

Prone Positioning in Venovenous Extracorporeal Membrane Oxygenation (VV-ECMO) in COVID-19 Acute Respiratory Distress Syndrome (ARDS)

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ABSTRACT

Background: There is a lack of scientific evidence on the beneficial effects of proning in COVID-19 ARDS patients on venovenous extracorporeal membrane oxygenation (VV-ECMO). This is the first original article from India that compared the effects of prone positioning in patients in VV-ECMO, the indication of ECMO being COVID-19-associated acute respiratory distress syndrome (ARDS).

Methodology: In this single-center retrospective observational study, we divided the COVID-19-associated ARDS patients on VV-ECMO into 2 groups, the supine group, and the prone group. The primary outcome parameter was 30 days mortality. Secondary outcome parameters were the length of ICU stay, days on VV-ECMO, and duration of mechanical ventilation.

Results: There was no statistical difference in mortality ($p = 0.9$) between the supine and prone groups. There were no statistically significant findings in the secondary outcome parameters too.

Conclusion: Prone positioning did not show a statistically significant benefit in mortality in COVID-19 ARDS patients on VV-ECMO. Although, there was a numerically lower percentage of mortality in prone patients. Additionally in numerical terms, patients had shorter ICU stays, fewer days on VV-ECMO, and shorter duration of mechanical ventilation who were prone.

Keywords: Acute respiratory distress syndrome, Coronavirus disease of 2019, Proning, Prone positioning, Venovenous ECMO.

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INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is a technique for providing prolonged support to human cardiac and/or respiratory systems when the human heart and lungs are incapable of meeting blood supply and/or gas exchange to sustain life.¹ Advent of SARS CoV-1 in 2002–2004 and SARS CoV-2 in the early 2020s, have led to the increased application and acceptance of ECMO worldwide. Extracorporeal membrane oxygenation consists of a circuit of drainage cannula, a centrifugal pump, a membrane gas exchanger (oxygenator), and a return cannula. The aim of ECMO is to bypass the heart and/or the lungs to provide them rest and time to adequately recuperate. Venovenous ECMO (VV-ECMO) supports the lungs, return cannula being placed in the venous system.²

Acute respiratory distress syndrome (ARDS) is characterized by acute respiratory hypoxemia, bilateral chest infiltrates unexplained by cardiac issues, or fluid overload. Acute respiratory distress syndrome is a result of dysregulated inflammation resulting in abnormal cytokine release in response to pulmonary or extrapulmonary insult. The injury causes alveolar epithelial–endothelial barrier disruption leading to lung exudates, surfactant dysfunction, compromised gas exchange, impaired pulmonary compliance, increased shunting and physiological dead space, alveolar hyalinization, and alveolar hemorrhages in varying orders.³

Multiple studies have shown the beneficial effects of prone ventilation in ARDS.⁴ Proning reduces the difference between dorsal and ventral transpulmonary pressure, reduces alveolar distension, increases recruitment potential, reduces shunting, and improves oxygenation and ventilation that is sustained when the patients are positioned supine.⁵

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There is a lack of scientific evidence on the beneficial effects of prone positioning in VV-ECMO done on ARDS associated with COVID-19 Infection. This is the first original article from India that compared the impact of prone positioning in patients on VV-ECMO, the indication of ECMO being COVID-19-associated

METHODOLOGY

The study was an observational and analytical, cross-sectional, retrospective study conducted in single tertiary-level hospital

Table 1: Baseline patient characteristics

Parameters	Supine group n = 20	Prone group n = 22	p-value
Median age (years)	57.1	59.3	p = 0.8
Female sex (%)	47.2%	45.5%	p = 0.9
Comorbidities			
Diabetes mellitus (n = 13)	5	8	p < 0.01
Hypertension (n = 11)	6	5	p = 0.9
Chronic kidney disease (n = 4)	2	2	p = 1
Morbid obesity (n = 6)	4	2	p < 0.01
Hypothyroidism (n = 7)	3	4	p = 0.8
Coronary artery disease (n = 6)	3	3	p = 1
Organ dysfunction			
Acute kidney injury	11	13	p = 0.9
Hepatic dysfunction	4	5	p = 0.9

in Kolkata (India). This study included patients who were put on venovenous ECMO from 1st April to 30th June in year 2021 during the second Indian wave of COVID-19. The study population comprised adults (age years: 18–60) with severe ARDS (PF ratio <150) associated with COVID-19, not clinically improving within the first 7 days on invasive mechanical ventilation. Exclusion criteria were underlying chronic lung disease, significant neurological injury, pregnancy, coagulopathy, cardiogenic shock, and non-responsive ARDS with more than 7 days of invasive mechanical ventilation. Necessary approvals and consents were obtained before commencing the study.

The patients (n = 42) were sorted into two groups. The first (supine group) of patients on VV-ECMO were kept in the supine position (n = 20) and the second (prone group) of VV-ECMO patients (n = 22) were prone as per ARDS proning protocol. The primary outcome parameter was 30 days of mortality between the two groups. Secondary outcomes were the duration of VV-ECMO, duration of ICU stay, and weaning from invasive mechanical ventilation.

Statistical analysis was done to compare these groups to evaluate the beneficial effects of proning in patients who were put on VV-ECMO due to severe ARDS associated with COVID-19. The p-value of < 0.01 was taken as statistically significant.

RESULTS

As per inclusion and exclusion criteria, 42 patients were included in the study. The baseline characteristics of the two groups are mentioned in Table 1. Only the incidences of diabetes and obesity were statistically different in the two groups.

The study's primary outcome, 30 days mortality was statistically analyzed between the supine and prone patients who were on VV-ECMO. There was no statistical difference (p = 0.9) documented in 30-days mortality in the two groups (Table 2). Although, the mortality was numerically less in the VV-ECMO patients who were prone as per ARDS proning protocol.

In the secondary outcomes, it has been found that the prone group of patients had less VV-ECMO duration, shorter ICU stay, and less number of ventilator days. However, there were no statistically significant differences in the secondary outcome parameters in both groups (Table 2).

Table 2: Outcome parameters

Parameters	Supine group n = 20	Prone group n = 22	p-value
Primary			
30 days mortality (%)	13 (65%)	14 (63.6%)	p = 0.9
Secondary			
Median days of VV-ECMO (days)	33.3	29.5	p = 0.8
Duration of ICU stay (days)	35.4	31.7	p = 0.8
Duration of ventilation (days)	37.8	33.1	p = 0.7

DISCUSSION

In this observational, retrospective study done in a single center, we tried to evaluate the beneficial effects of proning in VV-ECMO in patients of ARDS associated with COVID-19. The effect of proning in ECMO patients had been published earlier. A systematic review analyzing six clinical studies documented no mortality benefits of prone positioning in ECMO patients.⁶ In this study too, there was no difference in mortality attributed to proning in ARDS patients associated with COVID-19 on VV-ECMO.

There are a smaller number of studies on the effects of proning in ARDS patients with COVID-19 on VV-ECMO. In a study from the United States, Zaaqoq et al. had shown that hospital discharge was 33% in the ECMO-prone group against 22% in the ECMO supine group with a mortality hazard ratio of 0.31; 95% CI: 0.14–0.68.⁷ In contrast to this study, there was no statistically significant survival advantage found in our Indian patients who were prone during VV-ECMO. However, we observed a lesser percentage of mortality in patients in the prone group. In another study from France, Laghnam et al. found that proning helped in improved oxygenation and respiratory mechanical parameters in patients of COVID-19 ARDS and improvements persisted after patients were positioned supine.⁸

The second wave of COVID-19 in India claimed millions of lives in our homeland. The Indian ICUs were overwhelmed by the exponential rise of COVID-19 associated ARDS cases during the peak of the second wave of the pandemic. Our ICU was one of the few ICUs in India equipped with VV-ECMO facilities, running over a decade. The exhausted and overwhelmed medical facilities in India explain the lack of clinical studies during the COVID-19 pandemic. This is the only Indian study on proning in VV-ECMO of ARDS patients associated with COVID-19 performed till to date.

There are a few limitations in this study. This is a retrospective observational study performed in a single center in India. The sample size was taken as per convenience and there were minor statistically significant differences in the baseline characteristics of the two groups of patients. Therefore, the findings of this study cannot be considered representative of different patient groups. The results of this study are yet to be compared with prospective multicentric randomized controlled trials.

CONCLUSION

Prone positioning is a reliable clinical technique in ARDS patients to improve patient outcomes. We studied the effect of proning in ARDS patients associated with COVID-19 on VV-ECMO. Prone positioning did not contribute to a statistically significant difference in terms of mortality. Though, we found a numerically lower percentage of mortality in prone patients. Additionally, patients had shorter ICU stays, lesser days on VV-ECMO, and shorter

duration of mechanical ventilation who were prone as per ARDS proning protocol.

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