

# Sedation Practices during VV-ECMO in Indian Scenario: A Retrospective Survey

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## ABSTRACT

**Aim and background:** There has been an exponential rise in the use of venovenous extracorporeal membrane (VV-ECMO) in patients who develop acute respiratory distress syndrome (ARDS), as observed in Indian hospitals. In spite of the ever-increasing cases of patients being treated with VV-ECMO, there is scarcity of literature about sedation management in this patient group. This retrospective, online questionnaire-based survey was undertaken with an aim of gaining an overview of what majority institutes in India are practicing with respect to sedation during VV-ECMO, so that it can contribute to the smallest extent in forming policies and protocols.

**Materials and methods:** This survey was formulated on SurveyMonkey application and shared with members of ECMO society of India (ESOI) through WhatsApp. Their responses were recorded and analyzed through SurveyMonkey application.

**Results:** Fentanyl was found to be the most widely used drug followed by midazolam and fentanyl plus midazolam was the most commonly used combination. Majority of participants (83.33%) use Richmond Agitation-Sedation Scale (RASS) for monitoring agitation. Only other scale being used is the Ramsay scale. Incidence of delirium was less than 10% in most intensive care units (ICUs). Majority of participants (54.17%) required deep sedation for less than 5 days to keep their patients calm and comfortable. Physiotherapy was given during both deep and light sedation in most of the units (60%).

**Conclusion:** We found substantial uniformity with respect to choice of agitation scales used, initiation of physiotherapy, incidence of delirium and number of days on deep sedation among the centers across India.

**Clinical significance:** Although this survey gives a glimpse of sedation practices in VV-ECMO in many centers across India, more surveys and studies are required on this topic.

**Keywords:** Sedation, Survey, Venovenous extracorporeal membrane oxygenation.

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## INTRODUCTION

John Gibbon invented cardiopulmonary bypass circuit leading development of extracorporeal life support devices used in current era.<sup>1</sup>

Extracorporeal life support encompasses various modalities including extracorporeal membrane oxygenation (ECMO), which provides temporary cardiopulmonary assistance in failing heart and/or lung.<sup>2</sup>

Early bubble oxygenators had limitation of having higher chances of hemolysis.<sup>3</sup> In 1957, it was found that silicone efficiently allows gas exchange with lesser hemolysis. "Membrane oxygenator" was thus discovered and paved the way in coining the term ECMO. Prolonged extracorporeal support had become a possibility due to development of efficient oxygenators and use of continuous anticoagulation.<sup>4</sup>

Extracorporeal membrane oxygenation technology has seen a lot of evolution since then. The pump in ECMO functions like a heart, as it receives and propels the blood. An oxygenator does functions like that of a lung, by oxygenating the blood.

Venovenous extracorporeal membrane (VV-ECMO) provides respiratory support, whereas venoarterial ECMO (VA-ECMO) provides cardio-respiratory support.<sup>5</sup> There are various indications of VV-ECMO (e.g., bridge to lung transplant, status asthmaticus, bronchopleural fistula, acute lung injury, and viral/bacterial pneumonia); however, it is most commonly used worldwide for treating severe acute respiratory distress syndrome (ARDS).<sup>6</sup> The

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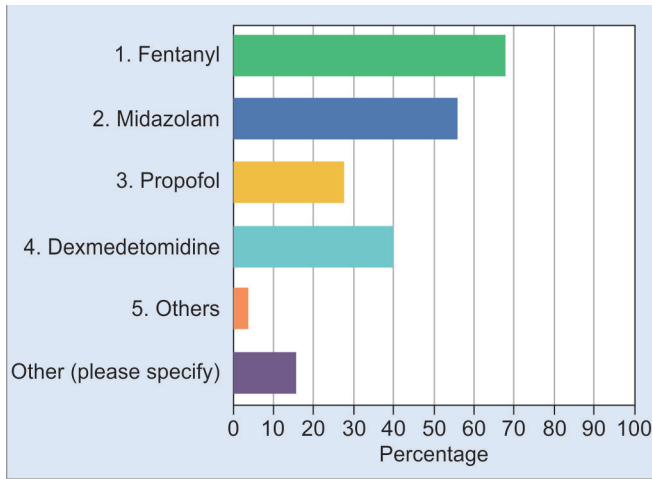
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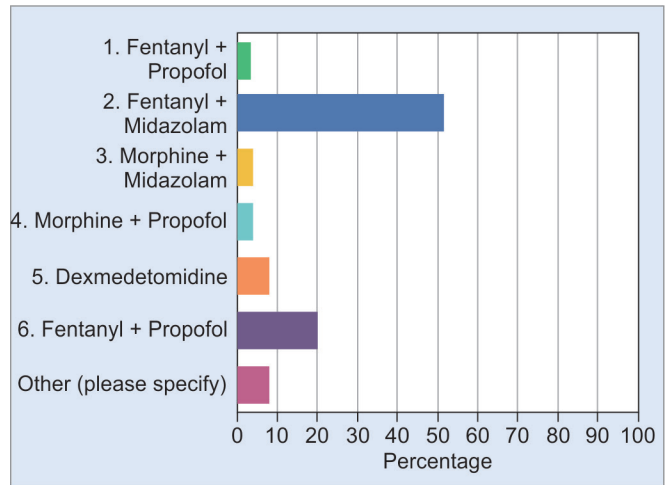
primary goal of supporting a patient with VV-ECMO is to promote lung rest via lung-protective ventilation.<sup>7</sup> Therefore, sedation forms important and integral part of management in patients on VV-ECMO.

Severe hypoxemia, ventilator dyssynchrony and fear of patient-initiated cannula removal are crucial challenges in VV-ECMO patients necessitating deep sedation and restricting mobility.<sup>8</sup> There are no widely accepted guidelines for the management of sedation and analgesia in patients on VV-ECMO, leading to diversity in sedation practices worldwide for this patient population.<sup>9</sup>

Last few years, especially since COVID-19 pandemic there is exponential rise in the number of patients being treated



**Fig. 1:** Responses to question 'which drugs are used in your ICU for sedation in patients on VV-ECMO'



**Fig. 2:** Responses to question 'drug combination preferred in your ICU for sedation in VV-ECMO'

**Table 1:** Percentage wise demonstration of responses to question 'which drugs are used in your ICU for sedation in patients on VV-ECMO'

| Answer choices         | Responses |    |
|------------------------|-----------|----|
| 1. Fentanyl            | 68.00%    | 17 |
| 2. Midazolam           | 56.00%    | 14 |
| 3. Propofol            | 28.00%    | 7  |
| 4. Dexmedetomidine     | 40.00%    | 10 |
| 5. Others              | 4.00%     | 1  |
| Other (please specify) | 16.00%    | 4  |
| Total respondents: 25  |           |    |

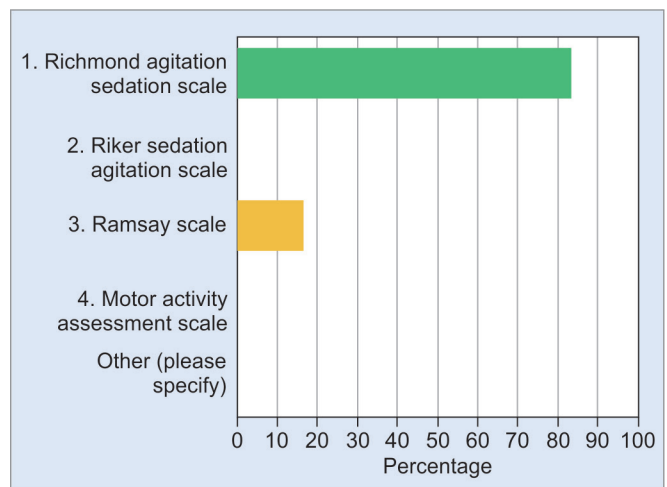
with VV-ECMO in the Indian scenario. Our survey focuses on understanding sedation practices in various institutes across India while managing patients on VV-ECMO.

## MATERIALS AND METHODS

In this retrospective survey, we collected data from intensivists and anesthesiologists managing patients on VV-ECMO in their respective institutes. The survey was created on SurveyMonkey application, which is available on android and apple devices. Survey link was shared with members of ECMO society of India (ESOI) through WhatsApp group. Responses received could be directly tracked and analyzed in the application. The survey was conducted in two parts, where 1st part had seven questions and 2nd part had two questions. The questions in both the parts had multiple choices and scope to mention any particular deviation. It was not mandatory to mention name of the unit or the respondent. Out of 412 members of ESOI, 25 responses were received for both the parts of the survey. The survey was conducted in December 2023.

## RESULTS

The drugs used for sedation in patients on VV-ECMO in Indian intensive care units (ICUs) were fentanyl, midazolam, dexmedetomidine, propofol, morphine, and ketamine. The



**Fig. 3:** Responses to question 'which agitation sedation scale is used in your ICU'

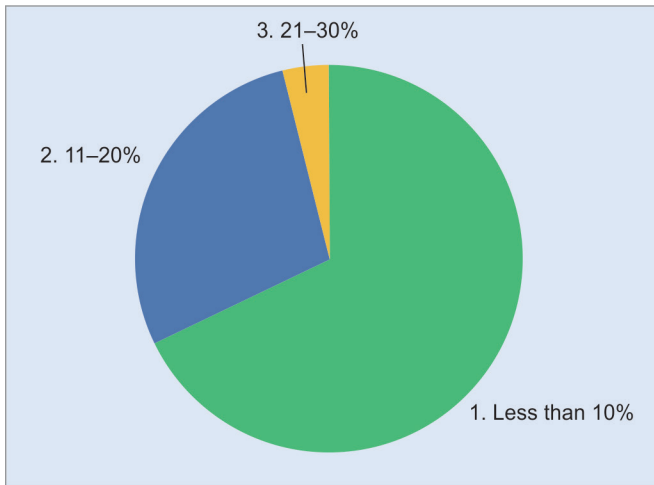
most commonly used drug is fentanyl followed by midazolam. Dexmedetomidine was the third most commonly used drug indicating its rising popularity (Fig. 1, Table 1).

Fentanyl and midazolam was the most commonly used combination followed by a combination of fentanyl, midazolam, and propofol. Interestingly, some centers use dexmedetomidine and ketamine combination (Fig. 2). One of the participant mentioned about use of combination dexmedetomidine infusion and fentanyl boluses in their unit.

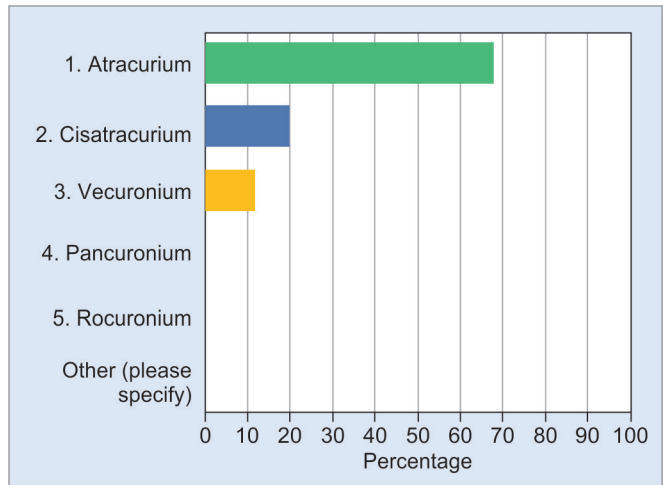
Majority participants (83.33%) use Richmond Agitation-Sedation Scale (RASS) for monitoring agitation. Only other scale being used is the Ramsay scale (Fig. 3).

Incidence of delirium was less than 10% in most ICUs. Approximately, 28% ICUs reported incidence of 11–20% and only 4% of ICUs had delirium percentage 21–30% (Fig. 4).

Majority of participants (54.17%) required deep sedation for less than 5 days to keep their patients calm and comfortable. Deep sedation was required in the patients for 6–10 days as per 45.83% of the respondents (Table 2).



**Fig. 4:** Responses to question 'Incidence of delirium in patients on VV-ECMO in your ICU'



**Fig. 5:** Responses to question 'which NMBAs preferred in your ICU, for patient on VV-ECMO'

**Table 2:** Percentage wise responses to question 'As an average for how many days most patients are deeply sedated when on VV-ECMO in your ICU'

| Answer choices         | Responses |    |
|------------------------|-----------|----|
| 1. Less than 5 days    | 54.17%    | 13 |
| 2. 6-10 days           | 45.83%    | 11 |
| 3. 11-14 days          | 0.00%     | 0  |
| 4. >14 days            | 0.00%     | 0  |
| Other (please specify) | 0.00%     | 0  |
| Total                  |           | 24 |

**Table 3:** Percentage wise responses to question 'how many patients required deep sedation when on VV-ECMO'

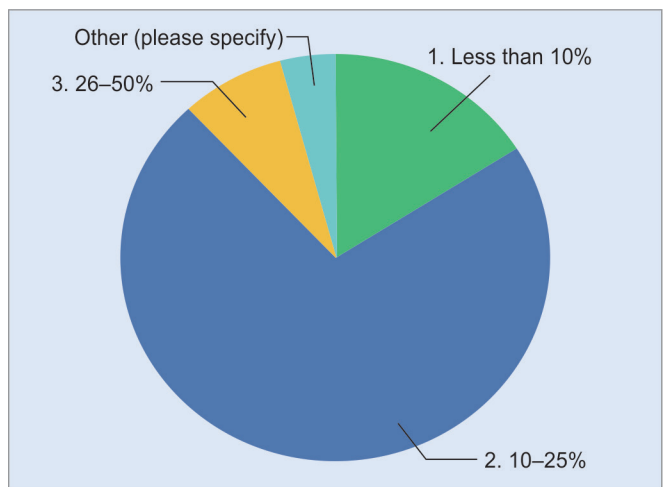
| Answer choices         | Responses |    |
|------------------------|-----------|----|
| 1. <25%                | 32.00%    | 8  |
| 2. 25-50%              | 56.00%    | 14 |
| Other (please specify) | 12.00%    | 3  |
| Total                  |           | 25 |

Approximately, 25-50% patients required deep sedation even after putting on VV-ECMO as per 56% of respondents. While one respondent reported that >50% cases required deep sedation, only one reported the requirement of deep sedation in all their cases (Table 3).

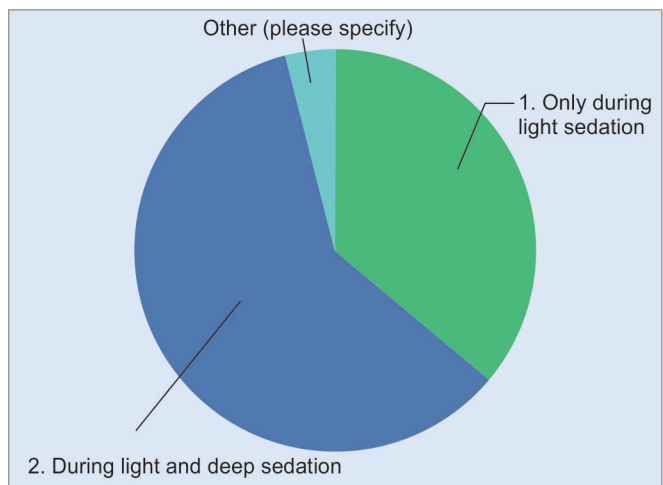
Atracurium is the most widely used neuromuscular blocking agent (NMBA) by 68% of respondents in patients on VV-ECMO. Cisatracurium (20%) and vecuronium (12%) are the only other agents used for the said purpose in the Indian scenario (Fig. 5).

Need of NMBAs for more than 48 hours in up to 25% patients was reported by 88% of participants; however, only 12% reported use of NMBAs in excess of 48 hours for more than 25% patients (Fig. 6).

Most ICUs start physiotherapy when a patient is in deep and/or light sedation. Approximately, 36% ICUs allow physiotherapy only when the patient is in light sedation (Fig. 7).



**Fig. 6:** Responses to question 'What percentage of patient required NMBA for more than 48 hours when on VV-ECMO'



**Fig. 7:** responses to question 'Is physiotherapy continued in your ICU during sedation in patients on VV-ECMO'

## DISCUSSION

Rising use of ECMO technology has imparted light on the supportive care which includes sedation management, pain management, delirium management, and physiotherapy.

In patients who are on life support but are not on ECMO, these areas are well researched and there are evidence-based guidelines available for the purpose.<sup>10</sup> Patients who had received daily interruption or light sedation showed a decreased in-hospital mortality rate, in comparison to those on deep sedation.<sup>11</sup> Delirium in ventilated patients causes longer stay on mechanical ventilator, prolonged hospitalization, and increased mortality.<sup>12</sup> Initiation of physiotherapy early in the course of mechanically ventilated patients has shown improved outcomes.<sup>13</sup> However, there is scarcity of data and practice guidelines in sedation management in patients on ECMO and there is substantial variation in daily practice from one center to another.<sup>9,14,15</sup>

Significant pharmacokinetic alterations happen in patients on ECMO, affecting drug dosing of the sedative agents.<sup>16</sup>

The most important reasons are as follows:

- Drug sequestration or adsorption to the circuit. It is observed more with highly lipophilic drugs like fentanyl. Circuit may act as reservoir prolonging the sedoanalgesia effect.<sup>16-18</sup>
- Higher volume of distribution due to drug adsorption and fluid resuscitation.<sup>16-18</sup>
- Drug clearance variabilities due to organ dysfunction.<sup>19</sup>  
This increased demand, sequestration, and reduced clearance leads to patients remaining sedated for considerably higher time than desired.

In our survey, we found that up to 32% participants reported the need of deep sedation in a quarter of their patients on VV-ECMO. Approximately, 56% participants felt the need of deep sedation in up to half of their patient population when on VV-ECMO. A multinational study involving more than 300 centers found that three out of every four patients on VV-ECMO required deeper sedation and one out of every four could be managed with minimal sedation.<sup>20</sup> Considerable difference is seen here if compared with findings in our survey.

The Extracorporeal Life Support Organization (ELSO) guidelines suggest light sedation to be preferred in patients receiving ECMO.<sup>21</sup> A single center retrospective study conducted at Toronto general hospital between year 2012 and 2015 by showed that patients on VV-ECMO required deep sedation for an average of 6 days.<sup>8</sup> In our study, we found that 54.17% respondents reported the need for deep sedation for <5 days for most of the patients. Deep sedation requirements for 6–10 days were reported by 45.83% respondents. None reported deep sedation beyond 10 days.

Extracorporeal Life Support Organization suggests to use of NMBAs during intravenous cannulation to avoid air embolism due to breathing efforts by the patient. The use of NMBAs may be considered when the ECMO flow optimization is in process and is not to be preferred during other times.<sup>21</sup> In our survey, we noticed that only 8% respondents reported the use of NMBAs beyond 48 hours in more than a quarter of patients. That indicates 92% of units had less than 25% patients who required NMBAs for more than 48 hours, which seems compliant with ELSO guidelines.

A single center observation study done over 8 years reported that physiotherapy if initiated in first week of ECMO support leads to lesser time on ECMO and shorter stay in ICU.<sup>22</sup> Munshi et al.

conducted a study between year 2010 and 2015 concluded that early physiotherapy can be initiated in patients on VV-ECMO and it may lead to reduction in mortality.<sup>23</sup> In our survey, 60% respondents conveyed that physiotherapy is initiated in their unit even when patient is deeply sedated while on VV-ECMO and it is continued during light sedation. Only 36% respondents stated that they initiate physiotherapy only when the patient is in light sedation. This is a buoyant trend in Indian ICUs that as majority of centers prefer early physiotherapy even when the patient is deeply sedated.

Meta-analysis done by Ho et al. included 10 studies and 8580 patients to assess prevalence of delirium in patients on ECMO. It found that 51.84% patients on VV-ECMO had delirium.<sup>24</sup>

As per our survey, 68% respondents reported that incidence of delirium was <10% in their unit when the patients were on VV-ECMO. Approximately, 28% reported incidence to be between 11 and 20%. Considerable difference between results of meta-analysis and our study indicates more research is needed in this area.

Multiple scales and scoring systems are used to assess agitation sedation in critically ill patients, including Ramsay scale, RASS, Riker sedation agitation scale (SAS), and motor activity assessment scale (MASS) to name a few.<sup>14</sup> Study done by deBacker et al. used SAS, while survey conducted by Buscher et al. used Ramsay scale for assessing agitation-sedation in patients on VV-ECMO.<sup>8,9</sup> In India, RASS seems to be the most widely used scale followed by Ramsay scale as per results of our survey.

There is wide variety in choice in the use of sedatives and analgesics at global level for patients on VV-ECMO. An international survey done by Minnen et al. across 48 centers found the most commonly used drugs for the purpose as propofol, midazolam, dexmedetomidine, fentanyl, morphine, and ketamine in reducing order.<sup>25</sup> International survey done by Buscher et al. found that midazolam was the most frequently used drug (79%), followed by morphine and fentanyl. While propofol was used in (36%), alpha-2 agonist was administered frequently in up to 66% cases on VV-ECMO. Neuromuscular blocking agents most commonly used were vecuronium (40%), followed by cis-atracurium (21%).<sup>9</sup> Pan-American and Iberian Federation guidelines on sedation and analgesia 2020, suggests the use of opioids like morphine along with ketamine. Morphine is preferred due to its lower lipophilicity.<sup>14</sup> Our study found that fentanyl (68%) was commonly used drug, followed by midazolam (56%), dexmedetomidine (40%), propofol (28%), and morphine (12%). Fentanyl and midazolam were the most widely used sedative combination (52%) as per our survey. There was a unique combination used at some centers in the form of dexmedetomidine and ketamine (8%). Approximately, 20% centers used fentanyl, propofol, and midazolam combination for deeper sedation. Atracurium was the preferred NMBA (68%), followed by cis-atracurium (20%) and vecuronium (12%). There is paucity of data on choices of sedatives, their combinations and NMBAs used in patients on VV-ECMO. Moreover, there are no widely accepted guidelines for sedation protocol in patients on VV-ECMO. More surveys, trials, and evidence-based guidelines are the need of the hour in this context.

## CONCLUSION

Our study highlighted a trend in choices of sedatives, NMBAs and their combinations used in centers across India in the treatment of patients on VV-ECMO. Findings like choices of drugs used for sedation also corroborated with international surveys. The survey

found substantial uniformity among the responses about the agitation scales used, initiation of physiotherapy, incidence of delirium, and number of days deep sedation were required.

### Clinical Significance

This survey gives a glimpse of sedation practices in VV-ECMO in many centers across India, though more surveys and studies are required on this topic.

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