

# Use of extracorporeal membranous oxygenation in the management of refractory trauma-related severe acute respiratory distress syndrome: a national survey of the Eastern Association for the Surgery of Trauma

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## ABSTRACT

**Objective** To report results of a national survey of provider attitudes, observations, and opinions regarding the use of extracorporeal membranous oxygenation (ECMO) to manage severe acute respiratory distress syndrome (ARDS) in trauma patients.

**Design** A survey was created to query providers on the use of ECMO in trauma, as well as general management principals related to care of the patient with refractory hypoxic respiratory failure. The survey was sent to all members of Eastern Association for the Surgery of Trauma (EAST). Once completed, the survey was returned to the University of Alabama at Birmingham and results were analyzed.

**Setting/patients** Trauma patients with refractory ARDS.

**Interventions** None.

**Measurements and main results** Respondents were from 37 states, the District of Columbia, and Puerto Rico. 56.9% reported institutional ECMO capabilities, but only 45.2% reported using ECMO for trauma patients. Most respondents (90.2%) reported ECMO use in less than or equal to five trauma patients per year. 20.9% think there is not enough data to support its use in trauma but only 4.7% would absolutely not consider ECMO use for trauma patients. Ranking the preferred modality of treatments for refractory ARDS from most to least preferable is as follows: airway pressure release ventilation, bilevel ventilation, paralysis, prone positioning, inhaled nitric oxide, epoprostenol, high-frequency oscillatory ventilation, corticosteroids, surfactant.

**Conclusions** ARDS has a high mortality among trauma patients. Despite its utility in treating severe ARDS and other pulmonary disease processes, ECMO has not been universally embraced by the trauma community. There are an increasing number of studies that suggest that ECMO is a safe and viable treatment option for trauma patients with ARDS. Based on the results of this survey, ECMO use remains limited by trauma providers that care for patients with refractory hypoxic respiratory failure and ARDS, likely due to a combination of knowledge gaps and lack of access to ECMO.

**Level of evidence** Level V.

## INTRODUCTION

Trauma remains a leading cause of mortality worldwide.<sup>1</sup> Complications associated with trauma such as systemic inflammation, pneumonia, and sepsis frequently will give rise to subsequent respiratory failure. It has been estimated from cross-sectional studies that 5%–20% of all mechanically ventilated patients will develop acute respiratory distress syndrome (ARDS) with the majority demonstrating moderate to severe forms of the disease.<sup>2,3</sup> Severe ARDS in the trauma patient continues to have a reported mortality rate as high as 60% despite appropriate and aggressive supportive care.<sup>4</sup> Despite widespread acknowledgement that excessive plateau pressures contribute to associated lung injury, variable implementation of ventilator strategies promoting lung protective ventilation may exist.<sup>5,6</sup> Furthermore, evidence to support the use of different advanced therapies frequently used in ARDS such as airway pressure release ventilation (APRV), inhaled nitric oxide (NO), extracorporeal membrane oxygenation (ECMO), and high frequency oscillatory ventilation (HFOV) is deficient. Currently, a widely accepted standardized approach to patients with severe ARDS does not exist in the form of guidelines.

Use of ECMO as a temporary rescue for trauma patients with hypoxic respiratory failure has been reported in multiple case reports and small case series during the last 15 years. Despite the associated risks of prior massive blood loss, coagulopathy, coexisting solid organ or traumatic brain injury, trauma patients placed on ECMO (with or without systemic anticoagulation) have improved survival with minimal complications or long-term morbidity.<sup>7–15</sup> However, consensus among trauma surgeons and intensivists regarding the use of ECMO for this patient group is lacking. This study seeks to ascertain current opinions from trauma providers regarding ECMO use for trauma patients with severe ARDS in the USA. In addition, we intend to obtain information on the current practices of surgical intensivists regarding the use of different therapies for severe ARDS, including the use of ECMO.

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## MATERIALS AND METHODS

### Severe ARDS definition

For purposes of this research survey, severe ARDS was defined using the Berlin definition of arterial oxygen pressure ( $\text{PaO}_2$ )/fractional inspired oxygen ( $\text{FiO}_2$ )  $<100\text{ mm Hg}$  with at least  $5\text{ cm H}_2\text{O}$  positive end-expiratory pressure (PEEP) being applied and having bilateral pulmonary infiltrates not totally due to pulmonary edema or cardiac failure. This definition was provided to all participants of the study.

### Survey development

After obtaining institutional review board approval at the University of Alabama at Birmingham, the survey was developed by PLB. The initial survey instrument was a 26-question inquiry using iterative process. It was then reviewed by JDK, DAR, and EDS for clarity. Changes in phrasing were then performed along with the addition of some answer choices for certain questions.

### Pretesting and pilot survey

Once the survey had been developed, a validation process was undertaken by pretesting the survey. This validation methodology is recommended to assess participants' understanding of items and whether items appear to tap the construct of interest.<sup>16,17</sup> The aim was for respondents to understand the pragmatic meaning of the questions, assess question ambiguity, ease of use, and adequacy of response categories to reduce response error. The survey was pretested by a small group of faculty trauma surgeons at the University of Alabama at Birmingham. An internet-based survey platform (Research Electronic Data Capture (REDCaps)) was used to distribute the pretest. Once the pretest had been completed, the respondents were interviewed as to their interpretation of specific survey items and the decision processes used to answer questions to reduce response error and increase construct validity. Based on the responses and comments received, modifications were made to add additional answer choices for several questions.

Prior to the national launch of the refined survey, the Eastern Association for the Surgery of Trauma (EAST) Research and Scholarship Section reviewed the refined survey instrument as the national launch was based on the EAST membership email roster. The scholarship section suggested two additional questions to increase the survey to 28 items. These questions were specific to the consideration of other diagnoses that ECMO might be used for other than ARDS.

### National launch of survey

Using the EAST membership email roster, the link to the survey was sent to individuals with active, senior, associate, fellow-in-training, and international categories of membership. After an initial email inviting members to participate, two subsequent

reminders were sent. The survey link was active between April 24, 2015 and May 22, 2016. Responses were compiled by the internet-based survey programme (REDCaps). Participant identity was kept confidential during the data collection process and no personally identifiable material was collected.

### Statistical analysis

Descriptive analyses of measured variables using means and SD or medians with IQRs as appropriate.

## RESULTS

The survey was distributed through email to 1626 individuals who were on the membership roster of EAST; 52 emails were returned due to non-deliverable status. Of the 1574 individuals that successfully had emails processed, 206 individuals responded to the link and initiated the survey (13.1% response rate). Respondents identified themselves as the following: 138 (67.0%) trauma faculty, 44 (21.4%) surgical intensivists, nine (4.4%) critical care fellows, eight (3.9%) ECMO medical/surgical directors, in addition to seven (3.4%) others. The respondents were from 37 states, the District of Columbia and Puerto Rico, in addition to three individuals from outside the USA (Canada and South Africa). More than half (56.9%) of respondents reported having institutional ECMO capabilities. Of the total respondents, 45.2% reported using ECMO in adult trauma patients. The institutional frequency of ECMO usage in trauma populations was 73.5% who perform 0–2 per year, 16.7% perform 2–5 per year, 5.8% perform 5–10 per year, and 3.9% perform >10 per year.

The respondents who did not use ECMO for trauma patients were queried as to all the reasons they would not consider ECMO, the most frequent response was 'not available at my institution' (65.7% of non-users). The remaining answers in descending frequency included 'not comfortable with use in trauma patients' (20.4%); 'cost prohibitive' (13.0%); 'bleeding risk is too high for trauma patients' (12.0%); 'do not believe it is appropriate for trauma patients' (7.4%); and 'do not believe it is appropriate for adults' (6.5%). If ECMO were available at the respondents' institutions, only 4.7% reported that they would not consider ECMO use for trauma patients with refractory hypoxic failure, with 11.4% unsure if they would use it or not.

When asked which trauma patients with ARDS are not amenable to using ECMO for severe hypoxia, most respondents (60.2%) think that patients with traumatic brain injury are not appropriate candidates, followed by spinal cord injured patients (24.8%). However, the overwhelming majority thinks that blunt trauma to the chest and abdomen (93.7%), and postsurgical abdominal (91.3%) and chest patients (91.3%) were suitable for ECMO (table 1).

**Table 1** Traumatic conditions respondents think are not amenable for extracorporeal membranous oxygenation in severe acute respiratory distress syndrome

	All respondents (n=196)	ECMO director (n=8)	Trauma surgeon (n=136)	Surgical intensivist (n=44)	Critical care fellow (n=8)
<b>Traumatic condition</b>					
Traumatic brain injury	60%	38%	64%	55%	25%
Spinal injury	25%	13%	24%	30%	13%
Blunt chest or abdominal trauma	6%	13%	6%	7%	0%
Postsurgical condition (splenectomy, colectomy, etc)	9%	0%	9%	11%	13%
Postsurgical condition of thorax (pneumonectomy, etc)	9%	38%	7%	11%	13%

**Table 2** Ranking of preference of additional treatments for patients with severe acute respiratory distress syndrome who fail conventional mechanical ventilation

Rank (all respondents)	Modality	Respondents that use modality (%)	ECMO directors ranking	Trauma surgeons ranking	Surgical intensivists ranking
1	APRV	82.0%	APRV	APRV	APRV
2	Bilevel	71.4%	Prone	Paralysis	Bilevel
3	Paralysis	83.0%	Paralysis	Bilevel	Paralysis
4	Prone	86.9%	NO	Prone	Prone
5	NO	75.7%	Bilevel	NO	Epo
6	Epo	59.2%	Epo	HFOV	NO
7	HFOV	61.7%	HFOV	Epo	HFOV
8	Steroids	60.2%	Steroids	Steroids	Steroids
9	Surfactant	44.2%	Surfactant	Surfactant	Surfactant

APRV, airway pressure release ventilation; Epo, epoprostenol; HFOV, high-frequency oscillatory ventilation; NO, nitric oxide; bilevel, bilevel ventilation; paralysis, pharmacological paralysis; prone, prone positioning; steroids, corticosteroids.

When queried about the preferred modality of treatments in patients with severe ARDS who deteriorate despite optimal ARDSnet ventilation practices, the respondents report using prone positioning (86.9%), pharmacological paralysis (83.0%), APRV (82.0%), and inhaled NO (75.7%) as most common methods to treat ARDS (table 2). Utilization of bilevel ventilation (71.4%), epoprostenol (61.7%), high-frequency oscillating ventilators (HFOV) (60.2%), corticosteroids (59.2%), and surfactant (44.2%) was reported as well. The ranking order of preference from most preferable to least preferable was: (1) APRV, (2) bilevel ventilation, (3) paralysis, (4) prone positioning, (5) inhaled nitric oxide, (6) epoprostenol, (7) HFOV, (8) corticosteroids, (9) surfactant.

Regarding the opinion of when to consider ECMO for a patient with severe ARDS, slightly over one-quarter (28.6%) of respondents reported that consideration for ECMO should occur with worsening hypoxic respiratory failure, but prior to maximal therapy being reached (table 3). More specifically, 13.1% would consider ECMO after maximizing conventional means of ventilation and 23.1% would wait for ECMO until failure to improve was noted on APRV or bilevel ventilation. An additional 16.6% of providers would add items such as prone positioning, inhaled NO, epoprostenol, corticosteroids, and surfactant; if failure to improve after these therapies were added, they would then consider ECMO.

Specifically related to the ECMO management of severe ARDS, respondents were queried as to parameters relating to patient care. Most respondents reported that they maintain

the patients' hemoglobin above 7 (51.8%), perform as needed bronchoscopies (as opposed to scheduled) (82.6%), and do not provide prophylactic antibiotics (86.5%) or antifungals (97.9%). PEEP is typically maintained below 12 cm H<sub>2</sub>O (67.7%), with most providers maintaining a PEEP range of 5 cm to 8 cm H<sub>2</sub>O. No specific ventilator mode was preferred by the respondents although patients are on ECMO. Related to the preferred approach to sedation of the ECMO patient, 84.7% of respondents reported using no sedation, minimal sedation, or moderate sedation with daily awakenings; 15.3% reported deep sedation with or without paralytic usage. The use of a lung protective ventilation strategy and timing (early vs late) was not addressed with this survey.

The respondents were queried regarding the preference of using venovenous (VV) and venoarterial (VA) ECMO modalities for other causes of hypoxia and right heart failure (RHF), namely, resulting from pulmonary thromboembolism (PTE), post-traumatic pneumonectomy, and pulmonary contusions (table 4). For pulmonary embolism causing hypoxia, most respondents would use ECMO (65% of respondents) with the majority beginning with VV ECMO (57.1%) with or without transitioning to VA ECMO if required. Nearly two-third of respondents would use ECMO for all these conditions either causing RHF or hypoxia in the trauma patient. Interestingly, when asked if they supported using ECMO modalities as a supportive bridge after cardiac arrest for hypoxia or RHF, over half (51.2%) endorsed ECMO.

**Table 3** Timing of when to initiate extracorporeal membranous oxygenation.

	All respondents (n=8)	ECMO directors (n=8)	Trauma surgeons (n=131)	Surgical intensivist (n=42)	Critical care fellows (n=8)
<b>Timing of ECMO initiation</b>					
Failure to improve after maximizing conventional ventilation	13.1%	25.0%	12.2%	7.1%	37.5%
Failure to improve after APRV/bilevel	23.1%	0.0%	23.7%	33.3%	0.0%
Failure to improve after addition of prone, NO, Epo, steroids and/or surfactant	16.6%	25.0%	16.0%	16.7%	25.0%
Hypoxic respiratory failure worsening but prior to maximal therapy being reached	28.6%	50.0%	26.7%	28.6%	12.5%
I never consider ECMO	10.6%	0.0%	12.2%	11.9%	0.0%
I do not know	8.0%	0.0%	9.2%	2.4%	25.0%

APRV, airway pressure release ventilation; ECMO, extracorporeal membranous oxygenation; Epo, epoprostenol; HFOV, high-frequency oscillatory ventilation; NO, inhaled nitric oxide; bilevel, bilevel ventilation; paralysis, pharmacological paralysis; prone, prone positioning; steroids, corticosteroids.

**Table 4** Use of VV versus VA extracorporeal membranous oxygenation other than for acute respiratory distress syndrome

	VV ECMO only	VA ECMO only	Initiate VV and transition to VA as needed		Would not use ECMO
			Don't know		
<b>Condition for ECMO</b>					
Hypoxia from pulmonary embolus	19.2%	7.9%	37.9%	26.6%	8.5%
Right heart failure from pulmonary embolus	9.7%	29.1%	25.1%	28.0%	8.0%
Right heart failure from traumatic pneumonectomy	11.0%	24.9%	26.6%	30.6%	6.9%
Hypoxia from pulmonary contusion	37.6%	2.3%	29.5%	24.3%	6.4%
Supportive 'bridge' after cardiac arrest from hypoxia/right heart failure	6.5%	22.6%	22.0%	33.3%	15.5%

ECMO, extracorporeal membranous oxygenation; VA, venoarterial; VV, venovenous.

## DISCUSSION

Trauma patients that develop severe ARDS with conventional mechanical ventilation have not been well studied; thus, there are no definitive therapeutic guidelines beyond the general principals established from ARDSnet.<sup>18</sup> Furthermore, guidelines supporting the use of adjunct therapies such as inhaled NO, epoprostenol, etc, are also lacking. The goal of this study was to query the trauma community at large to obtain a sense of preferences for these treatment modalities among providers caring for this complicated patient population.

This survey was sent to the entire EAST membership, composed of providers that care for trauma patients across all varieties of hospitals and trauma centers nationwide. Only 26.4% of the respondents report more than two ECMO runs annually for trauma patients. This could reflect a significant knowledge gap among providers or it could simply represent a lack of access to ECMO as a treatment option. In part, this may demonstrate a lack of comfort with this treatment modality for the trauma patient, given associated severe injuries such as traumatic brain injury or spinal cord injury or increased risk of hemorrhage and/or thrombosis. Despite these perceived contraindications, however, there are multiple case reports and case series that confirm both safety and efficacy even for the acutely multi-injured patient. In the future, it may prove beneficial to expand the educational curricula within Trauma/Critical Care/Acute Care Surgical fellowships to include clinical exposure to trauma patients on ECMO (where possible) or to at least incorporate relevant didactics and up to date evidence-based data on this topic. Doing so could help facilitate better patient evaluation and increased ECMO utilization at centers that have ECMO capabilities in appropriate patients. It could additionally help facilitate early referral to ECMO centers from hospitals that do not have an established ECMO programme, as there are currently only 269 hospitals with Extracorporeal Life Support Organization certified ECMO programmed in the USA.<sup>19</sup>

Based on the results of this survey, substantial variability persists in provider preferences and use of various adjunctive modalities such as prone positioning, pharmacological paralysis, etc, in severe ARDS in trauma patients. There are no standardized evidence-based protocols or treatment algorithms available to guide critical care providers in selecting among these therapies or in determining appropriate timing of initiation. Responding providers were asked to rank order their preferences for these therapies. The most preferable therapies were ventilator changes—switching from conventional ventilator settings to either APRV or bilevel. Chemical paralytics and prone positioning followed on the rank-order list with inhaled NO/Epo, HFOV, steroids and surfactant deemed to be generally less preferable. These preferences would be expected and are supported by available critical care literature. Ventilator changes are

relatively straightforward and typically are not associated with increased patient morbidity/mortality when managed appropriately (ie, minimizing tidal volumes, maintain plateau pressures, etc). Chemical paralysis and prone positioning have also shown benefit for patients with severe ARDS in several clinical trials.<sup>20-21</sup> In contrast, the less preferable treatment adjuncts have little to no data supporting clinical use even as rescue modalities; some may even cause patient harm.<sup>22-24</sup>

Future research should evaluate the appropriateness of these therapies within the trauma patient population. Additionally, future research should evaluate the timing of initiation of all these therapies, including ECMO, in conjunction with maintenance of low volume lung protective ventilation. Intuitively, early and aggressive management of patients with severe ARDS could potentially lead to better outcomes by decreasing ongoing hypoxia, hypercarbia, pulmonary hypertension, and inflammation that often drives high ventilator volumes and/or pressures. This was the hypothesis behind the marked improvement in outcomes noted in our recent ECMO study.<sup>7</sup> Trauma patients were placed on ECMO typically within 2 days of diagnosis of severe ARDS; ECMO then facilitated substantial reductions in ventilator volumes and pressures with less associated volutrauma and barotrauma, respectively. Clearly, when trying to analyze timing of escalation of therapy, it becomes important to balance risks of the therapy versus potential benefits, both in the short and long term. Future research should evaluate the timing, risks, and benefits of all adjunctive therapies for trauma patients with severe ARDS.

This study has limitations. The results of the survey reflect respondents' perceptions of the use of various therapies for severe ARDS and the questions are subject to possible misinterpretation and misperception.<sup>25</sup> The overall response rate was low at 13.1%. There is potential bias in the generalizability of the results of the survey given this low response rate. However, this response rate is in line with mean response rates reported for email and web-based surveys in healthcare research and in other fields.<sup>26-28</sup> Cook *et al* noted that geographic representativeness of responses is more critical than response rate alone.<sup>29</sup> Therefore, even though the overall response rate was low, the fact that 37 states were represented was a strength.

## CONCLUSIONS

Management of patients with severe ARDS remains a challenge. Outside of lung protective ventilation there are few therapies that improve patient mortality. Numerous studies are published on this topic but conclusions drawn regarding the appropriateness of these therapies are conflicting. Thus, substantial variation in clinical practice remains common. In particular, for trauma patients with severe ARDS, even less data exists to guide clinical

practice. This survey was intended to poll physicians caring for this specific patient population as to their practice patterns and beliefs regarding not only ECMO but also more traditional adjunct therapies for severe ARDS. It is important to understand the general practice patterns of the trauma critical care community at large so that, as new data emerge, educational directives can focus on bridging the gaps between anecdotal clinical practice and evidence-based medicine.

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