

# Management Strategies for Severe Respiratory Failure

## As Extracorporeal Membrane Oxygenation Is Being Considered

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### KEYWORDS

• Respiratory failure • ARDS • ECMO • Multiorgan failure • Mechanical ventilation

### KEY POINTS

- ARDS is an inflammatory disease that is perpetuated by ventilator-induced lung injury (VILI).
- ECMO offers an opportunity for ultraprotective lung protection and rest.
- Utility of ECMO is determined by disease cause and reversibility.
- Initiation of ECMO requires an organized, preplanned, coordinated effort.

### INTRODUCTION

The role of extracorporeal membrane oxygenation (ECMO) in the management of severe respiratory failure continues to evolve as increases in gained institutional experience and improvements in technology transform opinions regarding its utility.<sup>1-6</sup> Since the H1N1 influenza pandemic of 2009, the use of ECMO for severe respiratory failure has been on the rise.<sup>2,7,8</sup> This article facilitates the efficient coordination of care of the potential ECMO patient among the multidisciplinary members of the ECMO team. The exact parameters determining the ideal ECMO candidate have yet to be identified.<sup>9</sup> Numerous scoring systems exist to identify potential beneficiaries from this invasive technology.<sup>10-12</sup> There is no exact definition of severe respiratory failure; however, the Murray score, which is defined by oxygenation, positive end-expiratory pressure needs, compliance, and chest radiography, remains the gold standard.<sup>13</sup> There is

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no standard of care for the potential pre-ECMO patient with severe respiratory failure. Individual institutions should develop a multidisciplinary algorithm of management based on local resources, expertise, and opinions.<sup>1,14,15</sup> It is crucial for the team to set realistic expectations regarding ECMO candidacy and provide guidelines as to what levels of physiologic failure ECMO should be considered, initiated, or deemed futile.

Although early evidence from the late 1970s demonstrated no benefit in ECMO support, improvements in the understanding of acute respiratory distress syndrome (ARDS), ventilator management, and ECMO technology has been a game-changer.<sup>16–18</sup> Webb and Tierney<sup>19</sup> described lung inflammation and injury induced by the ventilator termed ventilator-induced lung injury (VILI). Understanding that ARDS is an inflammatory process is the key to overcoming it, and the subsequent multiorgan failure (MOF) that it causes.<sup>20</sup> Critical to the management of ARDS is to minimize continued lung injury.<sup>21,22</sup> The classic ARDS Network paper set the current gold standard of minimizing VILI by reducing volutrauma.<sup>23,24</sup> Additionally, multiple randomized studies support lower mortality with lower tidal volume ventilation.<sup>25</sup> The biologic plausibility for this may be lower cytokine levels, which decrease incidence of multiple organ system failure.<sup>26</sup> ARDS survivors show reductions in measured proinflammatory cytokines.<sup>27,28</sup> When ECMO is used, it is clear that ECMO itself is not the cause of improved cytokine levels; in fact, the initiation ECMO can initially increase inflammation.<sup>29</sup> ECMO does provide the opportunity for implementing a low stretch lung strategy and low driving pressure, which reduces VILI.<sup>15,17,30–32</sup> The reduction of high fractional inspired oxygen ( $F_{iO_2}$ ) provides another mechanism of ECMO benefit.<sup>33,34</sup> The basic premise of ECMO support is that it provides an opportunity for lung rest in the setting of ARDS.<sup>17,31,35</sup> Overall, ECMO serves as a means to reduce VILI, which can worsen ARDS.<sup>20,36,37</sup> The idea of “lung stress” is an emerging concept in mechanical ventilation in ARDS. Increases in lung stress as measured by driving pressure (plateau pressure minus positive end-expiratory pressure) have been associated with worse outcomes in ARDS.<sup>38</sup> Driving pressures of 15 cm H<sub>2</sub>O or higher were associated with poor outcomes and may identify a subset of patients for whom ECMO may be indicated. Serpa Neto and colleagues<sup>39</sup> studied outcomes of ECMO based on ventilator settings and found driving pressure to be the only ventilator setting associated with hospital mortality.

When to initiate ECMO as a means to prevent VILI and provide lung rest is unclear.<sup>40,41</sup> Early ventilator trauma can be identified in pre-ARDS, and strategies to reduce early cytokine release to avoid unbridled inflammation have led to a belief that initiation of ECMO after 7 days is not indicated.<sup>31,42,43</sup> Proponents of early ECMO believe the complication and severity of MOF is mitigated by early cannulation; however, no randomized, prospective human studies exist to compare timing of cannulation.<sup>44–46</sup> An observational study demonstrated that early cannulation led to a risk reduction of death, but a longer length of hospital stay. A small sheep study in ARDS induced by smoke failed to show advantage of early ECMO.<sup>47</sup> It is known that organ failure can recover on ECMO, but whether early ECMO prevents MOF is unclear.<sup>48</sup> However, it is clear that prolonged mechanical ventilation pre-ECMO does have worse outcomes.<sup>35,49,50</sup> Prankoff and colleagues conducted a retrospective study that exhibited that mortality correlated with duration of time in respiratory failure precannulation. The CESAR trial revealed that a coordinated effort of identification of ARDS patients and transfer to centers that are ECMO-capable improves outcomes.<sup>43</sup> This benefit likely extended beyond simply initiating patients on ECMO, because centers with high volume of ARDS and ECMO capabilities have improved outcomes.<sup>6,51</sup>

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