Is Extracorporeal Membrane Oxygenation Saving Lives, or Are We Just Using It in Healthier Patients?

In this issue of RESPIRATORY CARE, Natt et al[1] present a retrospective review of a large administrative database, looking at trends in use of extracorporeal membrane oxygenation (ECMO) in adults with ARDS. As the authors note, ECMO utilization for adult ARDS has undoubtedly increased, and that trend is continuing. Adult respiratory ECMO cases reported to the Extracorporeal Life Support Organization have continued to increase over the past several years, subsequent to the period reported in the current investigation[2] (Fig. 1). In this investigation, Natt et al[1] demonstrate a concomitant decrease in both mortality and hospital stay in subjects receiving ECMO during the course of the study period (2008–2012). Although this association is clear and statistically significant, the reasons for improvements in outcome are unclear. These data are consistent with prior studies that demonstrate improved mortality with ECMO in recent years associated with reductions in mechanical complications and improved ECMO strategies.[3-5] However, it is possible that the improved mortality that is described in the current era may simply represent a larger number of patients placed on ECMO with lower severity of illness or increasing numbers of patients placed on ECMO for ARDS due to etiologies with high acuity but a well-documented higher likelihood of survival, such as viral pneumonia.[5,6] Unfortunately, none of these details are reported in this investigation.

The trend of decreased hospital stay is similarly difficult to fully assess without additional patient data. The Conventional Ventilatory Support versus Extracorporeal Membrane Oxygenation for Severe Adult Respiratory Failure (CESAR) randomized trial[7] suggested that there may be some benefit in long-term morbidity for patients with ARDS treated with ECMO, presumably due to reduced ventilator-induced lung injury allowing faster recovery of lung function and functional status. Some have hypothesized that earlier institution of ECMO, perhaps even to avoid intubation, may have even more profound benefits.[8] Although this strategy has been utilized in the pre-lung transplant patient population with benefits in both morbidity and mortality,[9-11] such an approach is unproven in the general ARDS population, and it remains unclear how patient selection and severity of illness in recent years have impacted outcomes in patients receiving ECMO.

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As with the vast majority of ECMO studies, there are significant limitations to the study by Natt et al.[1] Administrative databases such as the Healthcare Cost and Utilization Project-National Inpatient Sample database may be prone to errors in coding, and these databases rarely contain severity of illness data and therefore lack the ability to control for the many confounding factors that may affect outcome in these complex patients.[12,13] These data can provide some guidance, but clinicians continue to be limited to making conclusions regarding the utility of ECMO based on associations from uncontrolled, retrospective data collection.

In lieu of better data to direct ARDS management, providers will continue to struggle with not only patient selection, but also the ideal time to initiate ECMO in a patient with severe ARDS. Despite the clear benefits in some circumstances, it is important to recognize that ECMO is a supportive therapy only, and it does nothing to fix the underlying process. As such, other therapeutic strategies must be optimized to provide the best chance of survival in this most critical population of patients. Despite research into a host of other adjunct therapies for ARDS, the single strategy that has had the greatest impact on mortality remains lung-protective ventilation.[14] ECMO arguably represents the extreme example of lung protection, allowing often dramatic reductions in ventilator settings in patients with severe respiratory failure, and using this logic, ECMO should be applied before the onset of irreversible lung injury.

However, ECMO is not a benign therapy, and weighing the inherent risks against the potential benefit in any given patient is challenging. Ventilator-induced lung injury begins within hours of initiation of mechanical ventilation, and although irreversible injury may take days to weeks to develop,[5] this timing is probably dependent on any given patient's ventilator settings in conjunction with the underlying disease process, various comorbidities, and individualized inflammatory response. The risk-benefit ratio is

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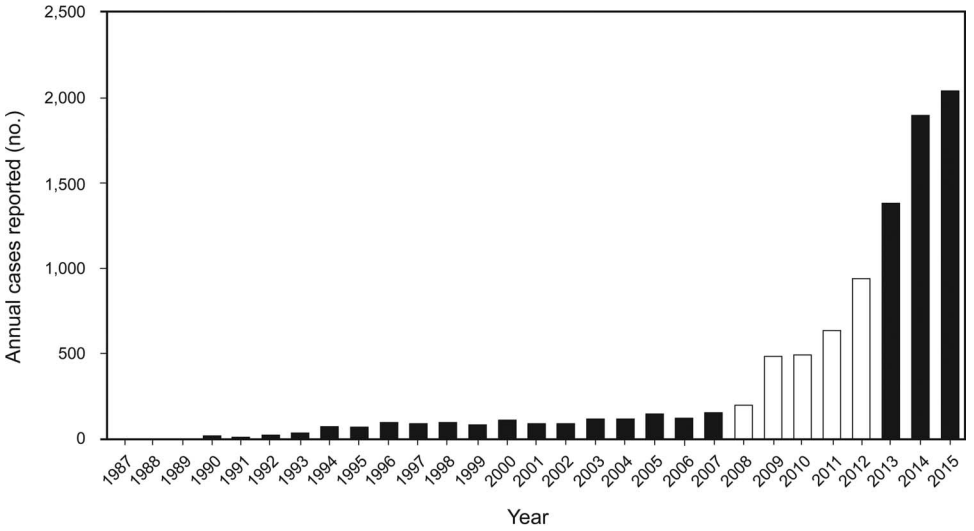

Fig. 1. Annual adult respiratory extracorporeal membrane oxygenation cases reported to the Extracorporeal Life Support Organization registry, with the years of the Natt et al study[1] highlighted in white.

further clouded by ongoing improvements in ECMO technology and strategies that reduce the risk of ECMO versus developments in other approaches to ARDS management that may reduce the benefit of ECMO compared with conventional therapy. It remains unclear whether other strategies with promise of therapeutic benefit in severe ARDS, such as prone positioning,[15] may provide superior outcomes to ECMO or whether their benefit may be further enhanced if coupled with ECMO. Given all of these unknowns, the need for well-designed randomized trials around ECMO use becomes even more important.

Epidemiologic studies such as this one by Natt et al[1] are important contributions to our knowledge and understanding of ECMO trends and the current state of clinical practice, and the authors should be applauded for a timely report during a time of exponential growth of this therapy. However, as was the case with the CESAR trial,[7] investigators need to continue to take positive steps toward attempting to address the question of how ECMO compares with optimal conventional therapies. Although a step in the right direction, CESAR has not adequately answered this question, and we look forward to the results of the new randomized trial of ECMO versus conventional therapy to hopefully provide some clarification regarding the utility of ECMO in this challenging population (ClinicalTrials.gov registration NCT01470703.) Clinicians and investigators need to go beyond descriptions of how we use ECMO and push for a thoughtful and more detailed investigation into true optimization of decision-making to guide the when and why of this complex therapy.

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