Published in final edited form as:

Pediatr Crit Care Med. 2013 November ; 14(9): 903–904. doi:10.1097/PCC.0000000000000008.

Neuromonitoring of neonatal ECMO patients using serial cranial ultrasounds

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Keywords

ECMO; extracorporeal; neonatal; brain injury; head ultrasound

Neurologic complications during extracorporeal membrane oxygenation (ECMO) remain a significant problem and rates have stayed constant over the last three decades despite advances in extracorporeal technology.(1, 2) Several neuromonitoring methods have been proposed to diagnose acute neurologic injury during ECMO, including neuroimaging, electroencephalograms, somatosensory evoked potentials, plasma brain injury biomarkers and cerebral blood flow velocity measurements by transcranial Doppler ultrasound.(2-4) So far, the only method that entered routine clinical care consists of serial cranial ultrasounds (CUS) in neonates and young infants with open anterior fontanel. While not very sensitive for detecting extra-axial lesions, CUS provide clinicians with an easy to use screening tool for intracranial hemorrhage, ischemic stroke and post-asphyxial changes.

In this issue of *Pediatric Critical Care Medicine*, Raets et al present a retrospective analysis of all neonatal ECMO CUS findings in the Netherlands from 1989 to 2010 (n=677) (5). They found a rate of brain injury by CUS (17.3%) similar to prior published reports (13.5%-24%) (6-8). There was no decline in the rate of intracranial abnormalities detected by CUS during the study period of 22 years (5). Interestingly, the authors found lateralization of lobar hemorrhage and ischemic stroke to the left hemisphere that has not been described before. Prior studies have shown either a lack of lateralization or a tendency towards right-sided lesions (9-13). While intriguing, the significance of this finding is unclear, as discussed by the authors, and warrants further investigation. Where this study truly stands out, though, is in the exquisite attention to detail in the classification of types of injury found by CUS. This is arguably the most comprehensive yet easy to follow schema for classifying brain injury during ECMO. It divides injury by 1) vessel occlusion (cortical and perforator arterial ischemic stroke vs sinus, deep vein or other sinovenous thrombosis); 2) primary hemorrhage (epidural, subdural or subarachnoid intracerebral hemorrhage vs choroid plexus hemorrhage vs supratentorial or infratentorial parenchymal hemorrhage); and 3) other (parenchymal brain infection, postasphyxial injury, preterm white matter injury, etc) (5). Advances in ultrasound technology allow for detailed description of intracranial lesions and detection of subtle findings that were not possible in the past (9).

The authors plan to use data presented in this study in the analysis of long-term neurodevelopmental outcomes in the neonatal Dutch cohort followed longitudinally up to 18 years of age (14). It will be interesting to examine the correlation of CUS findings with post-ECMO brain computed tomography (CT) and/or magnetic resonance imaging (MRI) and

with neurodevelopmental outcomes, as data on the subject are still inconclusive. Rollins et al in a series of 50 neonates with post-ECMO brain MRIs found that 50% of newborns with normal CUS during ECMO showed abnormalities on brain MRI (7). CUS was abnormal in 24% of neonates, and brain MRI was abnormal in 62% of neonates. Neither CUS nor brain MRIs, though, were predictive of neurodevelopmental outcomes (7). Glass et al examined 152 children at 5 years of age and correlated neurologic disability scores with severity of neuroimaging findings during and after ECMO in the neonatal period. A large proportion of children with mild, moderate and even severe lesions on neuroimaging had no neurologic disability detected (87%, 67% and 43%, respectively) (15). Conversely, 10%-13.5% of neonates with normal CUS or post-ECMO head CT or brain MRI did show neurodevelopmental delays (6, 15). Similarly, in a series of 22 patients cannulated for ECMO at an average age of 1.18 years (range 0.1-7.8 years), Wagner et al reported a lack of correlation between neuroimaging findings and cognitive outcomes at follow up at 7.2 years of age (range 1.8-13.9 years of age) (16). And in a group of 74 newborns who required ECMO for refractory respiratory failure, 13.5% had significant cognitive delay at serial follow up intervals up to 5 years post-ECMO, despite normal CUS and/or brain CT/MRI (6). This Dutch cohort will therefore be the largest to examine long-term neurodevelopmental outcomes post-neonatal ECMO and to bring more definitive answers as to correlation of abnormal neuroimaging findings with outcomes.

This study has the limitations of a retrospective review and lack of standardization of CUS studies within and between the two Dutch ECMO centers in Rotterdam and Nijmegen. Using a veno-arterial bridge (and opening it intermittently) is still practiced in some ECMO centers; it would be interesting to compare rates of acute neurologic events in the two Dutch ECMO centers before and after 2001, when “flushing” the bridge was discontinued in their patient care protocols.

The findings of the Raets et al study point to the persistent problem of acute neurologic injury during neonatal ECMO and provide a carefully crafted framework for classification of injury by CUS that will very likely serve as a template for future research into patterns of brain injury during neonatal and pediatric ECMO. Future studies will need to corroborate neuroimaging findings with other physiologic and biochemical markers of acute neurologic injury during ECMO to allow for early diagnosis and neuroprotective interventions, to improve predictive value for neurologic disability and to assess the need for early rehabilitation and treatment of patients post-ECMO, with the ultimate goal of optimizing neurodevelopmental outcomes.

Acknowledgments

Copyright Form Disclosures: Dr. Bambea received support for article research from the National Institutes of Health. Dr. Bambea's institution received grant support from NIH/NINDS.

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