Best Evidence

Journal Scan

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1. Extracorporeal membrane oxygenation for pediatric respiratory failure: Risk factors associated with center volume and mortality
Kirkland BW, Wilkes J, Bailly DK, et al.
Pediatric Critical Care Medicine 2016; 17:779–788

Objectives: Recent analyses show higher mortality at low-volume centers providing extracorporeal membrane oxygenation. Authors sought to identify factors associated with center volume and mortality to explain survival differences and identify areas for improvement. Design: Retrospective cohort study. Setting: Patients admitted to children’s hospitals in the Pediatric Health Information System database and supported with extracorporeal membrane oxygenation for respiratory failure from 2003 to 2014. Patients: A total of 5,303 patients aged 0–18 years old met inclusion criteria: 3,349 neonates and 1,954 children. Interventions: None. Measurements and Main Results: Low center volume was defined as less than 20, medium 20–49, and large greater than or equal to 50 cases per year. Center volume was also assessed as a continuous integer. Among neonates, clinical factors including intraventricular hemorrhage (relative risk, 1.4; 95% CI, 1.24–1.56) and acute renal failure (relative risk, 1.38; 95% CI, 1.20–1.60) were more common at low-volume compared to larger centers and were associated with in-hospital death. After adjustment for differences in demographic factors and primary pulmonary conditions, mild prematurity, acute renal failure, intraventricular hemorrhage, and receipt of dialysis remained independently associated with mortality, as did center volume measured as a continuous number. Among children, the risk of acute renal failure was almost 20% greater (relative risk, 1.18; 95% CI, 1.02–1.38) in small compared to large centers, but dialysis and bronchoscopy were used significantly less but were associated with mortality.

After adjustment for differences in demographic factors and primary pulmonary conditions, acute renal failure, acute liver necrosis, acute pancreatitis, and receipt of bronchoscopy remained independently associated with mortality. Center volume measurement was not associated with mortality given these factors.

Conclusions: Among neonates, investigation for intraventricular hemorrhage prior to extracorporeal membrane oxygenation and preservation of renal function are important factors for improvement. Earlier initiation of extracorporeal membrane oxygenation and careful attention to preservation of organ function are important to improve survival for children.

Reviewer’s comments
In the present study authors identified factors associated with both center volume and mortality to delineate factors that, at least in part, explain higher mortality at centers with low ECMO volume. Some of these factors can be modified and logically could be targeted to improve survival for neonates and children receiving ECMO for respiratory failure at these centers. Some of the factors are not modifiable like race but pre-ECMO identification of intraventricular hemorrhage especially in premature can certainly improve the ECMO outcome. Similarly prevention and early identification of acute renal failure which has been identified as independent mortality risk factor, can decrease odds for death. Similarly palliative care of complex congenital heart disease also improves the outcome of ECMO irrespective of the center volume. When these factors were added to models predicting death, the association with center volume and mortality no longer persisted as an independent risk factor for pediatric patients but remained for neonates. Also this study indicates improved survival with early use of ECMO preferably before the onset or establishment of multiorgan dysfunction.

2. Prognostic value of cerebral tissue oxygen saturation during neonatal extracorporeal membrane oxygenation
**Objectives:** Extracorporeal membrane oxygenation (ECMO) support is indicated in severe and refractory respiratory or circulatory failures. Neurological complications are typically represented by acute ischemic or haemorrhagic lesions, which induce higher morbidity and mortality. The primary goal of this study was to assess the prognostic value of cerebral tissue oxygen saturation (StcO\textsubscript{2}) on mortality in neonates and young infants treated with ECMO. A secondary objective was to evaluate the association between StcO\textsubscript{2} and the occurrence of cerebral lesions. Study design: This was a prospective study in infants < 3 months of age admitted to a pediatric intensive care unit and requiring ECMO support. Measurements: The assessment of cerebral perfusion was made by continuous StcO\textsubscript{2} monitoring using near-infrared spectroscopy (NIRS) sensors placed on the two temporo-parietal regions. Neurological lesions were identified by MRI or trans-fontanellar echography. Results: Thirty-four infants < 3 months of age were included in the study over a period of 18 months. The ECMO duration was 10±7 days. The survival rate was 50% (17/34 patients), and the proportion of brain injuries was 20% (7/34 patients). The mean StcO\textsubscript{2} during ECMO in the non-survivors was reduced in both hemispheres (p = 0.0008 right, p = 0.03 left) compared to the survivors. StcO\textsubscript{2} was also reduced in deceased or brain-injured patients compared to the survivors without brain injury (p = 0.002). Conclusion: StcO\textsubscript{2} appears to be a strong prognostic factor of survival and of the presence of cerebral lesions in young infants during ECMO.

**Reviewer’s comments:**
Near infrared spectroscopy (NIRS) measures cerebral tissue oxygenation saturation (StcO\textsubscript{2}). StcO\textsubscript{2} depends on oxygen blood transportation as well as CBF. Continuous StcO\textsubscript{2} monitoring can measure cerebral hemodynamic changes if no hypoxic events or rapid hemoglobin changes occur. Authors found that the mean StcO\textsubscript{2} decreased in non-surviving newborns and young infants during prolonged ECMO. Second, the mean StcO\textsubscript{2} and the duration of desaturation remained normal in patients without brain injury. This observational, non-interventional study has been done on neonates and infants only and investigators have focused on StcO\textsubscript{2} monitoring and changes in their values while infant is on ECMO. They have not studied the correlation between StcO\textsubscript{2} and PCO\textsubscript{2}, which have potent effects on cerebral blood flow. Changes in cerebral blood flow have direct effects on StcO\textsubscript{2}. Surprisingly authors have admitted that they have not monitored SpO\textsubscript{2} during the ECMO run! It suffices to mention that StcO\textsubscript{2} is an non-invasive device to monitor cerebral function in patients on ECMO who are at high risk for ischemic or haemorrhagic complications.

**3. PaO\textsubscript{2}/FiO\textsubscript{2} deterioration during stable extracorporeal membrane oxygenation associates with protracted recovery and increased mortality in severe acute respiratory distress syndrome**

**Background:** During extracorporeal membrane oxygenation (ECMO), arterial oxygen partial pressure to fractional inspired oxygen (PaO\textsubscript{2}/FiO\textsubscript{2}; PF ratio reflects native and artificial lung blood oxygenation). In this study authors analyzed PF ratio during ECMO support and its association with clinical outcome. Methods: This was a single-center observational study of adult patients (n = 81) undergoing veno-venous ECMO support for severe acute respiratory distress syndrome. Results: In 37 patients (46%) PF ratio decreased from ECMO-day 1 to ECMO-day 7 (PF ratio deterioration [PF-d]: −37 ± 6.1 mm Hg), whereas in 44 patients PF ratio improved (PF-i 65 ± 10.8 mm Hg). PF-d group required prolonged ECMO (median 21 days [interquartile range (IQR): 14–35 days] versus 13 days [IQR: 10–20 days]) and invasive mechanical ventilation (median 33 days [IQR: 24–52 days] versus 26 days [IQR: 22–34 days]), longer intensive care unit (median 44 days [IQR: 32–74 days] versus 30 days [IQR: 25–47 days]), and hospital (median 66 days [IQR: 39–95 days] versus 36 days [IQR: 28–54 days]) lengths of stay, with higher hospital mortality rates (48.7% versus 22.7%). ECMO oxygenation did not explain PF ratio variation that remained stable in PF-d and decreased in PF-i (198 ± 12.7 mL/min versus 171 ± 8.8 mL/min). Pre-ECMO PF ratio, neuromuscular blockade, and prone position, as well as ventilatory variables did not differ between groups. The PF-d group was older (49 ± 2.1 years versus 41 ± 1.8 years) and presented lower Respiratory Extracorporeal
Membrane Oxygenation Survival Prediction (RESP) scores (0.57 ± 0.63 versus 2.2 ± 0.52). With the use of logistic regression, PF ratio variation remained an independent predictor of hospital mortality after adjusting for age or RESP score. Conclusions: In severe ARDS, PF ratio deterioration during stable ECMO associates with protracted recovery and increased mortality, not accounted for by patient baseline characteristics, acute respiratory distress syndrome severity, or pre-ECMO management.

Reviewer’s comments:
Despite the widespread use of PaO2/FiO2 PF ratio as a simple index of hypoxemia to diagnose and grade ARDS severity, its prognostic utility in patients requiring ECMO support remains unknown. Importantly, in these patients, PF ratio reflects native lung function as well as artificial lung support. It is influenced by ECMO circuit blood flow, FiO2 in sweep gas flow, and blood recirculation in especially in VV-ECMO. In severe ARDS patients with residual native lung function undergoing VV-ECMO, cardiac output is also an important determinant of arterial blood oxygenation. In this study, authors have correlated the positive or negative changes in the PF ratio to the recovery or deterioration of native lung and VV-ECMO outcome. This study is useful for the intensivist to make important bedside decisions.

4. Serial lactate measurements as a prognostic tool in venovenous extracorporeal membrane oxygenation support

Background: Serial lactate measurements over time or lactate clearance has been reported to be clinically reliable than absolute values of lactate, as a surrogate for the magnitude and duration of global tissue hypoxia, for risk stratification in different pathologic conditions ranging from sepsis to trauma. In patients with acute respiratory distress syndrome (ARDS) lactate clearance within the first 72 hours of intensive care unit (ICU) admission was able to predict early mortality.

The main findings of the present investigation, performed in 126 consecutive patients with refractory ARDS supported by VV-ECMO are as follows: (1) lactate values, measured before ECMO initiation and at 6 and 24 hours after ECMO start, respectively, are predictors of ICU death; (2) lactate clearance at 72 hours after ECMO start is an independent predictor of death (together with age, BMI, and SOFA score). A lactate clearance of −16% with respect to baseline values identifies a subset of patients at higher risk of death. The higher lactate levels and poor clearance of lactate in non-survivors were not attributed to poor hemodynamics only but may be related to more
severe lung injury. Serum lactate is an easily available investigation and helps in prognostication and risk stratification and may be considered as therapeutic goal.

5. Clinical significance of spontaneous Echo contrast on extracorporeal membrane oxygenation
Unai S, Nguyen M, Tanaka D, et al
Ann Thorac Surg 2017; 103: 773-778

Background: Spontaneous echo contrast (SEC) is known to be a predisposition to thromboembolism and cerebrovascular accident. The aim of this study was to investigate the risk factors and the consequences of SEC in patients who were placed on venoarterial extracorporeal membrane oxygenation (VA-ECMO) because of cardiogenic shock. Methods: Between January 2011 and December 2014, 98 patients underwent the insertion of VA-ECMO because of cardiogenic shock in our institution. Transthoracic and transesophageal echocardiography was performed and interpreted by National Board of Echocardiography certified cardiologists. Patients were divided into 2 groups based on the presence or absence of SEC. Clinical data, echocardiographic measurements, and outcomes were compared between the 2 groups. Results: Of the 98 patients, 22 patients (22%) had SEC on echocardiography. Patients in the SEC group had a lower ejection fraction (8.0% versus 29%; \( p < 0.001 \)), a lower pulsatility index (defined by \([\text{systolic blood pressure} - \text{diastolic blood pressure}/\text{mean blood pressure}]\)) while receiving ECMO (0.13 ± 0.14 versus 0.26 ± 0.22; \( p = 0.009 \)). The SEC group had a higher rate of intracardiac thrombus (46% versus 13%; \( p = 0.002 \)) and stroke (36% versus 7.9%; \( p = 0.002 \)). On univariate analysis, intracardiac thrombus, SEC, and low pulsatility were significant risk factors for the development of stroke. On multivariate analysis, SEC was the only independent risk factor for stroke. Conclusions: SEC on VA-ECMO resulted in an increased risk of intracardiac thrombus and stroke. Maintaining pulsatility while the patient is on ECMO may result in a decreased chance of developing SEC and stroke.

Reviewer’s comments:

Spontaneous echo contrast is a smoke-like echo density observed on transthoracic or transesophageal echocardiograms caused by increased red blood cell aggregation during low-flow states and blood stasis. SEC is known to be a predisposition to thromboembolism. This paper has demonstrated the use of SEC in patients on VA-ECMO for cardiogenic shock. The presence of SEC increases the risk of thromboembolic complications in the presence of blood stasis in cardiac chambers. Judicious use of anticoagulants, antiplatelet therapy, maintaining pulsatility and ensuring opening of aortic valve to unload left ventricle prevent stasis of blood and risk of stroke.

6. The incidence of acute kidney injury and its effect on neonatal and pediatric extracorporeal membrane oxygenation outcomes: A multicenter report from the kidney intervention during extracorporeal membrane oxygenation study group
Pediatric Critical Care Medicine 2016; 17:1157–1169

Objective: In a population of neonatal and pediatric patients on extracorporeal membrane oxygenation (ECMO) to describe the prevalence and timing of acute kidney injury utilizing a consensus acute kidney injury definition and investigate the association of acute kidney injury with outcomes (length of ECMO and mortality).Design: Multicenter retrospective observational cohort study. Setting: Six pediatric ECMO centers. Patients: Pediatric patients (age, < 18 yr) on ECMO at six centers during a period of January 1, 2007, to December 31, 2011. Interventions: None. Measurements and Main Results: Complete data were analyzed for 832 patients on ECMO. Sixty percent of patients had acute kidney injury utilizing the serum creatinine Kidney Disease Improving Global Outcomes criteria (AKI\(_{\text{Scr}}\)) and 74% had acute kidney injury using the full Kidney Disease Improving Global Outcomes criteria including renal support therapy (AKI\(_{\text{Scr} + \text{RST}}\)). Of those who developed acute kidney injury, it was present at ECMO initiation in a majority of cases (52% AKI\(_{\text{Scr}}\) and 65% AKI\(_{\text{Scr} + \text{RST}}\)) and present by 48 hours of ECMO support in 86% (AKI\(_{\text{Scr}}\)) and 93% (AKI\(_{\text{Scr} + \text{RST}}\)). When adjusted for patient age, center of support, mode of support, patient...
complications and pre-ECMO pH, the presence of acute kidney injury by either criteria was associated with a significantly longer duration of ECMO support (AKISCr, 152 vs 110 hr; AKISCr + RST, 153 vs 99 hr) and increased adjusted odds of mortality at hospital discharge (AKISCr: odds ratio, 1.77; 1.22–2.55 and AKISCr + RST: odds ratio, 2.50; 1.61–3.90). With the addition of renal support therapy to the model, acute kidney injury was associated with a longer duration of ECMO support (AKISCr, 149 vs 121 hr) and increased risk of mortality at hospital discharge (AKISCr: odds ratio, 1.52; 1.04–2.21). Conclusion:Acute kidney injury is present in 60–74% of neonatal pediatric patients supported on ECMO and is present by 48 hours of ECMO support in 86–93% of cases. Acute kidney injury has a significant association with increased duration of ECMO support and increased adjusted odds of mortality at hospital discharge.

Reviewer’s comments:
This study is important and it systematically evaluates the KDIGO AKI definition in a broad multicenter cohort of pediatric ECMO patients. There are three important findings from this study which include: high incidence of AKI (60%-74%) in the neonatal and pediatric ECMO population, AKI occurs early in the ECMO course of the pediatric patient, with the majority of those with AKI identified at ECMO initiation and 93% of those identified with AKI by 48 hours and the third important result is the presence of AKI is associated with a longer duration of ECMO and increased mortality both at ECMO decannulation and by hospital discharge. The major limitation of this study is to define acute kidney injury and problem associated with serum creatinine immediately after birth. Moreover, the ECMO protocols and equipments were not standardised in the six participating centers.

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