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SEMINARS IN PERINATOLOGY

Neonatal ECMO: Neuroimaging and Neurodevelopmental Outcome

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Intracranial injury continues to be a major complication associated with extracorporeal membrane oxygenation (ECMO)-treated neonates. The reported frequency of abnormal neuroimaging has ranged from 28% to 52%, depending on neuroimaging techniques and methods of classification. The purpose of this chapter is to describe types of imaging techniques commonly used to evaluate the ECMO neonate, to specify different types of injuries that have been reported, and to identify factors which increase the risk of injury. We will then describe the functional impact at age 5 years following neonatal brain injury among ECMO infants.

KEYWORDS intracranial hemorrhage, intraventricular hemorrhage (IVH), extracorporeal membrane oxygenation (ECMO), neurodevelopmental outcome, ultrasound, magnetic resonance imaging (MRI), computer tomography (CT), cerebral ischemia

Risk Factors

Multiple factors increase the risk of intracranial injury in infants undergoing extracorporeal membrane oxygenation (ECMO).[1-6] In addition to the necessity for anticoagulant use during bypass, all candidates for ECMO have suffered from hypoxemia and acidosis, many with evidence of vasomotor shock. Hypercarbia, volume expansion, pneumothoraces, and blood pressure fluctuations alter cerebral blood flow.[1,7] Hypotension before or during ECMO may result in cerebral ischemia. Using near infrared spectrophotometry, Liem and coworkers demonstrated changes on ECMO including increased cerebral blood volume, loss of autoregulation, reactive hyperperfusion, and hemodilution.[8] Arterioles that are already maximally dilated may, in the presence of impaired autoregulation, rupture because of increased blood flow pressure.[9,10] Diminished pulsatility with venoarterial ECMO may also affect cerebral blood flow. Abnormal venous drainage resulting from jugular vein ligation has also been implicated as a cause of cerebrovascular injury subsequent to stasis within periventricular medullary veins.[11]

After unilateral carotid ligation, infants on ventilatory support have been noted to have decreased cerebral blood flow.[9] In a study by Hunter and coworkers, cerebral blood flow of lambs was measured by laser Doppler flowmetry during venoarterial (VA) and venovenous (VV) ECMO. Carotid ligation resulted in a decrease in the cerebral blood flow (CBF) of the right cerebral cortex. However, this decrease was only transient (60 seconds), with elevation of cerebral resistance. Using VV ECMO, no change in CBF was observed.[12]

There has been concern that ligation of the carotid artery may cause lateralized cerebrovascular injury. Several early small series noted an increase in injuries to the right hemisphere in infants who underwent ligation of the right carotid artery.[13-15] In larger series by Adolph and coworkers and Bulas and coworkers, however, no lateralization of lesions was noted by neuroimaging.[6,16] In a series of 355 infants using ultrasound (US), computer tomography (CT), magnetic resonance imaging (MRI), or clinical evaluation, Graziani and coworkers also demonstrated no selective or greater injury to the right hemisphere as compared with the left.[17] In a cohort of 31 infants treated with ECMO evaluated by MRI, there was no lateralization of major brain lesions.[18] No lateralization was noted in a group of infants studied by cerebral proton magnetic resonance spectroscopy following EMCM.[19] However, focal brain lesions were significantly associated with an asymmetric cerebrovascular response to carotid ligation of the right versus left middle cerebral artery as detected

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Figure 1 Axial CT image demonstrates mild prominence of the interhemispheric fissure and subarachnoid space.

by Magnetic Resonance Angiography (MRA) ($P < 0.5$).[18] Schumacher and his colleagues[5] have argued that *no lateralization* of lesions among ECMO-treated neonates is indicative of *increased vulnerability of the right hemisphere*, since reports of intraventricular hemorrhage (IVH) and stroke in non-ECMO patients indicate relative vulnerability of the left hemisphere.

It is believed that premature infants on ECMO are at high risk of intracranial hemorrhage due to the presence of a friable germinal matrix with poor supporting stroma.[1,2] Despite the exclusion of small premature infants from ECMO, studies have shown that younger infants continue to have a statistically significant increased risk of hemorrhage, even though the mean age was 38 weeks and only 27% of the hemorrhages originated in the germinal matrix.[6] Although regions of ischemia are at risk for hemorrhage when heparin is used, infarcts in term infants weighing over 3 kg typically do not progress to hemorrhages.

Infants with sepsis are also at high risk for intracranial hemorrhage likely due to additional problems with coagulopathy.[20] In a series by Hardart and coworkers, gestational age, sepsis, coagulopathy, and acidosis were all associated with a higher incidence of intracranial hemorrhage[21,22] Dela Cruz and coworkers demonstrated that elevated ACT and low platelet count were also associated with an increase in intracranial hemorrhages.[23]

Infants with long circuit runs, particularly those with congenital diaphragmatic hernia, have the highest rate of major nonhemorrhagic lesions. With more conservative use of heparin, the risk of partial venous occlusion and microemboli has been shown to increase.[6,24]

Widened interhemispheric fissures have been well described in infants on ECMO, with rates of occurrence as high as 59%[3,25] (Fig. 1). Rubin and coworkers (1990) believed this dilation was an intracranial manifestation of generalized edema.[26] Other authors have suggested that increased sagittal sinus pressure associated with internal jugular vein ligation and cannulation of the superior vena cava is the cause of this dilation due to decreased cerebrospinal fluid resorption of the arachnoid villi.[11,27] Widened extra axial space can develop as well, with severe cases noted following superior vena cava thrombosis.[28] VV ECMO is particularly prone to decreased venous drainage resulting in an increased incidence of dilated interhemispheric fissure and prominent subarachnoid space.[29] Due to the potential risk of venous stasis, cephalic drainage has been developed in an attempt to prevent neurologic complications by maintaining normal cerebral blood flow and increasing ECMO oxygen delivery.[30]

Cerebrovascular Imaging

Ultrasound

Ultrasound is particularly useful in the evaluation of infants on ECMO due to its portability and lack of ionizing radiation. The presence of a large intracranial hemorrhage is a contraindication for ECMO initiation, thus a screening examination before cannulation is critical in the assessment of potential therapeutic options. Ultrasound has been sensitive in the evaluation of large cranial hemorrhages. In a series by Bulas and coworkers, sonography successfully identified 46 (94%) of 49 major intracranial hemorrhages, lesions that most affect the way an infant is managed acutely.[31] Identification of isolated subependymal hemorrhages has been shown not to be at risk for progressive and should not prevent the initiation of ECMO therapy.[32]

As the risk of hemorrhage is greatest in the first few days of ECMO, daily cranial sonograms have been recommended for the potential identification of a developing bleed. The question as to how often daily sonograms should be performed

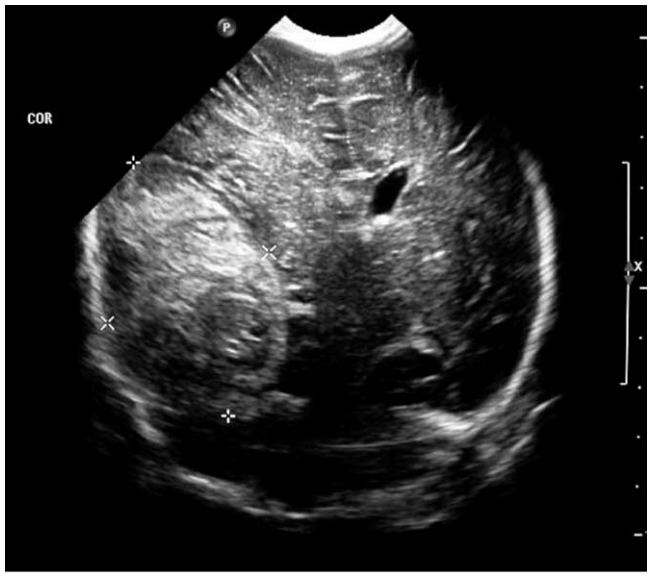

Figure 2 Coronal US image demonstrates a large hemorrhagic infarct of the right temporal lobe with herniation.