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Outcomes and risk stratification for severe ARDS treated with ECMO

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The acute respiratory distress syndrome (ARDS) is associated with a high mortality rate despite recent encouraging results from RCTs [1–3]. Initial profound hypoxemia is associated with the highest mortality rate [4]. In the subset of patients with the most severe hypoxemia ($\text{PaO}_2/\text{FiO}_2$ ratio <50 – 70) and/or when there is a high risk of severe ventilator-induced lung injury related to increased plateau pressure, some centers propose extracorporeal membrane oxygenation (ECMO) to minimize the trauma caused by mechanical ventilation and to promote lung rest and recovery. Biotechnological developments in the ECMO circuit, catheter and pump design have reinvigorated enthusiasm about using ECMO more than 20 years after initial disappointing results. In

addition to enhanced technology, there is also a greater understanding of the nuances of patient management while on ECMO [5, 6]. The recent CESAR trial results [7] and the favourable outcomes of patients who received ECMO as rescue therapy during the recent H1N1 influenza pandemic support this [8–11]. However, many uncertainties remain about the use of ECMO in the most severe ARDS patients. We do not know at the present time if this intervention is able to decrease mortality compared to proning [1] or other ARDS-supportive treatments, nor do we understand specific morbidities related to catheter placement and prolonged circuit and anticoagulant exposure. Eligibility and selection criteria need to be informed by both mortality and morbidity outcome data, which are only just beginning to emerge [12, 13]. The lung's ability to return to near-normal function after ARDS has been extensively reported [14]. We assume that pulmonary outcomes after ECMO will be similar, but what remains unclear are the other outcomes and in particular specific sequelae related to the application of this technology. As an example, placement of femoral cannulae may lead to ischemic nerve injury, and the resultant foot drop may have a profound impact on longer term function and mobility and other important patient and family-centered outcomes. These issues are of utmost importance because this intervention has very specific indications currently. First of all, ECMO is considered for the most hypoxemic patients. Although the relationship between hypoxemia and neurocognitive dysfunction was established by Hopkins and colleagues in 1999 [15], it remains unclear whether relatively brief hypoxemic exposures, for example, a $\text{PaO}_2/\text{FiO}_2 <50$ – 70 for several hours or days, would create substantial neuropsychological injury to justify early application of ECMO and the potential for other important long-term and potentially irreversible physical disabilities. We need detailed knowledge of how the components of ECMO therapy interact with the premorbid health status of our

patients to understand the relative harm to different end organs, to determine individualized acquired risk and to establish a hierarchy of different risk exposures. In addition, neurological outcomes may also be altered by the risk of bleeding, which is increased by ECMO because of the use of anticoagulant therapy but also by the thrombocytopenia that is frequently associated with prolonged use of ECMO. Depressive symptoms and memory complaints are still persistent at least 5 years after ICU discharge post-ARDS [16], but we do not know if ARDS patients requiring ECMO present with similar, improved or even more compromised outcomes.

In the present issue, Schmidt et al. [6] report various long-term outcomes in 67 ARDS patients who were successfully treated by ECMO. Comparing these to previously published series of ARDS patients, they conclude that SF-36 scores compare favorably with prior cohorts treated with conventional mechanical ventilation strategies. They also do not report higher rates of anxiety and depressive symptoms than other series. This is a timely and interesting contribution to our knowledge about long-term outcomes after ECMO, but some limitations remain and warrant further evaluation. It would be useful to compare ARDS survivors who did and did not receive ECMO using the same methodology, respecting the same oxygenation goals and using an adequate case mix with comparable age, cause of ARDS and comorbidities. However, currently there are very few studies evaluating long-term outcomes in ECMO patients [7, 17], and this study is a notable contribution.

The most commonly used tool to assess health-related quality of life (HRQOL) is the Short Form-36 (SF-36) general health survey. It is a generic questionnaire that

evaluates eight items from physical functioning to mental health. It was previously shown that surviving ARDS patients presented low SF-36 scores at 1 year [18–20]. Measuring only HRQOL does not give us the level of detail we need to understand morbidity or to help us construct rehabilitation programs to address specific limitations. HRQOL is too personal and subjective to give these detailed insights. Future work on ECMO outcomes would be strengthened by detailed physical, functional and neuropsychological outcome measures that help to inform the determinants of HRQOL in these patients.

One very important finding from the current study was the observation that low BMI was associated with poor outcome. We already understand that ICU-acquired weakness is an ubiquitous finding associated with severe critical illness and ARDS and that muscles undergo active proteolysis within hours of ICU admission. Premorbid muscle reserve is crucial to survival and restoring functional independence. One seminal contribution from this work may be the identification of low muscle mass as a key negative prognosticator that may be incorporated into more standardized ECMO eligibility criteria for future application and study.

Each of these discussion points needs to be answered prior to embracing ECMO as a standard treatment option and extending its indications to less hypoxemic patients. At the present time, it could be suggested to limit the ECMO indications to the most severely hypoxemic patients and/or when the criteria for protective mechanical ventilation are not fulfilled despite ventilator adjustments (Fig. 1). It is also important to evaluate the physical and neurocognitive impairments following ARDS treated by ECMO in order to understand whether

Fig. 1 Proposed algorithm for ECMO indications and areas of uncertainties

* $\text{PaO}_2/\text{FiO}_2 < 50$ in ECMO centers, close to 70 in non-ECMO centers requiring a mobile unit

there are treatment-specific repercussions that require directed therapy or whether morbidity is comparable to what is already described in the ARDS outcome literature and being addressed through the design of multimodal rehabilitation programs. This should be the next step. Finally, we should not forget the burden on caregivers associated with the recovery of patients with lung injury

[14]. There are important and prolonged psychological impairments sustained by family members, which may also have an important negative effect on patients' recovery and rehabilitative potential.

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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