The Challenges in Predicting ECMO Survival, and a Path Forward

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Extracorporeal membrane oxygenation (ECMO) support is a life-saving but complex technique for patients suffering from severe cardiac or pulmonary dysfunction. Increasingly greater utilization in the last 15 years means that a suite of mortality risk analytics is both feasible for researchers and required by clinicians, patients, administrators, and insurers. We argue that to date, research into such risk analytics has been insufficient and does not adequately reflect the various indications and configurations of extracorporeal life support (ECLS). We propose a path to address these challenges and ensure that clinicians and researchers obtain robust, specific, risk analytics. *ASAIO Journal* 2017; 63:847–848.

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ECMO risk prediction has three key goals. It should allow clinicians to prospectively stratify the outcome risk for ECMO candidate patients. It should also permit facilities and clinicians to retrospectively understand their risk-adjusted ECMO performance across all their patients. Finally, it should allow facilities and clinicians who wish to start an ECMO program to estimate future clinical performance from such a program.

Across these three objectives, the different indications for ECMO, modalities, and characteristics of the infrastructure and practice patterns all matter. Accordingly, the ideal model would be customized along those dimensions, be constructed in large datasets and successfully validated in external datasets.

To understand the extent that practical reality matches this ideal, we searched PubMed for all studies with all keywords "ECMO," "risk," "predict" published since January 1, 2010 through September 2, 2016. Of 48 studies meeting these inclusion criteria, 11 were focused on producing a risk model for adult populations.

Our analysis (**Table 1**) suggests several different conclusions. Some studies on the left side of the table are obviously not feasible for medical reasons such as veno-venous configuration in patients with cardiac function compromise. In other scenarios, it may not be sufficient to provide indirect cardiac support with veno-venous ECMO for some types of respiratory function compromise. Similarly, in cardiac arrest with aspiration pneumonia, a hybrid configuration with veno-arterial-venous configuration may be useful. Finally, in some patients with a purely respiratory support indication and with major double venous cannulation issues such as thrombosis or prior cannulation, but without indications for cannulation with bicaval dual lumen catheter, veno-arterial ECMO has been reported.

However, in much of the white space, our field has constructed relatively few risk models despite the many potential opportunities. We have only one model for witnessed cardiac arrest,[1] despite nearly 3,000 patients in the ELSO registry who have had ECMO for this indication. We have several published models in which either the indication is mixed,[2–4] or cannulation modes included both veno-arterial and veno-venous modes.[5–8] Klinzing *et al*. did construct separate risk models for veno-venous and veno-arterially treated patients, but the small number of patients failed to allow acceptable model predictive ability.[6]

We do have two good recent models that exclusively consider cardiogenic shock,[9,10] but three more that use older data including the important SAVE score.[11–13] Indeed, of the 13 risk models that have been published since 2010, five have accrued at least some patients before 2005. Yet such older data fail to incorporate the improvements in ECMO technology, processes and therefore in survival in more recent years. This might make those studies relying on older data less applicable to current practices.

We claim these points matter. Clinicians seeking to predict survival in a patient with severe acute respiratory disease could see estimated risk that diverges greatly from some "true" value if that risk model was partially derived from cardiogenic shock patients. Facility retrospective risk adjustment that relied a model constructed from patients in respiratory failure but including some patients whose initial diagnosis was cardiac arrest,[7] might similarly lead to biased estimates of facility performance.

Looking to the future, we believe these methodological issues can and should be dealt with. We see wider and systematic use of ELSO' ECLS Registry as a key part of a recommended program to deal with the white space in **Table 1**. Ideally, researchers should favor more recent data, corresponding as closely as possible to the modern ECMO infrastructure

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Table 1. Summary of ECMO Adult Risk Models Since 2010

	Focus in Study on ECMO Therapy Configuration		
ECMO Indication in Study	Exclusively Veno-venous	Both Veno-venous and Veno-arterial, or Hybrid	Exclusively Veno-arterial
Exclusively respiratory failure		Huang *et al*., 2016 Klinzing *et al*., 2015 [PRESERVE] Schmidt *et al*., 2013 [RESP]	
Large majority respiratory failure		Schmidt *et al*., 2014 [RESP]	
Mixed respiratory and cardiogenic indications		Kim *et al*., 2015	Chen *et al*., 2016*
Large majority cardiogenic shock			Schmidt *et al*., 2015 [SAVE]
Exclusively cardiogenic shock			Muller *et al*., 2016 [ENCOURAGE] Burrell *et al*. 2015 Li *et al*. 2015 Hsu *et al*., 2010 Formica *et al*., 2010
Exclusively witnessed cardiac arrest			Mégarbane *et al*., 2015

All studies published in PubMed January 1, 2010 to September 2, 2016. Light shading indicates published research with some study patients accrued before 2005.

*Added *post hoc*, appeared October 22, 2016.

ECMO, extracorporeal membrane oxygenation.

in widespread use today. While some may argue that "year of ECMO" could satisfy the question of impact, this may not be a workable solution for a prospective risk score calculated by a clinician in a facility.

Apart from the Registry, and continuing to increase the number of reporting centers, we also argue that we need separate risk models, for example, for veno-venous and veno-arterially treated patients with respiratory failure. Especially for witnessed cardiac arrest in hospital, we need substantially more models to understand the mortality risk (and neurological deficit) inherent in such use.

Some may argue that parceling out low numbers of patients into even smaller sets of indications and modes of treatment reduces predictive ability. This is a correct criticism, but suggests we should be conducting fewer own-institution retrospectives and more Registry-based work where more than 20,000 adult patients currently speak to our potential to "slice and dice" the data very finely.

Moreover, the dynamics in indication should be considered. Cardiogenic shock leading to acute respiratory distress syndrome and respiratory failure must be considered differently from viral pneumonia leading to respiratory failure. Similarly, acute respiratory disease syndrome in patients with septic shock complicated by circulatory shock should be considered a different case than cardiac failure without respiratory illness.

We acknowledge that none of these modeling tasks is simple or uncontroversial. However, the patients we start on ECMO and their families, the hospital clinicians, technologists and nursing staff who care for our patients, the insurers, and the society that ultimately provides scarce resources to enable ECMO—they all deserve our best attempts to produce more, and more refined risk models.

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