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Title: Examining Factors That May Contribute to Mortality For Pediatric Patients Started on ECMO For Respiratory Failure

Background: The use of ECMO in patients with respiratory failure has been chiefly studied in the adult population. While there are no pediatric randomized controlled trials, there is valuable Extracorporeal Life Support Organization (ELSO) data that validates ECMO's utilization in the population. For children with respiratory failure, the ability to maintain gas exchange is critical for survival. The timing regarding initiating VV-ECMO has been an issue of debate as there are many factors that influence the decision. These include the patient's current respiratory function, underlying disease etiology and comorbidities. Further examination of these factors presents an opportunity to improve treatment for this potentially poor-prognosis population.

Significance
Respiratory failure is one of the most common diagnoses made in pediatric intensive care units. Conditions such as asthma, acute respiratory distress syndrome, pneumonia, bronchiolitis, sepsis and aspiration represent some of the most common etiologies that lead to its diagnosis. Despite advances in therapy, respiratory failure remains one of the leading causes of pediatric mortality.

Management of pediatric respiratory failure includes, but is not limited to, prone positioning, nitric oxide, oxygen therapy, continuous positive airway pressure, and mechanical ventilation. These treatments are not without complications. Prolonged therapy on a ventilator can lead to both infection and pressure related injury. When these therapies have failed to stabilize the patient or have reached their maximal efficacy, extracorporeal membrane oxygenation (ECMO) can be introduced.

In venovenous ECMO, blood bypasses the compromised pulmonary circuit and is run through an external membrane oxygenator before returning to the patient. ECMO is only used in patients whose respiratory failure is reversible, as it affords the lungs time to heal organically. This strategy initially gained popularity in the 1970's in the neonatal population. Neonates who had severe hypoxia as a result of pulmonary hypertension that were treated with ECMO were shown to have significant improvements in overall survival. Adults in respiratory failure have also been shown to benefit from ECMO. The CESAR trial found that adult patients in the UK were more likely to survive at hospitals that combined conventional treatment and ECMO when compared to centers without established ECMO programs. More recently, it showed effectiveness in improving survival amongst adults with severe cases of the H1N1 influenza. However, in contrast to the neonatal and adult patient populations, much less is known about ECMO's efficacy in the older pediatric population.

ECMO has been utilized in severe cases of pediatric respiratory failure successfully. However, the prognosis is still quite poor for patients requiring ECMO. Current ELSO (Extracorporeal Life Support Organization) data suggests that pediatric patients who are placed on ECMO for various

types of respiratory failure exhibit a mortality rate slightly above 40%. Certain factors appear to contribute to improved mortality, such as limiting mechanical ventilation to under 2 weeks before cannulation onto ECMO. Additionally, the absence of preexisting organ dysfunction, immunosuppression, and restrictive lung disease are associated with improved mortality.

Similar to conventional therapy, ECMO carries its own risks. Unfortunately, the need to anti-coagulate patients for the therapy increases their risk of significant bleeding. While bleeding can occur anywhere, GI bleeds and intracranial hemorrhages are amongst the most common sites. Thromboembolic and ischemic strokes as well as death are all possible while on ECMO.

Importantly, while ECMO has been shown to be beneficial for some patients, many questions remain. For example, the optimal timing of cannulation and which patients would stand to gain the most benefit from ECMO are not yet clear. The aim of this study is to evaluate any preceding determining factors that could help to predict outcomes for patients when they are placed on ECMO for respiratory failure. Special attention will be paid to co-morbidities, severity of disease and timing of therapy.

Hypothesis: We hypothesize that there are clinical and patient specific factors that can predict ECMO's utility, which will guide clinical decision making in initiating ECMO for respiratory failure. To better understand the surrounding questions pertaining to ECMO for patients with respiratory failure, we will:

Aim 1. Evaluate the OI's of non-neonatal pediatric patients placed on ECMO for respiratory failure to determine whether the severity of the score is a significant factor in predicting survival
Aim 2. Determine whether length of ventilatory support prior to initiation of ECMO had an independent impact on mortality
Aim 3. Examine the specific etiologies of existing non-respiratory disease or comorbidities to assess for any correlation of worse outcomes depending on preexisting condition

Research Plan

Aim 1. Evaluate the OI's of non-neonatal pediatric patients placed on ECMO for respiratory failure to determine whether the severity of the score is a significant factor in predicting survival

Rationale. Patients with more severe degrees of respiratory failure are at higher risk of mortality. Because numerous studies have demonstrated a broad link between higher OI and poorer outcomes, closer examination of our ECMO population may help define the most appropriate timing for treatment.

Methods.

Clinical information will be abstracted from the electronic medical record. Abstracted data will be entered into a clinical database and includes the following: demographic features (age, gender, etc), therapeutic course (vent settings, length of ECMO, medications administered) OI at time of ECMO, clinical outcomes (successful decannulation, complications, survival).

Data Analysis. We will perform descriptive analysis of our respiratory failure population using abstracted data. Patients will be sorted based on the severity of their OI and their clinic outcomes will be correlated with their scores.

Aim 2. Determine whether length of ventilatory support prior to initiation of ECMO had an independent impact on mortality

Rationale. Current data suggests that ventilation greater than 14 days before starting ECMO had a negative impact on mortality. Evaluating how long patients have been ventilated at this institution before cannulation will help to elucidate whether patients are at higher risk of death, even before the intervention.

Methods. Clinical information including length of ventilatory treatment will be abstracted from the electronic medical record. Peak pressures on the vent will also be recorded. This new information will then be added to the clinical database.

Data Analysis. We will examine what percentage of patients started ECMO who received <14 days of mechanical ventilation vs. those who were ventilated for a longer than two weeks. Next, we will compare the outcomes of the two groups, looking at morbidity and mortality.

Aim 3. Examine the specific etiologies of existing non-respiratory disease or comorbidities to assess for any correlation of worse outcomes depending on preexisting condition

Rationale. It is known that preexisting comorbidities negatively impact outcomes of pediatric patients starting ECMO for respiratory failure. It is therefore worthwhile to examine how many of our patients had comorbidities, what their etiologies were and the patients clinical outcome in order to better assess the validity of our institution's mortality rate.

Methods. Patient's comorbidities, such as liver disease, renal failure, immunosuppression, cardiac history, and sepsis will be abstracted from the electronic medical record. This new information will then be added to the clinical database.

Data Analysis. We will separate patients based on whether they had any of the above mentioned comorbidities. Patients with more than one comorbidity will be evaluated separately. We will then examine their outcomes and compare the mortality statistics against current published data.

Conclusion

Expected Results.

It is possible that after examining the data, we may find that the mortality is lower in patients who received ECMO earlier in their clinical course. ECMO should be initially considered when OI is in the moderate range or low severe scores rather than extremely severe scores. It should always be initiated before 14 days of mechanical ventilation. As a tertiary care center, we are taking care of very sick children who have significant comorbidities, which increases the mortality rates at our hospital.

Future direction

Establishment of a protocol to initiate ECMO at a specific OI, similar to other children's hospitals.

Examples:

- UCSF: Initiates ECMO when OI >40
- Minnesota: When OI>45
- Washington: When OI>30

Citations

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