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Editorial

Role of Continuous Renal Replacement Therapy in Patients with Acute Respiratory Distress Syndrome Treated with Extracorporeal Membrane Oxygenation

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Extracorporeal membrane oxygenation (ECMO) is a modality of treatment used in the intensive care unit (ICU) to improve gas exchange in patients with acute respiratory distress syndrome (ARDS) and continuous renal replacement therapy (CRRT) is added to the treatment mainly for correction of fluid and electrolyte imbalance [1]. Although fluid overload and prevention of fluid overload constitute almost 60 percent of the indications to initiate renal replacement therapy in ECMO patients, the optimal time for initiation of renal replacement therapy is not well defined and impact of this on the outcomes of critically ill patients with ARDS is not completely understood [2].

Pathophysiology of ARDS is characterized by inflammatory insult to the endothelium of pulmonary capillaries and epithelium of alveoli leading to dysfunction of barrier function and formation of high permeability pulmonary edema [3]. Most of the ARDS patients are critically ill and in the mileu of intravascular hypovolemia, vasodilatation, capillary leak and third spacing compounded by inadequate assessment of volume status, receive massive amounts of fluids for resuscitation leading to pulmonary edema and generalized third spacing [4]. This will eventually result in an increase in interstitial pressure and impaired tissue perfusion/oxygenation necessitating the initiation of ECMO once mechanical ventilation fails to maintain oxygenation.

Assessing fluid balance in ARDS patient on ECMO has always been a challenge. It is often difficult to ascertain whether volume expansion, vasopressor use, inotropic support, or diuresis is the most appropriate strategy [5]. Experimental and observational data have shown that ECMO can have hemodynamic consequences and can interfere with the accurate assessment of volume status. Larrson et al in his experiments in swine model showed that veno-arterial ECMO can decrease systemic venous pressure while maintaining systemic perfusion leading to diminution of central venous pressure measurement [6]. Pyles et al in their experiment on Doset lambs found that initiation of ECMO is associated with decreased hemodynamic and echocardiographic measures of LV function despite accounting for changes in afterload [7]. ECMO can additionally result in cardiac stunning and cardiac dysfunction as reported by Martin et al [8]. All these factors in the background of acute renal failure and inadvertent fluid resuscitation result in development of fluid overload in patients with ARDS.

Fluid retention especially in the presence of acute kidney injury has been associated with an increase in morbidity and mortality in intensive care unit (ICU) patients and decreased survival in patients with ARDS [4, 9] Payen et al. has demonstrated a linear relationship between mortality and increasing positive fluid balance in patients admitted to the ICU especially in presence of acute kidney injury [10]. A similar observation was made by the PICARD group as well [11]. Goldstein et al, based on observational study in pediatric patients needing CVVH or CVVHDF, found that fluid overload at the initiation of CVVH or CVVHDF is associated with higher mortality independent of the severity of the illness [12]. There additionally seems to be a dose response effect of fluid overload on mortality [13]. These observations may be applicable to patients on ECMO as well. Excessive fluid resuscitation has been found to be associated with prolonged ECMO duration, mechanical ventilation, longer length of stay in the ICU and mortality [14]. Considering the evidence outlined above, fluid balance should become an essential parameter in patients undergoing ECMO for ARDS. CRRT is an important tool for managing fluid overload in these patients since it enables goal directed maintenance of fluid balance.

Efforts to keep a negative fluid balance may not be effective once patients become fluid overloaded and hemodynamically unstable requiring multiple vasopressors. Moreover, the use of diuretics and vasodilators (to reduce left ventricular end diastolic pressure) may not be effective in such scenarios. Hence early initiation of CRRT before the onset of fluid overload should be considered in patients on ECMO and ARDS. Blijdorp et al. observed that initiating preemptive CRRT during ECMO in neonatal patients improved outcomes by decreasing time on ECMO due to improved fluid management [15].

Although there is data supporting association between mortality and initiation of CRRT in ECMO patients, delayed start of CRRT could have been responsible for the observed increase in mortality. Kielstein et al. observed that the 90 day survival of patients on ECMO needing CRRT was only 17%; however, at the same time they found that the cohort of patients who had delayed start of CRRT had higher mortality [1]. The role of fluid overload contributing to mortality was not separately analyzed in this study. Randomized controlled studies comparing early vs. late initiation of CRRT before and after the occurrence of fluid overload in patients with ARDS on ECMO would be needed to further address this issue.

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