Original Article

Extracorporeal membrane oxygenation in COVID-19– Associated acute respiratory distress syndrome – Outcome and experience in a tertiary care intensive care unit – A retrospective study

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ABSTRACT

Background: Extracorporeal membrane oxygenation (ECMO) has been used in patients with severe acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19) who fail conventional treatment. **Methods:** A retrospective observational study was designed in patients who underwent ECMO for severe COVID-19 ARDS in a tertiary care centre from September 2020 to July 2021. The primary outcome was to assess factors influencing clinical outcomes and survival to hospital discharge. Secondary outcomes were to assess the clinical profile and pre-ECMO features, ECMO characteristics and complications. Collected data were entered in Excel software and analysed using R software version 4.0.2 (R foundation for statistical computing, Vienna, Austria). **Results:** A total of 19 patients underwent ECMO. Ten patients survived and discharge. Survivors had a longer median (interquartile range [IQR]) duration (days) on ECMO, that is, 25 (7–50), compared to non-survivors, that is, 12 (1–34) ($P = 0.133$). We also noted that patients who survived had a longer median (IQR) duration (days) of intensive care unit (ICU) stay, that is, 41.5 (30–70), compared to non-survivors, that is, 9 (2–40) ($P = 0.001$). **Conclusion:** In our study, 52.3% of patients survived and discharge, and with ECMO outcomes for COVID-19 ARDS were at par with ECMO outcomes for non-COVID-19 ARDS despite requiring ECMO for longer duration and increased ICU length of stay.

Key words: Acute respiratory distress syndrome, coronavirus disease, COVID-19, ECMO, extracorporeal membrane oxygenation, ICU, intensive care unit, length of stay

INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has affected millions across the globe.[1] Apart from pharmacotherapy and routine supportive measures, options for respiratory support in the intensive care unit (ICU) include non-invasive ventilation (NIV), high-flow nasal cannula (HFNC) oxygen, mechanical ventilation and prone ventilation.[2] Extracorporeal membrane oxygenation (ECMO) has been tried in patients who fail the above conventional therapies. ECMO has traditionally been used in patients with non-COVID-19–associated acute respiratory distress syndrome (ARDS) due to infections like influenza A (H1N1)[3] and Middle East Respiratory Syndrome-associated coronavirus (MERS CoV).[4] Patients on ECMO due to COVID-19 ARDS had longer duration on ECMO compared to non-COVID-19 ARDS patients, with no change in mortality.[5] The outcome in patients with severe COVID-19 ARDS treated with ECMO varied across studies, and there is no

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substantial data from countries like India.[6-8] A recent meta-analysis showed a pooled mortality of 48.8%.[9]

We conducted a retrospective study on patients who underwent ECMO for COVID-19 ARDS. The primary objective of our study was to assess factors influencing clinical outcomes and survival to hospital discharge. Secondary outcomes, that is, the clinical profile and pre-ECMO features, ECMO characteristics and complications, were assessed.

METHODOLOGY

After approval was obtained from the institutional ethics committee (vide approval number ECR/34/\Inst/KA/2013/RR-19 dated 9 October 2021) with a waiver for patient consent, this retrospective observational study was designed in patients who underwent ECMO for severe COVID-19 ARDS in a tertiary care centre from September 2020 to July 2021. The study was carried out as per the principles of the Declaration of Helsinki, 2013.

Adult patients aged 18 years or above were included in the study. All patients had severe ARDS with the ratio of partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2 ratio) being less than 100 with positive end-expiratory pressure (PEEP) $\geq$5 cmH_2O as per Berlin definition[10] and received lung-protective ventilation as per standard protocols. All patients received at least one session of prone ventilation before ECMO was initiated. The primary outcome of our study was to assess the factors influencing clinical outcomes and survival to hospital discharge. Secondary outcomes, that is, clinical profile and pre-ECMO features, ECMO characteristics and complications, were assessed. The clinical profile and pre-ECMO features included age, gender, body mass index (BMI), comorbidities, PaO_2/FiO_2 ratio and acute physiology and chronic health evaluation (APACHE) II score at ICU admission. The parameters assessed in ECMO characteristics were the type of ECMO initiated, anticoagulation, number of circuits used, complications and secondary sepsis. We considered factors that influenced the outcome, like the duration of mechanical ventilation before initiation of ECMO, the day of initiation of ECMO from conventional respiratory support, the duration (days) from the first day of symptom to hospital admission, duration (days) from the first day of symptom to ICU admission, number of days on ECMO and ICU length of stay.

Collected data were entered in Excel software and analysed using R software version 4.0.2 (R foundation for statistical computing, Vienna, Austria). Continuous variables following normal distribution, like age, BMI and APACHE II score, were presented as mean (standard deviation [SD]); continuous variables that were not normally distributed, like the duration of mechanical ventilation before initiation of ECMO, the day of initiation of ECMO from conventional respiratory support, the duration (days) from first symptom to hospital admission, the duration (days) from first symptom to ICU admission, the number of days on ECMO and ICU length of stay, were presented as median (interquartile range [IQR]). The Mann–Whitney U test was used to compare the two groups. Categorical variables like gender, complications and secondary sepsis were presented as count and percent; and Chi-square test was used for comparison between the groups. $P < 0.05$ was considered statistically significant.

RESULTS

There was no missing data in our study. Survival was noted till hospital discharge. Nineteen patients underwent ECMO during the study period; the mean (SD) age of survivors was 42.9 (10.30) years, and that of non-survivors was 44.7 (13.37) years ($P = 0.983$). Eighteen patients were male, and one was female. The mean (SD) BMI of survivors was 28.3 (3.77) kg/m^2, and of non-survivors was 28.4 (3.81) kg/m^2 ($P = 0.968$). All patients had bilateral chest infiltrates on radiological imaging, and 11 of the 19 patients had comorbidities. Diabetes mellitus was the most common comorbidity. All patients had a PaO_2/FiO_2 ratio of less than 100 and received at least one session of prone ventilation before ECMO initiation. The mean (SD) APACHE II score was 16.7 (7.07) in survivors and 19.6 (5.83) in non-survivors ($P = 0.222$).

Most patients were initiated on venovenous ECMO (17/19), except two patients who had to be initiated on venoarterial ECMO due to associated cardiogenic shock. Once the cardiogenic shock resolved, the two patients initiated on venoarterial ECMO were converted to venovenous ECMO. All patients received a femoral–jugular approach. Unfractionated heparin was used for anticoagulation in all patients except for one in whom fondaparinux was used due to suspected heparin-induced thrombocytopenia. In our study, 13 patients needed renal replacement therapy (six among survivors, seven among non-survivors, $P = 0.986$) during ECMO. Two patients required temporary

pacemaker insertion for refractory bradycardia. Ten patients survived hospital discharge, and nine died. The study parameters are summarised in Figure 1.

Complications were seen in 12/19 patients. Bleeding was the most common complication observed in six patients; bilateral peripheral gangrene and deep vein thrombosis were seen in one patient each; two patients had barotrauma, and two had coagulopathy. Secondary sepsis was seen in 15/19 patients on ECMO. *Acinetobacter baumannii* was seen in seven patients, and *Klebsiella pneumoniae* and *Candida* species were detected in four patients each.

DISCUSSION

Our study on ECMO in COVID-19 ARDS noted a mortality of 47.2%, and 52.8% patients survived to hospital discharge.

The mortality in patients who received ECMO for COVID-19 ARDS ranged from 40% to 48.1%.[9,11-13] The duration of ECMO also varied from 10 days to more than 30 days.[3,5,14] In our study, the time in the ICU was longer in patients who survived to hospital discharge than patients who died. A recent meta-analysis[9] showed a pooled ICU length of stay of 33.5 days. Our study noted that bleeding was the most common complication. It was higher in non-survivors, which could indicate the shorter duration of ECMO and reduced length of ICU stay in these patients. In a multicentric study of 152 patients,[15] the incidence of major bleeding was 30.9. We noted that 78.9% of patients (no difference between survivors and non-survivors) had secondary sepsis. However, it did not contribute to mortality.

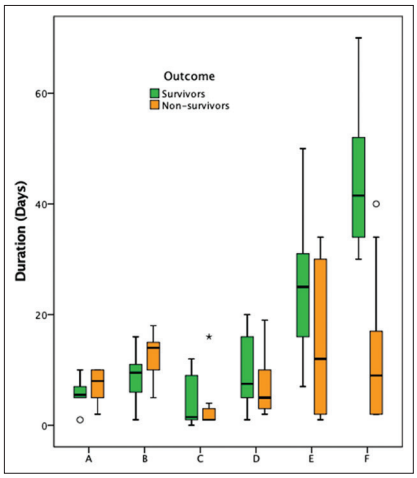

Figure 1: Study parameters among survivors vs non-survivors. A: duration from the first symptom to hospital admission; B: duration from the first symptom to intensive care unit admission: C: duration of mechanical ventilation before initiation of ECMO; D: day of initiation of ECMO from conventional respiratory support; E: number of days on ECMO; F: length of intensive care unit stay. ECMO = extracorporeal membrane oxygenation

Our study noted that age, BMI, APACHE II score, duration of mechanical ventilation before initiation of ECMO and secondary sepsis did not influence mortality. However, we noted that patients who survived had a trend towards longer duration on ECMO and longer length of ICU stay than non-survivors.

Ours was a single-centre study with a limited sample size. We noted that non-survivors had a trend towards shorter duration of ECMO and decreased length of stay in ICU, which might have been influenced by significant bleeding complications (cannula displacement, intracranial bleeding and vascular), patients in the initial days of ECMO and ICU stay.

CONCLUSION

In our study on ECMO in COVID-19 ARDS, 52.3% of patients survived. ECMO is a promising modality for patients with severe COVID-19 ARDS not responding to conventional ventilatory measures.

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Conflicts of interest

There are no conflicts of interest.

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