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SYSTEMATIC REVIEW

Temporary mechanical circulatory support for COVID-19 patients: A systematic review of literature

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Abstract

Objective: Myocardial damage occurs in up to 25% of coronavirus disease 2019 (COVID-19) cases. While veno-venous extracorporeal life support (V-V ECLS) is used as respiratory support, mechanical circulatory support (MCS) may be required for severe cardiac dysfunction. This systematic review summarizes the available literature regarding MCS use rates, disease drivers for MCS initiation, and MCS outcomes in COVID-19 patients.

Methods: PubMed/EMBASE were searched until October 14, 2021. Articles including adults receiving ECLS for COVID-19 were included. The primary outcome was the rate of MCS use. Secondary outcomes included mortality at follow-up, ECLS conversion rate, intubation-to-cannulation time, time on ECLS, cardiac diseases, use of inotropes, and vasopressors.

Results: Twenty-eight observational studies (comprising both ECLS-only populations and ECLS patients as part of larger populations) included 4218 COVID-19 patients (females: 28.8%; median age: 54.3 years, 95%CI: 50.7–57.8) of whom 2774 (65.8%) required ECLS with the majority (92.7%) on V-V ECLS, 4.7% on veno-arterial ECLS and/or Impella, and 2.6% on other ECLS. Acute heart failure, cardiogenic shock, and cardiac arrest were reported in 7.8%, 9.7%, and 6.6% of patients, respectively. Vasopressors were used in 37.2%. Overall, 3.1% of patients required an ECLS change from V-V ECLS to MCS for heart failure, myocarditis, or myocardial infarction. The median ECLS duration was 15.9 days (95%CI: 13.9–16.3), with an overall survival of 54.6% and 28.1% in V-V ECLS and MCS patients. One study reported 61.1% survival with oxy-right ventricular assist device.

Conclusion: MCS use for cardiocirculatory compromise has been reported in 7.3% of COVID-19 patients requiring ECLS, which is a lower percentage compared to the incidence of any severe cardiocirculatory complication. Based on

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the poor survival rates, further investigations are warranted to establish the most appropriated indications and timing for MCS in COVID-19.

KEYWORDS
COVID-19, extracorporeal life support, extra-corporeal membrane oxygenation, mechanical circulatory support

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a pandemic in March 2020 by the World Health Organization (WHO) and resulted in a globally devastating effect, with over 180 million people being affected and about 6 million deaths.[1] COVID-19 is the clinical manifestation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Although respiratory symptoms have dominated COVID-19 clinical presentation, up to 20%–25% of overall patients show cardiac involvement[2–6] as reflected by increased biomarker levels.[7] The underlying mechanisms for cardiac failure are severe immune system overreaction, the downregulation of the angiotensin-converting enzyme 2, the increased levels of Angiotensin II, the development of hypertension, thrombosis, and direct damage to the cardiomyocytes.[8] Moreover, COVID-19 patients might experience arrhythmias due to underlying comorbidities, polypharmacy, and disease progression.[8] Finally, COVID-19 patients suffering from acute respiratory distress syndrome (ARDS) and severe systemic hypoxia are at risk of type 2 myocardial infarction.[9] All these mechanisms involved in COVID-19-related cardiac damage might adversely affect prognosis.[10]

According to data reported by the Extracorporeal Life Support Organization (ELSO),[11] until April 2022, extracorporeal life support (ECLS) has been used as respiratory and/or circulatory support in over 13000 COVID-19 patients.[12–14] Overall, veno-venous (V-V) ECLS has been the most used configuration in the case of refractory respiratory failure[15,16] primarily due to acute respiratory distress syndrome (ARDS). However, a subset of COVID-19 patients might experience persistent concomitant hemodynamic instability and cardiac dysfunction requiring temporary mechanical circulatory support (MCS).[17,18] Due to both the underlying pulmonary and cardiac pathologies and the complications from interventions, these patients are usually burdened with higher mortality and complication rates.[18] This might especially account for cases of delayed MCS initiation or cases where initial V-V ECLS had undergone a configuration change to veno-arterial (V-A) or veno-venoarterial (V-VA) ECLS for further hemodynamic deterioration. Unfortunately, despite the growing knowledge on cardiac involvement in COVID-19, data on MCS use during or after a SARS-CoV-2 infection are scarce. Based on the discrepancy between the reported incidence of cardiac damage in COVID-19 and the lack of evidence on MCS use for SARS-CoV-2 infection, we hypothesize the underuse of MCS in COVID-19 patients with consequent high cardiac-related morbidity and mortality. Therefore, this systematic review investigates the rate of MCS use, outcomes, and cardiac disease drivers for MCS initiation and ECLS configuration change in COVID-19 patients supported with ECLS.

2 | SPECIFIC AIMS AND METHODS

2.1 | Data sources and search strategies

The protocol for this systematic review was completed before the start of the literature screening. The study was undertaken and reported in accordance with the preferred reporting items for systematic review and meta-analyses (PRISMA) guidelines[19] and was registered with PROSPERO (Registration No. CRD42021266433). PubMed/EMBASE databases were searched from inception to October 14, 2021. Details of the search strategy are provided in Supporting Information. After removing duplicates, the remaining titles and abstracts were assessed for inclusion by two independent reviewers (S.M. and J.M.R.) using a free, open-source citation screening program.[20] Full texts of relevant articles were retrieved and independently assessed by three authors (S.M., M.E.D.P., and J.M.R.). Disagreements over article inclusion were resolved by consensus. Reference lists of assessed full texts were screened for further relevant studies.[21]

2.2 | Population, intervention, comparison, and outcome (PICO)

We included randomized clinical trials, controlled before-and-after studies, prospective and retrospective cohort studies, cross-sectional studies, case–control studies, and case series. Conference abstracts, books or gray literature, articles not written in English, reviews, and animal studies were excluded.

Studies reporting on adult patients (age ≥ 18 years old) diagnosed with COVID-19 and undergoing V-A, V-VA, venoveno-arterial (VV-A) ECLS, or other MCS devices such as Impella (Abiomed, Danvers, USA) and TandemHeart (TandemLife, Pittsburgh, Pennsylvania) were considered eligible.[22] The use of intra-aortic balloon pump was not subject of this review based on the different mechanism and magnitude of circulatory support compared to the abovementioned MCS types. Inclusion required documentation of used MCS type and/or ECLS configuration for all patients. In addition, pediatric patients and patients with no proven diagnosis of COVID-19 were excluded.

Articles analyzing only patients supported with V-V ECLS and not reporting any reference to their MCS use were excluded to minimize the risk of selection and information bias for centers that used but not reported ECLS configurations or MCS other than V-V ECLS. Moreover, studies excluding all V-A ECLS were not considered.[23] Finally, case series reporting less than five patients were excluded.[24] When possible, comparisons were performed between patients supported with V-V ECLS and patients supported with MCS devices. The primary outcome measure was the use rate of cardiac support identified as V-A ECLS, V-VA, VV-A ECLS, or other MCS devices such as Impella (Abiomed, Danvers, USA) or TandemHeart (TandemLife, Pittsburgh, Pennsylvania) in COVID-19 patients requiring ECLS. Secondary outcome measures included mortality at follow-up, ECLS conversion rate, intubation-to-cannulation time, time on ECLS, cardiac-related complications, use of inotropes, and vasopressors.

2.3 | Data extraction and risk-of-bias assessment

Using a standardized electronic report form, data were extracted by a first reviewer (A.S.) and independently checked for accuracy by three other reviewers (S.M., M.E.D.P., and J.M.R.). Details of extracted variables are reported in the Supporting Information. In addition, the Newcastle-Ottawa Scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) was used for assessing the quality of such studies (Table S1).

2.4 | Data synthesis

Available evidence was summarized using systematic review methodology and standard summary statistics overall.[25] An additional analysis was performed to estimate the pooled median values for available continuous variables. The quantile estimation (QE) method for pooling median was based on interquartile ranges and minimum to maximum values. The sampling variance of the effect size for each study was estimated via the QE method. After estimating the sampling variances for all studies, studies were meta-analyzed using the restricted maximum likelihood estimator (REML) in a random-effects model.[26] The analysis was performed with R 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). Given the significant clinical,[27] methodological, and statistical heterogeneity among published studies, further meta-analytic methods were not applied.

3 | RESULTS

3.1 | Literature search

A total of 1309 abstracts were identified through PubMed/Medline/EMBASE search (Figure 1), and reference list screening yielded one additional publication. Six duplicates were identified. After title and abstract screening, 841 potentially relevant records were reviewed and evaluated regarding study type. Finally, 83 studies were selected based on the inclusion criteria. Additional four more articles were excluded based on the lack of reported outcomes,[28,29] lack of ECLS type definition for all patients,[30,31] or methodological uncertainties.[32] In this last case, the study was based on data reported weekly by the European ELSO and not on an original database including single patient data. Therefore, the data source was considered unreliable. As a possible population overlap was identified in 22 articles[13,31,33–52] (Table S1), only the most recent or complete studies reporting the larger cohorts of patients were included.[13,33,34,36–40,48] As one of the included study reports data from the ELSO registry accounting for 213 contributing centers worldwide (Figure 2), it was not possible to exclude with certainty the presence of a partial overlap with other selected studies published by centers contributing to the ELSO registry. In the case of possible large overlap of a study[12] with the ELSO registry cohort,[13] the latest was considered for inclusion based on the larger data availability at publication time. Finally, 28 articles were considered for the qualitative analysis (Figure 1).[13,33,34,36–40,48,53–71] Most of the included studies had a retrospective design.[37,40,47,48,53,54,56,59,62,64,66,69,71] Only four studies reported prospectively collected data[33,38,63,67] and two studies showed data from multicenter registries.[13,34] Randomized trials were not identified (Table 1). According to the Newcastle-Ottawa Scale, the risk of bias assessment of observational studies is presented in Table S2. Eighteen articles reported studies developed on

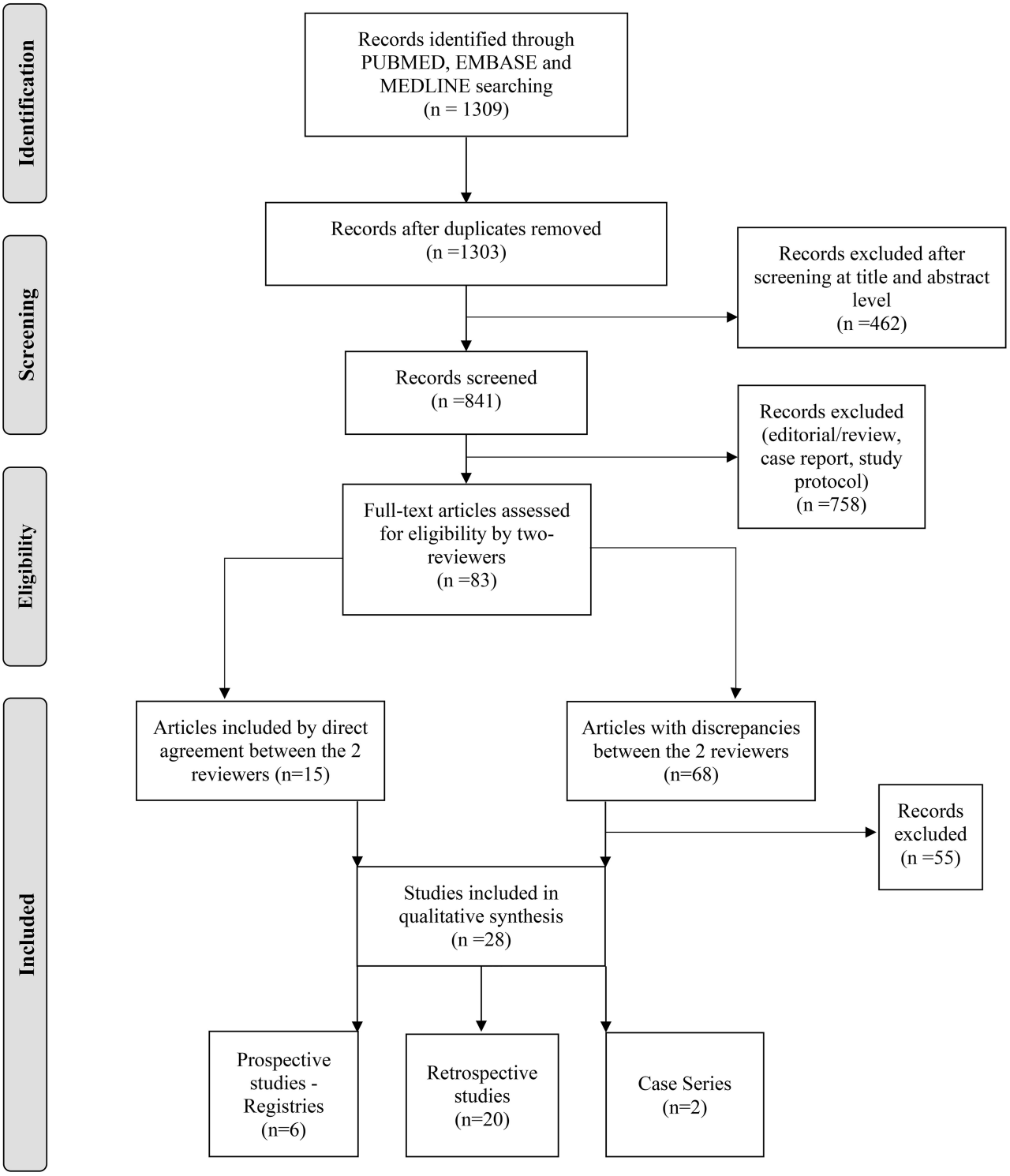

FIGURE 1 Flowsheet of the included studies

ECLS patients only,[13,33,34,36–40,48,53,54,56,60,62,66,67,70,71] while other 10 reported data on mixed populations including both ECLS and not ECLS patients.[55,57–59,61,63–65,68,69] Studies were performed in Europe (n = 15), North America (n = 8), China (n = 3), Middle East, and India (n = 1) and inclusion criteria were comparable among them (Table S3).[13]

3.2 | Overall COVID-19 patient profiles

A total of 4218 COVID-19 patients, including 2774 patients (65.8%) supported with ECLS, were comprised in the final analysis (Table 1). Even though the literature search included all publications until October 2021, only four studies reported data referred to patients who received ECLS

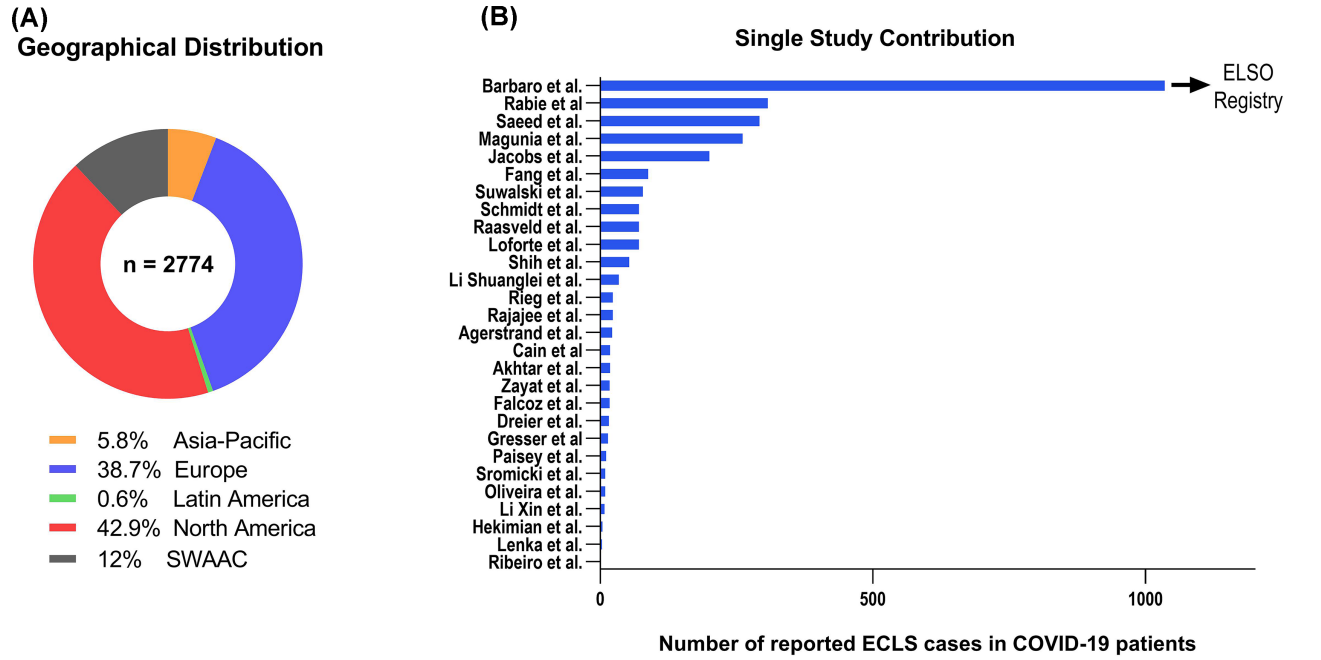

FIGURE 2 Summary of selected literature. (A) Geographical distribution of reported ECLS patients. (B) Single study contribution to the literature synthesis. SWAAC, Southwest Asia and Africa Chapter [Color figure can be viewed at wileyonlinelibrary.com]

in 2021.[38,39,57,63] However, only Schmidt et al. compared the results of patients receiving ECLS for COVID-19 during the first wave (before July 1, 2020) and the following waves (from July 1 2020 to January 28 2021). Baseline characteristics were available for the overall population and not only for the ECLS subgroup in studies reporting on mixed populations. Females accounted for 28.8% of the overall population (n = 1214) and males for the 71.2% (n = 3004). The reported median age was 54.3 years (95%CI: 50.7–57.8), with one case series reporting on a population of much younger patients (median: 19; IQR: 17–29).[58] Most of the studies (Table 1) reported data on body mass index (BMI) referring a median BMI of 29.7 (95% CI: 27.8–30.3), which indicates an overweight or obese status of the population.[13,36–38,40,53,54,56–58,60,62,63,65–67,70,71] The overall survival was 51.9% (n = 2190). Fourteen studies (50%) reported data on possible cardiac causes of dea th.[33,34,37,40,45,48,53,54,56,58,59,61,62,71] Overall, a group of 71 patients were identified as dead from cardiac-related causes, such as tamponade,[33,40] heart failure,[37,48,62,69] cardiogenic shock,[69] or cardiac arrest[34] (Table 1).

3.3 | COVID-19 patients' cardiac-related characteristics

Data depicting patients' cardiac impairment were reported inconsistently, and substantial amount of data were not available (Table 2). Most patients (n = 2884/3214, 89.7%) were clearly identified as suffering from ARDS, with 558 patients (13.9%, data available for 3996 patients) diagnosed with pre-existent cardiac disease. Interestingly, more patients were described as experiencing cardiac complications than septic shock (n = 73/565, 12.9%). Indeed, acute heart failure (n = 139/1789) and/or cardiogenic shock (n = 37/383) were reported in 7.8% and 9.7% of patients, respectively. One case series reporting single patient data described that left ventricular ejection fraction was moderately-to-severely impaired in all cases and this was the only report specifically focused on adult patients diagnosed with myocarditis or multisystem inflammatory syndrome.[58] Only four studies[33,40,56,66] reported data on possible right heart failure, and myocarditis was rarely reported, while it was described as uncommon by Lenka et al.[59] Cardiac arrest was reported in 6.6% of patients (n = 114/1739), occurring before or after ECLS initiation. Vasopressors were used in 37.2% (n = 834/2240), while the use of inotropes was rarely reported (Table 2). Specific cardiac-related characteristics for the ECLS subgroups were not available.

3.4 | ECLS strategies and outcomes

The overall median Pa/FiO_2 ratio was 77.5 (95% CI: 62.3–92.7; data available for 2384 patients from 18 studies). Pre-ECLS median APACHE and SOFA scores were rarely reported.

Veno-venous ECLS was used as single organ support in 92.7% of the patients (n = 2571/2774) while

TABLE 1 Study characteristics, baseline patient data, and overall survival

Author	Country	Year of publication	Study type (*N* centers)	Study period	Overall COVID-19 patients (*N*)	Age (years)	Females (*N*, %)	Body mass index	Overall survival (*N*, %)	Reported possible cardiac cause of death (*N*, %)
Agerstrand et al.[53]	United States	2021	Retrospective (1)	March 2020–May 2020	22	52 (range: 19–68)	4 (18.2)	28.2 (21.3–55)	12 (54.5)	0
Akhtar et al.[54]	United Kingdom	2020	Retrospective (1)	March 2020–July 2020	18	47.3 ± 9.8	2 (11)	31 ± 6.6	14 (78)	0
Barbaro et al.[13]	International—ELSO Registry	2021	Registry (349)	January 2020–May 2020	1035	49 (41–57)	269 (26)	31 (27–37)	Discharged: 588 (56.8) Hospitalized: 67 (6.5)	Na
Cain et al.[55]	United States	2021	Retrospective (1)	Mar 2020–July 2020	39	53 (44–61)	20 (51.3)	Na	26 (66.7)	Na
Dreier et al.[56]	Germany	2021	Retrospective (1)	March 2020–May 2020	16	59 (51–65)	3 (18.7)	27.5 (24.7–32.6)	11 (68.8)	0
Falcoz et al.[33]	France	2020	Prospective (1)	March 2020–April 2020	17	56 (30–76)	1 (6)	Na	11 (64.7)	1 (5.9) Tamponade
Fang et al.[48]	China	2021	Retrospective (7)	January 2020–June 2020	88	58.5 (47–66.5)	32 (36.4)	Na	23 (26.1)	22 (25) Heart failure
Gresser et al.[57]	Germany	2021	Retrospective (1)	March 2020–January 2021	95	66 (55–74)	21 (22.1)	27 (25–33)	59 (62.1)	Na
Hekimian et al.[58]	France	2021	Case series (1)	February 2020–June 2020	11	19 (17–29)	5 (45.5)	24 (22–32)	10 (90.9)	0
Jacobs et al.[34]	United States	2021	Registry (29)	March 2020–December 2020	200	51 (40–59)	62 (31)	Na	90 (45)	6 (3) Cardiac arrest
Lenka et al.[59]	United States	2020	Retrospective (1)	March 2020–April 2020	32	62.2 ± 11.2	12 (37.5)	Na	Discharged: 11 (34.5) Hospitalized: 16 (50)	Na
Li X. et al.[60]	China	2020	Case series (1)	January 2020–March 2020	8	64.5 (62.3–78)	2 (25)	24 (22.7–24.4)	Survivors: 3 (37.5) Ongoing ECLS: 1 (12.5)	Na
Li S. et al.[61]	China	2021	Retrospective (1)	January 2020–March 2020	65	67 (60.5–72)	18 (27.7)	ECLS group: 24.4 (22.5–25.3)	16 (24.6)	6 (12.2) Respiratory/heart failure
Loforte et al.[62]	Italy	2021	Retrospective (12)	March 2020–September 2020	71	55.4 ± 9.3	10 (14)	30.2 ± 6.1	26 (36.6)	2 (2.8) Acute heart failure
Magunia et al.[63]	Germany	2021	Retrospective/ prospective (27)	January 2020–May 2021	1186	63 (54–73)	333 (28.1)	28.3 (25.2–32.8)	403 (34)	Na
Oliveira et al.[64]	United States	2021	Retrospective (9)	March 2020–May 2020	131	61 (49.5–71.5)	85 (64.9)	≤25: 40 (30) ≥40: 7 (5.3)	Discharged: 94 (79.4) Hospitalized: 11 (8.4)	Na
Paisey et al.[65]	United Kingdom	2021	Retrospective (1)	March 2020–May 2020	15	51 (48–54)	3 (20)	29 (23–32)	8 (53.3)	Na
Raasveld et al.[66]	Netherlands, Belgium, Sweden, Spain	2021	Retrospective (13)	March 2020–April 2020	71	52 (47–57)	14 (19.7)	29.2 (26.1–32.1)	45 (63.4)	Na
Rabie et al.[36]	Saudi Arabia, Kuwait, Qatar, India, Egypt	2021	Retrospective (19)	March 2020–September 2020	307	43 (37–52)	59 (19)	28.6 (25.4–33.3)	178 (58)	Na

TABLE 1 (Continued)

Author	Country	Year of publication	Study type (*N* centers)	Study period	Overall COVID-19 patients (*N*)	Age (years)	Females (*N*, %)	Body mass index	Overall survival (*N*, %)	Reported possible cardiac cause of death (*N*, %)
Rajajee et al.[67]	United States	2021	Prospective (1)	March 2020–July 2020	23	47 (37–52)	18 (35)	33 (27–37)	In-hospital: 15 (65.2); 1 year: 13 (56.5)	0
Ribeiro Queiros et al.[68]	Portugal	2021	Retrospective (1)	March 2020–April 2020	35	62.6 ± 6.0	12 (34.3)	Na	26 (74.3)	Na
Rieg et al.[69]	Germany	2020	Retrospective (1)	February 2020–May 2020	213[a]	65 (54–79)	84 (39.5)	Na	162 (76.1)	15[b] (29.4)
Saeed et al.[37]	United States	2021	Retrospective (17)	March 2020–September 2020	292	49 (39–57)	81 (28)	32 (29–37)	Discharged: 135 (46) Hospitalized: 25 (9)	18 (16)
Schmidt et al.[38]	France	2021	Prospective (1)	March 2020–January 2021	71	54 (49–60)	21 (29.6)	31.0 (27.2–37.0)	Estimates of 90-day survival: 52%	Na
Shih et al.[70]	United States	2021	Retrospective (2)	February 2013–May 2020	53	50 (41–56)	17 (32.1)	33.6 (30.6–37.9)	33 (62.3)	Na
Sromicki et al.[71]	Switzerland	2021	Retrospective (1)	March 2020–May 2020	9	59 (46–69)	2 (22)	27.2 (24–37.9)	7 (77.8)	0
Suwalski et al.[39]	Poland	2021	Retrospective (1)	March 2020–May 2021	78	47 ± 11.3	18 (23.1)	31.3 ± 9.5	19 (24.4)	Na
Zayat et al.[40]	Germany	2020	Retrospective (1)	March 2020–April 2020	17	57 (53–62)	6 (35)	28.2 (24.7–31.1)	9 (52.9)	1 (5.9) Tamponade

Note: Data are presented as *n* (%), mean ± standard deviation, or median (interquartile range) as appropriate and reported by the original article.

Abbreviations: ECLS, extracorporeal life support; ELSO, extracorporeal life support organization; Na, not available.

[a]Overall reported patients: $n = 213$; ICU patients: $n = 70$.

[b]Data reported only for patients who died ($n = 51$), possible cause of death.

TABLE 2 Cardiac-related and diagnostic characteristics of included patients

Author	ARDS (*N*, %)	Septic shock (*N*, %)	Preexistent cardiac disease (*N*, %)	Troponin (ng/ml)	Acute HF (*N*, %)	Cardiogenic shock (*N*, %)	Right HF (*N*, %)	Myocardial infarction (*N*, %)	Possible myocarditis (*N*, %)	Cardiac arrest (*N*, %)	ECPR (*N*, %)	Use of inotropes (*N*, %)	Use of vasopressors (*N*, %)
Agerstrand et al.[53]	21 (95.4)	Na	1 (4.5)	Na	7 (31.8)	7 (31.8)	Na	1 (4.5)	Na	4 (18.2)	Na	Na	22 (100)
Akhtar et al.[54]	Na	Na	0	Na	Na	5 (28)	Na	0	5 (28)	0	0	Na	Na
Barbaro et al.[13]	819 (79)	Na	24 (2)	Na	50 (5)	Na	Na	Na	22 (2)	48 (5)/1019[a]	11 (1)	Na	561 (55)/1015[a]
Cain et al.[55]	39 (100)	Na	CAD: 3 (7.7)	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na
Dreier et al.[56]	16 (100)	Na	Na	Na	1 (6.3)	Na	1 (6.3)	Na	Na	Na	Na	Na	Na
Falcoz et al.[33]	17 (100)	Na	Na	Na	1 (5.9)	1 (5.9)	1 (5.9)	Na	Na	Na	Na	Na	Na
Fang et al.[48]	88 (100)	Na	8 (9.1)	cTnI: 0.033 (0.013–0.239)	22/65[a] (33.8)	7 (8)	Na	Na	Na	Na	Na	26 (30)	
Gresser et al.[57]	92 (96.8)	Na	32 (33.7)	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na
Hekimian et al.[58]	3 (27.3)	0	1 (9.1)	0.81 (0.17–2.55)	11 (100%)	Na	0	0	6 (54.5)	1 (9)	Na	6 (54.5)	6 (54.5)
Jacobs et al.[34]	Na	Na	22 (11)	Na	Na	Na	Na	Na	Na	6[c] (5.5)/110	0	Na	Na
Lenka et al.[59]	28 (87.5)	Na	14 (43.7)	0.03 (0.01–0.15)	Na	Na	Na	1 (3.1)	Uncommon	Na	Na	Na	12 (36.3)
Li X. et al.[60]	8 (100)	Na	1 (12.5)	Na	0	0	0	Na	Na	1 (12.5)	1 (12.5)	Na	Na
Li S. et al.[61]	65 (100)	10 (15.4)	3 (4.6)	Na	4 (6.2)	1 (1.5)	0	0	0	1 (1.5)	1 (1.5)	Na	40 (61.5)
Loforte et al.[62]	71 (100)	Na	15 (21.1)	Na	3 (4)	Na	Na	Na	2 (3)	Na	Na	14 (19.7)	55 (77.5)
Magunia et al.[63]	1098 (92.6)	Na	311 (26.2)	Na	Na	Na	Na	Na	Na	Na	Na	Na	Na
Oliveira et al.[64]	131 (100)	Na	CAD: 21 (16) HF: 12 (9.2)	0.01 (0.01–0.02)	Na	Na	Na	Na	Na	Na	Na	Na	95 (72.5)
Paisey et al.[65]	11 (73.3)	Na	0	0.031 (0.010–0.105)	Na	Na	Na	Na	Na	Na	Na	Na	Na
Raasveld et al.[66]	71 (100)	Na	1 (2)	Na	4 (5.6)	Na	4 (5.6)	Na	Na	Na	Na	Na	Na
Rabie et al.[36]	Na	Na	CAD: 8 (2.6)	Na	Na	Na	Na	Na	Na	Na	Na	Na	179 (58.3)
Rajajee et al.[67]	23 (100)	1 (4.3)	Na	Na	Na	3 (13)	Na	Na	Na	Na	Na	3 (13)	Norepinephrine: 23 (100) Vasopressin: 16 (70)
Ribeiro Queiros et al.[68]	Na	Na	CAD: 1 (2.9) HF: 4 (11.4)	TnT: 0.112	Na	2 (5.7)	Na	Na	Na	Na	Na	2 (5.7)	31 (88.6)
Rieg et al.[69]	64[b] (91.4)	43[b] (61.4)	45 (21)	TnT: 0.016 (0.007–0.039)	15[c] (29.4) /51	13[b] (19)	Na	Na	Na	6[b] (9)	Na	Na	Na
Saeed et al.[37]	Na	9 (8)	12 (4)	Na	18 (16)	Na	Na	Na	Na	34 (12)	Na	Na	176 (64)
Schmidt et al.[38]	71 (100)	Na	Na	Na	Na	Na	Na	Na	Na	Pre-ECLS: 2 (3); during ECLS: 8 (11)	Na	Na	Na
Shih et al.[70]	53 (100)	Na	Na	Na	Na	Na	Na	Na	Na	3 (5.7)	3 (5.7)	Na	24 (45.3)

TABLE 2 (Continued)

Author	ARDS (*N*, %)	Septic shock (*N*, %)	Preexistent cardiac disease (*N*, %)	Troponin (ng/ml)	Acute HF (*N*, %)	Cardiogenic shock (*N*, %)	Right HF (*N*, %)	Myocardial infarction (*N*, %)	Possible myocarditis (*N*, %)	Cardiac arrest (*N*, %)	ECPR (*N*, %)	Use of inotropes (*N*, %)	Use of vasopressors (*N*, %)
Sromicki et al.[71]	Na	3 (33.3)	Na	Na	3 (33.3)	Na	Na	Na	Na	Na	Na	Na	Na
Suwalski et al.[39]	78 (100)	1 (1.3)	CAD: 1 (1.3); Previous MI: 3 (3.8); HF: 3 (3.8)	TnI: 0.060 (0.025–0.203)	Na	2 (2.6)	Na	1 (1.3)	Na	Na	Na	Dobutamine: 12 (15.4); Adrenaline: 13 (16.7); Dopamine: 3 (3.8); Levosimendan: 1 (1.3)	Noreadrenaline: 74 (94.9)
Zayat et al.[40]	17 (100)	10 (59)	12 (70.5)	TnT: 0.022 (0.012–0.052)	1 (6)	1 (6)	7 (41.2)	1 (6)	Na	Na	Na	12 (70.6)	15 (88.2)

Note: Data are presented as *n* (%), mean ± standard deviation, or median (interquartile range) as appropriate and reported by the original article.

Abbreviations: ARDS, acute respiratory distress syndrome; CAD, coronary artery disease; ECLS, extracorporeal life support; ECPR, extracorporeal cardiopulmonary resuscitation; HF, heart failure; Na, not available; TnT, troponin T.

[a]Data reported for a subgroup of patients indicated as the denominator.

[b]Data reported only for ICU patients ($n = 70$).

[c]Data reported only for patients who died, possible cause of death.

4.7% ($n = 130/2774$) of cases required V-A ECLS as single or subsequent support (Figure 3). Among these patients, Rieg et al. described the included population as undergoing V-A ECLS or left ventricular unloading with Impella.[69] While large series reporting on the use of Impella in COVID-19 patients are not available, few case reports have been identified.[72–78] V-VA ECLS was chosen in 1.6% of cases ($n = 43/2774$). Only 1% of patients ($n = 30/2774$) required another type of ECLS. From their initial ECLS configuration, 3.1% of the patients ($n = 54/2774$) underwent a configuration change during ECLS. Of these 54 patients, 33.3% ($n = 18$) were converted from V-V to V-A, 18.5% ($n = 10$) from V-V to V-VA, and 9.3% ($n = 5$) were converted from V-V to VV-V. Details of the configuration change were unknown in the 21 remaining patients (38.9%). Among patients who underwent configuration change, five patients were temporarily weaned from V-V ECLS and required a second run with V-A ECLS due to refractory hemodynamic instability and recurrent respiratory failure.[62] The main reported reasons for configuration change were the presence of heart failure, myocarditis, or myocardial infarction. Furthermore, the timing between cannulation and conversion was rarely reported. The median times from intubation to ECLS start (3.8 days; 95% CI: 3.1–4.5) and the overall ECLS duration (15.9 days; 95% CI: 13.9–16.3) are reported in Figures S1 and S2. An awake ECLS strategy was reported in only one patient, described as patient receiving ECLS while awake and without mechanical ventilation.[48] Survival according to specific configuration groups was rarely provided. However, 54.6% ($n = 677/1241$) and 28.1% ($n = 16/57$) of patients survived in the V-V and the V-A/V-VA ECLS group, respectively (Table 3). Cain et al. reported a 61.1% ($n = 11/18$) survival rate with the use of a right ventricular support (RVAD) including a membrane lung (OxyRVAD).

4 | DISCUSSION

This systematic review summarizes the results of 28 published studies reporting on the use of extracorporeal respiratory and circulatory support to manage COVID-19 patients. V-V ECLS was the most common support (92.7%) compared to V-A ECLS or other ECLS configurations, which were used in 4.7% and 2.6% of patients, respectively. Among both V-V and V-A ECLS patients, 3.1% of them required conversion to a different ECLS configuration, mainly to provide full cardiorespiratory support. Impella use was rarely reported. ECLS was initiated on a median time of 3.8 days after intubation, and the median ECLS duration was 15.9 days. A considerable number of patients experienced acute heart failure (7.8%),

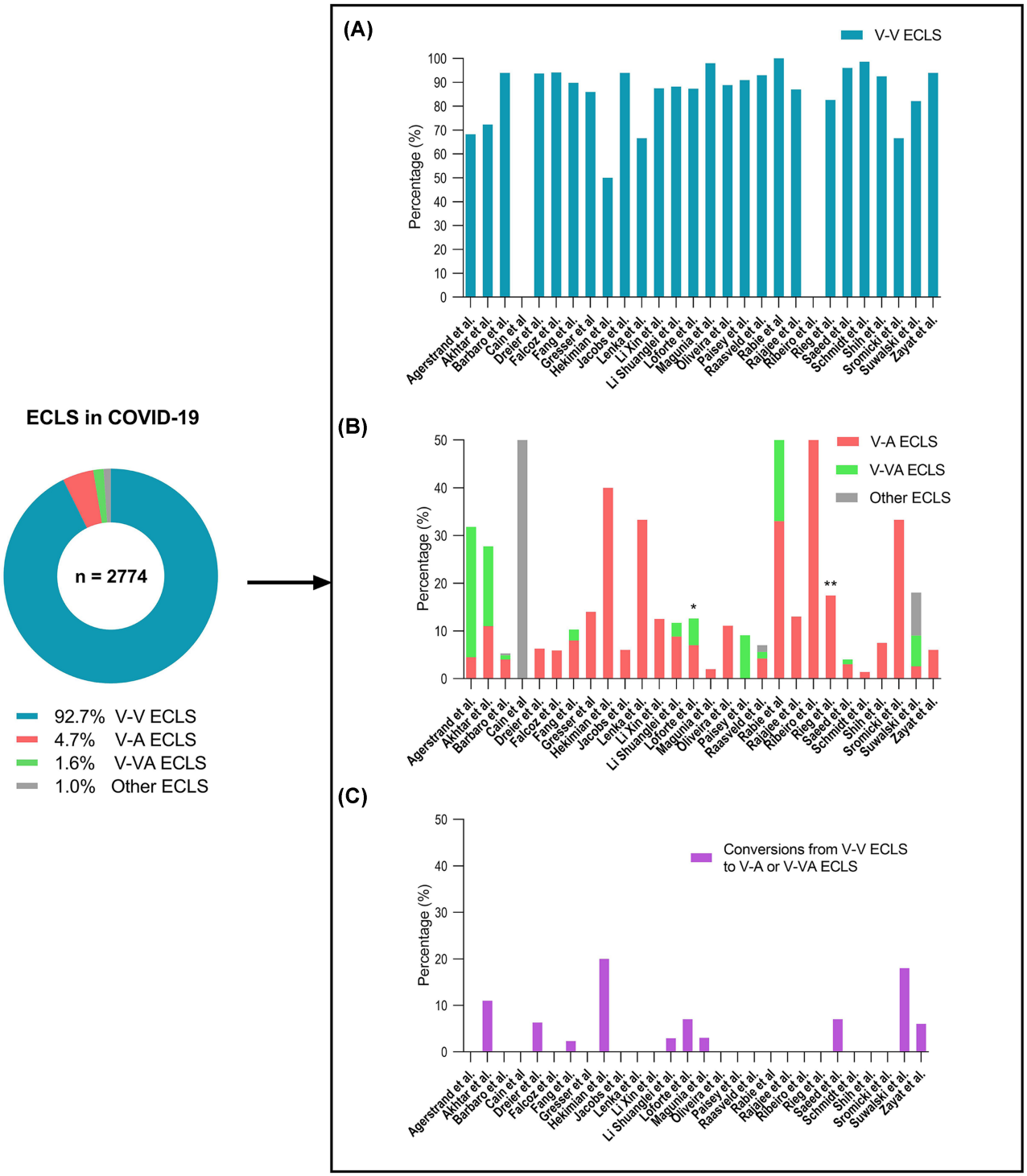

FIGURE 3 Distribution of extracorporeal life support (ECLS) types use among studies. (A), Veno-venous ECLS (V-V ECLS). (B), Veno-arterial ECLS (V-A ECLS) and Veno-venoarterial ECLS (V-VA ECLS); *Five V-V ECLS-weaned patients required a second course of ECLS with a V-A ECLS. **V-A ECLS or left ventricular unloading (Impella, Abiomed, Danvers, USA). (C), Rate of conversions from V-V ECLS to V-A or V-A ECLS [Color figure can be viewed at wileyonlinelibrary.com]

cardiogenic shock (9.7%), and cardiac arrest (6.6%) over the COVID-19 patients with the availability of these data. Vasopressors (36.7%) were often used. Survival for ECLS patients was inconsistently reported and, overall, was ranging from 28.1% for V-A/V-VA ECLS patients to 54.6% for V-V ECLS patients and 61.1% for patients supported with OxyRVAD, respectively.

Severe COVID-19 illness defined based on the American Thoracic Society guidelines for community-acquired pneumonia[79] may occur in up to 16% of SARS-CoV-2

TABLE 3 Extracorporeal life support-related data

	Pre-ECLS data				ECLS characteristics						ECLS outcomes		
Author	**Proning (*N*, %)**	**Pa/FiO2**	**APACHE II**	**SOFA**	**Overall ECLS (*N*, %)**	**Intubation-to-cannulation time (days)**	**Conversion (*N*, %)**	**Reason for conversion**	**Awake ECLS (*N*, %)**	**Median duration (days)**	**Survival V-A/V-VA (*N*, %)**	**Survival V-V (*N*, %)**	**Still ongoing (*N*, %)**
Agerstrand et al.[53]	8 (36.4)	63 (49–100)	31 (20–36)	Na	22 (100)	3.5 (range: 1–10)	0		Na	24.5 (7–74)	4 (57.1)	8 (53.3)	0
Akhtar et al.[54]	16 (89)	Na	12.2 ± 4	Na	18 (100)	2.3 ± 2	2 (11)	Myocarditis	Na	17.7 ± 9.4	Na	Na	0
Barbaro et al.[13]	612 (60) /1019[a]	72 (59–94) /868[a]	Na	Na	1035 (100)	4 (1.8–6.4)	Na		Na	13.9 (7.8–23.3)	Na	483 (62) /779[a]	31 (3)
Cain et al.[55]	37 (97.4)	71.9 (62–85)	Na	Na	18 (49.2)	Na	0		Na	Na		11 (61)	5
Dreier et al.[56]	15 (93.8)	83 (60–109)	Na	10 (9–12)	16 (100)	8 (5–18)	1 (6.3)	Biventricular heart failure	Na	Non-survivors: 24 (5–74) Survivors: 28 (13–64)	0	11 (73.3)	0
Falcoz et al.[33]	16 (94.1)	71 (52–134)	Na	8 (3–15)	17 (100)	4 (1–17)	0		Na	9 (0–16)	Na	Na	0
Fang et al.[48]	35 (39.8)	88.8 (66–128)	Na	8 (6–10)	88 (100)	3 (1–7)	2 (2.3)	Na	1 (1.1)	13 (5.8–24.3)	Na	Na	0
Gresser et al.[57]	8 (57.1)	Na	Na	12 (10–14)	14 (14.7)	1.4 (0.2–4)	0		Na	Na	2 (14.3)		Na
Jacobs et al.[34]	126 (63.3)	69.5 ± 27	Na	Na	200 (100)	4 (1–6)	0		Na	15 (9–28)	3 (25)	87 (46.3)	0
Lenka et al.[59]	Na	Na	Na	1 (0–1)	3 (13)	Na	0		Na	Na	Na	Na	Na
Li X. et al.[60]	Na	66.5 (59–74)	Na	Na	8 (100)	7.5 (4.3–12.8)	0		0	35 (19–45)	0	3 (37.5)	1 (12.5)
Li S. et al.[61]	9 (72.7)/33[a]	69.6 ± 30.1	Na	Na	34 (52.3)	5 (2–12.2)	1 (2.9)	Hemodynamic instability	1 (2.9)	15 (5.8–22.8)	1 (33)	13 (43.3)	1 (2.9)
Loforte et al.[62]	60 (85)	78.7 ± 39.3	Na	Na	71 (100)	5.5 (1.6–7.1)	5 (7)	Heart failure[b]	Na	15 (8–23)	2 (22.2)	25 (40.3)	0
Magunia et al.[63]	Na	Na	Na	Overall: 5 (3–8)	261 (22)	Na	8 (3)	Na	Na	16 (9–26)	92 (35.3)		Na
Oliveira et al.[64]	51 (46.8)	195 (174–231)	SOFA IVB: 50.5 (37–66)	3 (2–5)	9 (7)	Na	0		Na	Na	1 (100)	7 (87.5)	0
Paisey et al.[65]	Na	Na	14 (7–30)	Na	11 (73)	Na	0		Na	40 (5–96)	0	6 (54.5%)	0
Raasveld et al.[66]	56 (79)	58 (46–76)	Na	9 (7–12)	71 (100)	5 (3–10)	0		Na	13 (7–20)	Na	Na	0
Rabie et al.[36]	160 (52.1)	60 (52–68)	Na	12 (9–14)	307 (100)	2.5 (1–5)	0		Na	15 (9.5–24)	178 (58)		0
Rajajee et al.[67]	23 (100)	69 (57–79)	Na	12 (10–14)	23 (100)	7 (4–10)	0		Na	16 (8–32)	1 (33.3)	14 (70)	0
Ribeiro Queiros et al.[68]	Na	Na	Na	Na	1 (2.9)	Na	0		Na	Na	1 (100)		0
Rieg et al.[69]	Na	Na	Na	Na	23 (33)	Na	0		Na	11 (7–21)	0	9 (47.4)	Na
Saeed et al.[37]	220 (77)	77 (63–101)	Na	Na	292 (100)	3 (1–6)	19 (7)	Na	Na	Non-survivors: 19 (9–37) Survivors: 15 (9–25)	Na	Na	19 (6.5)

TABLE 3 (Continued)

Author	Pre-ECLS data				ECLS characteristics						ECLS outcomes		
	Proning (*N*, %)	Pa/FiO2	APACHE II	SOFA	Overall ECLS (*N*, %)	Intubation-to-cannulation time (days)	Conversion (*N*, %)	Reason for conversion	Awake ECLS (*N*, %)	Median duration (days)	Survival V-A/V-VA (*N*, %)	Survival V-V (*N*, %)	Still ongoing (*N*, %)
Schmidt et al.[38]	64 (90)	60 (54–74)	Na	11 (8–13)	71 (100)	3 (1–7)	0		Na	18 (5–35)	Estimates of 90-day survival: 52%		1% (0.2%–8%)
Shih et al.[70]	35 (66)	Na	Na	Na	53 (100)	Na	0		Na	14 (9–30)	33 (62.3)	0	Shih et al.[70]
Sromicki et al.[71]	Na	Na	Na	Na	9 (100)	15 (6–22.5)	0		Na	7 (5–13.5)	1 (33.3)	6 (100)	0
Suwalski et al.[39]	Na	64.1 ± 22.8	14.4 ± 6.6	8.5 ± 3.2	78 (100)	Na	14 (18)	Inadequate drainage (35.7%), inadequate perfusion (14.3%), acute myocardial infarction (7.1%), hypovolemic shock (14.3%), cardiogenic shock (14.3%) septic shock (7.1%)	Na	16.5 ± 10.0	0	20 (31.3)	0
Zayat et al.[40]	17 (100)	<100 (range: 53–75)	Na	11.9 ± 9.4	17 (100)	3 (3–15)	1 (6)	MI, RHF	Na	16 (11–21)	1 (100)	8 (50)	0

Note: Values are presented as *n* (%), mean ± standard deviation, or median (interquartile range) as appropriate and reported by the original article.

Abbreviations: A, arterial; APACHE, acute physiology and chronic health evaluation; ECLS, extracorporeal life support; MI, myocardial infarction; Na, not available; RHF, right heart failure; SOFA, Sequential Organ Failure Assessment; V, venous.

[a]Data reported for a subgroup of patients indicated as the denominator.

[b]Five V-V ECLS-weaned patients required a second course of ECLS with a V-A ECLS.

TABLE 4 MCS case report study and patient characteristics

Author	Country	Year of publication	Age (years)	Sex	ARDS	Cardiac arrest	Cardiac disease	Troponin (ng/ml)	Use of inotropes	Use of vasopressors	First ECLS	Second ECLS	Third ECLS	Duration (days)	Survival
Bemtgen et al.[72]	Germany	2020	52	Male	Yes	No	Cardiogenic shock	Na	Yes	Yes	Impella CP	V-A ECLS + Impella CP	V-V ECLS + Impella CP	Impella: 19; V-V ECLS: still ongoing	Yes
Kaki et al.[73]	United States	2020	57	Female	No	No	Cardiogenic shock, pulmonary embolism	0.21	Na	Na	Impella RP	No	No	4	Yes
Mahrokhian et al.[74]	United States	2021	65	Male	No	No	Cardiogenic shock	Na	Yes	Yes	Impella 5.5	No	No	21	Yes
Papageorgiou et al.[75]	Sweden	2021	43	Male	No	No	Cardiogenic shock, myocarditis	0.59	Yes	Yes	Impella CP	V-A ECLS + Impella CP	No	7	Yes
Ruiz et al.[76]	United States	2020	35	Female	No	Yes	Cardiogenic shock, myocarditis	0.28	Yes	Yes	Bi-V Impella	No	No	14	Yes
Valchanov et al.[77]	United Kingdom	2020	43	Male	Yes	Yes	Cardiac arrest, myocardial infarction	18.509	Yes	Yes	V-A ECLS	V-A ECLS + Impella 5.0	Impella 5.0	14	No
Yeleti et al.[78]	United States	2020	25	Female	No	No	Cardiogenic shock, myocarditis	Okt 65	Na	Na	Impella CP + Impella RP	V-A ECLS + Impella CP	No	3	Yes

Abbreviations: A, arterial; ARDS, acute respiratory distress syndrome; Bi-V, biventricular; ECLS, extracorporeal life support; IABP, intra-aortic balloon pump; Na, not available; V, venous.

cases,[80] leading to an overall mortality rate estimated at 2.2% of the total cases in the WHO reports (accessed on June 13, 2021). The first wave of the COVID-19 pandemic was characterized by an ICU admission rate of 21%, and 69% of cases needed invasive mechanical ventilation (IMV).[81] ICU and IMV mortality were 28.3% and 43%, respectively.[81] This highlights the pivotal role of lung involvement in COVID-19. Indeed, the typical presentation of COVID-19 patients requiring intensive care is bilateral pneumonia and acute hypoxemic respiratory failure.[18] Despite this, up to 20%–25% of patients can manifest a concomitant cardiac involvement.[2]

It has been described that 22.6% of COVID-19 patients have elevated troponin values at presentation and median B-natriuretic peptide (BNP) above the reference range.[2,5,82] Moreover, cardiac involvement is more frequent in ICU patients[83] and impacts the prognosis dramatically, with over 50% mortality rate when the myocardial damage occurs.[84,85] The broad spectrum of COVID-19 cardiac involvement includes multiple mechanisms such as the ability of the virus to enter cardiomyocytes and to indirectly damage the heart through systemic hyperactivation of inflammatory and coagulation patterns, such as in the case of the multisystem inflammatory syndrome, heparin resistance and thrombosis, endothelial injury of the coronary arteries, and hypoxemia causing pulmonary hypertension.[85–90] The right heart might be particularly affected by increased pulmonary afterload and loss of right ventricular radial function.[91] Furthermore, many drugs applied in COVID-19 and concomitant infections might have direct but intercurrent cardiac adverse events, such as hydroxychloroquine and azithromycin.

The role of ECLS for patients with cardiorespiratory failure due to COVID-19 has evolved over time, as described by the ELSO guidelines,[92] but the specific role of MCS in COVID-19 patients has yet to be established. Data shared through the EuroELSO COVID-19 dashboard, accessed on November 1, 2021, suggest that 4547 (92.4%) adults have received V-V ECLS for respiratory insufficiency and 216 (4.4%) underwent V-A ECLS during a COVID-19 infection. Data from this literature review match the percentages reported by the online ELSO dashboards and, thus, reflect real-world scenarios. Even though the majority of included studies reported data only on the first wave of COVID-19 infections, we assume that these results are still applicable to the current situation, as the online ELSO dashboards report a constant V-V/V-A ratio over time.

Between the first and second wave, clinicians and researchers have increased awareness of the significant cardiac involvement in COVID-19 but without changing the balance between the use of V-V and V-A ECLS. Furthermore, Barbaro et al. demonstrated that 90-day in-hospital mortality in ECMO COVID-19 patients increased by about 15% between the first phase of the pandemic (before May 2020) and a later phase (between May and December 2020).[31] This large ELSO registry report showed that cardiac arrest before starting ECMO and initial mode (V-A or V-VA vs. V-V) were associated with an increased relative risk of mortality but further analyses on this specific aspect are lacking.[31] This review highlights the significant number of patients experiencing acute heart failure, cardiogenic shock, or cardiac arrest before or after initiation of ECLS. Moreover, a cardiac-related cause of death has been described in several ECLS cases, and Saeed et al. identified the need for cardiopulmonary resuscitation before ECLS placement as a risk factor for in-hospital mortality (hazard ratio: 1.87; 95% CI: 1.01–3.46). Nevertheless, a particular discrepancy still exists between the numbers of ECLS patients experiencing severe cardiac and hemodynamic compromise and those receiving MCS. Indeed, most patients received isolated respiratory support but, despite several authors reporting cardiac causes of death in their patients, it is difficult to understand if a combined respiratory and circulatory support could have prevented many deaths in the V-V ECLS population. Factors such as healthcare system strain, the timing of the cardiocirculatory complication, and patient's response to non-MCS interventions could play an important role in answering this question.[93] Therefore, special attention in future reports on COVID-19 patients and ECLS should focus on this open topic whose solution might significantly impact the ECLS selection and indication process for future non-COVID-19 patients. An important hint to better understand the interplay between the lungs and heart is provided by Cain et al. and Mustafa et al. who approached COVID-19 patients with the use of an OxyRVAD to provide lung and right ventricular heart support.[51,52,55] These authors reported higher survival rates ranging 61–75% and good outcomes compared to standard invasive mechanical ventilation. Nevertheless, a direct comparison between the use of an OxyRVAD and a V-V ECMO is still not available.

Within the MCS field, not only V-A ECLS devices have been used in COVID-19 patients. Indeed, the cardiac Society of Australia and New Zealand[94] and the American Society for Artificial Internal Organs[95] suggested that Impella could be considered for a selected subgroup of COVID-19 patients suffering acute cardiac failure without severe respiratory failure (Table 4). However, few clinical reports are now emerging regarding the use of this device, and they indicate that Impella alone might not be enough to support these patients often affected by biventricular failure and hypoxia.[72,75,78] Contrarily, it seems more effective as left ventricular unloading

combined with V-A ECLS[72,75,77,78] or circulatory support associated with V-V ECLS.[72]

Finally, the conversion from a V-V ECLS to V-A or V-VA ECLS in several patients indicates two possible scenarios: a delayed recognition of a cardiac condition already existing at cannulation or a subsequent deterioration of the patient's status with consequent cardiac involvement. Unfortunately, the timing of conversion was rarely reported, but Loforte et al. reported the cases of five patients weaned from V-V ECLS and requiring a second V-A ECLS run due to refractory hemodynamic instability. This observation highlights again the fundamental concept of missed, delayed, or rescue use of MCS in COVID-19 patients, which might have negatively influenced outcomes and survival.

The initial difficulties in recognizing COVID-19-related cardiac involvement, the need for advanced hybrid configurations[96] which are rarely available in less experienced centers, and the increased risk of bleeding and thrombosis related to complex ECLS settings might explain the underuse of V-A and hybrid ECLS in COVID-19 patients. Indeed, these patients are affected by a severely impaired coagulation homeostasis, altered response to anticoagulation agents, and complex monitoring of the coagulation status, which can further complicate the ECLS management.[86] Furthermore, the ethical circumstances surrounding the allocation of scarce resources during the first wave of the COVID-19 pandemic tended to favor a utilitarian approach, minimizing the use of ECMO, to maximize collective benefit. Important ethical considerations have been outlined by Emanuel et al.[97] for allocating medical resources: maximize benefits; prioritize healthcare workers; avoid allocation on a first-come, first-served basis; be responsive to evidence; recognize research participation; and apply the same principles to all COVID-19 and non-COVID-19 patients. ELSO has published guidance[92] regarding the use of ECLS during this pandemic that aligns with these principles: the highest priority should be given to younger patients, those with minor/no medical comorbidities, and only if a center had the resources and expertise to afford this challenge. Unfortunately, it was not possible to extrapolate data regarding ICU capacity from the articles included in this review. Indeed, data such as the minimum and maximum length of ECLS run, useful to evaluate bed availability in each ICU during the pandemic, were not routinely reported.

Predictive factors for cardiac involvement and hemodynamic instability during ECLS for COVID-19 might be identified to help clinicians to decide on the best mechanical support for each patient. Unfortunately, most of the studies included in this review lacked data on baseline cardiac markers such as troponin, pro-BNP, or echocardiographic data and reported only indirect markers of hemodynamic instability such as the need for vasopressors. Moreover, data on the pre-ECLS median APACHE and SOFA scores as well as the use of inotropes were rarely reported. A call for more attention in reporting and describing ECLS patients' data is needed, especially in COVID-19 patients. It is advised to screen critically ill COVID-19 patients for acute heart failure in the early and late phases of the disease. Appropriate nomenclature, measurement instruments, and a core outcome set are recommended to standardize research efforts internationally and provide good evidence-based guidelines.[22,98]

This is the first systematic review analyzing the use of MCS in COVID-19 patients requiring ECLS. Strengths of this study include a comprehensive review of the literature performed according to the PRISMA guidelines,[19] robust inclusion criteria, and relevant exclusion criteria. Inclusion required documentation of ECLS type for all patients, and articles analyzing only patients supported with V-V ECLS were excluded to minimize the risk of selection and information bias. Duplicated and overlapping populations were excluded (Table S1). We assessed study quality using a validated tool and identified and discussed reporting limitations and knowledge gaps.

The main limitation of this systematic review is the lack of published randomized controlled trials and the high heterogeneity of included studies. Indeed, the high variability in reported data, the small sample size of the population undergoing MCS, and the inconsistency in reported variables precluded a comparative meta-analysis. For example, some studies have a small sample size and do not detect differences in clinical outcomes, while most of the patients are provided by a large international registry.[13] Despite the methods adopted to prevent overlapping populations, it is not possible to completely exclude partial overlapping. In addition, heterogeneous variable reports and a significant lack of data on outcomes, such as renal failure and hemodialysis, prevented a meaningful comparative meta-analysis on these data. Moreover, there is great variability among patient management, and none of the studies reported a clear management strategy for patients requiring ECLS. Furthermore, no study directly compared V-V ECLS patients and patients requiring MCS with a consequent lack of evidence regarding differences in outcomes. Finally, several articles reporting on ECLS outcomes were excluded based on the lack of details on ECLS types and configurations or reporting only V-V ECLS cases without any reference to their policy for MCS use. Notably, the large ELSO Registry report by Barbaro et al. describing 4812 COVID-19 patients supported with ECLS could not be included for a lack of details on ECLS configurations.[31]

5 | CONCLUSIONS

V-A ECLS or hybrid ECLS configurations have been used in 7.3% of COVID-19 cases requiring ECLS. As the number of patients with severe cardiac involvement is higher and the outcome in these patients is poor, a possible underuse of this support might negatively affect patients' outcomes. Furthermore, based on the emerging literature, it can be assumed that the rate of cardiocirculatory complications in ECLS patients has been so far underreported, leaving an open question on the severity of the cardiocirculatory complications, their timing in the COVID-disease course, and the subsequent importance of MCS. Indeed, based also on the high mortality of these patients, further investigations are warranted to establish the correct indications and timing for MCS use in COVID-19 patients.

CONFLICT OF INTEREST

RL is a consultant for Medtronic, Getinge, and LivaNova and Advisory Board Member of Eurosets: all honoraria are paid to the University for research support.

AUTHOR CONTRIBUTIONS

Silvia Mariani conceptualized and designed the study and was involved in data collection, data analysis/interpretation, statistics, drafting the article, and manuscript revision, approval, and submission. Maria Elena De Piero was involved in data analysis/interpretation, statistics, drafting the article, and manuscript revision and approval. Justine M. Ravaux conceptualized and designed the study and was involved in data collection, data analysis/interpretation, statistics, drafting the article, and manuscript revision and approval. Alexander Saelmans was involved in data collection, data analysis/interpretation, drafting the article, and manuscript revision and approval. Michal J. Kawczynski, Michele Di Mauro, and Tong Li were involved in statistics and manuscript revision and approval. Bas C. T. van Bussel was involved in data analysis/interpretation and manuscript revision and approval. Anne Willers, Justyna Swol, Mariusz Kowalewski, Thijs S. R. Delnoij, Iwan C. C. van der Horst, and Jos Massen were involved in manuscript revision and approval. Roberto Lorusso conceptualized and designed the study and was involved in data analysis/interpretation and manuscript revision and approval.

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REFERENCES

1. WHO. Coronavirus (COVID-19) dashboard. 2022. Available from: https://covid19.who.int
2. Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res. 2020;116:1666–87.
3. Basso C, Leone O, Rizzo S, De Gaspari M, van der Wal AC, Aubry MC, et al. Pathological features of COVID-19-associated myocardial injury: a multicentre cardiovascular pathology study. Eur Heart J. 2020;41:3827–35.
4. Ramadan MS, Bertolino L, Marrazzo T, Florio MT, Durante-Mangoni E, The Monaldi Hospital Cardiovascular Infection Study Group. Cardiac complications during the active phase of COVID-19: review of the current evidence. Intern Emerg Med. 2021;16:2051–61.
5. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the new York City area. JAMA. 2020;323:2052–9.
6. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan. China JAMA Cardiol. 2020;5:802–10.
7. Awad WI, Idhrees M, Kennon S, Bashir M. Coronary artery bypass grafting surgery versus percutaneous coronary intervention: what is the clinical decision framework amid COVID-19 era? J Card Surg. 2020;35:2464–6.
8. Shafi AMA, Shaikh SA, Shirke MM, Iddawela S, Harky A. Cardiac manifestations in COVID-19 patients-a systematic review. J Card Surg. 2020;35:1988–2008.
9. Musher DM, Abers MS, Corrales-Medina VF. Acute infection and myocardial infarction. N Engl J Med. 2019;380:171–6.
10. Santoso A, Pranata R, Wibowo A, Al-Farabi MJ, Huang I, Antariksa B. Cardiac injury is associated with mortality and critically ill pneumonia in COVID-19: a meta-analysis. Am J Emerg Med. 2021;44:352–7.
11. COVID-19 Cases on ECMO in the ELSO Registry. Available from: https://wwwelsoorg/COVID19aspx
12. Lorusso R, Combes A, Coco VL, De Piero ME, Belohlavek J, Euro EC-W, et al. ECMO for COVID-19 patients in Europe and Israel. Intensive Care Med. 2021;47:344–8.
13. Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the extracorporeal life support organization registry. Lancet. 2020;396:1071–8.

14. Broman LM, Eksborg S, Coco VL, De Piero ME, Belohlavek J, Lorusso R. Extracorporeal membrane oxygenation for COVID-19 during first and second waves. Lancet Respir Med. 2021;9:e80–1.
15. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet. 2009;374:1351–63.
16. Combes A, Hajage D, Capellier G, Demoule A, Lavoue S, Guervilly C, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. N Engl J Med. 2018;378:1965–75.
17. Lo Coco V, Swol J, De Piero ME, Massimi G, Chiarini G, Broman LM, et al. Dynamic extracorporeal life support: a novel management modality in temporary cardio-circulatory assistance. Artif Organs. 2021;45:427–34.
18. De Piero ME, Lo Coco V, Taccone FS, Belliato M, Broman LM, Malfertheiner MV, et al. Has venoarterial ECMO been underutilized in COVID-19 patients? Innovations (Phila). 2020;15:317–21.
19. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6:e1000097.
20. Wallace B, Small K, Brodley C, Lau J, Trikalinos T. Deploying an interactive machine learning system in an evidence-based practice center: abstrackr. Proceedings of the ACM International Health Informatics Symposium (IHI); 2012. p. 819–24.
21. Wohlin C. Guidelines for snowballing in systematic literature studies and a replication in software engineering. Proceedings of the 18th International Conference on Evaluation and Assessment in Software Engineering—EASE '14; 2014. p. 1–10.
22. Broman LM, Taccone FS, Lorusso R, Malfertheiner MV, Pappalardo F, Di Nardo M, et al. The ELSO Maastricht treaty for ECLS nomenclature: abbreviations for cannulation configuration in extracorporeal life support—a position paper of the extracorporeal life support organization. Crit Care. 2019;23:36.
23. Bergman ZR, Prathibha S, Bauman BD, Yannopoulos D, Brunsvold ME. Venoarteriovenous ECMO in concomitant acute respiratory distress syndrome and cardiomyopathy associated with COVID-19 infection. Case Rep Crit Care. 2021;2021:8848013.
24. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. BMJ Evid Based Med. 2018;23:60–3.
25. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane handbook for systematic reviews of interventions. 2nd ed. Chichester (UK): John Wiley & Sons; 2019.
26. McGrath S, Zhao X, Qin ZZ, Steele R, Benedetti A. One-sample aggregate data meta-analysis of medians. Stat Med. 2019;38:969–84.
27. Barbateskovic M, Koster TM, Eck RJ, Maagaard M, Afshari A, Blokzijl F, et al. A new tool to assess clinical diversity in meta-analyses (CDIM) of interventions. J Clin Epidemiol. 2021;135:29–41.
28. Onorati F, Myers P, Bajona P, Perrotti A, Mestres CA, Quintana E. Effects of COVID-19 pandemic on cardiac surgery practice in 61 hospitals worldwide: results of a survey. J Cardiovasc Surg (Torino). 2020;61:763–8.
29. Nie Q, Ye A, Wei S. Nursing management of severe COVID-19 patients undergoing extracorporeal membrane oxygenation combined with prone position ventilation. Heart Surg Forum. 2020;23:E422–5.
30. Zhang W, Hou W, Jin R, Liang L, Xu B, Hu Z. Clinical characteristics and outcomes in elderly with coronavirus disease 2019 in Beijing, China: a retrospective cohort study. Intern Emerg Med. 2020;16:875–82.
31. Barbaro RP, MacLaren G, Boonstra PS, Combes A, Agerstrand C, Annich G, et al. Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international extracorporeal life support organization registry. Lancet. 2021;398:1230–8.
32. Marullo AG, Cavarretta E, Biondi Zoccai G, Mancone M, Peruzzi M, Piscioneri F, et al. Extracorporeal membrane oxygenation for critically ill patients with coronavirus-associated disease 2019: an updated perspective of the European experience. Minerva Cardioangiol. 2020;68:368–72.
33. Falcoz PE, Monnier A, Puyraveau M, Perrier S, Ludes PO, Olland A, et al. Extracorporeal membrane oxygenation for critically ill patients with COVID-19-related acute respiratory distress syndrome: worth the effort? Am J Respir Crit Care Med. 2020;202:460–3.
34. Jacobs JP, Stammers AH, St Louis JD, Hayanga JWA, Firstenberg MS, Mongero LB, et al. Multi-institutional analysis of 200 COVID-19 patients treated with extracorporeal membrane oxygenation: outcomes and trends. Ann Thorac Surg. 2022;113:1452–60.
35. Li R, Hu S, Chen P, Jiang J, Cui G, Wang DW. Saving critically ill COVID-19 patients with mechanical circulatory support. Ann Transl Med. 2021;9:1221.
36. Rabie AA, Azzam MH, Al-Fares AA, Abdelbary A, Mufti HN, Hassan IF, et al. Implementation of new ECMO centers during the COVID-19 pandemic: experience and results from the Middle East and India. Intensive Care Med. 2021;47:887–95.
37. Saeed O, Tatooles AJ, Farooq M, Schwartz G, Pham DT, Mustafa AK, et al. Characteristics and outcomes of patients with COVID-19 supported by extracorporeal membrane oxygenation: a retrospective multicenter study. J Thorac Cardiovasc Surg. 2021;S0022-5223:00801-1.
38. Schmidt M, Langouet E, Hajage D, James SA, Chommeloux J, Brechot N, et al. Evolving outcomes of extracorporeal membrane oxygenation support for severe COVID-19 ARDS in Sorbonne hospitals. Paris Crit Care. 2021;25:355.
39. Suwalski P, Staromlynski J, Braczkowski J, Bartczak M, Mariani S, Drobinski D, et al. Transition from simple V-V to V-A and hybrid ECMO configurations in COVID-19 ARDS. Membranes (Basel). 2021;11:434.
40. Zayat R, Kalverkamp S, Grottke O, Durak K, Dreher M, Autschbach R, et al. Role of extracorporeal membrane oxygenation in critically ill COVID-19 patients and predictors of mortality. Artif Organs. 2020;45:E158–70.
41. Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020;46:1089–98.
42. Jacobs JP, Stammers AH, St Louis J, Hayanga JWA, Firstenberg MS, Mongero LB, et al. Extracorporeal membrane oxygenation in the treatment of severe pulmonary and cardiac compromise

in coronavirus disease 2019: experience with 32 patients. ASAIO J. 2020;66:722–30.
43. Jacobs JP, Stammers AH, Louis JS, Hayanga JWA, Firstenberg MS, Mongero LB, et al. Multi-institutional analysis of 100 consecutive patients with COVID-19 and severe pulmonary compromise treated with extracorporeal membrane oxygenation: outcomes and trends over time. ASAIO J. 2021;67:496–502.
44. Schmidt M, Hajage D, Lebreton G, Monsel A, Voiriot G, Levy D, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. Lancet Respir Med. 2020;8:1121–31.
45. Lebreton G, Schmidt M, Ponnaiah M, Folliguet T, Para M, Guihaire J, et al. Extracorporeal membrane oxygenation network organisation and clinical outcomes during the COVID-19 pandemic in greater Paris, France: a multicentre cohort study. Lancet Respir Med. 2021;9:851–62.
46. Durak K, Kersten A, Grottke O, Zayat R, Dreher M, Autschbach R, et al. Thromboembolic and bleeding events in COVID-19 patients receiving extracorporeal membrane oxygenation. Thorac Cardiovasc Surg. 2021;69:526–36.
47. Yang X, Hu M, Yu Y, Zhang X, Fang M, Lian Y, et al. Extracorporeal membrane oxygenation for SARS-CoV-2 acute respiratory distress syndrome: a retrospective study from Hubei, China. Front Med (Lausanne). 2020;7:611460.
48. Fang J, Li R, Chen Y, Qin JJ, Hu M, Huang CL, et al. Extracorporeal membrane oxygenation therapy for critically ill coronavirus disease 2019 patients in Wuhan, China: a retrospective multicenter cohort study. Curr Med Sci. 2021;41:1–13.
49. Xuan W, Chen C, Jiang X, Zhang X, Zhu H, Zhang S, et al. Clinical characteristics and outcomes of five critical COVID-19 patients treated with extracorporeal membrane oxygenation in Leishenshan Hospital in Wuhan. J Clin Anesth. 2020;67:110033.
50. Suwalski P, Drobinski D, Smoczynski R, Franczyk M, Sarnowski W, Gajewska A, et al. Analysis of 75 consecutive COVID-19 ECMO cases in Warsaw Centre for Extracorporeal Therapies. Kardiol Pol. 2021;79:851–4.
51. Mustafa AK, Alexander PJ, Joshi DJ, Tabachnick DR, Cross CA, Pappas PS, et al. Extracorporeal membrane oxygenation for patients with COVID-19 in severe respiratory failure. JAMA Surg. 2020;155:990–2.
52. Mustafa AK, Joshi DJ, Alexander PJ, Tabachnick DR, Cross CA, Jweied EE, et al. Comparative propensity matched outcomes in severe COVID-19 respiratory failure-extracorporeal membrane oxygenation or maximum ventilation alone. Ann Surg. 2021;274:e388–94.
53. Agerstrand C, Dubois R, Takeda K, Uriel N, Lemaitre P, Fried J, et al. Extracorporeal membrane oxygenation for coronavirus disease 2019: crisis standards of care. ASAIO J. 2021;67:245–9.
54. Akhtar W, Olusanya O, Baladia MM, Young H, Shah S. SARS-CoV-2 and ECMO: early results and experience. Indian J Thorac Cardiovasc Surg. 2020;37:1–8.
55. Cain MT, Smith NJ, Barash M, Simpson P, Durham LA 3rd, Makker H, et al. Extracorporeal membrane oxygenation with right ventricular assist device for COVID-19 ARDS. J Surg Res. 2021;264:81–9.
56. Dreier E, Malfertheiner MV, Dienemann T, Fisser C, Foltan M, Geismann F, et al. ECMO in COVID-19-prolonged therapy needed? A retrospective analysis of outcome and prognostic factors. Perfusion. 2021;36:582–91.
57. Gresser E, Reich J, Sabel BO, Kunz WG, Fabritius MP, Rubenthaler J, et al. Risk stratification for ECMO requirement in COVID-19 ICU patients using quantitative imaging features in CT scans on admission. Diagnostics (Basel). 2021;11:1029.
58. Hékimian G, Kerneis M, Zeitouni M, Cohen-Aubart F, Chommeloux J, Bréchot N, et al. Coronavirus disease 2019 acute myocarditis and multisystem inflammatory syndrome in adult intensive and cardiac care units. Chest. 2021;159:657–62.
59. Lenka J, Chhabria MS, Sharma N, Tan BE, Boppana LKT, Venugopal S, et al. Clinical characteristics and outcomes of critically ill patients with COVID-19 in a tertiary community hospital in upstate New York. J Community Hosp Intern Med Perspect. 2020;10:491–500.
60. Li X, Guo Z, Li B, Zhang X, Tian R, Wu W, et al. Extracorporeal membrane oxygenation for coronavirus disease 2019 in Shanghai China. ASAIO J. 2020;66:475–81.
61. Li S, Xiong J, Du Z, Lai W, Ma X, Feng Z, et al. Extracorporeal membrane oxygenation (ECMO) for critically ill patients with coronavirus disease 2019 (COVID-19): a retrospective cohort study. J Card Surg. 2021;36:3554–60.
62. Loforte A, Di Mauro M, Pellegrini C, Monterosso C, Pelenghi S, Degani A, et al. Extracorporeal membrane oxygenation for COVID-19 respiratory distress syndrome: an Italian Society for Cardiac Surgery Report. ASAIO J. 2021;67:385–91.
63. Magunia H, Lederer S, Verbuecheln R, Gilot BJ, Koeppen M, Haeberle HA, et al. Machine learning identifies ICU outcome predictors in a multicenter COVID-19 cohort. Crit Care. 2021;25:295.
64. Oliveira E, Parikh A, Lopez-Ruiz A, Carrilo M, Goldberg J, Cearras M, et al. ICU outcomes and survival in patients with severe COVID-19 in the largest health care system in Central Florida. PLoS ONE. 2021;16:e0249038.
65. Paisey C, Patvardhan C, Mackay M, Vuylsteke A, Bhagra SK. Continuous hemadsorption with cytokine adsorber for severe COVID-19: a case series of 15 patients. Int J Artif Organs. 2021;44:664–74.
66. Raasveld SJ, Delnoij TSR, Broman LM, Lansink-Hartgring AO, Hermans G, De Troy E, et al. Extracorporeal membrane oxygenation in patients with COVID-19: an international multicenter cohort study. J Intensive Care Med. 2021;36:910–7.
67. Rajajee V, Fung CM, Seagly KS, Park PK, Raghavendran K, Machado-Aranda DA, et al. One-year functional, cognitive, and psychological outcomes following the use of extracorporeal membrane oxygenation in coronavirus disease 2019: a prospective study. Crit Care Explor. 2021;3:e0537.
68. Queiros PR, Ferreira ND, Caeiro D, Ponte M, Guerreiro C, Silva M, et al. Fighting the pandemic with collaboration at heart: report from cardiologists in a COVID-19-dedicated Portuguese intensive care unit. Rev Port Cardiol (Engl Ed). 2021;40:923–8.
69. Rieg S, von Cube M, Kalbhenn J, Utzolino S, Pernice K, Bechet L, et al. COVID-19 in-hospital mortality and mode of death in a dynamic and non-restricted tertiary care model in Germany. PLoS ONE. 2020;15:e0242127.
70. Shih E, Squiers JJ, DiMaio JM, George T, Banwait J, Monday K, et al. Outcomes of extracorporeal membrane oxygenation in patients with severe acute respiratory distress syndrome caused by COVID-19 versus influenza. Ann Thorac Surg. 2021;113:1445–51.
71. Sromicki J, Schmiady M, Maisano F, Mestres CA. ECMO therapy in COVID-19: an experience from Zurich. J Card Surg. 2021;36:1707–12.

72. Bemtgen X, Kruger K, Supady A, Duerschmied D, Schibilsky D, Bamberg F, et al. First successful treatment of coronavirus disease 2019 induced refractory cardiogenic plus Vasoplegic shock by combination of percutaneous ventricular assist device and extracorporeal membrane oxygenation: a case report. ASAIO J. 2020;66:607–9.
73. Kaki A, Singh H, Cohen G, Schreiber T. A case report of a large intracardiac thrombus in a COVID-19 patient managed with percutaneous thrombectomy and right ventricular mechanical circulatory support. Eur Heart J Case Rep. 2020;4:1–5.
74. Mahrokhian SH, Nordan T, Ortoleva JP, Cobey FC, Chen FY, Kapur NK, et al. Successful use of Impella 5.5 to manage cardiogenic shock complicated by COVID-19. J Card Surg. 2021;36:4783–5.
75. Papageorgiou JM, Almroth H, Tornudd M, van der Wal H, Varelogianni G, Lawesson SS. Fulminant myocarditis in a COVID-19 positive patient treated with mechanical circulatory support—a case report. Eur Heart J Case Rep. 2021;5:ytaa523.
76. Ruiz JG, Kandah F, Dhruva P, Ganji M, Goswami R. Case of coronavirus disease 2019 myocarditis managed with biventricular Impella support. Cureus. 2021;13:e13197.
77. Valchanov K, Krishnan U, Hoole SP, Davies WR, Pettit S, Jones N, et al. COVID-19 patient with coronary thrombosis supported with ECMO and Impella 5.0 ventricular assist device: a case report. Eur Heart J Case Rep. 2020;4:1–6.
78. Yeleti R, Guglin M, Saleem K, Adigopula SV, Sinha A, Upadhyay S, et al. Fulminant myocarditis: COVID or not COVID? Reinfection or co-infection? Future Cardiol. 2021;17:1307–11.
79. Jackson CD, Burroughs-Ray DC, Summers NA. Clinical guideline highlights for the hospitalist: 2019 American Thoracic Society/Infectious Diseases Society of America update on community-acquired pneumonia. J Hosp Med. 2020;15:743–5.
80. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708–20.
81. Chang R, Elhusseiny KM, Yeh YC, Sun WZ. COVID-19 ICU and mechanical ventilation patient characteristics and outcomes—a systematic review and meta-analysis. PLoS ONE. 2021;16:e0246318.
82. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5:811–8.
83. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497–506.
84. Kotecha T, Knight DS, Razvi Y, Kumar K, Vimalesvaran K, Thornton G, et al. Patterns of myocardial injury in recovered troponin-positive COVID-19 patients assessed by cardiovascular magnetic resonance. Eur Heart J. 2021;42:1866–78.
85. Ramadan MS, Bertolino L, Marrazzo T, Florio MT, Durante-Mangoni E. Cardiac complications during the active phase of COVID-19: review of the current evidence. Intern Emerg Med. 2021;1–11:2051–61.
86. Hulshof AM, Brüggemann RAG, Mulder MMG, van de Berg TW, Sels JEM, Olie RH, et al. Serial EXTEM, FIBTEM, and tPA rotational thromboelastometry observations in the Maastricht intensive care COVID cohort-persistence of hypercoagulability and Hypofibrinolysis despite anticoagulation. Front Cardiovasc Med. 2021;8:654174.
87. Dutch C, Thrombosis C, Kaptein FHJ, Stals MAM, Grootenboers M, Braken SJE, et al. Incidence of thrombotic complications and overall survival in hospitalized patients with COVID-19 in the second and first wave. Thromb Res. 2021;199:143–8.
88. Streng AS, Delnoij TSR, Mulder MMG, Sels J, Wetzels RJH, Verhezen PWM, et al. Monitoring of unfractionated heparin in severe COVID-19: an observational study of patients on CRRT and ECMO. TH Open. 2020;4:e365–75.
89. Willers A, Arens J, Mariani S, Pels H, Maessen JG, Hackeng TM, et al. New trends, advantages and disadvantages in anticoagulation and coating methods used in extracorporeal life support devices. Membranes (Basel). 2021;11:617.
90. Levy JH, Connors JM. Heparin resistanc—clinical perspectives and management strategies. N Engl J Med. 2021;385:826–32.
91. Bleakley C, Singh S, Garfield B, Morosin M, Surkova E, Mandalia MS, et al. Right ventricular dysfunction in critically ill COVID-19 ARDS. Int J Cardiol. 2021;327:251–8.
92. Badulak J, Antonini MV, Stead CM, Shekerdemian L, Raman L, Paden ML, et al. Extracorporeal membrane oxygenation for COVID-19: updated 2021 guidelines from the extracorporeal life support organization. ASAIO J. 2021;67:485–95.
93. Mesotten D, Meijs DAM, van Bussel BCT, Stessel B, Mehagnoul-Schipper J, Hana A, et al. Differences and similarities among coronavirus disease 2019 patients treated in seven ICUs in three countries within one region: an observational cohort study. Crit Care Med. 2021;50:595–606.
94. Lal S, Hayward CS, De Pasquale C, Kaye D, Javorsky G, Bergin P, et al. COVID-19 and acute heart failure: screening the critically ill—a position statement of the Cardiac Society of Australia and New Zealand (CSANZ). Heart Lung Circ. 2020;29:e94–8.
95. Rajagopal K, Keller SP, Akkanti B, Bime C, Loyalka P, Cheema FH, et al. Advanced pulmonary and cardiac support of COVID-19 patients: emerging recommendations from ASAIO-A "living working document". ASAIO J. 2020;66:588–98.
96. Brasseur A, Scolletta S, Lorusso R, Taccone FS. Hybrid extracorporeal membrane oxygenation. J Thorac Dis. 2018;10:S707–15.
97. Emanuel EJ, Persad G, Upshur R, Thome B, Parker M, Glickman A, et al. Fair allocation of scarce medical resources in the time of Covid-19. N Engl J Med. 2020;382:2049–55.
98. Hodgson CL, Fulcher B, Mariajoseph FP, Burrell AJC, Pellegrino V, Brodie D, et al. A core outcome set for research in patients on extracorporeal membrane oxygenation. Crit Care Med. 2021;49:e1252–4.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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