Pediatric RESEARCH

COMMENT

Fronto-temporal horn ratio: yet another marker of ventriculomegaly?

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Posthemorrhagic ventricular dilatation (PHVD) continues to be a significant complication of prematurity that carries a high risk of adverse neurodevelopmental outcome.[1,2] Multiple animal and human studies have consistently demonstrated that the increase in ventricular size correlates with long-term outcome; however, it remains a matter of debate when best to treat PHVD.[3–8] Recent retrospective studies and two randomized controlled trials (RCTs) have shown beneficial effects of cranial ultrasonography (cUS)-based decisions.[9–13] In these studies, deciding when to intervene mostly relied on practical and reproducible cUS measurements, such as the ventricular index (VI), anterior horn width (AHW), and thalamo-occipital distance (TOD).[14,15] In studies reported mostly by neurosurgeons, the frontal and occipital horn ratio has been shown to be a reliable surrogate for ventricular volumes,[16] and more recently the fronto-temporal horn ratio (FTHR)[17] has been correlated with magnetic resonance imaging (MRI) measurements by Radhakrishnan et al.[18] However, until a recent study by Leijser et al.,[19] no comparison was made between these different sonographic indices. The investigators explored inter-observer reliability of the sonographic indices for prediction of severe PHVD and showed a better reliability for VI and AHW measurements (intra-class correlation coefficient of 0.49–0.84 and 0.51–0.81, respectively) than for FTHR (0.41–0.82). The predictive value for neurodevelopmental outcomes after severe PHVD was also higher for the AHW than for the FTHR.[19]

In this issue, Obeid et al.[20] retrospectively assessed preterm infants with PHVD to define normative FTHR values as a marker of ventriculomegaly in cUS. The investigators found that the FTHR can be a useful quantitative biomarker of ventriculomegaly in preterm infants and it may help standardize ventricular measurements to direct intervention. While defining the normative values of FTHR is a noteworthy contribution to the literature, it should be emphasized that, due to the limited peripheral field view in cUS scans, it may be difficult to clearly visualize the parietal bone and both ends of the horizontal line indicating the biparietal width sometimes have to be estimated by judgment, as can be seen in their figure. Additionally, as there was a larger number of infants included in Obeid's study and these infants also had a lower gestational age than that of Radhakrishnan et al.,[18] it would have been a great opportunity to compare the VI, AHW, and FTHR in this large dataset. Besides, to assess additional brain injury, Obeid et al.[20] used the Kidokoro score[21] but with different thresholds for the classification of white matter injury to that used by Kidokoro. In the original description, >4 was taken as the cut-off to differentiate between moderate to severe and normal to mild white matter injury, while in the present study the cut-off was ≥8, which makes it difficult to compare the extent of white injury in this cohort with previous studies that used the same scoring.

The findings of this study also prompt us to revisit the effect of grade of intraventricular hemorrhage on the development of progressive PHVD. The close association between these two entities is particularly evident in Figure 4, where there is a sharp increase in FTHR in infants with periventricular hemorrhagic infarction (PVHI) even though some of these infants received intervention. It was recently shown that development of PHVD is an additional prognostic factor in infants with PVHI.[22] It is not clear in the text how many infants underwent transfontanelle ventricular taps, but this procedure should no longer be used, as it has been linked to the development of needle tracts. Additionally, it is not surprising to see a higher (77%) ventriculo-peritoneal shunt rate than reported in the literature, as there are FTHR values approaching and even exceeding 0.75 before initiation of the temporizing interventions. This finding is in line with the previous observation by Leijser et al.[9] that late interventions result in more surgical procedures.

What is novel and of great interest is the use of diffusion tensor imaging (DTI) in this study. DTI examines the integrity of white matter in the neonatal brain by utilizing the three-dimensional anisotropy of water diffusion and has gained interest for characterizing changes in tissue microstructure associated with a wide range of neurologic disorders.[23] However, DTI region of interest was used rather than measures of the entire fiber tract, which are likely to be more helpful in a condition such as PHVD where effects on the whole brain are to be expected. Additionally, DTI-assessed asymmetry of the posterior limb of the internal capsule (PLIC) has shown that the fractional anisotropy value is lower on the affected side in infants with a PVHI and predictive of development of unilateral spastic cerebral palsy.[24] It would, therefore, have been more informative to have ipsilesional and contralesional fractional anisotropy values of the PLIC rather than reporting left and right sides separately regardless of the presence of a hemispheric lesion.

There are significant differences regarding neurodevelopmental outcome in the literature following PHVD with more data suggesting that early intervention does improve outcome.[9,13] A recent retrospective study compared neurodevelopmental outcomes at 18–24 months between preterm infants undergoing either an early cUS-based approach or late intervention by waiting until clinical signs occurred.[9] The investigators showed that the latter approach was associated with an increased risk of adverse outcome.

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The randomized controlled ELVIS (Early versus Late Ventricular Intervention Study) trial[12] also demonstrated less brain injury assessed by the Kidokoro score as well as smaller ventricular volumes on MRI performed at term-equivalent age.[25] At 2 years of age, the risk of composite outcome of death or severe neurodevelopmental disability was lower in infants undergoing earlier interventions, after adjustment for gestational age and severity of the hemorrhage. Also of note is that the ELVIS trial showed a significant relationship between the maximal frontal and occipital horn ratio (FOHR) and cognitive and motor outcomes.[13] The present study by Obeid et al.[20] also contributes to the accumulating evidence that size of the ventricles correlates with adverse neurodevelopmental outcome.

It is unfortunate that the outcome data in this study were restricted to 16–20 months corrected age and lacks reporting of cognitive and motor scores using a standardized tool. The gross motor function classification system (GMFCS) is a standardized method to evaluate the child's function, rehabilitative potential, and expected trajectory over time.[26] However, the use of GMFCS to assess cerebral palsy between 16 and 20 months is questionable as the distinctions between levels are less pronounced at this age and this score is considered to be more reliable from 24 months onwards. One is now left with the question as to how many of the infants classified as GMFCS Level I do in fact have cerebral palsy and how many have cerebral palsy related to a PVHI that would occur even with effective treatment for the PHVD.

While the FTHR used by Obeid et al.[20] can be used in a future clinical trial of interventions in preterm infants with PHVD, aimed at minimizing tissue injury and optimizing outcomes, we recommend that the VI, AHW, and TOD are also included as these measures have been shown to be robust in previous RCTs and that they continue to be standard approach for assessing the progression of PHVD.

ADDITIONAL INFORMATION

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