Clinical Pearl: Post Hemorrhagic Ventricular Dilatation Management: Neurodevelopmental Outcomes

Mingshan Lai, MBBS, Joseph R. Hageman, MD. Mitchell Goldstein, MD, MBA, CML

"Ever since I heard about IVH and PHVD, I think of all of the premature infants I cared for and wonder about their neurodevelopmental outcomes."

As I discussed in a previous clinical pearl, after I instilled surfactant into the endotracheal tube of a 500-gram extremely premature infant born at 24 weeks gestation in 1983, we were able to wean him to room air and a rate of 3 breaths per minute by the following day. My friend and colleague, Dr. Elaine Farrell, learned the interpretation of neonatal cranial ultrasound from her husband, Dr. Jason Birnholtz, a pediatric radiologist, both of whom were at Harvard before Elaine came to work with us at the Evanston Hospital Infant Special Care Unit, wheeled the ultrasound machine to the bedside and placed the transducer on the anterior fontanelle and told me "this baby has a grade II intraventricular hemorrhage (IVH) as per the Papile classification system (1)". I was surprised and worried that he might develop post-hemorrhagic ventricular dilation (PHVD), which would have been classified as a grade III IVH as Papile proposed in 1978 when I was a second-year pediatric resident. Ever since I heard about IVH and PHVD, I think of all of the premature infants I cared for and wonder about their neurodevelopmental outcomes. I still remember those infants with PHVD whom I had to perform lumbar punctures and those on whom we consulted the neurosurgeons to place Ommaya reservoirs for serial taps to hopefully attenuate PHVD (2).

Here we are at a conference with an excellent presentation by Dr. Mingshan Lai, one of our very bright neonatal fellows, and he is reviewing three papers about the management of Post hemorrhagic ventricular dilatation and neurodevelopmental outcomes (4-6).

In the observational study by Shankaran et al., the authors demonstrated the impact of post-hemorrhagic ventricular dilatation (PHVD) by assessing the neurodevelopmental outcomes of a cohort of infants born ≤26 weeks gestation. This study included 17 centers in the NICHD network and spanned 4.5 years, divided infants based on head ultrasound findings at 28 days and 36 weeks corrected age into three groups: normal head ultrasound (62.4%), intracranial hemorrhage without ventricular dilatation (18.2%), and post-hemorrhagic ventricular dilatation (19.3%). The primary outcome of this study was death or neurodevelopmental impairment, defined as moderate or severe cerebral palsy, Bayley III cognitive or motor scores <70, bilateral blindness, or profound deafness despite amplification. Of the 4216 infants included in this study, 3069 (72.8%) returned to follow-up at 18-26 months, and the primary outcome was found in 28% with normal head ultrasounds, 39% with intracranial hemorrhage without ventricular dilatation, and 68% with PHVD. Furthermore, infants with PHVD were at significantly higher risk for rehospitalization after discharge, hospitalization for seizures, needing ventriculoperitoneal (VP) shunt revisions, and smaller head circumference when compared to infants in the other two groups (6).

However, there remains no consensus among neonatologists, neurologists, and neurosurgeons on when is the best time for intervention. The Early versus Late Ventricular Intervention Study (ELVIS) trial explored this knowledge deficit with a randomized controlled trial that compared intervening on PHVD with lumbar punctures at a low threshold (ventricular index (VI) >97%tile and anterior horn width (AHW) >6mm) versus a high threshold (VI >97%tile + 4mm and AHW >10mm) with a primary outcome of death and/or VP shunt placement. Though this trial did not show a significant difference between the groups in terms of primary outcome, it did show a significant difference in Kidokoro scores calculated from brain MRIs taken at term-corrected age, with the low threshold group having lower scores (p<0.001) (4).

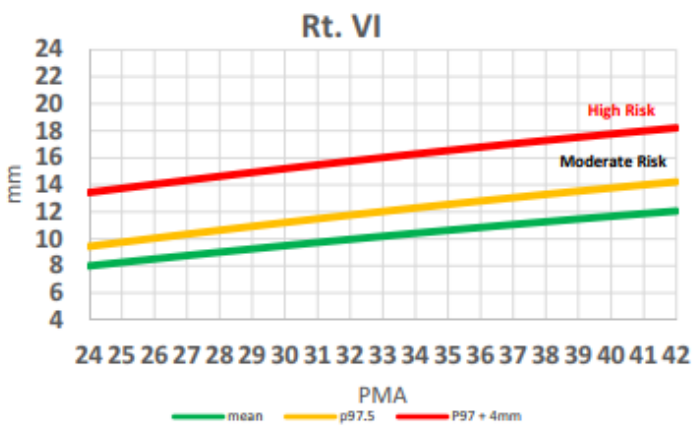
"However, there remains no consensus among neonatologists, neurologists, and neurosurgeons on when is the best time for intervention."

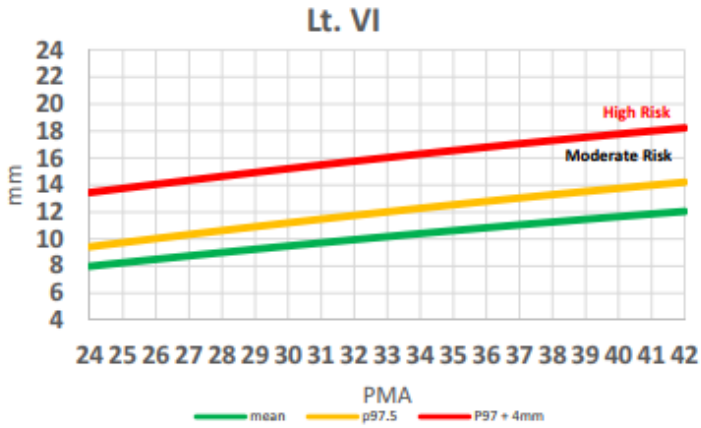
Mehmet et al. further explored the long-term impact of the ELVIS trial by assessing outcomes at two years. The composite adverse outcome was death, cerebral palsy, or Bayley composite cognitive/motor scores <-2 SDs at 24 months. This study found no difference in composite adverse outcomes between the two groups (p=0.07). However, when corrected for gestational age, severity of intraventricular hemorrhage, and cerebellar hemorrhage, the low threshold intervention group was associated with a decreased risk for adverse outcomes (p=0.03). Furthermore, infants in the low threshold group that required VP shunts had similar cognitive and motor scores compared to infants in the low threshold group that did not (p=0.3 and p=0.3, respectively).

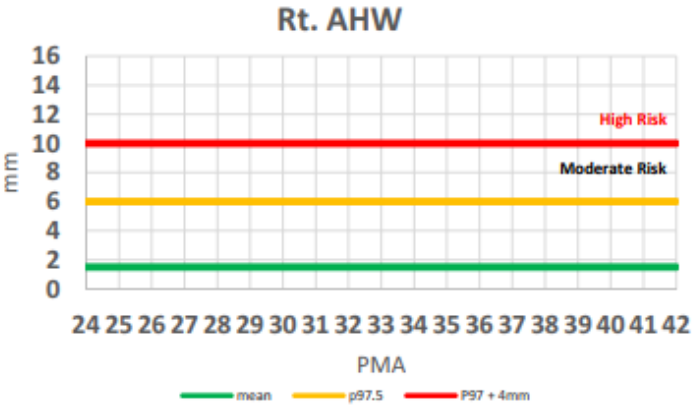
In contrast, infants in the high threshold group that required VP shunts had significantly lower cognitive and motor scores when

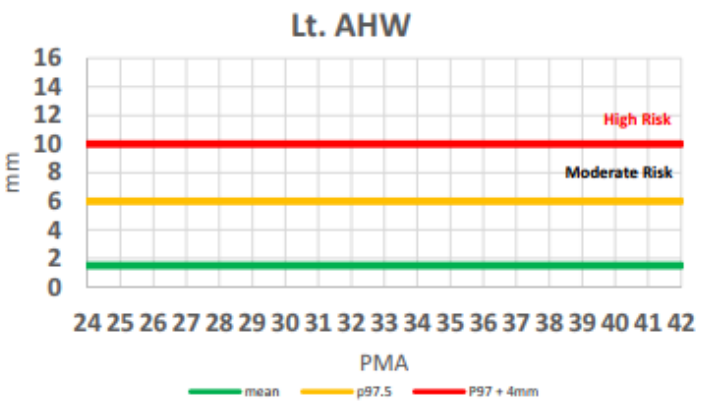
Name:
DOB:

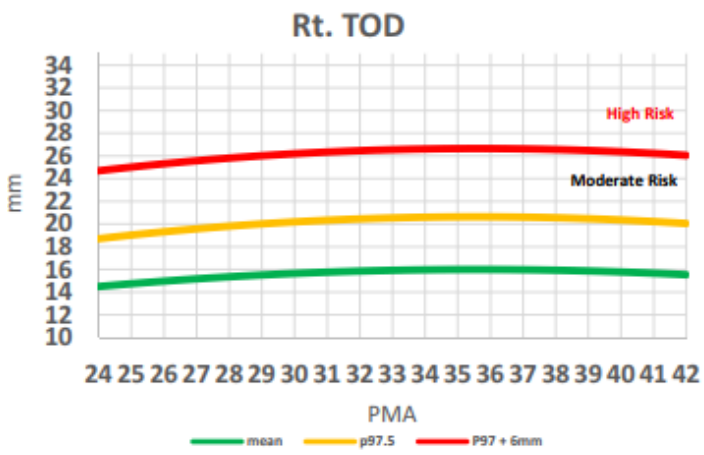
Ventricular Measurement Risk Zones

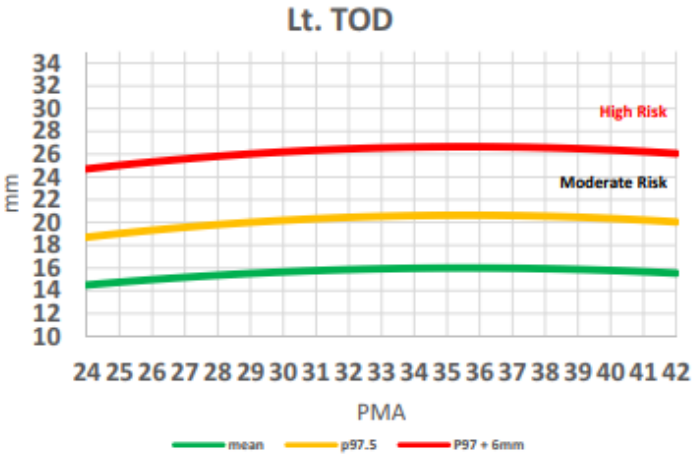




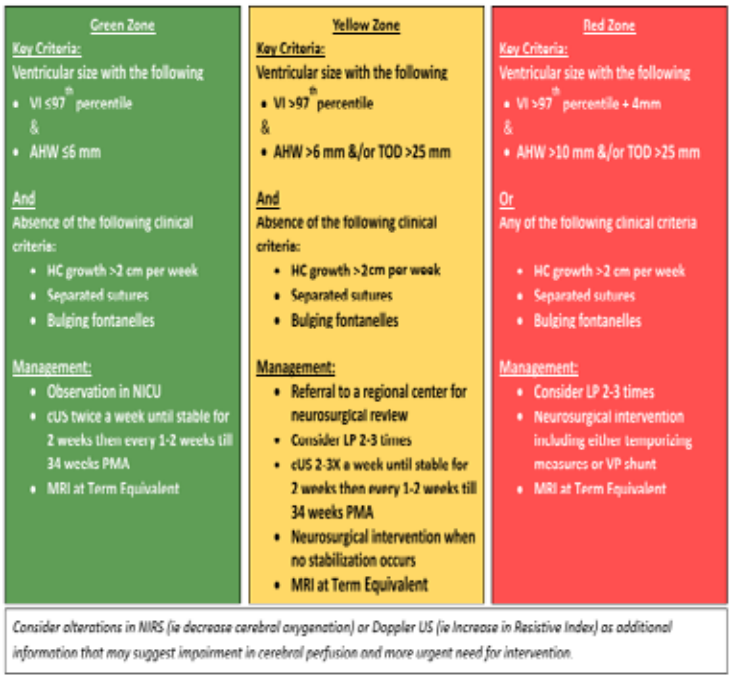








Date	PMA	Rt. VI	Rt. AHW	Rt. TOD	Lt. VI	Lt. AHW	Lt. TOD



compared to infants in the high threshold group that did not require VP shunts (p=0.01 and p=0.004, respectively). Additionally, this study demonstrated that higher Kidokoro scores were associated with adverse composite outcomes (p<0.001), and infants with normal or mildly abnormal Kidokoro scores had higher Bayley cognitive and motor scores than infants with moderate or severe scores (p=0.02 and p=0.01, respectively). As previously stated, in the ELVIS trial, infants in the low threshold group had significantly lower scores than infants in the high threshold group. This suggests that neurodevelopmental outcomes improve by intervening earlier before the ventricles dilate to a critical state. Their finding supports that larger frontal occipital horn ratio (FOHR) was negatively associated with cognitive and motor score, irrespective of group allocation (p<0.001 and p<0.001, respectively), and infants with adverse outcomes had larger FOHR than infants without adverse outcomes (p<0.001) (5).

"In contrast, infants in the high threshold group that required VP shunts had significantly lower cognitive and motor scores when compared to infants in the high threshold group that did not require VP shunts (p=0.01 and p=0.004, respectively)."

In light of these new studies, El-Dib et al. suggested changes in the management of PHVD should be made, shifting away from timing intervention around clinical symptoms of increased intracranial pressure and increasing head circumference and towards utilization of cranial head ultrasound (cUS) measurements, especially VI and AHW. Their article provided tools to stratify infants with PHVD into low-, moderate-, and high-risk groups. The low-risk group (VI <97%tile and AHW ≤6mm) was recommended to obtain twice-weekly cUS until stable for two weeks, then every 1-2 weeks until 34 weeks corrected age. MRI was recommended to be obtained at term-equivalent age. The moderate-risk group (VI >97%tile and AHW >6mm) was recommended to be referred to a regional center for neurosurgical review and to consider serial lumbar punctures as early intervention, in addition to the imaging recommendations of the low-risk group. If no stabilization occurred after serial lumbar punctures, neurosurgical intervention was recommended. The high-risk group (VI >97%tile +4mm and AHW >10mm or clinical signs of rapid head circumference growth, separated sutures, or bulging fontanelles) was recommended to consider serial lumbar punctures while planning for neurosurgical interventions. This group was also recommended to obtain an MRI at term-equivalent age (4).

Infants with PHVD are at high risk for adverse outcomes, including death and neurodevelopmental impairment, and their management requires a multidisciplinary approach and remains a developing field. Recent evidence suggests that more aggressive imaging with cUS and earlier intervention with serial lumbar punctures and neurosurgical interventions may be beneficial in avoiding adverse outcomes.

"by intervening early, before the ventricles dilate to a critical state, neurodevelopmental outcomes improve. Their finding supports this that larger frontal occipital horn ratio (FOHR) was negatively associated with cognitive and motor score, irrespective of group allocation (p<0.001 and p<0.001, respectively), and infants with adverse outcomes had larger FOHR than infants without adverse outcomes (p<0.001)."

"changes in the management of PHVD should be made, shifting away from timing intervention around clinical symptoms of increased intracranial pressure and increasing head circumference, and towards utilization of cranial head ultrasound (cUS) measurements, especially VI and AHW"

References:

1. Gupta P, Sodhi KS, Saxena AK et al. Neonatal cranial sonography: A concise review for clinicians. *J Pediatr Neurosci 20116;11(1):7-13. Doi. 10.4103/1817-1745.181261.*
2. Papile LA,Burstein J, Burstein R et al. Incidence and evolution of subependymal and intraventricular hemorrhage: A study of infants with birthweights of less than 1500 gm. *J Pediatr. 1978;Apr;92(4):529-534.*
3. Ommaya reservoir. www.mskcc.org/pe.
4. El-Dib M, Limbrick DD, Inder T, et al. Management of post-hemorrhagic ventricular dilatation in the infant born preterm. *J Pediatr 2020;226:16-27.e3.*
5. Mehmet NC, Groenendaal F, Liem KD et al. Randomized controlled early vs late ventricular intervention study in post-hemorrhagic ventricular dilatation: Outcome at 2 years. *J Pediatr. 2020;226:28-35.*
6. Shankaran S, Majaj M, Natarajan G et al. Outcomes following post-hemorrhagic ventricular dilatation among infants of extremely low gestational age. *J Pediatr 2020;226:36-44.*

Disclosures: *There are no reported disclosures*

NT

Corresponding Author

Mingshan Lai, MBBS
Fellow in Neonatology
Comer Children's Hospital
5721 S Maryland Ave
Chicago, IL 60637
email: mingshan.lai@uchicagomedicine.org

Corresponding Author

Joseph R. Hageman, MD
Senior Clinician Educator
Pritzker School of Medicine
University of Chicago MC6060
5841 S. Maryland Ave.
Chicago, IL 60637
Phone: 773-702-7794
Fax: 773-732-0764
Email: jhageman@peds.bsd.uchicago.edu

Mitchell Goldstein, MD, MBA, CML
Professor of Pediatrics
Loma Linda University School of Medicine
Division of Neonatology
Department of Pediatrics
Loma Linda, CA
Email: mgoldstein@llu.edu

Clinical Pearls are published monthly.

Submission guidelines for "Clinical Pearls":

1250 word limit not including references or title page.

May begin with a brief case summary or example.

Summarize the pearl for emphasis.

No more than 7 references.

Please send your submissions to:

jhageman@peds.bsd.uchicago.edu