**Project Title: Risk factors for neurologic injury and mortality in critically ill children supported on ECMO.**

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**Problem Statement**: Critically ill children on ECMO are at high risk for neurologic injury and death. Neurologic injury occurs in approximately one third of pediatric ECMO patients, in the form of intracranial hemorrhage, embolic stroke, hypoxic brain injury, or combination thereof. Mortality is seen in almost half of all ECMO patients, and is usually due to irreversible (multi)organ failure or intractable hemorrhage. When neurologic injury occurs, the risk of death increases by 89%. In this project, we propose to pursue two independent aims: 1) identify coagulation-related risk factors for intracranial hemorrhage or embolic stroke; 2) develop early prediction scores for patient- and circuit-related complications during ECMO, using well-established existing definitions for such complications.

**Background**: Aim 1: ECMO is a well-established method of support used in more than 2400 pediatric patients annually with severe cardiac and/or respiratory failure unresponsive to maximal medical therapy, when estimated chances of mortality exceed 80%. It involves direct cannulation of the heart or of one or two large vessels, typically the right carotid artery and the right internal jugular vein, to circulate blood through an extracorporeal circuit that includes a pump to maintain blood flow and an oxygenator to provide gas exchange. A continuous infusion of unfractionated heparin is used to prevent thrombus formation. Prolonged anticoagulation needed during ECMO is a major risk factor for intracranial hemorrhage. Despite anticoagulation, thrombi can still form in the circuit due to activation of inflammatory and coagulation pathways as the blood gets exposed to the foreign surfaces of the circuit. When dislodged from the circuit, thrombi can migrate into the patient’s blood vessels and reach the brain, producing one or multiple embolic strokes. It is currently unknown what the optimal methods are for anticoagulation during ECMO, especially in children, who have hemostatic systems that are still developing. We hypothesize that specific patterns of abnormalities in the coagulation system (based on laboratory tests assessing coagulation) can predict onset of intracranial hemorrhage or embolic strokes.

Aim 2: Patient- and circuit-related complications during ECMO can occur at any time during extracorporeal life support. Until now, the field has lacked the ability to collect and utilize comprehensive physiologic, laboratory, and circuit data to develop early prediction scores for onset of complications. The Extracorporeal Life Support Organization (ELSO) has developed definitions for complications during ECMO support that are grouped into the following categories: mechanical, hemorrhagic, neurologic, renal, cardiovascular, pulmonary, metabolic, and patient limb complications (<https://www.elso.org/Portals/0/ELSOECLSRegistryForm5_0%202018-03-01.pdf>). We hypothesize that patient time-series physiologic data, level of mechanical support, status of the coagulation system, and indicators of individual organ dysfunction can be used to develop risk scores for patient- and circuit-related complications during ECMO.

**Preliminary Data/Relevant Experience**: Our group has published extensively on various topics related to ECMO, including management of anticoagulation during pediatric ECMO, neurologic injury in ECMO patients, and neurologic outcomes of ECMO patients. The clinical PI has a research program including multicenter NIH-funded studies in ECMO.

**Data Set Identification**: We will use Epic data (demographics, diagnoses, vital signs, continuous infusions, ECMO flowsheet, laboratory results, imaging reports) from consecutive patients in the Johns Hopkins Children’s Center supported on ECMO between 2011-2018.

**References:**

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