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Extracorporeal membrane oxygenation outcome in adults with acute respiratory distress: Systematic review

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ABSTRACT

Background: An increased death risk is associated with acute respiratory distress syndrome. For patients with advanced respiratory and circulatory problems, ECMO provides temporary heart and lung replacement as well as breathing support. This study aims to identify the outcomes and evaluate the findings of recent studies involving ARDS patients receiving ECMO. *Method:* The PRISMA guidelines were followed throughout the review. A thorough search of the literature was done on Embase, Medline, PubMed Central, and PubMed. We next screened the articles based on our inclusion criteria, and key terms. *Results:* In this review, we considered eight trials with 3642 patients overall: one cohort study, one randomized controlled trial, and six observational studies. Rates of mortality showed notable variance. A number of variables surfaced as possible predictors of the outcomes, including the age of the patient, the level of hypoxemia, the degree of mechanical ventilation, comorbidities, and ECMO-related variables. *Conclusion:* Many factors, particularly those connected to the patient, such as age, the degree of hypoxemia, and the cause of ARDS, can explain the heterogeneity of outcomes. Mortality rates are also influenced by ECMO-related issues, such as bleeding from anticoagulation, the development of thrombocytopenia, and cannula-related problems.

Keywords: Outcome, extracorporeal membrane oxygenation, acute respiratory distress

1. INTRODUCTION

Despite the use of low-volume, low-pressure breathing methods intended to reduce ventilator-induced lung injury, acute respiratory distress syndrome (ARDS) is linked to a high mortality rate (Thompson et al., 2017). Mortality rates over 60% were recorded as the most severe forms of ARDS (Bellani et al., 2016). Some facilities will employ venovenous extracorporeal membrane oxygenation (VV ECMO) in certain circumstances (Brodie and Bacchetta, 2011). In the last few years, significant progress has been made in the field of ECMO circuit technology (Combes et al., 2014). When traditional treatment fails to improve a patient's ARDS, ECMO can be a lifesaver (Combes et al., 2018). By replacing the lungs and heart temporarily, ECMO offers respiratory and circulatory assistance. The treatment is pumping blood through an oxygenator, or artificial lung, with a mechanical pump. The oxygenator absorbs carbon dioxide and replaces it with oxygen before pumping the blood back into the patient's body (Bartlett et al., 2020).

For ARDS patients, ECMO can act as a method for treatment, providing ventilation and oxygenation while giving a period of time for the lungs to heal (Brodie and Bacchetta, 2011). Recent advances in technology and better patient selection and care have led to an increase in ARDS patient's ECMO use. Nonetheless, there is ongoing debate on the best way to treat patients with ARDS who received ECMO, and different studies have found varying rates of death for these patients (Munshi et al., 2019). Furthermore, a number of variables, such as the timing of ECMO beginning, patient characteristics, the duration of ECMO, and comorbidities related to ECMO use, can impact outcomes in patients with ARDS who received ECMO (Peek et al., 2009). This review's purpose is to assess the results of current research involving patients with ARDS who received ECMO and pinpoint the risk factors for mortality. Future research will benefit from the review, which will offer clinicians treating ARDS patients useful information.

2. METHOD

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 standards were adhered to in this systematic review. We looked through Medline, Embase, PubMed, and PubMed Central, for pertinent publications. We searched through all the databases using different combinations of ARDS, mortality, and ECMO. Keywords for search include Extracorporeal Membrane Oxygenation, Oxygenators, Membrane, Respiratory Distress Syndrome, Adult, Respiratory Insufficiency, Carbon Dioxide, Hypercapnia, people, adolescent, and adult. We chose scholarly works that were written in English and included the most recent works published between Janauary 2018 and March 2024. We only considered research articles with human subjects and studies conducted on people who were at least eighteen years old. Articles that are observational, cohort, and randomized controlled trials were searched; case series and case reports were not included.

Articles that could not be obtained in their entirety were eliminated. Articles that did not have outcome data or those that had a sample size of fewer than 100 patients were also disqualified. Proposal papers and grey literature were excluded as well. We screened the articles using the Endnote program version 21. Identical items were eliminated. All authors carefully considered each piece to ensure it was eligible. All authors participated in the discussion and resolution of the issues. After additional screening, the final screened articles were subjected to inclusion criteria, and only those that met the requirements were considered. In the Initial screening, we collected 424 articles; after duplication removal and screening for title and abstract, 58 full-text articles remained, which were assessed for eligibility criteria, then 50 full-text articles were eliminated with reasons; 19 case studies, 23 not reported outcomes, and 8 due to other reasons (Figure 1). Finally, we included 8 full-text articles in the systematic review.

3. RESULTS

We included 8 studies in our systematic review with a total of 3642 patients; one study was conducted in 2023, one in 2022, one in 2021, 3 in 2020, one in 2019, and one study in 2018. Of the included studies, 2 were conducted in the USA, 2 in Korea, 1 in the United Kingdom, 1 in Maryland, 1 in Germany, and 1 in Canada. Six studies were observational Urner et al., (2022), Seeliger et al., (2021), Galvagno et al., (2020), Na et al., (2019), Warren et al., (2020), Lim et al., (2020), one randomized controlled trial Combes et al., (2018), and one cohort study (Snyder et al., 2023) (Table 1). When compared to a normal mechanical breathing regimen that includes ECMO as rescue therapy, ECMO did not significantly lower 60-day mortality among patients with severe ARDS (Combes et al., 2018).

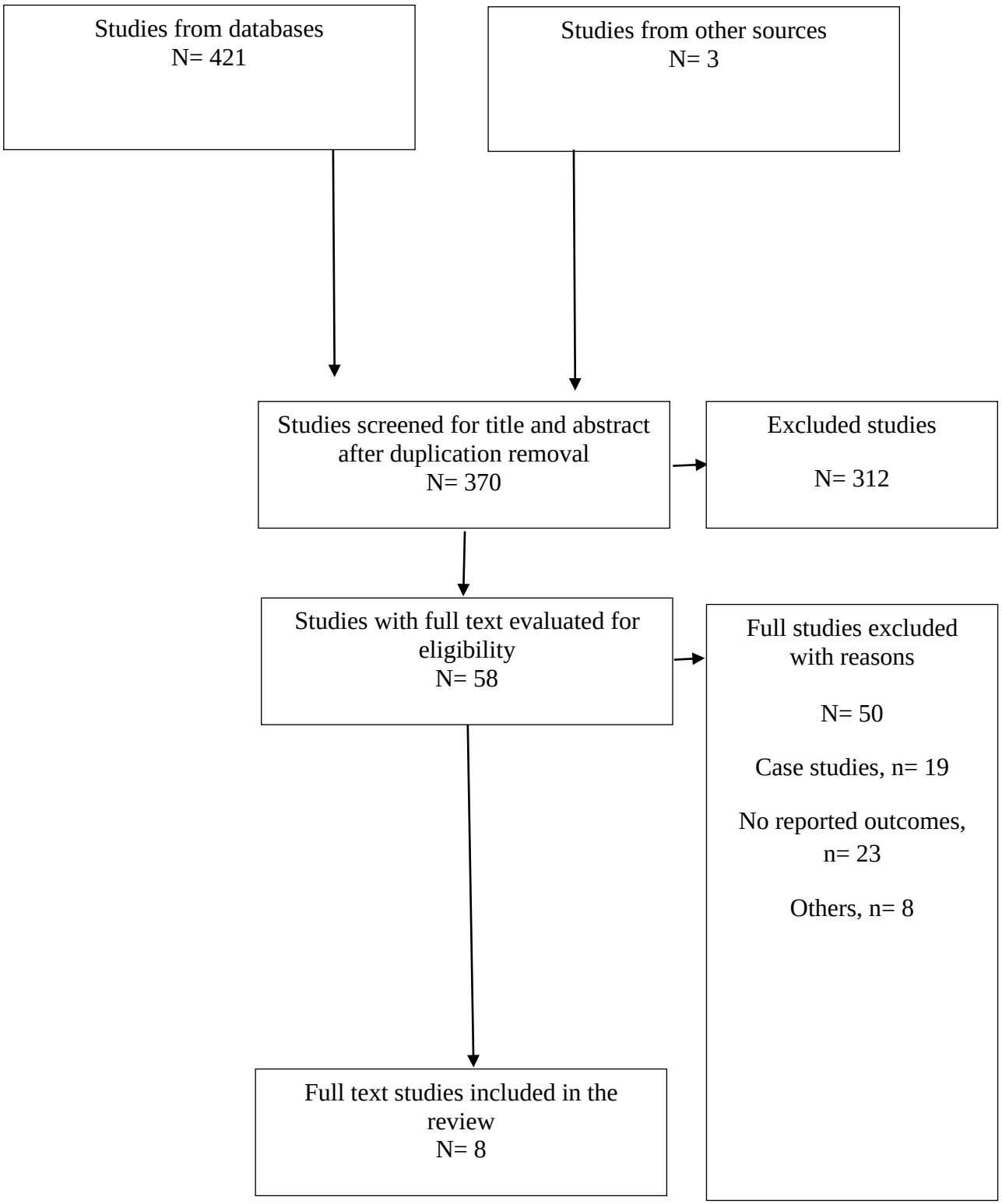

Figure 1 PRISMA consort chart of included studies

Regardless of the cannula placement, patients with ARDS getting ECMO showed comparable clinical outcomes in terms of short-term oxygenation and long-term mortality, according to Lim et al., (2020) study. ECMO can have favorable outcomes for patients with respiratory insufficiency who are not responding to conventional therapy (Warren et al., 2020) (Table 2). According to Na et al., (2019), patients who experienced severe acute respiratory failure and were on ECMO support for more than 28 days did not exhibit reduced short- or long-term survival rates compared to those who were on ECMO for 28 days or less. Obesity was not associated with a greater death rate in patients who needed VV ECMO for acute respiratory failure, according to (Galvagno et al., 2020).

There were no discernible differences in the predicted FVC% or other pulmonary functional markers of recovery outcomes between patients receiving ECMO and those not (Snyder et al., 2023). ECMO treatment with heparinization of high-dose was linked to lower rates of thromboembolic events and oxygenator changes as compared to heparinization with a low-dose method (Seeliger et al., 2021). When setting up ECMO for COVID-19 patients, considerations like age, the severity of hypoxaemia, and the duration and intensity of mechanical ventilation have been shown to affect therapeutic efficacy. ECMO was linked to decreased death rate in some respiratory failure patients related to COVID-19 (Urner et al., 2022).

Table 1 Characteristics of included studies

Citation	Country	Sample size	Population characteristics	Method	Aim
Combes et al., 2018	USA	Control group, n= 125 ECMO group, n= 124	ARDS Patients who had been on mechanical ventilation for less than seven days and endotracheal intubation.	Randomized controlled trial	To ascertain the impact of starting ECMO early in individuals who have the most severe ARDS symptoms
Lim et al., 2020	Korea	Internal jugular vein, n = 157 Femoral vein, n = 178	Study included ECMO-treated adult patients with acute severe respiratory failure.	Retrospective observational study	To assess the mortality and oxygenation over the short and long term depending on cannula configuration in patients receiving VV ECMO for ARDS.
Warren et al., 2020	United Kingdom	1205	Adult respiratory failure patients received ECMO	Observational multicenter cohort study	To describe ECMO patients, the outcome, and the traits that might be linked to survival.
Na et al., 2019	Korea	ECMO for 28 days or less, n=411 More than 28 days ECMO, n= 76	Study included ECMO-treated adult patients with acute severe respiratory failure.	Retrospective observational study	To look into the results of patients with acute severe respiratory failure who were kept on extended for more than 28 days ECMO.
Galvagno et al., 2020	Maryland	194	All adults' patients hospitalized to a VV ECMO unit specifically.	Retrospective observational study	The relationship between body mass index (BMI) and survival in acute hypoxic or hypercarbic respiratory failure patients on VV ECMO was assessed.
Seeliger et al., 2021	Germany	218	Acute respiratory failure patients were supported by VV ECMO for longer than 24 hours.	Observational retrospective cohort study	This study examined two anticoagulation techniques with an emphasis on thromboembolic events together with adjustments

					to oxygenators.
Urner et al., 2022	Canada	844	COVID 19 adults who had respiratory failure	Observational study	To calculate ECMO impact in relation to traditional mechanical ventilation on the outcomes of patients suffering from respiratory failure related to COVID-19.
Snyder et al., 2023	USA	ECMO, n= 34 Non ECMO, n= 76	Adult ARDS patients.	Retrospective cohort	To evaluate the relationship in a cohort of ARDS patients between ECMO and non ECMO groups.

Table 2 Findings of included studies

Citation	Main findings	Conclusion
Combes et al., 2018	At 60 days, 46% of the control group and 35% of ECMO group patients died. In the control group, 28% of patients switched to ECMO on average 6.5 days following randomization, and 57% of those patients died. With the exception of more transfusion-related bleeding events, more cases of severe thrombocytopenia, and fewer occurrences of ischemic stroke, the frequency of complications did not differ substantially between the groups.	ECMO did not significantly reduce 60-day mortality among patients with extremely severe ARDS as compared to a standard mechanical breathing regimen that included ECMO as rescue therapy.
Lim et al., 2020	Ninety pairs were produced using the matching of propensity score technique, and the groups' baseline characteristics at admission, such as PaO2, were comparable. PaO2 did not vary based on cannula configuration at 1, 4, or 12 hours following the start of ECMO. Furthermore, no difference in oxygenation from the baseline levels between the jugular and femoral groups. The jugular group's PaCO2 level was noticeably lower at 1, 4, and 12 hours. At 180 days following ECMO, no statistical significant difference between the two groups' mortality rates; however, the jugular group experienced greater problems due to the cannula.	ARDS patients receiving ECMO demonstrated similar clinical results in terms of long-term mortality and short-term oxygenation, regardless of the cannula arrangement.
Warren et al., 2020	Seventy-four percent of patients were still alive upon ECMO ICU discharge. The median age of survivors was lower than that of non-survivors. The higher degree of hypoxaemia was linked to a decreased survival chance. Survivors had a median Sao2 of 90%. Asthma patients who needed ECMO had a higher chance of surviving than respiratory failure patients from other causes.	For undifferentiated respiratory failure patients who are not responding to traditional therapy, ECMO can provide positive short-term results.
Na et al., 2019	The long-term group experienced a longer period of mechanical ventilation prior to ECMO, and a larger percentage of interstitial lung disease exacerbation was identified as the respiratory failure cause. There was no statistically significant difference in the 6-month or hospital death rates between the groups. Both multivariable and univariable analyses showed no correlation between ECMO support and hospital mortality for more than 28 days.	Acute severe respiratory failure patients on ECMO assistance for more than 28 days did not have lower short- or long-term survival rates than patients on ECMO for 28 days or less.

Galvagno et al., 2020	At the time of cannulation, obese patients needed greater mean airway pressure and positive end-expiratory pressure. When stratified by BMI categorization, there were no statistically significant differences in any group's survival to discharge. After adjusting for BMI and other covariates, multivariable regression did not show any correlation with increased chances of dying or prolonged hospital stays.	Obesity was not linked to a higher death rate in patients needing VV ECMO for acute hypoxic or hypercarbic respiratory failure.
Seeliger et al., 2021	ECMO runtime was 8 (high dose) versus 11 (low dose) days, and the disease severity, as determined by the SAPS II score, was 46 versus 47. In the high-dose group, there were 14 oxygenator modifications, while in the low-dose group, there were 48. At 15 days, 73% had not changed from the oxygenator in the high-dose group, compared to 55% in the low-dose group. Patients' experienced severe bleeding episodes in 19.7% compared to 13.9%, and thromboembolic events in 6.8% compared to 19%. Thirty-day mortality was 33.3% as opposed to 30.7% in high-dose and low-dose groups, respectively.	When compared to heparinization in low doses, ECMO treatment with heparinization in high doses was linked to decreased rates of oxygenator alterations and thromboembolic events.
Urner et al., 2022	If the PaO2/FiO2 ratio dropped by less than 80 mm Hg, the adherence-adjusted death rate for ECMO patients was 26.0%, as opposed to 33.2% for patients who got traditional treatment without ECMO. According to secondary analyses, patients under 65 years old, with a PaO2/FiO2 less than 80 mmHg or driving pressures more than 15 cmH2O for the first ten days of mechanical breathing, benefited most with ECMO.	In certain COVID-19 patients related respiratory failure, ECMO was linked to a lower death rate. In COVID-19 patients, factors such as age, the degree of hypoxaemia, and the intensity of mechanical ventilation have been reported to modify the efficiency of treatment and should be taken into account when setting up ECMO.
Snyder et al., 2023	Patients on ECMO experienced noticeably longer hospital stays, ICU stays, and mechanical ventilation durations. Both ECMO and non-ECMO group experienced comparable functional outcomes. After controlling for hospital stay period, age, SOFA, and COVID-19 status, ECMO was not able to predict lung function changes.	When comparing ECMO with non ECMO patients, there were no appreciable changes in the forced vital capacity predicted or other indicators of pulmonary functional recovery outcomes.

4. DISCUSSION

The purpose of this study is to ascertain the outcomes and assess the conclusions of previous investigations involving ARDS patients on ECMO. Our research indicates that a variety of parameters, especially those related to the patient, like age, the severity of hypoxemia, and the underlying etiology of ARDS, might be utilized to account for the variation in results. ECMO-related disorders, such as bleeding from anticoagulation, thrombocytopenia, and cannula-related complications, also have an impact on mortality rates. The study by Combes et al., (2018) found no correlation between early ECMO application and a mortality rate at 60 days that was noticeably lower than that of the control group. Even though the use of ECMO for severe respiratory failure has grown significantly in the last ten years Karagiannidis et al., (2016), its use is still debatable (Toufen et al., 2011). Although the first two randomized studies of ECMO had dismal outcomes, they were carried out decades ago.

The results of a multicenter randomized controlled trial conducted by Peek et al., (2009), which compared ECMO with conventional treatment for severe adult respiratory failure, were encouraging; however, not all patients in the ECMO group received ECMO, and the control group used of mechanical ventilation was not standardized. A multicenter study by Lim et al., (2020) examined the variation in oxygenation in VV ECMO patients treated for ARDS in relation to the position of the infusion catheter. Following the start of ECMO, arterial oxygen levels were consistently noted in the propensity score-matched cohort, between the femoral and jugular groups. Additionally, there were no discernible changes in the two groups' mortality rates 90 days following the start of ECMO. On the other

hand, the jugular group had a considerably higher incidence of cannula-related problems, such as bleeding at the cannulation site and infection, than the femoral group (Lim et al., 2020).

Due to concerns about diminished oxygenation and the possibility of recirculation, the jugular site is frequently used for infusion catheter insertion during VV ECMO (Frenckner et al., 2018). In contrast to jugular access, femoral venous access did not seem to lower oxygenation (Lim et al., 2020). Similar arterial PaO2 and arterial oxygen content were reported in a retrospective investigation with a very limited sample size between fem–jug and fem–fem configurations by (Guervilly et al., 2014). According to Na et al., (2019) study, in-hospital mortality among patients receiving long-term ECMO did not differ statistically from that of patients receiving short-term ECMO. Additionally, there was no discernible difference in the two groups' 6-month mortality. The survival rate of patients receiving ECMO support for 21 days or more, however, did not differ from that of patients receiving ECMO treatment for fewer than 21 days in two recent single-center investigations (Kon et al., 2015; Menaker et al., 2019).

The study by Galvagno et al., (2020) found no correlation between BMI and length of hospital stay or mortality prior to release. The association between VV ECMO mortality and BMI has been found to be inconsistent in a number of recent studies, some of which show lower mortality with higher obesity class (Powell et al., 2023; Lazzeri et al., 2017). According to Galvagno et al., (2020) findings, there is no correlation between a patient's BMI and death when they receive VV ECMO. While there is no BMI criterion in the current ECMO guidelines that would rule out VV ECMO for obese patients, many practitioners continue to maintain that patients who are morbidly obese should not be considered for VV ECMO in the event of severe respiratory failure.

The same research shows that there is no BMI threshold at which VV ECMO should be withheld in obese patients, which is consistent with the findings of recent studies (Galvagno et al., 2020). Prognostic ratings have an important role in predicting outcomes in ARDS patients on ECMO. The SOFA score is one such often-used metric that, depending on the level of dysfunction in six organ systems, aids in the prediction of ICU mortality (Vincent et al., 1996). Comparably, it has been demonstrated that the ECMO Net Mortality Prediction model, a particular prognostic score created for ECMO patients, offers accurate outcome predictions and can be used to compare center performance (Pappalardo et al., 2013).

5. CONCLUSION

Many characteristics, particularly those associated with the patient, such as age, degree of hypoxemia, and ARDS origin, can be utilized to explain the variability of outcomes. ECMO-related complications, including bleeding from anticoagulation, thrombocytopenia, and cannula difficulties, also impact mortality rates.

Abbreviations

ARDS: Acute respiratory distress syndrome
ECMO: Extracorporeal membrane oxygenation
VV ECMO: Venovenous extracorporeal membrane oxygenation
BMI: Body mass index
PaO2: Partial pressure of oxygen
ICU: Intensive care unit
PaCO2: Partial pressure of carbon dioxide
SOFA: Sequential Organ Failure Assessment

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Ethical approval

Not applicable.

Informed consent

Not applicable.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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