of postoperative MRI with outcome in large cohorts of neonates with CHD are urgently needed.

Clearly, brain development is complex and dynamic, whereas acquired injuries noted in newborns with CHD are focal and small, with imaging characteristics that may be evanescent. Each MR study is a snapshot in time, whereas acquired injury in the setting of CHD may be cumulative. CHD in many ways offers an ideal paradigm for the application of MRI to guide neuroprotection: The injury burden is high, and opportunities for intervention can be anticipated. The work by Petit et al is a valuable contribution toward defining the complete portfolio of risk factors confronting newborns with TGA. Moving forward, the challenge is to connect imaging to outcome and to define what risk factor to modify. For MRI to become the sensitive early outcome variable that will make novel trial design possible, the questions of which MRI method to use, when to use it, and how to uniformly describe findings are critically important.

Disclosures

None.

References


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