International Survey on Mechanical Ventilation During Extracorporeal Membrane Oxygenation

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The optimal ventilation strategy for patients on extracorporeal membrane oxygenation (ECMO) remains uncertain. This survey reports current mechanical ventilation strategies adopted by ECMO centers worldwide. An international, multicenter, cross-sectional survey was conducted anonymously through an internet-based tool. Participants from North America, Europe, Asia, and Oceania were recruited from the extracorporeal life support organization (ELSO) directory. Responses were received from 48 adult ECMO centers (response rate 10.6%). Half of these had dedicated ventilation protocols for ECMO support. Pressure-controlled ventilation was the preferred initial ventilation mode for both venovenous ECMO (VV-ECMO) (60%) and venoarterial ECMO (VA-ECMO) (34%). In VV-ECMO, the primary goal was lung rest (93%), with rescue therapies commonly employed, especially neuromuscular blockade (93%) and prone positioning (74%). Spontaneous ventilation was typically introduced after signs of pulmonary recovery, with few centers using it as the initial mode (7%). A quarter of centers stopped sedation within 3 days after ECMO initiation. Ventilation strategies during VA-ECMO focused less on lung-protective goals and transitioned to spontaneous ventilation earlier. Ventilation strategies during ECMO support differ considerably. Controlled ventilation is predominantly used initially to provide lung rest, often facilitated by sedation and neuromuscular blockade. Few centers apply "awake ECMO" early during ECMO support, some utilizing partial neuromuscular blockade. ***ASAIO Journal*** **2024; 70:300–304**

Key Words: ECMO, acute respiratory distress syndrome, mechanical ventilation

Background

Venovenous (VV) and venoarterial extracorporeal membrane oxygenation (VA-ECMO) support are potentially lifesaving therapies for respiratory and cardiac failure after conventional therapies have failed. Despite best efforts, even on ECMO, mortality remains high, and optimal care strategies during ECMO support remain unclear in various areas. Mechanical ventilation strategies during ECMO support are one of these areas. Acute respiratory distress syndrome (ARDS) is a condition characterized by respiratory failure that may warrant using ECMO support to provide adequate gas exchange, whereas minimizing ventilator-induced lung injury (VILI) risk. Avoiding injurious forces of mechanical ventilation using low tidal volumes and subsequent low driving pressure (ΔP) are principles of lung-protective ventilation.[1] In ARDS, lower ΔP is independently associated with increased survival.[2,3] Extracorporeal membrane oxygenation is an invasive therapy, but its deployment allows the ΔP to be set at lower levels, whereas maintaining adequate oxygenation and ventilation to give the lungs time to rest and recover.

An increasing number of centers aim for "awake ECMO," allowing spontaneous mechanical ventilation or even endotracheal extubation early after initiation of ECMO support.[6,7,9–12]

All taken together, the optimal mechanical ventilation strategy during ECMO support is unclear. Previous surveys of mechanical ventilation have shown ventilator settings and subsequent sedation strategies differ widely between centers and that only 3–16% of centers aim for early spontaneous ventilation after initiating ECMO support. Therefore, this survey aimed to describe current ventilation strategies and the subsequent use of sedation and rescue therapies during ECMO support.[13,14]

Materials and Methods

We conducted a cross-sectional, semistructured international survey on mechanical ventilation practices during ECMO that was e-mailed to 454 ECMO centers in Northern America, Europe, Asia, and Oceania. The ELSO directory was used to retrieve each center's e-mail addresses of the ECMO program directors. We included centers providing either or both VV-ECMO and VA-ECMO support in adult patients only. The survey was conducted through an internet-based tool (Survey Monkey, Palo Alto, CA, Supplemental Digital Content, http://links.lww.com/ASAIO/B155).

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Two intensivists and a PhD-student developed this survey after an extensive review of the available literature. The e-mail to potential respondents consisted of a cover letter explaining the purpose of the survey and a hyperlink to the survey tool. We sent one follow-up reminder 3 weeks after the first invitation.

The final survey contained 34 targeted questions about demographics, mechanical ventilation mode and settings, rescue therapies, sedative use, and support ventilation during ECMO support. The survey was divided into VV- and VA-ECMO parts. Skip logic was used to ask relevant questions only. The survey was not publicly available. After completion, no reentry was allowed. Responses were exported anonymously from the survey tool 1 month after the reminder e-mail. Surveys with no answers were removed. The number of respondents to each question was recorded, and each question was analyzed separately. The answers were combined in case of more than one response from a single center. Demographic and qualitative data (multiple choice questions) were expressed as frequencies and percentages (n, %). Qualitative data (open questions) were categorized when possible. If not, we described the answers.

Results

Of all the surveys sent, we received responses from 48 centers in 18 countries (response rate 10.6%) (Table 1); 30 (63%) from Europe, 15 (31%) from North America, six (13%) from Oceania, and one (2%) from Asia. Of these responding centers, 47 (98%) completed the relevant questions. Most respondents were intensivists (n = 39, 81%) and practiced in a university medical center (n = 39, 81%).

Venovenous Extracorporeal Membrane Oxygenation

Demographics. Table 1 summarizes the general demographics of the centers. Most centers had a VV-ECMO load of 10–29 per annum (n = 30, 64%). Half of all centers (n = 25, 52%) had a dedicated protocol available regarding mechanical ventilation during VV-ECMO support.

Ventilator mode and settings. Most centers (n = 40, 93%) considered lung rest as the primary goal of mechanical ventilation during VV-ECMO support. This was reflected by the most preferred initial ventilation mode, which was pressure-controlled ventilation (n = 26, 60%), volume-controlled ventilation was the second most used initial ventilation mode (n = 7, 16%), and only three centers (7%) stated that pressure support was their preferred initial ventilation mode. In line with the goal of lung rest were the preferred ventilator settings as shown in Table 2, describing characteristics of mechanical ventilation settings during ECMO support: a targeted positive end-expiratory pressure (PEEP) of 10 cm H_2O (n = 18, 44%), ΔP of 10 cm H_2O (n = 14, 39%), plateau pressure lower than 20 cm H_2O (n = 14, 41%), tidal volumes lower than 4 ml/kg (n = 10, 30%) and respiratory rate targeted equal or below 10 breaths per minute (n = 21, 54%). None of the centers targeted an initial PEEP or ΔP above 15 cm H_2O, plateau pressure above 30 cm H_2O, tidal volumes, and respiratory rate of more than 8 ml/kg and 20 breaths/minute.

Pulmonary rescue therapies and monitoring. Neuromuscular blockade was used by most respondents (n = 40, 93%). Most

Table 1. Summary of Survey Mechanical Ventilation During ECMO

General Demographics (n)	n (%)
Role (48)	
Intensivist	39 (81)
Nurse	1 (2)
Anesthesiologist	2 (4)
Other	6 (13)
Setting (48)	
Academic	39 (82)
Regional	9 (19)
Continent (48)	
Europe	30 (63)
Oceania	6 (13)
North America	15 (31)
Asia	1 (2)
Ventilation protocol, yes (48)	25 (52)
VV-ECMO	
Goal (43)	
Lung rest	40 (93)
Lung-recruitment	1 (2)
Other	2 (5)
Initial ventilation mode (43)	
PC	26 (61)
VC	7 (16)
PRVC	3 (7)
PS	3 (7)
Nonintubated	1 (2)
Varies on physician	2 (5)
Other	1 (2)
Rescue therapies (43)	
Neuromuscular blockade	40 (93)
Prone positioning	32 (74)
Beta-blockade	18 (42)
Partial NMB use, yes (39)	5 (13)
Stop sedatives (43)	
As soon as possible	4 (9)
After 3 days	5 (12)
Ventilator support diminishes	15 (35)
Compliance increase	15 (35)
Never during ECMO run	2 (5)
Other	2 (5)
Restart sedatives (43)	
Ventilator dyssynchrony	20 (47)
High TV/upper DP	13 (30)
Persistent hypoxemia	7 (16)
Other	3 (7)
Permanently stop sedative (43)	
When pulmonary recovery	24 (56)
Other	19 (44)
Tracheostomy (43)	41 (93)
Wean, ECMO first (43)	34 (79)
VA-ECMO	
Different strategy than VV-ECMO, yes (41)	30 (73)
Initial ventilation mode (29)	
PC	10 (35)
VC	7 (24)
PRVC	7 (24)
PS	0
Nonintubated	0
Varies on physician	2 (7)
Other	1 (2)
Stop sedatives (29)	
Immediate after starting ECMO	7 (24)
Hemodynamic stability	19 (66)
Other	3 (10)
Tracheostomy, yes (41)	33 (81)

DP, driving pressure; ECMO, extracorporeal membrane oxygenation; NMB, neuromuscular blockade; PC, pressure-controlled; PRVC, pressure released volume-controlled; PS, pressure support; TV, tidal volume; VA, venoarterial; VC, volume-controlled; VV, venovenous.

Table 2. Mechanical Ventilation Setting During ECMO Support

	VV-ECMO n (%)	VA-ECMO n (%)(%)
PEEP (cm H_2O)	41	28
<10	7 (17%)	15 (54%)
10	18 (44%)	8 (29%)
10–15	10 (26%)	3 (11%)
>15	0	1 (4%)
Based on the esophagus balloon	3 (7%)	0
Based on the pre-ECMO level	2 (5%)	0
Driving pressure (cm H_2O)	36	23
<104	7 (19%)	0
10	14 (39%)	5 (22%)
10–15	13 (36.1%)	15 (65%)
>15	0	1 (4%)
Based on the esophagus balloon	2 (6%)	0
Not targeted	0	2 (9%)
Plateau pressure (cm H_2O)	34	22
<20	14 (41%)	2 (9%)
20–25	13 (38%)	11 (50%)
25–30	5 (15%)	7 (32%)
Not targeted	2 (6%)	2 (9%)
Tidal volume (ml/kg)	33	26
<4	10 (30%)	0
4–5	8 (24%)	3 (12%)
<6	9 (27%)	16 (62%)
>6	2 (6%)	6 (23%)
Not targeted	4 (12%)	1 (4%)
Respiratory rate/minute	39	25
Spontaneous	1 (3%)	2 (8%)
<10	21 (54%)	6 (24%)
10–15	12 (31%)	13 (52%)
15–20	5 (13%)	4 (16%)

ECMO, extracorporeal membrane oxygenation; PEEP, positive end-expiratory pressure; VA, venoarterial; VV, venovenous.

centers aim to stop neuromuscular blockade as soon as possible. Partial neuromuscular blockade was used in five centers (13%) to facilitate lung-protective spontaneous ventilation, whereas maintaining diaphragm activity. Prone positioning was used by (n = 32) 74% of the centers during VV-ECMO support. An esophagus balloon was used to titrate PEEP by three centers (7%) and ΔP by two centers (6%).

Sedatives. Table 3 provides an overview of the most used sedatives. The top three sedatives, whether or not in combination, were propofol (74%), midazolam (50%), and α-2 adrenergic receptor agonists (clonidine or dexmedetomidine) (48%).

Discontinuing of sedatives. Most centers discontinued sedation and started spontaneous ventilation only when there were signs of pulmonary recovery (n = 30, 70%). Almost one-fourth of the centers attempted to switch to spontaneous ventilation within 3 days after initiating ECMO. The main reasons for restarting controlled ventilation and sedation were high tidal volumes or ΔP (n = 13, 30%) and patient-ventilator dyssynchrony (n = 20, 47%). After the restart of sedatives, more than two-thirds performed daily wake-up calls. Sedatives were permanently stopped in case of pulmonary recovery (n = 24, 56%) when tolerated in terms of hypoxia, agitation, work of breathing, and dyssynchrony (n = 17, 40%). Only two centers declared that they never stopped sedatives or used spontaneous ventilation unless weaning from ECMO was started.

Weaning practices. Almost every center performed tracheostomy in patients supported with VV-ECMO (n = 41, 93%), and one-third routinely placed a tracheostomy after an expected specified duration, usually 2 weeks, of mechanical ventilation (n = 15, 35%).

Most centers (n = 39, 79%) chose to wean and discontinue ECMO before mechanical ventilation.

Table 3. Top Three Sedative Use During ECMO

	VV-ECMO n = 42 (%)	VA-ECMO n = 29 (%)
Clonidine/dexmedetomidine	20 (48)	13 (45)
Fentanyl	16 (38)	8 (28)
Ketamine	4 (10)	2 (7)
Midazolam	21 (50)	16 (55)
Morphine	10 (24)	6 (21)
Propofol	31 (74)	20 (69)
Other	11 (26)	9 (31)
None	1 (2)	4 (14)

ECMO, extracorporeal membrane oxygenation; VA: venoarterial; VV, venovenous.

Venoarterial Extracorporeal Membrane Oxygenation

Demographics. The average VA-ECMO load was 10–29 per annum (n = 20, 48%). Nearly three-quarters of all respondents indicated that they used different ventilation strategies in patients supported with VA-ECMO for a cardiac indication depending on respiratory compromise.

Ventilator mode and settings. Lung rest was barely used during VA-ECMO support (Table 1). Initial ventilator settings were partly different from those reported during VV-ECMO. In general, targeted PEEP was lower, and targeted ΔP, tidal volumes, and respiratory rate were higher (Table 2).

Sedatives. The sedatives used were comparable to those used in patients supported with VV-ECMO (Table 3). Sedatives were stopped, and support ventilation was started directly after ECMO initiation (n = 7, 24%) or as soon as hemodynamic stability was achieved (n = 19, 66%). The reason for restarting sedatives was less focused on ventilatory problems but more based on hemodynamic instability (n = 18, 62%). After restarting sedation, almost every respondent performed a daily interruption of sedation when hemodynamically allowed.

Weaning practices. Tracheostomy was performed less in patients supported with VA-ECMO (n = 33, 80%). Like in VV-ECMO patients, a third of the centers performed a tracheostomy routinely when a mechanical ventilation duration of more than 2 weeks was expected.

Discussion

The major finding of our survey was that most centers preferred controlled mechanical ventilation as the initial mode in the early phase after ECMO start. Despite its potential benefits, awake ECMO was not widely adopted.[6,10–12,15] However, spontaneous ventilation was increasingly used as the initial ventilation mode or applied early, within 3 days after start of ECMO, compared to previously conducted studies.[10–12] Nevertheless, these studies included only VV-ECMO. The preferred initial ventilator settings during VV-ECMO support ranged from lung-protective to ultra-lung-protective.

Two studies showed that although ultraprotective lung ventilation during VV-ECMO support was largely adopted, mechanical ventilator settings and mechanical power during the first 2 days of ECMO support did not impact the patient's prognosis.[6,7] These findings raise important questions about optimal ventilation strategies for patients on ECMO.

Mechanical ventilation strategies during VA-ECMO were less lung-protective, and spontaneous ventilation was used earlier compared to VV-ECMO. The transition to spontaneous ventilation could be divided into two strategies: 1) switch as soon as possible to spontaneous ventilation after starting ECMO, or 2) wait for the lung to recover before switching to spontaneous ventilation.

Considering that controlled ventilation can contribute to diaphragmatic atrophy and injury, which is linked to unfavorable outcomes, the application of spontaneous breathing during invasive mechanical ventilation also raises questions. So far, studies focusing on applying spontaneous ventilation modes during ECMO are underrepresented. Limited literature shows the safety and benefits of early spontaneous or nonintubated ventilation in patients supported with VV- and VA-ECMO. Potential benefits include maintaining respiratory muscle function, decreased hospital length of stay, and increased survival. Potential adverse effects are ventilation dyssynchrony, patient discomfort, and possibly self-inflicted lung injury.[8]

We found that the vast majority of the centers used controlled ventilation (pressure or volume-controlled) as the preferred initial ventilation mode, which makes it possible to strictly control the ΔP and assumingly avoid VILI.[15] This was in agreement with earlier conducted studies.[13,14,16] To achieve lung rest, patients usually require sedation and neuromuscular blockade. The high rate of neuromuscular blockade was consistent with other studies.[2,13] In general, interrupting sedation or no sedation with spontaneous breathing is a beneficial strategy in critically ill patients.[17] In most patients on ECMO as a bridge to transplant or patients with chronic obstructive pulmonary disease, spontaneous breathing was possible. However, in patients on ECMO with ARDS, it was only possible in less than 30%.[18] Crotti *et al.*[18] postulated that the different underlying pathophysiological mechanisms might account for this finding. As an increased work of breathing was a primary reason for an unsuccessful switch to spontaneous ventilation, some centers now use partial neuromuscular blockade, which is a new phenomenon compared with previous surveys. Partial neuromuscular blockade may facilitate lung-protective spontaneous ventilation without inducing self-inflicting lung injury while maintaining diaphragm activity. This potentially allows a safe compromise between the risks and benefits of "awake ECMO" but requires careful and repeated monitoring of diaphragmatic function.[19] More studies are needed to determine the safety and efficacy of this strategy.

Most centers (79%) decannulate from ECMO before extubation, per the 2019 EuroELSO weaning survey.[20] However, ECMO reduces breathing effort sufficiently in extubated patients,[21] and therefore, extubation before decannulation seems safe and may be beneficial in selected cases.[22–24]

Prone positioning was used to a greater extent in our study compared to previously reported studies.[13,14,16] A possible explanation could be that the study from Camporota *et al.*[13] contains data from before the proning severe ARDS patients (PROSEVA) trial that showed that prone positioning was beneficial, as the authors already stated.[25] During the coronavirus disease 2019 (COVID-19) pandemic, clinicians widely adopted prone positioning; therefore, expertise in the maneuver has increased, which may lead to the earlier application of this rescue therapy during ECMO support. Moreover, recent studies have shown that prone positioning during ECMO improves gas exchange and may reduce hospital mortality.[26–29] We included beta-blockers as possible respiratory rescue therapy during ECMO support because we suspect these were still widely used. However, one should note there is no physiologic background to use them during ECMO support. Beta-blockers reduce cardiac output; this decreases the amount of oxygenation provided by the native lung, which consequently leads to an apparent increase in arterial oxygenation. However, this increase is misleading and appears at the expense of a reduction in venous oxygenation and, thus, organ perfusion and oxygenation.[30]

Our survey has several limitations, of which a low response rate is the most obvious. An explanation for this might be that e-mails did not reach the recipient due to spam filters or incorrect e-mail addresses. Surveys can be subject to different types of bias. Responders might differ in their practices from nonresponders, considering that most respondents work in university or academic hospitals. Most centers who completed the survey were from Europe and the United States, and only a minority from other parts of the world. Another limitation is that, generally, a survey represents what doctors think they are doing, which may not always reflect what they actually do. When no protocol was available, answers might reflect the individual doctor's view rather than the view of the ECMO center. Also, we have no information about the outcome of the different mechanical ventilation strategies. Finally, this survey did not categorize practices during specific indications for ECMO, which could affect the results, particularly during VA-ECMO support in patients without respiratory compromise. Strengths of this survey were the high completion rate of questions if the survey was opened, the possibility to use open answers to explore this subject and generate hypotheses for further study, and the distinction between VA- and VV-ECMO support.

Conclusions

Mechanical ventilation in patients supported with ECMO varies between centers. Controlled mechanical ventilation was the preferred initial mode in almost all centers to provide lung rest during VV-ECMO. Sedation and neuromuscular blockade were widely used during ECMO support to achieve this. A small number of centers apply "awake ECMO" early in the course of ECMO support, some with the use of partial neuromuscular blockade.

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