VV-ECMO in severe COVID-19: multidimensional perspectives on the use of a complex treatment

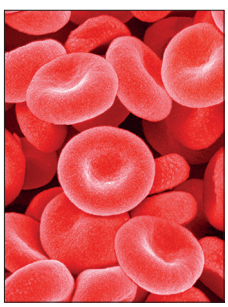
Accurately selecting patients who are likely to benefit from venovenous extracorporeal membrane oxygenation (VV-ECMO) for severe respiratory failure is crucial given its low availability, substantial invasiveness, associated complications, and high financial costs. Existing selection criteria are influenced by multidimensional factors, including local logistics and geographical variation in health-care provision, expert opinion, and data from observational studies and a single randomised controlled trial of ECMO for severe acute respiratory distress syndrome.[1,2] Evolving outcomes of patients on VV-ECMO during the COVID-19 pandemic showed that current selection criteria might not effectively guide decision making under unprecedented levels of health-care system strain, and accentuated the need for reliable prognostic models and better understanding of both short-term and long-term outcomes.[3] In this context, we read with interest the two studies by Roberto Lorusso and colleagues[4] and by Matthieu Schmidt and colleagues,[5] published in *The Lancet Respiratory Medicine*.

In their prospective, multicentre observational cohort study, Lorusso and colleagues[4] sought to identify associations between clinical characteristics at the time of VV-ECMO cannulation and in-hospital mortality, and to report 6-month functional outcomes in patients supported with VV-ECMO during the first wave of the COVID-19 pandemic (March–September, 2020). Data from 1215 patients were analysed using mixed Cox proportional hazards models. In-hospital mortality was 50% (602/1215 patients died), and 95% (549/577) of those with available follow-up data who survived to hospital discharge were still alive at 6 months. Factors associated with in-hospital mortality included being age 60 years or older, use of inotropes or vasopressors before initiation of VV-ECMO, and time from intubation to ECMO of 4 days or longer.

Schmidt and colleagues[5] did a retrospective, multicentre observational cohort study to describe patient characteristics and outcome at 90 days after the initiation of ECMO in patients with COVID-19, and to identify independent risk factors for mortality according to different SARS-CoV-2 variants during the first 2 years of the COVID-19 pandemic (Jan 1, 2020–Sept 30, 2021). Data from 1345 patients were analysed using multivariable Cox regression models. Crude mortality to day 90 was 42% (569/1345) for the overall cohort, and 43% (297/686) for patients infected with the wild-type variant, 39% (152/391) for those with the alpha variant, 40% (78/195) for those with the delta variant, and 58% (42/73) for patients with other variants (mainly beta and gamma). Independent predictors of mortality were age, immunocompromised status, longer time from intensive care unit admission to intubation, need for renal replacement therapy, use of vasopressors (Sequential Organ Failure Assessment haemodynamic component score ≥3), higher partial pressure of arterial carbon dioxide, and higher lactate concentration before cannulation. After adjusting for independent risk factors, infection with the delta variant was associated with higher likelihood of death in reference to the wild-type strain.

We commend the authors for endeavouring to analyse such extensive amounts of data from multicentre sources, with solid internal validity and strict methodological principles. We now have granular data about the short-term to long-term mortality of severe COVID-19 respiratory failure supported with ECMO at particular timepoints of the pandemic, evidence of the association of some prognostic factors with mortality, and confirmation of the potential effects of restricted deployment of VV-ECMO (ie, in patients with younger age, reduced duration of respiratory support before cannulation, low frequency of comorbidities, and severe hypoxaemia, treated at an experienced ECMO centre) on mortality. Moreover, findings of both studies are in concordance with the results of the recently published systematic review and meta-analysis by Tran and colleagues[6] of prognostic factors associated with mortality, and with evidence from other registries.[3]

However, the generalisability of the findings from these studies, their effect on current clinical practice, and their role in shaping our patient selection decision-making process might be limited. First, these results reflect the unprecedented situation in which ECMO centres found themselves as we plunged into a



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life-threatening pandemic. Second, the circumstances of the early waves of the COVID-19 pandemic—with uncertainty about the benefit of ECMO in patients with COVID-19, poor understanding of the disease, low resource availability, unavailability of crisis management protocols, and technology-driven optimism—are unlikely to be repeated in the near future. Third, evidence-based prognostication should not be used in isolation to define ECMO eligibility, since study results reflect prognosis only in those patients who were ultimately cannulated. Indeed, the results of these important studies are difficult to put into context, and deciding which patients should receive VV-ECMO (with or without resource scarcity) will still be made on a case-by-case basis, bearing in mind these and other identified prognostic factors.

It is increasingly recognised that patient-centred outcomes should not be limited to survival, and as health-care systems evolve to models of shared decision making, a turn towards multidimensional outcomes and away from mortality in isolation is warranted. In their study, Lorusso and colleagues[4] attempted to provide such information by reporting 6-month survival and functional outcomes, and demonstrated that a substantial proportion of patients had persistent dyspnoea, cardiac and neurocognitive symptoms, and overall low back-to-work rates (both full-time or part-time). Unfortunately, data collection was not standardised and did not include recommended assessment scales for disability, mood disorders, and cognitive dysfunction (functional independence measure, 6-min walk test, pulmonary function test, and Short Form-36 questionnaire),[7–9] increasing the risk of recall bias, missing data, and competing risks, among other confounding factors. Properly collecting these important outcomes requires, as the authors state, dedicated clinics and post-ECMO follow-up programmes, which are not widely implemented.

In conclusion, we welcome the valuable results of the studies by Lorusso and colleagues[4] and Schmidt and colleagues,[5] but we are still limited in our ability to effectively identify candidates for VV-ECMO and to provide patients, families, and other members of the health-care team with a precise expectation of what surviving VV-ECMO entails. We do not yet have a comprehensive understanding of the physical, cognitive, and psychological sequelae of critical illness and ECMO support, or the impact on caregivers. Standardised reporting of multidimensional outcomes in addition to survival will be a fundamental step to advance critical care and to adapt subsequent care transitions according to the opportunities and challenges provided by rapid and continuous medical and technological innovation.

We declare no competing interests.

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