Editorial

A novel survival prediction model of ECMO in acute respiratory distress syndrome: things to consider for optimal use

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Comment on: Hilder M, Herbstreit F, Adamzik M, *et al.* Comparison of mortality prediction models in acute respiratory distress syndrome undergoing extracorporeal membrane oxygenation and development of a novel prediction score: the PREdiction of Survival on ECMO Therapy-Score (PRESET-Score). Crit Care 2017;21:301.

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Acute respiratory distress syndrome (ARDS) is the most severe form of acute inflammatory lung injury and is caused by various etiologies (1). Mechanical ventilation is the mainstay of supportive therapy (2). However, ventilator induced lung injury continues to be unresolved problems. Lung protective ventilation, based on low tidal volume and decreased driving pressure, is the standard of care; however, it is not always possible to keep this strategy in patients with severe ARDS (3). Extracorporeal membrane oxygenation (ECMO) is a promising rescue therapy and has been increasingly used in patients with ARDS (4). In 2009, Conventional ventilation or ECMO for Severe Adult Respiratory failure (CESAR) trial showed positive results but the survival benefits remain unclear (5). Despite the potential benefit, the debate on the efficacy of ECMO results from the technical invasiveness and high rate of complications (6-8). Furthermore, ECMO requires specialized personnel with a specific skill set and is an economic burden. Therefore, appropriate selection of patients and appropriate use of this limited resource are important issues. Various scoring systems have been proposed to select patients most likely to benefit from ECMO (9-13). However, these scoring systems have several limitations. They were derived from a heterogeneous group of ECMO devices, with a variety of ECMO practice parameters, various levels of ECMO technical support, and various patient populations. There has been no consistent validation of the proposed predictive scores (14,15).

In a single ECMO center, Hilder *et al.* conducted independent validation of the previous scoring systems to investigate their usefulness in predicting survival (16). They developed the PRESET score, a novel and practical categorical system based on pre-ECMO clinical data. The score was validated with two independent validation cohorts. In a derivation cohort, medical records of 108 patients with ARDS on veno-venous ECMO were retrospectively analyzed. Four scoring systems were used: ECMOnet score; Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP score); Prediction dEath for Severe ARDS on VV-ECMO (PRESERVE) score; and Roch score; to predict mortality and to identify independent variables by performing multivariate logistic regression analysis for mortality for developing the new PRESET score (9-12).

Based on the results, the median (25–75% quartile) for Sequential Organ Failure Assessment (SOFA) score was 14 [12–16] and for Simplified Acute Physiology Score II (SAPS II) was 62.5 [57–72.8]. The median intensive care unit stay was 17 days (range, 1–124 days) and mortality was 62%. Only the ECMOnet score [area under curve (AUC) 0.69] and

the RESP score (AUC 0.64) distinguished between survivors and non-survivors. Admission arterial pH, mean arterial pressure, lactate, platelet count, and pre-ECMO hospital stay were independent predictors of death, and were used to develop the PRESET-score. Internal (AUC 0.845; 95% CI: 0.76–0.93, P<0.001) and external (AUC 0.70; 95% CI: 0.56–0.84, P=0.008) validation revealed excellent discrimination. Interestingly, among clinical variables measured immediately before the initiation of ECMO, only extrapulmonary variables were predictors of survival; respiratory variables were not predictive of survival. This suggests important issues regarding the practical aspects of ECMO support. The use of ECMO suggests the time for the resolution of primary lung disease. It is important to determine whether the patient has already irreversible pulmonary damage or serious damage to other organs at the beginning of ECMO support. These factors provide prognostic information, indicative of reversibility of the patient's condition.

The study has a number of strengths. All patients were treated with an identical ECMO system, so patients were well matched. The authors created a new scoring system for outcome prediction and validated it in two independent cohorts. In addition, they compared the new scoring system with previous scoring systems and demonstrated comparable outcome prediction power. The strongest point of this new model is that only simple variables, including three hemodynamic variables, heart rate, mean arterial blood pressure, and vasopressor requirement, were used. This new scoring system is complementary to previous models, which depend upon baseline epidemiologic variables and comorbidity.

Despite the strengths, cautious interpretation is required to use this model appropriately. First, the study was conducted at a single center and the study population had severe disease. The SOFA and SAPS II scores of the patients were high, approximately 20% of patients had cardiac arrest before initiation of ECMO, and individuals transferred from other hospitals were included in the study population. This suggests that implementation of ECMO may have been delayed. Recently, the timing of initiation of ECMO has become an important issue. Early initiation of ECMO improved survival in patients with ARDS (15,17,18). In the study by Hilder *et al.*, each additional hospital stay before the initiation of ECMO was associated with a 10% increase in mortality. This may be the reason that pre-ECMO hospital stay was used as a prediction parameter in the PRESET score. Furthermore, it should be noted that this predictive model is more likely effective for patients who are hemodynamically unstable. Because this study included the severe shock patients requiring very high doses of vasopressor. Therefore, the results and the prognostic relevance of the PRESET score may not be directly applicable to other institutions with different severity and circumstance. Validation with larger cohorts is required for general use of this new scoring system. Additional issues are related to the definition of outcomes. Unlike previous scoring systems, this study suggested short-term outcomes. It is not well defined whether the short-term outcomes are ICU or hospital outcomes. However, this may explain why hemodynamic variables had substantial prognostic significance in this scoring system. Therefore, the PRESET score may not be suitable to predict long term, such as 6 months or 1 year, outcomes.

Although the PRESET score is a useful prediction model, the use should be based on individual clinical judgement of the specific patient including history, etiology of ARDS, patient characteristics, patient conditions, and the status of a living will. It is useful to have a simpler method to assess predicted ECMO survival. However, scoring systems should not be a substitute for clinical evaluation in decision to initiate ECMO therapy. Furthermore, outcome prediction scoring systems should be used to select optimal patients without contraindications, rather than exclude patients with a low probability of survival. Beyond scores, treatment decisions require a multidisciplinary team approach by experienced physicians.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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