

## A Step Up for Extracorporeal Membrane Oxygenation: Active Rehabilitation

Extracorporeal membrane oxygenation (ECMO) has been used in an increasing number of centers as a bridge to lung transplant.<sup>1-4</sup> It is recognized that as the lungs fail, invasive mechanical ventilation may not fulfill the optimal goals as a bridge to transplant. There have now been several international reports of ECMO as a successful bridge to transplant in patients who are awake and non-ventilated ("awake ECMO"). There is sound physiological rationale to minimize both mechanical ventilation and sedation in these cohorts, particularly when the waiting times for lung transplantation are increasing. In fact, invasive mechanical ventilation is potentially associated with ventilator-induced lung injury,<sup>5,6</sup> ventilator-associated pneumonia, and ICU acquired weakness<sup>7,8</sup> which may reduce the likelihood of transplant success and survival.<sup>9</sup> Overall, outcomes following lung transplantation in patients bridged with extracorporeal life support, including ECMO, have been variable, depending on the patients, their indication for transplantation, and the configuration and duration of extracorporeal support.<sup>10-14</sup>

The main benefits of awake ECMO are that the patient can eat, drink, communicate, *and* participate in active rehabilitation, which may be an important predictor of outcome, as reported in this issue by Rehder et al.<sup>15</sup> In theory, early use of awake ECMO may result in more physically and physiologically stable patients, as compared to those receiving invasive mechanical ventilation at the time of lung transplantation, which may translate into improved post-transplant outcomes. Indeed, some investigators have cautioned that the use of awake ECMO may lower the risk profile of recipients, resulting in a lower priority on the waiting list.<sup>12</sup>

In the largest case series to date, Fuehner and colleagues reported data from a retrospective single center analysis of 26 patients receiving awake ECMO, compared to a historical control group of 34 patients receiving conventional mechanical ventilation.<sup>2</sup> Survival at 6 months after lung transplant was 80% in the awake ECMO group, compared to 50% in the mechanical ventilation group. Of note, the survival rate of the awake ECMO group decreased to 43% when secondary intubation became necessary, highlighting the importance of careful patient selection.

In this issue of the Journal, Rehder and colleagues take the management of awake ECMO one step further and include

active rehabilitation. They report unique data from a case series of 9 consecutive patients bridged to lung transplant with ECMO at a single tertiary center, comparing 5 patients who received awake ECMO, active rehabilitation, and ambulation pre-transplant to 4 patients who received ECMO with sedation and mechanical ventilation and without active rehabilitation.<sup>15</sup> While the study in itself was a small, retrospective case series, it helps to build a stronger case for awake and ambulatory ECMO as a safe and feasible option for pre-transplant rehabilitation as a bridge to transplant and recovery.

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Few centers that have utilized awake ECMO have reported specific rehabilitation exercises undertaken by their patients. The Table summarizes the available data on rehabilitation during awake ECMO.

Rehder et al report that all patients managed with awake ECMO pre-transplant mobilized within 5 days, and 3 patients within 48 hours of ECMO cannulation. Four of the patients in the active rehabilitation group ambulated on ECMO, and one patient participated in resistance exercises and sitting balance exercises over the edge of the bed prior to transplant. They had increased duration of mechanical ventilation and ECMO pre-transplant, possibly due to delayed listing for transplant during the rehabilitation process. All patients in the active rehabilitation group survived to 1-year follow-up, and they had reduced stay in both ICU and hospital. These 1-year outcomes for bridge to transplant are comparable to recent studies (range for survival 74–96%).<sup>10,12,17,18</sup>

Safety considerations for the use of awake ECMO include careful patient selection, early cannulation with ECMO, using a single cannulation site in the upper body (ie, internal jugular or subclavian vein) to allow for maximal mobility, and a multidisciplinary effort. Importantly, the ability to use a single, dual-lumen cannula in the upper body for extracorporeal life support may be limited by patient size and/or flow rate required to provide adequate gas exchange support.<sup>19</sup> Persistent hypoxemia despite maximal flow with a single dual-lumen cannula may necessitate an additional venous drainage cannula (eg, femoral vein), limiting the safety and feasibility of awake

Table. Rehabilitation During Awake ECMO

First Author	Year	Awake ECMO no.	Age y	Primary Diagnosis Cystic Fibrosis no.	ECMO Duration d	Ambulation as Rehabilitation no.	ICU Stay d	Survived to Transplant %
Rehder <sup>15</sup>	2013	5	28	4	8	4	27	100
Hoopes <sup>12</sup>	2013	28	45	7	14	19	31	100
Fuehner <sup>2</sup>	2012	26	44	5	9	0	18	77
Chierichetti <sup>1</sup>	2012	7	32	ND	12	0	29	100
Hayes <sup>16</sup>	2012	4	28	4	8	4	ND	100
Garcia <sup>4</sup>	2011	10	45	0	20	4	28	67

Values are mean, except for survived to transplant.

ECMO = extracorporeal membrane oxygenation

ND = no data available

ECMO. Other studies have reported successful rehabilitation with treadmill walking,<sup>16</sup> and transfers from bed to chair.<sup>4</sup>

Early mobilization may be an important intervention to reduce the negative side effects of intubation, mechanical ventilation, and bed rest.<sup>20</sup> It may be particularly important in the cohort of patients who are critically ill pre-transplant and require ECMO as a bridge to transplant with an uncertain waiting period for donor lungs. There may also be potential for the use of extracorporeal life support in other patient populations to facilitate rehabilitation and prevent intubation, such as severe respiratory failure with ARDS or exacerbations of COPD.<sup>4</sup> Indeed, recent case series have demonstrated the feasibility of using low-flow extracorporeal carbon dioxide removal to obviate the need for invasive mechanical ventilation in hypercapnic COPD patients failing noninvasive ventilation.<sup>21,22</sup> However, many of the patients in these studies had femoral cannulation, limiting the ability to provide more intensive rehabilitation, which may have synergistic benefits when coupled with reduced analgesedation off invasive mechanical ventilation.

This is an area of critical care that is difficult to study using randomized controlled trials, due to small available numbers of patients and rapidly evolving medical practice; however, the need for validation of this study is clear. Further studies are required to confirm that rehabilitation during extracorporeal life support is safe and feasible. These studies will need to describe the most effective type of rehabilitation exercises to maximize pa-

tient-important outcomes, with particular emphasis on investigating the long-term effects of awake extracorporeal life support on physical function, health related quality of life, and return to work.<sup>23</sup>

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The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.02606

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