ECMO and the Risk of Cholestasis in Children

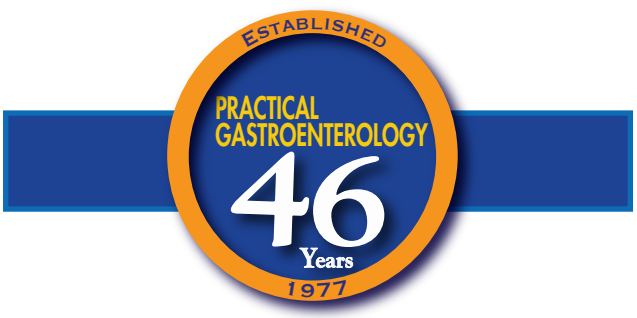
Extracorporeal membrane oxygenation (ECMO) is a life-saving procedure which provides oxygen while removing carbon dioxide to critically ill patients by removing blood from a patient before returning it via a circuit. The returning blood is not pulsatile which can lead to hepatic injury and direct hyperbilirubinemia (DHB), and the occurrence of DHB in the setting of ECMO is associated with increased patient mortality. The authors of this study looked at risk factors for pediatric patients on ECMO developing DHB or experiencing mortality.

This single-center retrospective study at a tertiary medical center evaluated all pediatric patients under eight years of age who received ECMO over a 10-year period (2010-2020). Children on ECMO for less than 48 hours duration were excluded from the study, and DHB was defined as a direct bilirubin level greater than 1 mg / dL. Causes for ECMO and ECMO duration were determined, and risk factors for DHB which included total parenteral nutrition (TPN), continuous renal replacement therapy (CRRT), and central cannulation were evaluated. Illness severity while on ECMO included two scores: the vasoactive-ionotropic score (VIS) and Acute Physiology and Chronic Health Evaluation (APACHE II) score. Finally, outcomes were compared between patients with DHB on ECMO and a control group consisting of patients without DHB on ECMO.

A total of 106 patients in the intensive care unit (ICU) were included in the study, and 51% of patients were male while 46% of patients were neonates. The median age at time of ECMO was 0.2 years (range 0-2.3 years), and the most common cause leading to ECMO was post-surgical care for congenital heart disease (39%). The median time spent on ECMO was 8 days (range 5-19 days), and 34% of patients on ECMO developed DHB. None of the patients with DHB while on ECMO had underlying previous liver disease. Serum AST and ALT were not significantly different between patients with DHB and the control group at the time of ECMO initiation. Neonates were not at a higher risk of developing DHB while on ECMO. TPN was utilized in 83% of patients, and central cannulation was utilized in 34% of patients; neither therapeutic was a risk factor for DHB. However, patients who developed DHB while on ECMO spent a significantly longer time on ECMO (19 days (interquartile range or IQR 8-30 days)) versus 6 days (IQR 4-13 days, $P<0.001$) and were significantly more likely to require CRRT (50% versus 13%, $P<0.001$). A total of 46 of the 106 patients (43%) died, and patients with DHB were statistically more likely to die while on ECMO compared to the control group (72% versus 29%, $P<0.001$). Although the APACHE II score was not significantly different between study groups at the time of ICU admission, logistic regression analysis demonstrated that DHB development during ECMO was associated with a significantly higher mortality rate independent of the VIS score or CRRT use ($P=0.006$).

This retrospective study provides some initial insight as to potential causes of mortality for children with DHB undergoing ECMO. The simple presence of DHB was a risk factor for mortality in this study, and CRRT was a possible aggravating risk factor. The authors state that more work is needed to prevent DHB from occurring in children receiving ECMO.

Alexander E, O'Sullivan D, Aganga D, Hassan S, Ibrahim S, Absah I. Clinical implications for children developing direct hyperbilirubinemia on extracorporeal membrane oxygenation. Journal of Pediatric Gastroenterology and Nutrition 2022; 74: 333-337.



Malnutrition in Children with Congenital Heart Disease

Congenital heart disease (CHD) is a common pediatric congenital disorder worldwide, and malnutrition can be a co-morbidity in children

with CHD leading to poor health outcomes. The authors of this study performed a meta-analysis to determine the prevalence of malnutrition in children with CHD before and after cardiac surgery. This meta-analysis followed the guidelines of the PRISMA statement (http://www.prisma-statement.org/), and the authors searched for several CHD terms utilizing an "or" for combination wording through several large medical databases. Cross-sectional or cohort studies were identified through September 2021 with an emphasis on preoperative and postoperative malnutrition. Malnutrition (underweight, stunting, and wasting) was defined by using World Health Organization *z*-scores in which "underweight" was defined as a weight-for-age *z*-score less than -2; "stunting" was defined as a height-for-age *z*-score less than -2; and "wasting" was defined as a weight-for-height *z*-score of less than -2.

The authors initially found 3415 publications; however, only 39 studies fit all inclusion criteria (33 studies on malnutrition in the preoperative period; 17 studies on malnutrition in postoperative period). Using these specific studies, the meta-analysis determined that 79,719 patients were evaluated preoperatively for underweight status; 78,572 patients were evaluated for stunting; and 77,249 patients were evaluated for wasting. The Newcastle-Ottawa Scale demonstrated that all such studies were of moderate to high quality. Pooled estimate analysis determined that 27.4% (95% CI, 21.7-34.0) of children with CHD were underweight, 24.4% (95% CI, 19.5-30.0) of children with CHD had stunting, and 24.8% (95% CI, 19.3-31.3) of children with CHD had wasting. Q testing further demonstrated that children with CHD had significantly more malnutrition compared to healthy children with no CHD (for underweight, $Q = 16.24$, $P < .0001$; for stunting, $Q = 6.21$, $P = .013$ for stunting; for wasting $Q = 66.82$, $P < .0001$). Post-operative CHD repair improved malnutrition prevalence from 33.1% (95% CI, 26.2-40.8) at one month to 7.2% (95% CI, 4.7-10.8) at 12 months; improved stunting prevalence from 18.2% (95% CI, 10.8-29.0) at one month to 8.9% (95% CI, 4.5-16.7) at 12 months; and improved wasting prevalence from 22.1% (95% CI, 13.2-24.5) at one month to 5.4% (95% CI, 2.4-11.7) at 12 months. Of note, significant heterogeneity between studies using I^2 testing was present when a pooled analysis was done for patients with underweight, stunting, and wasting. The main cause of heterogeneity depended on the continent where the study was performed. Funnel plot and Egger test analysis demonstrated no publication bias for the factors of overweight and stunting although this effect was seen for wasting.

This study demonstrates that malnutrition is a significant issue in pediatric patients with CHD, and surgical correction of CHD may improve malnutrition. However, this study also demonstrates significant outcome heterogeneity when studies throughout the world are considered. Well-defined definitions of outcomes in the setting of malnutrition and CHD are sorely needed, and better research is needed for preoperative malnutrition management (supplemental feedings, dietician management, etc.).

Diao J, Chen L, Wei J, Shu J, Li Y, Li J, Zhang S, Wang T, Qin J. Prevalence of malnutrition in children with congenital heart disease: a systematic review and meta-analysis. Journal of Pediatrics 2022; 242: 39-47.

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