

Extracorporeal Membrane Oxygenation for COVID-19: A Systematic Review and Meta-Analysis

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Abstract

Background: There are several reports of extracorporeal membrane oxygenation (ECMO) use in patients with coronavirus disease 2019 (COVID-19) who develop severe acute respiratory distress syndrome (ARDS). We conducted a systematic review and meta-analysis to guide clinical decision-making and future research.

Methods: We searched MEDLINE, Embase, Cochrane, and Scopus databases from 1st December 2019 to 10th January 2021 for observational studies or randomized clinical trials examining ECMO in adults with COVID-19 ARDS. We performed random-effects meta-analyses and metaregression, assessed risk of bias using the Joanna Briggs Institute checklist and rated the certainty of evidence using the GRADE approach. Survival outcomes were presented as pooled proportions while continuous outcomes were presented as pooled means, both with corresponding 95% confidence intervals [CIs]. The primary outcome was in-hospital mortality. Secondary outcomes were duration of ECMO therapy and mechanical ventilation, weaning rate from ECMO and complications during ECMO.

Results: We included twenty-two observational studies with 1896 patients in the meta-analysis. Venovenous ECMO was the predominant mode used (98.6%). The pooled in-hospital mortality in COVID-19 patients (22 studies, 1896 patients) supported with ECMO was 37.1% (95% CI: 32.3%-42.0%, high certainty). Pooled mortality in the venovenous ECMO group was 35.7% (95% CI: 30.7%-40.7%, high certainty). Duration of ECMO support (18 studies, 1844 patients) was 15.1 days (95% CI: 13.4-18.7). Weaning from ECMO (17 studies, 1412 patients) was accomplished in 67.6% (95% CI: 50.5%-82.7%) of patients. There were a total of 1583 ECMO complications reported (18 studies, 1721 patients) and renal complications were the most common.

Conclusion: Majority of patients received ECMO support for COVID-19-related ARDS. In-hospital mortality in patients receiving ECMO support for COVID-19 was 37.1%, similar to those with non-COVID-19-related ARDS. Increasing age was a risk factor for death. Venovenous ECMO appears to be an effective intervention in selected patients with COVID-19-related ARDS.

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Introduction

The use of extracorporeal membrane oxygenation (ECMO) for acute respiratory distress syndrome (ARDS) during outbreaks of emerging infections was previously reported during the 2009 influenza A(H1N1) pandemic, as well as the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreaks. [1–4] More recently, there are reports on the use of ECMO in patients with coronavirus disease 2019 (COVID-19), who develop severe ARDS.[5, 6] The Extracorporeal Life Support Organisation (ELSO), the World Health Organization and the Surviving Sepsis Campaign (SSC) Guidelines recommend considering ECMO, in specialised centres, for patients with COVID-19 who develop severe ARDS. In addition, venovenous (VV) ECMO is recommended in selected patients who develop hypoxaemia that is refractory

to optimal ventilator management and prone positioning, depending on the availability of resources. [7–11]

Initial case reports and case series on the use of ECMO for COVID-19-related ARDS were disappointing and raised concerns regarding ECMO use in this patient population.[12, 13] However, several reports of ECMO use have subsequently emerged and have reported considerably better outcomes.[5, 6, 14, 15] The first update of SSC guidelines published recently, suggested that ECMO should be considered only for carefully selected patients with COVID-19 and severe ARDS, with a weak strength of recommendation.[16] Given the resource implications of providing ECMO in a pandemic and variability in the reported outcomes, we performed a systematic review of the literature to summarise outcome data and identify risk factors for an unfavourable outcomes in order to guide clinical-decision making and further research.

Methods

Search strategy and selection criteria

This study was registered with PROSPERO (CRD42020192627), and was conducted in adherence with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement.[17] We searched MEDLINE, Embase, Cochrane and Scopus databases from 1st December, 2019, to 10th January 2021, using the following keywords and their variations: “extracorporeal membrane oxygenation”, “extracorporeal life support”, “adult”, “SARS-CoV-2” and “COVID-19” (Supplementary Table 1). We assessed all relevant studies and their citation lists to identify articles for inclusion.

We included data from all studies as well as available online national registries reporting on 10 or more adult patients with COVID-19 supported on ECMO. We excluded any animal or paediatric studies (< 18 years). In the case of overlapping patient data, we included the largest study and excluded any other overlapping studies. Studies from centres that contributed to the ELSO registry report [5] were also excluded to avoid duplication. Two reviewers (RRL and KR) independently screened the articles for eligibility by going through the titles and abstract. Full text of the shortlisted articles was searched thereafter; any conflicts were resolved by consensus or by a third reviewer (KS).

Data collection

Data were collected independently by two reviewers (RRL and KR) using a prespecified data extraction form; any conflicts were resolved by consensus or by a third reviewer (KS). Data collection covered study characteristics (study design, study duration, year of publication, name and country of origin of ECMO centre, indications for ECMO); patient demographics (number of patients, proportion of male/female patients, age, body mass index [BMI], comorbidities); pre-ECMO characteristics (ventilation parameters: partial pressure of arterial oxygen to fraction of inspired oxygen ratio [$\text{PaO}_2/\text{FiO}_2$], serum pH, lactate, duration of mechanical ventilation before ECMO initiation, adjunctive therapies, Sequential Organ Failure Assessment [SOFA] score); ECMO characteristics (type of ECMO at initiation, cannulation site, adjunctive therapies [prone positioning, neuromuscular blockade, inotropes/vasopressors, inhaled nitric oxide,

corticosteroids, and immunomodulatory agents]); mortality (in-hospital as well as substitution of the closest common mortality time point); and other relevant clinical outcomes (intensive care unit [ICU] and hospital length of stay [LOS], ECMO duration, and complications during ECMO). Complications were represented broadly as per the ELSO reporting guidelines. Authors were contacted for additional data where necessary.

Assessment of risk of bias and certainty of evidence

Using the Joanna Briggs Institute (JBI) checklists for case series and cohort studies (Supplementary Table 2), we assessed studies for quality. We assessed the possibility of publication bias using Egger's test. We assessed statistical heterogeneity using the I^2 statistics, the Chi-squared test and visual inspection of the forest plots. We used the Grading of Recommendations, Assessments, Developments and Evaluations (GRADE) approach to assess the certainty of evidence[18, 19] (GRADEpro app available online: <https://www.gradepro.org> [accessed on 10 January 2021]).

Statistical analysis

We performed statistical analyses in R 3.6.1, using the *meta* (v4.12-0) and *dmetar* (v0.0.9000) packages. [20–22] For continuous variables, we pooled the means from the aggregate data presented in each study as per Wan et al.[23] The primary outcome was in-hospital mortality. Secondary outcomes were analysed in the overall cohort, and included those remaining in hospital, and on ECMO, ICU and hospital length of stay, duration of mechanical ventilation before ECMO, duration of ECMO, and complications during ECMO.

We anticipated significant interstudy heterogeneity given the varied presentation of COVID-19 and general lack of guidelines for patient management with ECMO during the early pandemic. As such, we conducted random-effects meta-analyses (DerSimonian and Laird), and 95% confidence intervals (CIs) were computed using the Clopper-Pearson method.[24–26] Survival outcomes are presented as pooled proportions, while continuous outcomes are presented as pooled means, both with corresponding 95% CIs.

Subgroup/Sensitivity analysis

We conducted planned subgroup analyses with continuity correction to include studies with zero events and include geographical region (Asia, Europe, North America, and International). Summary-level meta-regression was conducted when at least 6 data points were collected to explore potential sources of heterogeneity or prognostically-relevant pre specified study-level covariates.[26] Two sensitivity analyses were conducted for our meta-analysis: analysing the mortality among studies where all patients were supported with VV-ECMO, and another by excluding studies with a JBI score of less than 7.

Results

Study details and demographics

Of 2259 references screened, we identified 37 potentially relevant studies and one national database that reported on the outcomes of ECMO in COVID-19 patients (Fig. 1).[5, 6, 12–15, 27–43] After excluding 11 studies with overlapping information, we included twenty-two retrospective observational studies with 1896 patients in the meta-analysis. There were 20 single centre studies and two registry reports (Tables 1 and 2). There were 4 studies (422 patients) from Asia, 13 studies (320 patients) from Europe, 4 studies (102 patients) from North America and one multinational study (1035 patients). Modality of ECMO support was reported in 19 studies (1845 patients) and VV-ECMO was the predominant technique used (98.6%). 89 patients required venoarterial or venoarterial-venous configurations. The pooled patient demographics are summarised in supplementary Table 2.

Table 1
Demographics of the included studies

| First Author | Country | Number of patients | Male patients n(%) | Age* | VV ECMO | P/F ratio* |
|--------------|--------------------------|--------------------|--------------------|----------------|---------|------------------|
| Alnababteh | United States of America | 13 | 8 (61.5) | 44.54 ± 9.49 | 13 | 97.96 ± 49.87 |
| Akhtar | UK | 18 | 16 (88.9) | 47.3 ± 0.9 | 18 | NR |
| Barbaro | International | 1035 | 764 (73.8) | 49 (41–57) | 978 | 72 (59–94) |
| Charlton | UK | 34 | 27 (79.4) | 46.3 ± 7.5 | 34 | 64.5 (54.7–74.3) |
| Cousin | France | 30 | 24 (80) | 33.33 ± 7.00 | 30 | 69 ± 9.34 |
| Falcoz | France | 17 | 16 (94.1) | 56 [30–76] | 16 | 71 [52–134] |
| Guihaire | France | 24 | 20 (83.3) | 48.8 ± 8.9 | 24 | 67 [52–78] |
| Huette | France | 12 | 12 (100) | 62 (58–64) | 14 | 76 (66–83) |
| Jackel | Germany | 15 | 11 (73.3) | 60.8 (54.2–67) | 15 | 63.7 (51.9–94.5) |
| Jang | Korea | 19 | 15 (79) | 63 ± 4.81 | 16 | 97.7 ± 61.11 |
| Le Breton | France | 13 | 10 (77) | 49.31 ± 7.75 | 13 | 60.62 ± 15.23 |
| Jozwiak | France | 11 | 7 (63.6) | 50 (38–59) | 11 | 68 (58–89) |
| Masur | United States of America | 12 | 8 (66.7) | 53.83 ± 13.18 | NR | NR |
| Mustafa | United States of America | 40 | 30 (75) | 48.4 ± 1.5 | 40 | 68.9 ± 3.1 |
| Roedl | Germany | 20 | NR | NR | 20 | NR |
| Schmidt | France | 83 | 61 (73.5) | 48.0 ± 11.0 | 81 | 62 ± 18 |

Abbreviations: VV-ECMO: venovenous extracorporeal membrane oxygenation, P/F: partial pressure of arterial oxygen to fraction of inspired oxygen ratio [PaO₂/FiO₂], NR: not reported

*Age and P/F ratio reported as mean ± SD, median (interquartile range) or median [range].

| First Author | Country | Number of patients | Male patients n(%) | Age* | VV ECMO | P/F ratio* |
|---|---------|--------------------|--------------------|--------------------|---------|------------------|
| Shih | USA | 37 | 27 (73.0) | 51 (40–59) | 37 | 95 (73–147) |
| Takeda | Japan | 237 | 196 (82.7) | NR | 230 | NR |
| Yang | China | 21 | 12 (57.1) | 58.5 (42.75–67.25) | 21 | 60 (55.6–72) |
| Zayat | Germany | 17 | 11 (64.7) | 57 (53–62) | 17 | NR |
| Zeng | China | 12 | 11 (91.7) | 50.9 ± 13.5 | NR | NR |
| Zhang | UK | 43 | 33 (76.7) | 46 (35.5–52.5) | 43 | 67.5 (58.9–77.8) |
| Abbreviations: VV-ECMO: venovenous extracorporeal membrane oxygenation, P/F: partial pressure of arterial oxygen to fraction of inspired oxygen ratio [PaO ₂ /FiO ₂], NR: not reported | | | | | | |
| *Age and P/F ratio reported as mean ± SD, median (interquartile range) or median [range]. | | | | | | |

Table 2
Outcomes of the included studies

| First Author | Mortality | Survivors | Not discharged | Still on ECMO | Complications on ECMO | Days on ECMO* |
|--------------|-----------|-----------|----------------|---------------|--|-----------------|
| Alnababteh | 6 | 4 | 3 | NR | 3 mechanical 7 haemorrhagic 6 renal 4 pulmonary 2 infectious 3 metabolic 2 limb | 12.85 ± 6.04 |
| Akhtar | 4 | 14 | 0 | 0 | | 17.7 ± 9.4 |
| Barbaro | 380 | 588 | 67 | 31 | 295 mechanical 69 neurologic 444 renal | 13.9 (7.8–23.3) |
| Charlton | 16 | 18 | 0 | 0 | | |
| Cousin | 16 | NR | NR | NR | 8 mechanical 27 haemorrhagic 4 neurologic 15 renal 2 pulmonary 4 infectious 3 limb | 10.67 ± 5.45 |

Abbreviations: ECMO: extracorporeal membrane oxygenation, NR: not reported.

*Days on ECMO reported as mean ± SD, median (interquartile range), or median [range].

| First Author | Mortality | Survivors | Not discharged | Still on ECMO | Complications on ECMO | Days on ECMO* |
|--------------|-----------|-----------|----------------|---------------|--|----------------|
| Falcoz | 6 | 10 | 1 | 0 | 7 mechanical 62 haemorrhagic 1 neurologic 12 renal 1 cardiovascular 3 pulmonary 10 infectious 1 others (thrombocytopenia) | 9 [0–16] |
| Guihaire | 4 | 16 | 4 | 3 | 18 mechanical 1 neurologic 10 pulmonary 3 infectious 1 other (mesenteric ischemia) | 19.0 ± 10.1 |
| Huette | 4 | 8 | 0 | 0 | 5 mechanical 3 hemorrhagic 8 renal 1 cardiovascular 4 pulmonary 10 infectious 3 others (2 liver failure, 1 HIT) | 12 (9–22) |
| Jackel | 8 | 7 | 0 | 0 | | |

Abbreviations: ECMO: extracorporeal membrane oxygenation, NR: not reported.

*Days on ECMO reported as mean ± SD, median (interquartile range), or median [range].

| First Author | Mortality | Survivors | Not discharged | Still on ECMO | Complications on ECMO | Days on ECMO* |
|--------------|-----------|-----------|----------------|---------------|--|---------------|
| Jang | 10 | 4 | 5 | 2 | 5 neurologic 9 renal 1 cardiovascular 6 pulmmonary | 17.27 ± 16.42 |
| Jozwiak | 6 | 5 | 0 | 0 | | |
| Le Breton | 2 | 11 | 0 | 0 | 2 mechanical 3 hemorrhagic 2 infectious | 14.53 ± 8.84 |
| Masur | 5 | 1 | 6 | NR | 6 neurologic | 9.60 |
| Mustafa | 6 | 29 | 5 | 2 | 10 pulmonary | 29.9 ± 3.6 |
| Roedl | 13 | 7 | 0 | 0 | | |
| Schmidt | 25 | 38 | 20 | 5 | 25 mechanical 45 hemorrhagic 5 neurologiv 38 renal 11 cardiovascular 50 pulmonary 129 infectious 7 others (5 thrombocytopenia, 2 HIT) | 20 (10–40) |
| Shih | 16 | 21 | 0 | 0 | | |
| Takeda | 67 | NR | 20 | 20 | NA | 14.42 ± 9.01 |

Abbreviations: ECMO: extracorporeal membrane oxygenation, NR: not reported.

*Days on ECMO reported as mean ± SD, median (interquartile range), or median [range].

| First Author | Mortality | Survivors | Not discharged | Still on ECMO | Complications on ECMO | Days on ECMO* |
|---|-----------|-----------|----------------|---------------|---|---------------|
| Yang | 12 | 6 | 3 | 0 | 3 hemorrhagic 8 renal 8 cardiovascular 6 pulmonary 3 infectious | NR |
| Zayat | 8 | 9 | 0 | 0 | | |
| Zeng | 5 | NR | 7 | 4 | NA | 11.3 ± 7.8 |
| Zhang | 14 | 29 | 0 | 0 | | |
| Abbreviations: ECMO: extracorporeal membrane oxygenation, NR: not reported. | | | | | | |
| *Days on ECMO reported as mean ± SD, median (interquartile range), or median [range]. | | | | | | |

Assessment of study quality

Appraisal using the JBI checklist for cohort studies and case series suggested a high level of quality across the included studies for this review. All studies, except two,[13, 32] had scores above 8/10 (Supplementary Table 3). A summary of the GRADE assessment for certainty of evidence is provided in Supplementary Table 4.

Pre-ECMO variables

Fifteen studies (1344 patients) reported on PaO₂/FiO₂ prior to ECMO initiation. The pooled mean PaO₂/FiO₂ was 67.76 (95% CI: 64.72–70.80). Pre-ECMO SOFA score was reported in 11 studies (275 patients) with a pooled mean SOFA score prior to ECMO initiation of 9.62 (95% CI: 8.40-10.84)

Pre-ECMO adjunctive therapies

Patients with COVID-19 who received ECMO also received various adjunctive therapies prior to ECMO. Pooled incidence of prone positioning prior to ECMO was 85.3% (95% CI: 74.6%-93.7%) while 96.3% (95% CI: 87.6%-100.0%) of the patients received neuromuscular blockers. Additional details on the use of inotropic agents, corticosteroids, immuno-modulators and antiviral drugs are highlighted in supplementary Table 5.

In-Hospital Mortality

The pooled in-hospital mortality of COVID-19 patients receiving ECMO (22 studies, 1896 patients) was 37.1% (95% CI: 32.3%-42.0%, high certainty). (Fig. 2) Two studies had a JBI score lower than 8; pooled in-hospital mortality after excluding these studies was 37.9% (95% CI: 32.9%-42.9%). There was no evidence

of publication bias (Supplementary Fig. 1) ($p_{\text{egger}} = 0.21$). We also analyzed the proportion of non-survivors supported on VV ECMO for COVID-19 (17 studies, 1737 patients); pooled in-hospital mortality was 35.7% (95% CI: 30.7%-40.7%, high certainty). (Fig. 3) Mortality, after removal of studies that did not report on pre ECMO $\text{PaO}_2/\text{FiO}_2$ ratio, was 36.4% (95% CI: 30.2%-42.9%). Two studies compared mortality rates of patients on mechanical ventilation to those on ECMO; patients needing mechanical ventilation had mortality rates of 47.8% and 63.2% as compared to 46.15 % and 57.1% respectively in those needing ECMO in these two studies.

Subgroup analysis

There were no overall differences in regional outcomes for COVID-19 patients treated with ECMO (Supplementary Fig. 2).

Meta-regression analysis

Univariable meta-regression analysis identified increasing age and reduced ECMO duration as variables associated with mortality, while increasing BMI were protective. (Supplementary Figs. 3,4 and 5). Increasing SOFA score was not associated with higher mortality. Other pre-ECMO factors ($\text{PaO}_2/\text{FiO}_2$ ratio, duration of mechanical ventilation prior to ECMO) or coexisting comorbidities (diabetes mellitus, hypertension, smoking) were not associated with increased mortality. (supplementary table 6)

Secondary outcomes

141 of 1733 patients (21 studies) remained in hospital, while 68 of 1720 patients (20 studies) were still being supported with ECMO at the time of publication. Pooled ICU LOS (8 studies, 216 patients) and hospital LOS (6 studies, 1177 patients) were 32 days (95% CI: 26–38, moderate certainty) and 40 days (95% CI: 30–49, low certainty), respectively. There were 17 studies (1412 patients) that reported on weaning from ECMO with 67.6% (95% CI: 50.5%-82.7%, low certainty) of patients successfully weaned off ECMO. The pooled mean duration of mechanical ventilation prior to ECMO (16 studies, 1427 patients) was 4.40 days (95% CI: 4.03–4.79, moderate certainty), while the pooled ECMO duration (18 studies, 1711 patients) was 15.81 days (95% CI: 13.26–18.35, moderate certainty). Complications during ECMO were reported in 18 studies (1721 patients) There were a total of 1583 reported complications; renal complications (559/1583) were the most common, followed by mechanical (429/1583) and infectious complications (171/1583). A summary of all the outcomes including complications is provided in Table 2.

Discussion

This systematic review and meta-analysis examined the use of ECMO in adult patients with COVID-19. The pooled in-hospital mortality in 1896 patients with COVID-19 who predominantly had severe ARDS and were supported with ECMO was 37%, and this estimate was based on high certainty evidence. Mortality was slightly lower (35.7%) in patients exclusively receiving VV ECMO. This pooled mortality rate

is comparable to the mortality rates seen in ECMO treated patients in the ECMO to Rescue Lung Injury in Severe ARDS [EOLIA] and Conventional ventilation or ECMO for Severe Adult Respiratory failure [CESAR] trials[44, 45] as well as the recent individual patient data meta-analysis of the two randomized controlled trials evaluating the use of VV ECMO in patients with ARDS from non-COVID etiologies (32.1 vs. 36%).[46] The pooled mean duration of ECMO support in COVID-19 patients was 16 days and the pooled mean ICU length of stay was 29 days. A large proportion of patients received neuromuscular blockade (96.2%) and were positioned prone (84.5%) prior to initiation of ECMO. The patients more commonly suffered renal, mechanical and infectious complications and the complication rates in COVID-19 patients were similar to those seen in the EOLIA trial.[44] The review also identified increasing age as a risk factor for increased mortality.

The use and efficacy of ECMO in pandemics have been previously reported. [1–3] (1–3) The incidence of ECMO use in patients with 2009 influenza A(H1N1)-associated ARDS in Australia and New Zealand was estimated to be 2–6 cases per million [1, 8], whereas 6% of critically ill patients were supported with ECMO for MERS-CoV-associated ARDS.[4] A meta-analysis of the studies that reported on the use of ECMO for the 2009 influenza A(H1N1) pandemic showed an overall mortality of 35% in a relatively younger population (mean age 40 years).[2] Patients with MERS-CoV who were supported with ECMO had a higher reported mortality of 40–70%.[3] By comparison, this review demonstrated that the cumulative mortality for patients with COVID-19 receiving ECMO support was 37.1% in a group of patients who were older (mean age 51.6 years) and were predominantly men. These results may also alleviate some concerns regarding VV ECMO use in the context of COVID-19-related ARDS.[13, 47] During a pandemic, ECMO use will be subject to resource availability, given that prolonged ECMO support may be needed in these patients and the ELSO guidelines provide recommendations to assist clinicians in selecting patients judiciously in order to maximise benefit to patients with available resources.[7, 8] Our metaregression analysis showed that outcomes appear worse in patients with increasing age. Clinicians may have to exercise considerable discretion when offering ECMO to older patients during a pandemic where resources may be stretched, with no definitive age cut-off to guide this decision-making.

Interestingly, greater duration of ECMO support and illness severity (SOFA score) were not independently associated with death. The duration of VV ECMO support was longer when compared with patients in the EOLIA trial receiving ECMO (median: 15.92 days vs 11 days). Prolonged ECMO runs outside COVID-19 have been reported with good success.[48] However, the association between prolonged ECMO duration and improved mortality seen in this study stems likely from immortal time bias49, commonly reported in observational studies. For patients on ECMO, such individuals must survive long enough to be weaned off, whereas their peers have no minimum survival requirements. The mean duration of mechanical ventilation prior to ECMO was 4.4 days and was not associated with mortality in the metaregression analysis. Higher SOFA score was not an independent predictor for death in this review, a finding that contradicts previously published experience.[50] SOFA scores in patients requiring ECMO for COVID-19 can be variable, depending on their underlying phenotype.[51] Therefore, caution should be exercised when placing patients with advanced extrapulmonary organ failures on ECMO. Even though VV ECMO appears to be a viable therapy, the potential need for prolonged ECMO support may be a

significant consideration when selecting patients during the pandemic. Other uncertainties regarding the long-term outcomes and the maximum duration of ECMO where recovery is still possible remain and may become clearer as more data becomes available. [52]

Strengths of this study include robust inclusion criteria and relevant exclusion criteria. Our review included 15 studies covering 6 geographical regions. We reduced confounding by elucidating factors correlating with mortality via subgroup analysis and meta-regression. Single centre data that overlapped with international registries were excluded thereby avoiding duplication of data. We assessed study quality using a validated tool and assessed certainty in our estimates using GRADE. Nonetheless, we recognise several limitations of this study. Firstly, we included studies written only in English for the review. The variability in ECMO initiation and management across centres and regions, as well as additional variability during the pandemic may have contributed to increased heterogeneity in our results. The outcomes of patients who were still in hospital or on ECMO at the time of publication were not known. These aspects could have introduced various confounders given the lack of risk adjustment or propensity-score weighting. Even though the paper from ELSO registry contributed to a majority of patients in the review, the overall weightage to the entire analysis was only 12%, highlighting that the data was not skewed by one study. In addition, manuscripts published from centres that contributed to the ELSO registry report were excluded to avoid duplication. Meta-regression analyses are also inherently constrained by a lack of power, resulting in an increased risk of type 2 errors. Nonetheless, there was no publication bias in the studies included and JBI critical appraisal deemed most of the articles as high quality and suitable for inclusion while the GRADE assessment suggested a high certainty of evidence for the primary outcome.

Conclusions

The outcomes from VV ECMO use in patients with COVID-19-related severe ARDS during the early pandemic appear similar to those reported in patients who receive VV ECMO for non-COVID-19-related severe ARDS. Increasing age is a risk factor for death. The duration of ECMO appears to be prolonged in patients with COVID-19 and a prolonged ECMO run was not in itself a predictor of death.

Abbreviations

ECMO

Extracorporeal membrane oxygenation

ARDS

Acute respiratory distress syndrome

MERS-CoV

Middle East Respiratory Syndrome Coronavirus

COVID-19

Coronavirus disease 2019

ELSO

Extracorporeal life support organisation
SSC
Surviving Sepsis Campaign
VV
Venovenous

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and materials: All data generated or analysed during this study are included in the published studies and their supplementary information files.

Competing interests: DB receives research support from ALung Technologies. He has been on the medical advisory boards for Baxter, Abiomed, Xenios and Hemovent, and is the President-elect of ELSO. RPB receives research support unrelated to this project from National Institutes of Health's National Heart, Lung and Blood Institute K12 HL138039 and R01 HL153519 and the National Institute of Child Health and Human Development R01 HD015434. He is the ELSO Registry Chair. EF reports personal fees from ALung Technologies, Baxter, Fresenius Medical Care, Getinge, and MC3 Cardiopulmonary outside the submitted work.

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Author contributions: The study was designed by KS and KR. RRL and KR screened the articles, assessed the risk of bias and extracted the data. RPB and ST aided with the data from Extracorporeal Life Support Organisation and Japan ECMOnet for COVID-19 registries respectively. SNW helped with the search criteria. RRL analysed and interpreted the data under the supervision of CST and KR. BR and SF helped with GRADE analysis. Tables and figures were produced by RRL. KR and KS had primary responsibility of writing the manuscript, to which all authors contributed to and revised. DB, EF, RPB, GM critically revised the manuscript for important intellectual content. All authors provided critical conceptual input, interpreted the data analysis, read, and approved the final draft.

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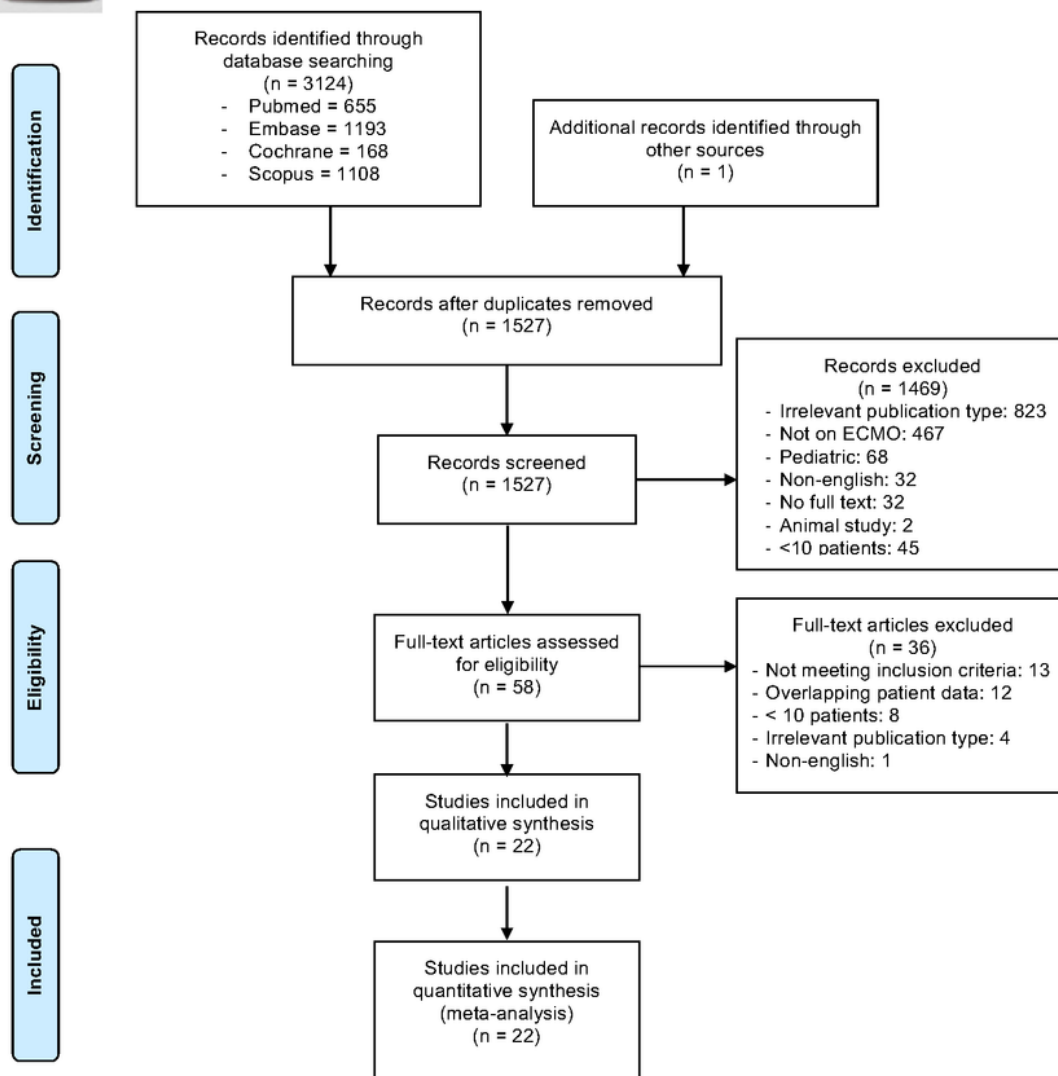
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Figures



PRISMA 2009 Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Figure 1

Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flowchart

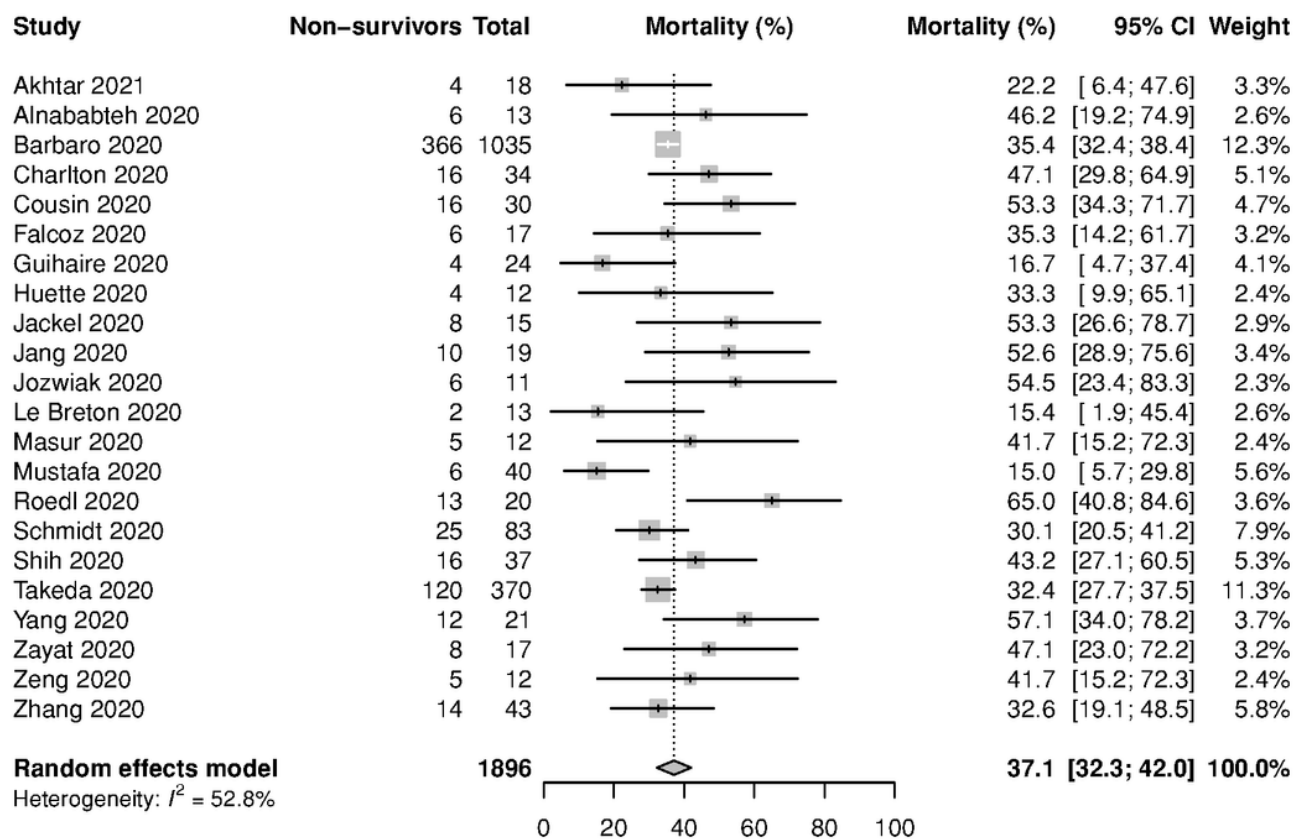


Figure 2

Proportion of nonsurvivors among coronavirus disease 2019 patients requiring extracorporeal membrane oxygenation support

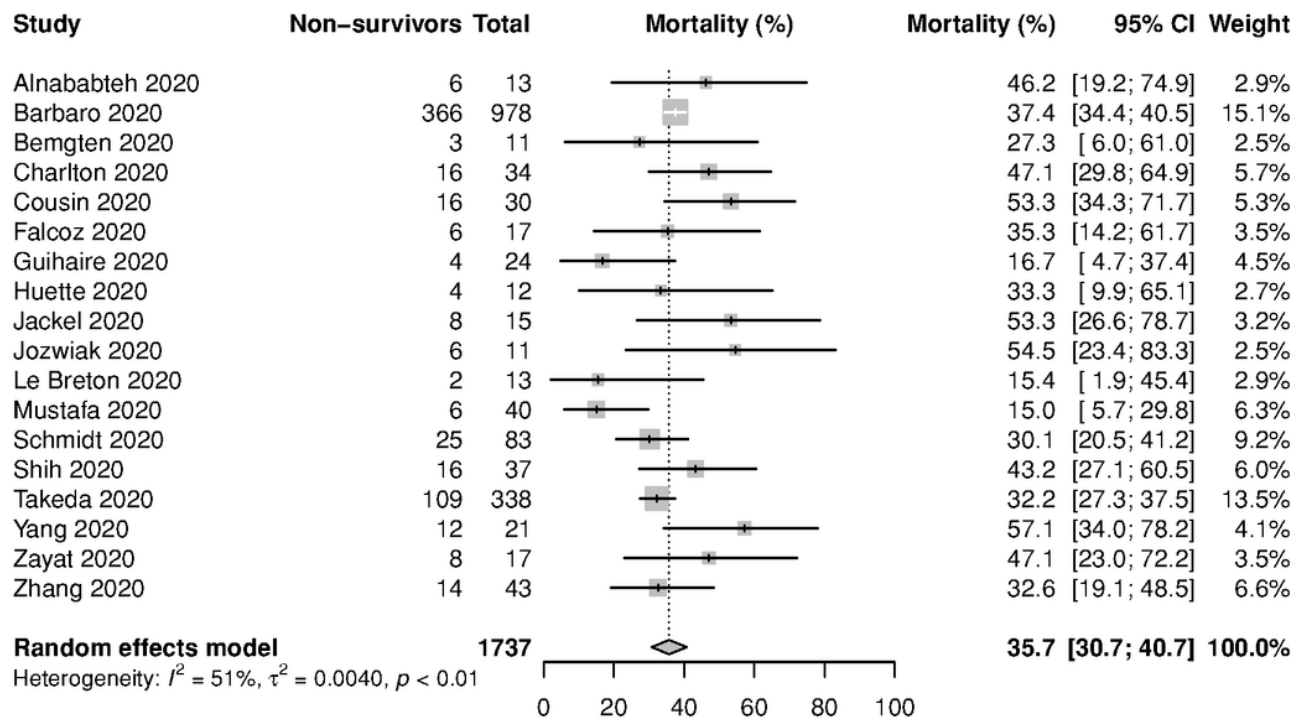


Figure 3

Proportion of nonsurvivors among coronavirus disease 2019 patients requiring venovenous extracorporeal membrane oxygenation support

Supplementary Files

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