Extracorporeal Membrane Oxygenation in Adult Acute Respiratory Distress Syndrome

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KEYWORDS

- Extracorporeal membrane oxygenation
- Extracorporeal life support
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The role of extracorporeal membrane oxygenation (ECMO) in supporting refractory respiratory failure in adults continues to evolve. Interest in ECMO surged after reports of severe acute respiratory distress syndrome (ARDS) associated with the 2009 H1N1 pandemic viral infection.[1] As physicians struggled to treat young, previously healthy patients failing conventional therapy,[2] heightened media and Internet coverage drove the discussion of rescue measures into the public forum. Published systematic review[3] and pooled analyses[4,5] point out that high-quality experimental evidence available for guidance is limited. While the results of further randomized controlled trials are awaited,[6] considerable new experience with adult ECMO continues to accrue.

ECMO is supportive care and is not intended as a primary ARDS treatment; an artificial membrane lung and blood pump (a modified cardiopulmonary bypass circuit) provides gas exchange and ensures systemic perfusion to sustain the life of the patient when native heart and lung function cannot.[7] Continuous cardiopulmonary support stabilizes critical derangements of oxygenation and ventilation and allows additional time to continue to diagnose, treat, and allow recovery from the underlying cause of respiratory failure. During this period, typically days to weeks, further iatrogenic ventilator-induced lung injury can be avoided.

At its heart, ECMO is an invasive, complex, resource-intensive form of support. Safe delivery requires considerable institutional and caregiver commitment. Because of

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this, its use is advocated only in those patients believed to be at substantial risk of death. Nevertheless, as cardiac surgery and destination support of heart failure have become more commonplace, the personnel and devices required to provide prolonged support are now routinely deployed in many intensive care units (ICUs). The availability of simpler, compact support devices, combined with improved clinical management, has lowered the barriers to broader adoption of ECMO as a rescue therapy for refractory respiratory failure. This article reviews the current evidence supporting the use of extracorporeal support in refractory respiratory failure and discusses contemporary management of adult patients receiving ECMO.

REVIEW OF SUPPORTING EVIDENCE

In a recently published systematic review,[3] Mitchell and colleagues identified only 3 randomized controlled trials[8–10] and 3 cohort studies[11–13] evaluating ECMO in patients with acute respiratory failure. Meta-analysis of the randomized controlled trials revealed significant heterogeneity in risk of mortality, with the summary risk ratio 0.93 (95% confidence interval, 0.71–1.22); however, it was noted that the most recent trial showed a reduction in mortality and severe disability in patients randomized to receive ECMO. These trials are reviewed in the following sections, followed by discussion of additional available data.

Randomized Controlled Trials of ECMO Versus Conventional Ventilation

Interest in ECMO support of adult respiratory failure was stimulated after its successful use in a trauma patient.[14] By 1974, there were 20 case reports in adults and children. In response, the US National Institutes of Health sponsored a multicenter randomized trial comparing venoarterial (VA) ECMO with conventional mechanical ventilation in adult patients with severe acute respiratory failure.[8] At that time, the standard ECMO circuit was based on a servoregulated roller pump coupled to a high-resistance, thrombogenic membrane lung that required full anticoagulation, technology that is no longer in use. Patients were drawn from a larger cohort of 686 hypoxemic patients; 90 patients who met prespecified criteria for severity of illness (ECMO entry criteria, fast-entry: PaO_2 <50 mm Hg for >2 hours at inspired oxygen fraction [FiO_2] of 1.0 and positive end-expiratory pressure [PEEP] $\geq$5 cm H_2O; or slow-entry: after 48 hours of maximal medical therapy, PaO_2 <50 mm Hg for >12 hours at FiO_2 1.0 and PEEP $\geq$5 cm H_2O and Q_s/Q_T >30% of cardiac output) were enrolled. Overall survival of the larger group of patients was 34%[15]; the high-risk patients randomized to receive VA ECMO plus conventional ventilation and those receiving conventional ventilation alone had dismal survival rates of 8.7% and 9.5%.

In 1994, Morris and colleagues[9] reported a second single-center, randomized, controlled trial. Based on Gattinoni and colleagues[16] initial experience with extracorporeal CO_2 removal ($ECCO_2R$), 40 patients meeting the ECMO entry criteria were randomized to receive either $ECCO_2R$ with venovenous (VV) ECMO or pressure-controlled inverse ratio ventilation. No survival difference was noted between the 2 study arms (33% vs 42%); however, overall ARDS survival at that institution was significantly higher than in the previous decade.[17] Based on the negative results from these 2 trials, use of ECMO support for adult respiratory failure was largely restricted to a few centers.

Most recently, a pragmatic randomized controlled trial was conducted in the United Kingdom, following the design used in the previous UK study of ECMO in neonatal respiratory failure.[18] The Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR) trial[10] used different entry criteria (severe, but potentially