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Clinical Outcomes and Complications of Extracorporeal Membrane Oxygenation (ECMO) in Adult Patients With COVID-19 in Central and Eastern Europe: A Systematic Review and Meta-Analysis

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Statistical Analysis C
Data Interpretation D
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Background: Extracorporeal membrane oxygenation (ECMO) is a rescue therapy for severe COVID-19–related acute respiratory distress syndrome (ARDS). International datasets do not consistently report Central and Eastern Europe (CEE) separately. We aimed to assess mortality, clinical characteristics, and complications of ECMO-treated COVID-19 patients across the CEE region.

Material/Methods: We conducted a systematic review with single-arm meta-analyses of observational studies. PubMed, Scopus, Embase, and Web of Science were searched from January 2020 to August 2025 for studies reporting ECMO outcomes in adult (≥18 years) COVID-19 patients from CEE countries, with at least 10 ECMO-treated patients. Conference abstracts and overlapping cohorts were excluded. The study protocol was registered with PROSPERO (CRD420251077593).

Results: Twelve studies included 802 patients from 6 countries. Pooled in-hospital mortality was 65% (95% CI 0.57-0.72; $I^2 = 70.6\%$; 10 studies; n = 691), and ICU mortality was 61% (95% CI 0.47-0.74; $I^2 = 85.8\%$; 7 studies, n = 526). Country-level in-hospital mortality estimates were 54% for the Czech Republic and 76% for Poland but were descriptive because of the small number of studies and wide CIs. Mean pre-ECMO mechanical ventilation duration was 4.8 days (95% CI 3.7-5.8; $I^2 = 4.4\%$), ECMO duration was 17.8 days (95% CI 12.8-22.9; $I^2 = 79.8\%$), and ICU length of stay was 23.6 days (95% CI 7.5-39.7; $I^2 = 92.6\%$). Serious bleeding occurred in 40% (95% CI 22-61%; $I^2 = 85.7\%$). Certainty was very low for all pooled outcomes.

Conclusions: These CEE-specific estimates provide regional benchmarks, but substantial heterogeneity and very low certainty limit international comparisons and country-level interpretation. Standardized regional registries, prospective multicenter data, harmonized complication reporting, and long-term outcome assessment are needed.

Keywords: COVID-19 • Europe, Eastern • Extracorporeal Membrane Oxygenation • Meta-Analysis • Respiratory Distress Syndrome

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Introduction

Extracorporeal membrane oxygenation (ECMO) became a key rescue therapy for adult patients with severe COVID-19 acute respiratory distress syndrome (ARDS) refractory to conventional management. Early international registry data suggested in-hospital mortality near 37% to 40%, comparable to non-COVID-19 ARDS [1,2]. However, subsequent analyses have revealed a trend toward higher mortality as the pandemic progressed, with rates exceeding 50% in later waves and significant heterogeneity across regions and centers [3-5]. Despite this expanding evidence base, outcomes from Central and Eastern Europe (CEE) remain poorly characterized: large registries and meta-analyses provide broad benchmarks but rarely report CEE as a discrete regional stratum, and the available CEE evidence is fragmented across small national or single-center reports with little formal synthesis.

This gap matters because healthcare delivery, critical-care capacity, and research output remain unevenly distributed across Europe despite nearly 2 decades of political and institutional integration [6], and several CEE countries recorded some of the highest excess mortality among high-income nations during the first pandemic wave [7]. The SepsEast network, an independent consortium of intensive-care specialists from across CEE [6], has responded to these disparities through dedicated research and educational initiatives [8,9], and its prospective work has reported significantly higher mortality among mechanically ventilated COVID-19 patients in Central European intensive care units (ICUs) than in Western European cohorts. Whether comparable disparities extend to ECMO-treated patients has not yet been systematically examined.

Available regional data reinforce this concern. A Polish multicenter study reported 74% ICU mortality in COVID-19 ECMO patients [10], while EuroECMO-COVID linked poorer outcomes to age, comorbidities, delayed ECMO initiation, organ dysfunction, and major complications [4,11]. Because referral pathways, ECMO capacity, and center experience can differ substantially between healthcare systems, and because ECMO retains clear benefit in selected patients, including younger individuals, those with profound hypoxemia, and those treated early in high-volume, experienced centers [12-14], CEE-specific benchmarking is warranted in a region less consistently represented in large Western European and international registries.

This systematic review and meta-analysis aimed to estimate pooled in-hospital and ICU mortality, major complications, and selected clinical characteristics among adult patients with COVID-19 treated with ECMO in CEE, and to assess between-study heterogeneity and between-country variability where data permitted. These findings may help direct future prospective and registry-based studies toward the potential role of referral pathways, center experience, and resource availability.

Material and Methods

Protocol and Registration

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [15]. Formal ethical committee authorization was unnecessary for this work; nonetheless, all procedures adhered to the ethical principles set forth in the Declaration of Helsinki.

The study protocol was developed before study initiation and was registered with PROSPERO (CRD420251077593).

Sources

We conducted a structured search of PubMed, Scopus, Embase, and Web of Science databases in August 2025. The strategy combined terms related to ECMO, COVID-19, and CEE countries. We included only full-text, peer-reviewed articles published in English, Polish, or Czech, from January 1, 2020, up to the date of search (August 1, 2025); conference abstracts were excluded. Complete database-specific search strategies, including database syntax and the number of records retrieved before deduplication, are provided in **Table 1**. The search combined controlled vocabulary, where available, with free-text terms, and syntax was adapted for each database. Duplicate records were removed before screening by matching title, authors, journal, year, and DOI. Remaining potential duplicates were checked manually.

Study Selection

A Population, Exposure, Outcome (PEO) framework was used to structure and guide the article selection process (**Table 2**). For the purpose of this review, CEE was defined as a group of the following countries: Poland, the Czech Republic, Slovakia, Hungary, Slovenia, Croatia, Romania, Lithuania, Latvia, and Estonia.

Studies were eligible if they: (1) reported ECMO outcomes in adult (≥18 years) patients with COVID-19; (2) included at least 10 ECMO-treated patients; and (3) were observational studies (cohort, case series, or cross-sectional) conducted in any of the CEE countries and published in English, Polish, or Czech. This language restriction reflected the languages that were native for the review team. Studies were excluded if they involved pediatric patients, reported overlapping cohorts, or did not provide sufficient quantitative data for the pre-defined outcomes. When cohorts overlapped, the report with the largest COVID-19 ECMO sample or the most complete outcome data was retained. Conference abstracts and duplicate reports were also excluded.

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Table 1. Search strategy and database results.

Database	Search terms	Number of articles
Pubmed	("Extracorporeal Membrane Oxygenation" [Mesh] OR ECMO [Title/Abstract]) AND ("COVID-19" [Mesh] OR "SARS-CoV-2" [Title/Abstract] OR "coronavirus" [Title/Abstract]) AND ("Poland" [Affiliation] OR "Czech Republic" [Affiliation] OR "Slovakia" [Affiliation] OR "Hungary" [Affiliation] OR "Slovenia" [Affiliation] OR "Croatia" [Affiliation] OR "Romania" [Affiliation] OR "Lithuania" [Affiliation] OR "Latvia" [Affiliation] OR "Estonia" [Affiliation] OR "Central Europe" [Affiliation] OR "Eastern Europe" [Affiliation]) AND ("2020/01/01" [Date – Publication]: "3000" [Date – Publication]) AND ("prospective" [Title/Abstract] OR "retrospective" [Title/Abstract]) NOT ("Review" [Publication Type])	21
Scopus	TITLE-ABS-KEY ("extracorporeal membrane oxygenation" OR ECMO) AND TITLE-ABS-KEY ("COVID-19" OR "SARS-CoV-2" OR coronavirus) AND (AFFIL ("Poland") OR AFFIL ("Czech Republic") OR AFFIL ("Slovakia") OR AFFIL ("Hungary") OR AFFIL ("Slovenia") OR AFFIL ("Croatia") OR AFFIL ("Romania") OR AFFIL ("Lithuania") OR AFFIL ("Latvia") OR AFFIL ("Estonia") OR AFFIL ("Central Europe") OR AFFIL ("Eastern Europe")) AND PUBYEAR > 2019 AND (TITLE-ABS-KEY (prospective) OR TITLE-ABS-KEY (retrospective)) AND NOT DOCTYPE (rev)	54
Embase	('extracorporeal membrane oxygenation'/exp OR 'extracorporeal membrane oxygenation': ab,ti OR ecmo: ab,ti) AND ('coronavirus disease 2019''/exp OR 'covid-19': ab,ti OR 'sars-cov-2': ab,ti OR coronavirus: ab,ti) AND (poland: ad OR 'czech republic': ad OR slovakia: ad OR hungary: ad OR slovenia: ad OR croatia: ad OR romania: ad OR lithuania: ad OR latvia: ad OR estonia: ad OR 'central europe': ad OR 'eastern europe': ad) AND (2020: py OR 2021: py OR 2022: py OR 2023: py OR 2024: py OR 2025: py) AND (prospective: ab,ti OR retrospective: ab,ti) NOT 'review'/it	71
Web of Science	TS = ("extracorporeal membrane oxygenation" OR ECMO) AND TS = ("COVID-19" OR "SARS-CoV-2" OR coronavirus) AND (AD = Poland OR AD = "Czech Republic" OR AD = Slovakia OR AD = Hungary OR AD = Slovenia OR AD = Croatia OR AD = Romania OR AD = Lithuania OR AD = Latvia OR AD = Estonia OR AD = "Central Europe" OR AD = "Eastern Europe") AND PY = (2020-2025) AND (TS = prospective OR TS = retrospective) NOT DT = REVIEW	30
Total articles after duplicates removal		89

Table 2. Population, Exposure, and Outcome (PEO) framework.

PEO	Description
Population	Adult patients (≥ 18 years) with severe respiratory failure due to COVID-19 admitted to intensive care units in countries included in the review's operational definition of Central and Eastern Europe: Poland, the Czech Republic, Hungary, Slovakia, Slovenia, Croatia, Romania, Lithuania, Latvia, and Estonia
Exposure	Extracorporeal membrane oxygenation (ECMO), including veno-venous (VV) and veno-arterial (VA) modalities
Outcome	Primary outcomes: O1: In-hospital mortality O2: ICU mortality Secondary outcomes: O3: ICU severity scores at ECMO initiation O4: Duration of mechanical ventilation before ECMO initiation (days) O5: Duration of ECMO therapy (days) O6: ICU length of stay (days) O7: Major complications (n,%)

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Title and abstract screening were performed independently by 2 reviewers (KA and MM1), followed by independent full-text assessment (MM1 and MM2). Disagreements were resolved through consensus.

Primary and Secondary Outcomes

The primary outcomes (O) were in-hospital mortality among adult patients receiving ECMO for COVID-19–related respiratory failure (O1) and ICU mortality (O2). Secondary outcomes included ICU severity scores at ECMO initiation (O3), duration of mechanical ventilation before ECMO initiation (days) (O4), duration of ECMO therapy (days) (O5), ICU length of stay (days) (O6), and major ECMO-related complications (O7), such as serious bleeding, sepsis, pneumothorax, deep venous thrombosis, oxygenator failure, multiorgan failure, and delirium, expressed as number and percentage of affected patients.

Data Extraction and Analysis

Data extraction was independently performed by 2 reviewers using a standardized form. Extracted data included study details (author, year, design, country, and sample size), patient characteristics (age, sex, BMI, severity scores, and pre-ECMO ventilation), ECMO parameters (type, duration, cannulation, ventilation days before ECMO, ICU stay), and outcomes (mortality at different time points and major complications such as bleeding, sepsis, multiorgan failure, pneumothorax, oxygenator failure, DVT, and delirium). Discrepancies were resolved through discussion with a third reviewer. Data not reported in the source studies were recorded as missing and were not imputed; each analysis used only the available data for the relevant outcome.

Meta-analyses of proportions (PEO O1, O2, and O7) were conducted using a random-intercept logistic regression model to account for both within- and between-study variability. The between-study variance (τ^2) was estimated using the maximum-likelihood method. Random-effects confidence intervals were calculated using the t-distribution, accounting for uncertainty in τ^2 estimation. To stabilize variances, proportions were logit-transformed prior to pooling, and Clopper-Pearson confidence intervals (CI) were computed for individual study estimates.

All meta-analyses of means (PEO O3 to O6), were conducted using the inverse-variance method under a random-effects model to account for both within- and between-study variability. The between-study variance (τ^2) was estimated using the restricted maximum-likelihood method, and its CI was derived using the Q-profile approach. Random-effects CIs were adjusted using the Hartung-Knapp method to provide more accurate coverage in the presence of heterogeneity. Analyses were based on untransformed (raw) means.

The results of meta-analyses were presented with forest plots. For individual study estimates and heterogeneity indices, 95% CIs were reported. A P value ≤ 0.05 was considered statistically significant.

Heterogeneity was quantified using the I^2 statistic, calculated from Cochran's Q; the I^2 interpretation was guided by thresholds described in the Cochrane Handbook for Systematic Reviews [16] as follows: 0%-40%: not important; 30%-60%: moderate; 50%-90%: substantial; and 75%-100%: considerable heterogeneity.

Meta-analyses were performed using R version 4.4.2, and packages 'meta' version 8.0-2 [17] and 'estmeansd' version 1.0.1. [18].

Several included studies reported continuous outcomes, including Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, duration of mechanical ventilation before ECMO, ECMO duration, and ICU length of stay, as medians with interquartile ranges (IQRs) rather than as means with standard deviations (SDs). For studies reporting the median, first and third quartiles, and sample size, the mean and SD were estimated using the Box-Cox method implemented in the `bc.mean.sd()` function of the `estmeansd` R package (version 1.0.1) [18]. **Table 3** indicates studies that reported raw means and SDs and those that required conversion from median-based summaries.

Subgroup analyses by country were pre-specified for the primary outcome (in-hospital mortality) and for ICU mortality. Eligibility for country-stratified synthesis required a minimum of 2 independent studies from a given country to ensure stable variance estimation. Countries represented by only 1 study were included in the overall pooled estimate but were not reported as separate subgroups. Subgroup results are presented as forest plots with country-specific pooled estimates and 95% CIs (**Figure 1**).

Quality Assessment

Risk of bias was assessed using the JBI Checklist for Cohort Studies [19] and the JBI Checklist for Case Series (2017) [20]. Each item was rated as "Yes", "No", "Unclear", or "Not applicable". A rating of "Unclear" indicated insufficient information, while "Not applicable" was used only when the item did not apply to the study design. No numerical summary score or overall quality category was assigned. Two authors (KA and KZ) performed the assessment independently and resolved disagreements by consensus.

Certainty of Evidence Assessment

The overall certainty of evidence for each outcome was evaluated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework [21], adapted for single-arm

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Table 3. Characteristics of the included studies.

First Author	Publication date	Study period	Study design	Country	Sample size (N)	Male (%)	Age (years)	BMI (kg/m²)
Balik	Dec 2022	2020-2022	Retrospective cohort study	Czech Republic	119	65%	57b	NA
Barbura*	Jun 2025	2018-2025	Retrospective cohort study	Romania	25	68%	46.7a	30.1a
Burša	Feb 2025	2020-2023	Retrospective cohort study	Czech Republic	63	60%	50b	31.2b
Drmić	Jun 2023	2020-2021	Retrospective cohort study	Croatia	18	33%	53a	NA
Genzor	Apr 2023	NA	Prospective cohort study	Czech Republic	41	65%	NA	NA
Golicnik*	Jul 2023	2016-2021	Retrospective cohort study	Slovenia	41	76%	53b	30b
Kutleša	Apr 2023	2020-2022	Retrospective cohort study	Croatia	112	75%	NA	NA
Rypulak	May 2024	2020-2023	Retrospective case series	Poland	86	72%	46a	33.9a
Sitina	May 2023	2020-2021	Retrospective cohort study	Czech Republic	86	NA	NA	29.4a
Trejnowska	Apr 2022	2020-2021	Retrospective cohort study	Poland	158	75%	46.3a	30.9a
Ulakcsai	Aug 2023	2021	Prospective cohort study	Hungary	35	63%	37b	29.5b
Zöllei	May 2024	2021-2022	Retrospective case series	Hungary	18	72%	44a	NA

First Author	ECMO types	ECMO type: VV-ECMO (%)	SOFA before ECMO	Mechanical bentilation before ECMO (days)	Duration of ECMO (days)	Length of ICU stay (days)	Serious bleeding (%)	In-hospital mortality (%)	ICU mortality (%)
Balik	VV + VA	92%	NA	NA	NA	NA	NA	52%	43%
Barbura*	VV	100%	13.8 a	NA	NA	14.2b	NA	NA	NA
Burša	VV	100%	NA	NA	16b	NA	16%	56%	NA
Drmić	VV	100%	3.5 b	4.5b	11.5b	21.5b	NA	61%	61%
Genzor	VV	100%	NA	1.9	NA	NA	NA	59%	NA
Golicnik*	VV	100%	8 b	NA	15b	32b	51%	59%	59%
Kutleša	VV	100%	NA	NA	NA	NA	NA	70%	NA
Rypulak	VV	100%	8.2b	2.83a	12.9a	17.7a	36%	80%	80%
Sitina	VV	100%	NA	NA	NA	NA	NA	NA	56%
Trejnowska	VV + VA	99%	NA	5.3a	18a	26.3a	55%	74%	74%
Ulakcsai	VV	100%	NA	2b	13b	NA	NA	74%	NA
Zöllei	VV	100%	NA	2.5b	26a	40a	50%	50%	44%

Abbreviations: BMI, body mass index; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment; VV-ECMO, veno-venous extracorporeal membrane oxygenation.

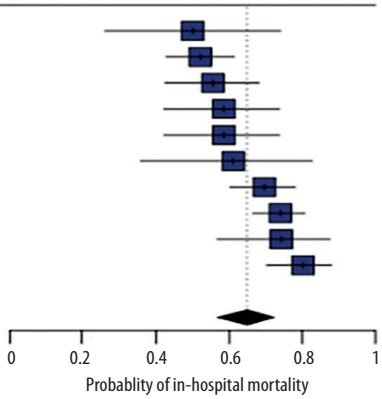
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A

Study	Events	Total	GLMM, random, 95% CI
Zöllei 2024	9	18	0.50 [0.26; 0.74]
Balik 2022	62	119	0.52 [0.43; 0.61]
Burša 2025	35	63	0.56 [0.42; 0.68]
Genzor 2023	24	41	0.59 [0.42; 0.74]
Golicnik 2023	24	41	0.59 [0.42; 0.74]
Drmić 2023	11	18	0.61 [0.36; 0.83]
Kutleša 2023	78	112	0.70 [0.60; 0.78]
Trejnowska 2022	117	158	0.74 [0.66; 0.81]
Ulakcsai 2023	26	35	0.74 [0.57; 0.88]
Rypulak 2024	69	86	0.80 [0.70; 0.88]
Total (95% CI)		**691**	**0.65 [0.57; 0.72]**

Heterogeneity: $Tau^2 = 0.1384$; $Chi^2 = 30.58$, df = 9 (P = 0.0003); $I^2 = 70.6\%$



B

Study of subgroup	Events	Total	GLMM, random, 95% CI
Country = Czech Republic			
Balik 2022	62	119	0.52 [0.43; 0.61]
Burša 2025	35	63	0.56 [0.42; 0.68]
Genzor 2023	24	41	0.59 [0.42; 0.74]
Total (95% CI)		**223**	**0.54 [0.40; 0.68]**

Heterogeneity: $Tau^2 = 0$; $Chi^2 = 0.57$, df = 2 (P = 0.7530); $I^2 = 0\%$

Country = Hungary			
Zöllei 2024	9	18	0.50 [0.26; 0.74]
Ulakcsai 2023	26	35	0.74 [0.57; 0.88]
Total (95% CI)		**53**	**0.55 [0.02; 1.00]**

Heterogeneity: $Tau^2 = 0.0930$; $Chi^2 = 3.03$, df = 1 (P = 0.0819); $I^2 = 67\%$

Country = Poland			
Trejnowska 2022	117	158	0.74 [0.66; 0.81]
Rypulak 2024	69	86	0.80 [0.70; 0.88]
Total (95% CI)		**244**	**0.75 [0.32; 0.96]**

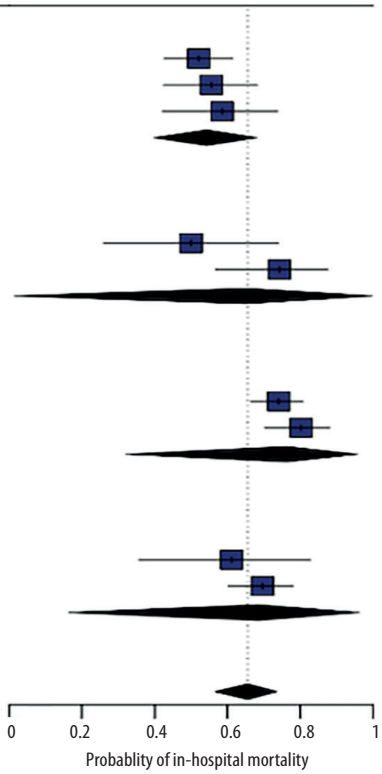
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 1.17$, df = 1 (P = 0.2796); $I^2 = 14.4\%$

Country = Croatia			
Drmić 2023	11	18	0.61 [0.36; 0.83]
Kutleša 2023	78	113	0.70 [0.60; 0.78]
Total (95% CI)		**130**	**0.68 [0.16; 0.96]**

Heterogeneity: $Tau^2 = 0$; $Chi^2 = 0.52$, df = 1 (P = 0.4714); $I^2 = 0\%$

Total (95% CI)			

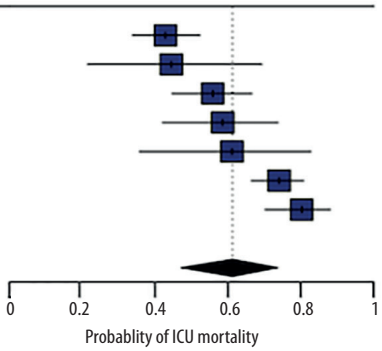
Heterogeneity: $Tau^2 = 0.1509$; $Chi^2 = 29.75$, df = 8 (P = 0.0002); $I^2 = 73.1\%$
Test for subgroup difference: $Chi^2 = 24.89$, df = 3 (P < 0.0001)



C

Study	Events	Total	GLMM, random, 95% CI
Balik 2022	51	119	0.43 [0.34; 0.52]
Zöllei 2024	8	18	0.44 [0.22; 0.69]
Sitina 2022	48	86	0.56 [0.45; 0.67]
Golicnik 2023	24	41	0.59 [0.42; 0.74]
Drmić 2023	11	18	0.61 [0.36; 0.83]
Trejnowska 2022	117	158	0.74 [0.66; 0.81]
Rypulak 2024	69	86	0.80 [0.70; 0.88]
Total (95% CI)		**526**	**0.61 [0.47; 0.74]**

Heterogeneity: $Tau^2 = 0.2864$; $Chi^2 = 42$, df = 8 (P < 0.0001); $I^2 = 85.8\%$



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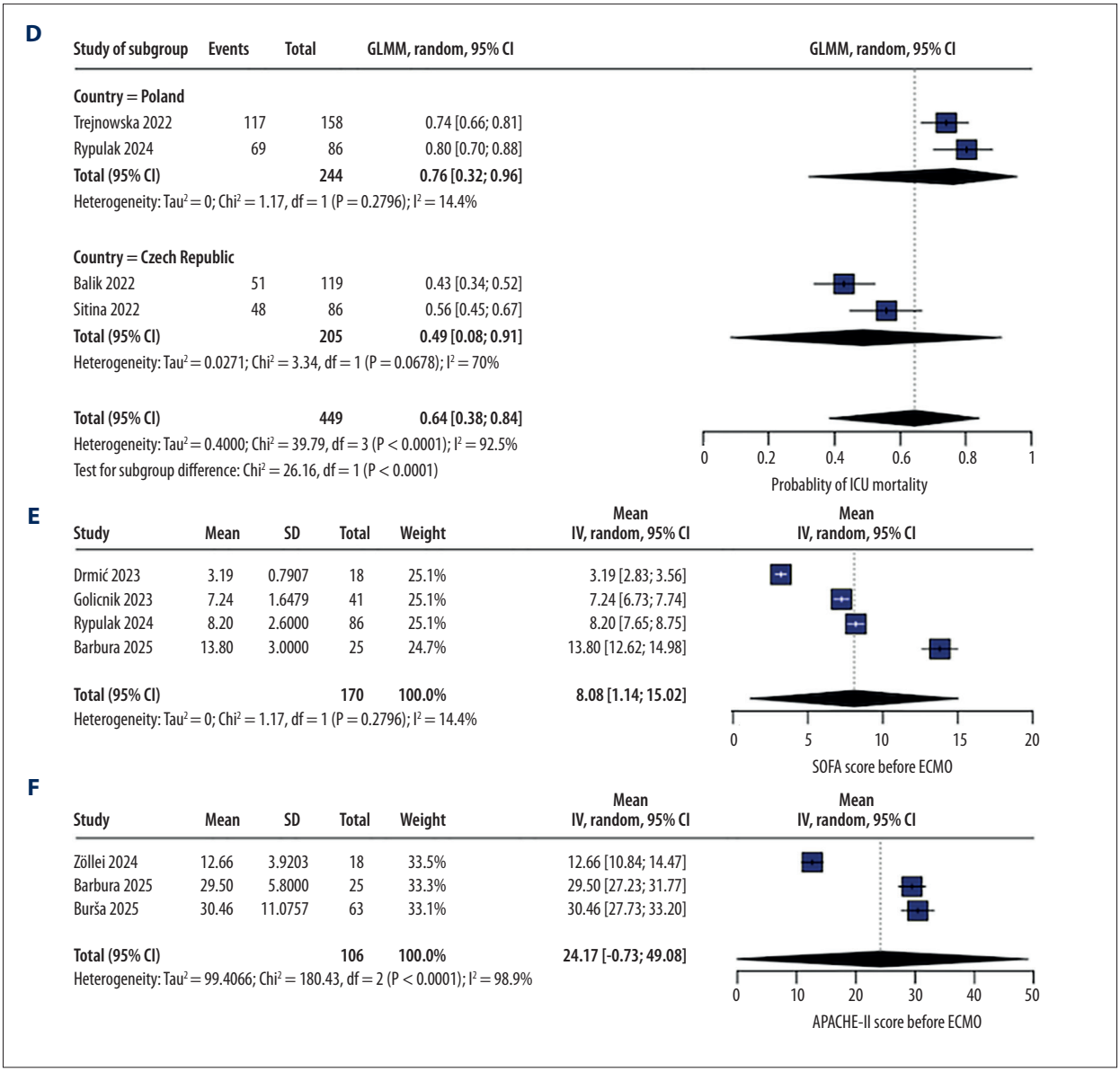


Figure 1. Forest plots of in-hospital mortality, in-ICU mortality, and ICU severity scores at extracorporeal membrane oxygenation (ECMO) initiation in the Central and Eastern European (CEE) ECMO cohort. (**A**) Pooled in-hospital mortality across all CEE studies (random-effects generalized linear mixed model [GLMM]). (**B**) Subgroup analysis by country for nations with at least two studies reporting in-hospital mortality (Czech Republic, Hungary, Poland, and Croatia). Slovenia, represented by a single study, is included in the overall pooled estimate but not in the subgroup panel. (**C**) Pooled ICU mortality across all CEE studies (random-effects GLMM). (**D**) Subgroup analysis by country (Czech Republic and Poland), the only two nations with at least two studies reporting ICU mortality. (**E**) Pooled mean Sequential Organ Failure Assessment (SOFA) score before ECMO (inverse-variance, random-effects). (**F**) Pooled mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score before ECMO (inverse-variance, random-effects).

observational meta-analyses. The evidence started at low certainty, because all included studies were observational, and was downgraded where appropriate for risk of bias, inconsistency, indirectness, imprecision, and publication bias [22]. For inconsistency, we applied an operational threshold of I^2 greater than 50% to 75% for downgrading by 1 level and I^2 greater than 75% for downgrading by 2 levels. The I^2 value was considered together with the direction and magnitude of study estimates and the overlap of their CIs. The GRADE assessment is summarized in **Table 4**.

Sensitivity Analysis

A post hoc sensitivity analysis was conducted by re-analyzing the primary outcome after excluding studies with at least 1

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Table 4. Summary of findings with Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment.

Outcomes	No. of participants (studies)	Certainty assessment					Overall certainty	Pooled estimate (95% CI)	Heterogeneity (I^2)
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication bias			
In-hospital mortality	691 (10 studies)	Serious[a]	Serious[b]	Not serious	Not serious	Undetected, but uncertain[f]	⊕⊖⊖⊖ Very low	Pooled proportion: 0.65 (95% CI: 0.57 to 0.72)	70.6%
ICU mortality	526 (7 studies)	Serious[a]	Very serious[c]	Not serious	Serious[d]	Not reliably assessable[g]	⊕⊖⊖⊖ Very low	Pooled proportion: 0.61 (95% CI: 0.47 to 0.74)	85.8%
SOFA score before ECMO	170 (4 studies)	Serious[a]	Very serious[c]	Not serious	Serious[d]	Not reliably assessable[g]	⊕⊖⊖⊖ Very low	Pooled mean: 8.08 (95% CI: 1.14 to 15.02)	99.4%
APACHE-II score before ECMO	106 (3 studies)	Serious[a]	Very serious[c]	Not serious	Very serious[e]	Not reliably assessable[g]	⊕⊖⊖⊖ Very low	Pooled mean: 24.17 (95% CI: -0.73 to 49.08) [h]	98.9%
Duration of mechanical ventilation before ECMO (days)	229 (4 studies)	Serious[a]	Not serious	Not serious	Not serious	Not reliably assessable[g]	⊕⊖⊖⊖ Very low	Pooled mean: 4.77 (95% CI: 3.70 to 5.85)	4.4%
Duration of ECMO therapy (days)	378 (6 studies)	Serious[a]	Very serious[c]	Not serious	Not serious	Not reliably assessable[g]	⊕⊖⊖⊖ Very low	Pooled mean: 17.83 (95% CI: 12.80 to 22.86)	79.8%
ICU length of stay (days)	287 (4 studies)	Serious[a]	Very serious[c]	Not serious	Serious[d]	Not reliably assessable[g]	⊕⊖⊖⊖ Very low	Pooled mean: 23.55 (95% CI: 7.45 to 39.65)	92.6%
Serious bleeding	366 (5 studies)	Serious[a]	Very serious[c]	Not serious	Serious[d]	Not reliably assessable[g]	⊕⊖⊖⊖ Very low	Pooled proportion: 0.40 (95% CI: 0.22 to 0.61)	85.7%

Abbreviations: ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; APACHE II, Acute Physiology and Chronic Health Evaluation II SOFA, Sequential Organ Failure Assessment.

[a] Downgraded for risk of bias because the evidence was derived from single-arm observational studies, predominantly retrospective cohorts, with concerns regarding selection, confounding, and incomplete reporting. [b] Downgraded by 1 level for inconsistency because I^2 was > 50% and ≤ 75%. [c] Downgraded by 2 levels for inconsistency because I^2 was > 75% and study estimates varied markedly. [d] Downgraded for a wide confidence interval spanning clinically different values. [e] Downgraded by 2 levels because the confidence interval was extremely wide and included a clinically implausible negative lower limit. [f] Funnel plot inspection and Egger's test did not detect asymmetry, but only 10 studies were available and statistical power was limited. [g] Publication bias could not be reliably assessed because fewer than 10 studies contributed to the outcome. This was not interpreted as evidence that publication bias was absent. [h] The negative lower confidence limit results from the unbounded normal-scale confidence interval used in the random-effects model and has no clinical meaning; the pooled estimate is highly uncertain.

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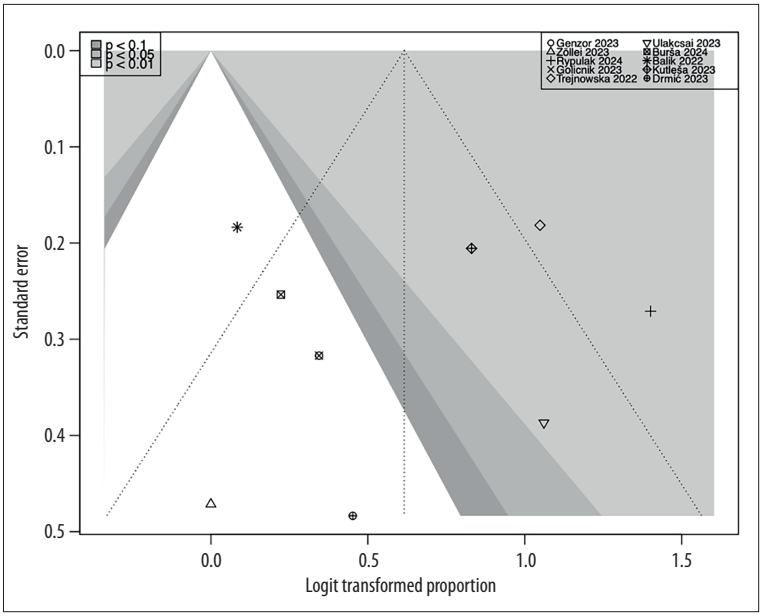


Figure 2. Funnel plot for assessment of publication bias in pooled in-hospital mortality.

"No" or "Unclear" rating in an applicable JBI item. "Not applicable" ratings were not treated as methodological concerns. This item-based rule excluded the studies of Burša et al [23], Genzor et al [24], Kutleša et al [25], and Zöllei et al [26]. The same random-effects generalized linear mixed model used in the primary analysis was then fitted to the remaining studies. This rule was used only for the sensitivity analysis and was not used to assign overall study-quality categories.

Publication Bias

Publication bias was assessed only for outcomes with at least 10 contributing studies, using visual inspection of funnel plots (**Figure 2**) [27] and Egger's regression test [28].

Results

Literature Search and Study Characteristics

The literature search results are presented in the PRISMA flow diagram (**Figure 3**). Of 23 full-text articles, 10 were excluded after author contact confirmed population overlap, and 1 due to wrong study type (conference abstract). Twelve studies were included in the final analysis: 10 retrospective cohort analyses and 2 case series encompassing a total of 802 patients with COVID-19 supported with ECMO across Central and Eastern European countries (Czech Republic, 4 studies; Poland, Hungary, and Croatia, 2 studies from each country; and Slovenia and Romania, 1 study from each country) [10,23-26,29-35]. The characteristics and results of the included studies are presented in **Table 3**. Because not all studies reported every outcome, the number of contributing studies and patients is reported separately for each pooled analysis.

Primary Outcome

Mortality

Mortality outcomes varied across studies: 10 of 12 studies (83.3%) reported in-hospital mortality, and 7 of 12 (58.3%) reported ICU mortality. Short- and mid-term post-discharge mortality were rarely reported, with only 1 study of 12 (8.3%) each reporting 28-, 30-, 60-, and 180-day mortality, and 2 of 12 studies (16.7%) reporting 90-day mortality.

The pooled in-hospital mortality was 65% (95% CI 0.57-0.72; $I^2 = 70.6\%$) based on 10 studies (n = 691). The certainty of this estimate was rated as very low according to the GRADE framework, downgraded due to serious inconsistency (**Table 4**). Stratification by country was performed for nations represented by at least 2 studies reporting the relevant mortality outcome. Among the 9 studies with stratifiable in-hospital mortality data (n = 650), the Czech Republic (3 studies, n = 223) and Poland (2 studies, n = 244) yielded pooled estimates of 54% (95% CI 0.40-0.68; $I^2 = 0.0\%$) and 76% (95% CI 0.32-0.96; $I^2 = 14.4\%$), respectively (**Figure 1**). Country subgroups were presented for the Czech Republic, Hungary, Poland, and Croatia. Estimates for Hungary and Croatia were highly imprecise because of small sample sizes and wide CIs and should be interpreted descriptively. Slovenia, represented by a single study, was included in the overall pooled estimate but not in the subgroup panel. Romania did not contribute data to the in-hospital mortality analysis. The GRADE certainty was very low (**Table 4**)

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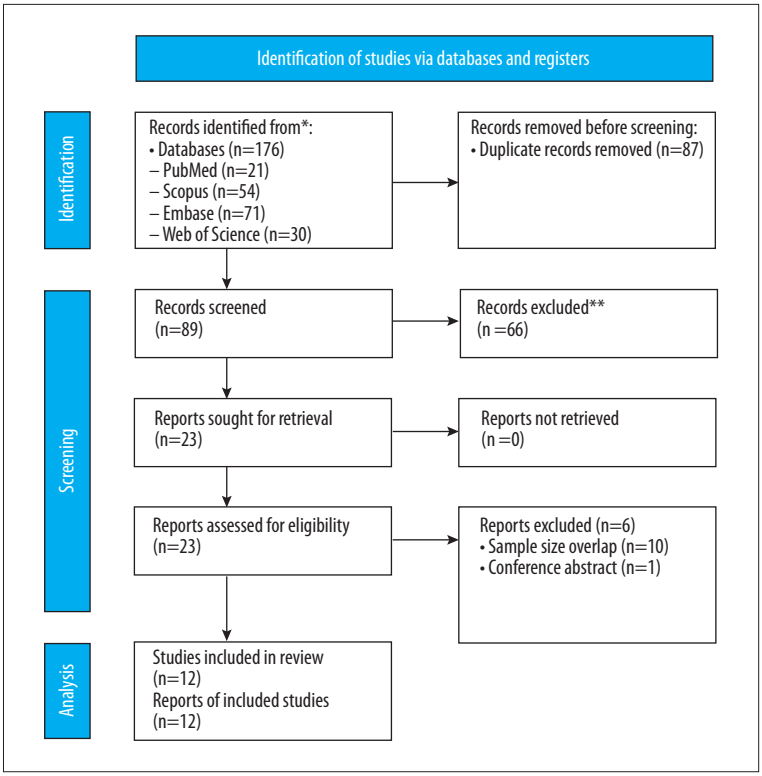


Figure 3. PRISMA flow diagram illustrating the study selection process.

The pooled ICU mortality was 61% (95% CI 0.47-0.74; $I^2 = 85.8\%$). Country-stratified analysis of ICU mortality included the Czech Republic and Poland (4 studies, n = 449) (**Figure 1**). Other countries were not eligible for ICU mortality subgroup analysis because fewer than 2 studies per country reported this outcome. For mortality outcomes, country-level estimates were treated as descriptive only, particularly when based on 2 studies or accompanied by wide CIs. The GRADE certainty was very low (**Table 4**).

In the post hoc sensitivity analysis excluding 4 studies with at least 1 "No" or "Unclear" JBI item, 6 studies (n = 457) remained. The pooled in-hospital mortality was 68% (95% CI 0.55-0.78; I^2=79.2%), compared with 65% (95% CI 0.57-0.72) in the primary analysis. The exclusion did not materially change the pooled estimate or its interpretation, although substantial between-study heterogeneity remained.

Secondary Outcomes

ICU Severity Scores at ECMO Initiation

A total of 4 studies (n = 170) reported SOFA scores prior to ECMO initiation. Individual study means for this outcome ranged from 3.2 to 13.8. The pooled mean SOFA score was 8.1 (95% CI 1.1-15.0), with high heterogeneity ($I^2 = 99.4\%$) (**Figure 1**). The GRADE certainty of this estimate was very low, downgraded for very serious inconsistency and serious imprecision (**Table 4**).

A total of 3 studies (n = 106) reported APACHE II scores prior to ECMO initiation. Individual study means for this outcome ranged from 12.7 to 30.5. The pooled mean APACHE II score was 24.2 (95% CI -0.7 to 49.1), with high heterogeneity ($I^2 = 98.9\%$) (**Figure 1**). The negative lower confidence limit arises from the unbounded normal-scale confidence interval used in the random-effects meta-analysis and has no clinical meaning. The pooled estimate should therefore be interpreted as highly uncertain rather than as a clinically plausible range. The GRADE certainty was very low (**Table 4**).

The Simplified Acute Physiology Score II (SAPS II), which was predefined as a secondary outcome, was not reported in any of the included studies (**Table 3**).

Duration of Mechanical Ventilation Before ECMO Initiation

A total of 4 studies (n = 229) reported the duration of mechanical ventilation prior to ECMO initiation, with individual study means ranging from 4.2 to 6.5 days. The pooled mean duration was 4.8 days (95% CI 3.7-5.8). No significant heterogeneity was observed among studies ($I^2 = 4.4\%$), indicating consistent findings across study populations (**Figure 4**). The GRADE certainty was very low (**Table 4**).

Duration of ECMO Therapy

A total of 6 studies (n = 378) were included in the analysis of total ECMO duration. Individual study means of days on ECMO ranged

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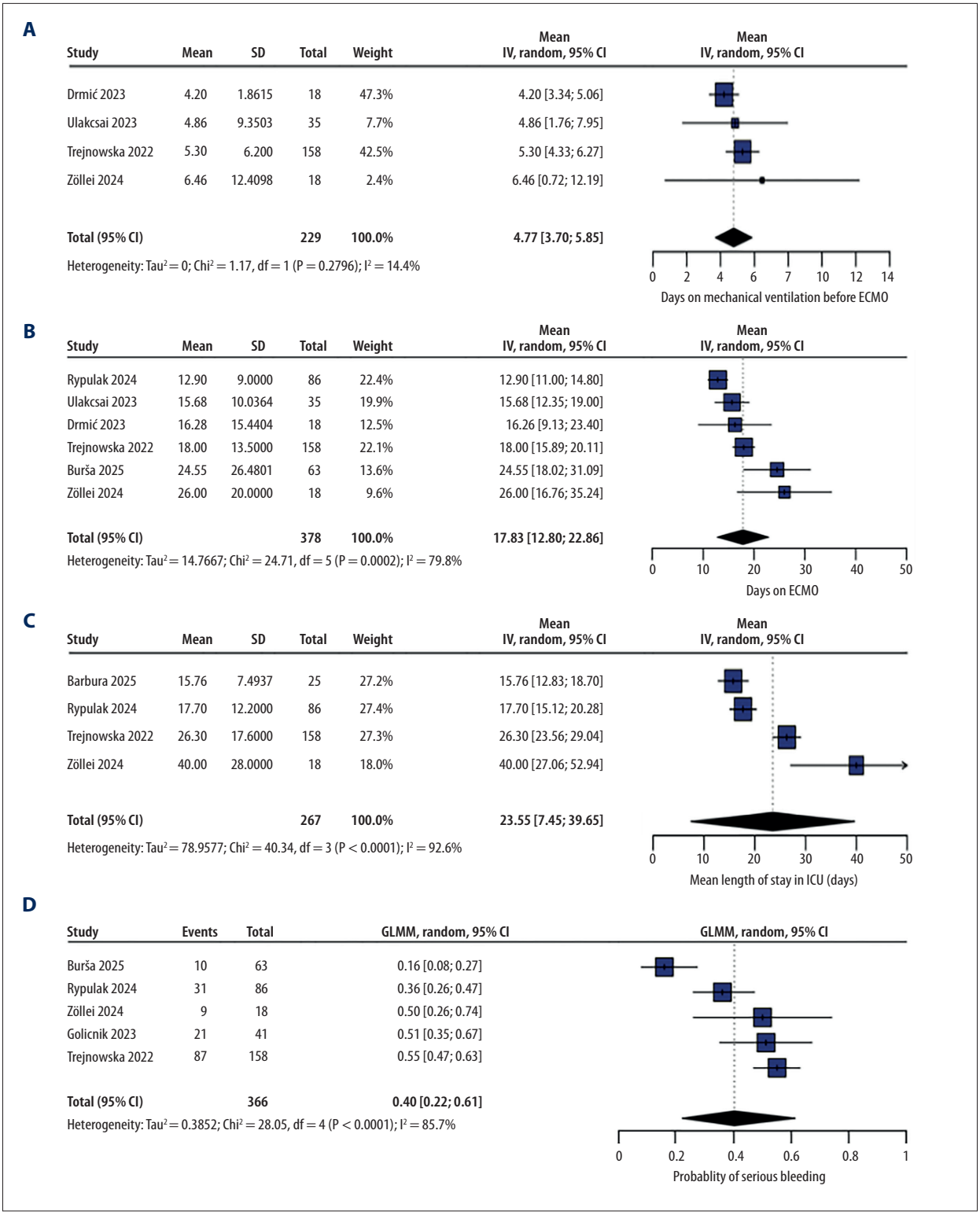


Figure 4. Forest plots of procedural timelines, ICU length of stay, and serious bleeding in the Central and Eastern European (CEE) extracorporeal membrane oxygenation (ECMO) cohort. (**A**) Duration of mechanical ventilation before ECMO initiation (inverse-variance, random-effects). (**B**) Duration of ECMO therapy (inverse-variance, random-effects). (**C**) ICU length of stay (inverse-variance, random-effects). (**D**) Pooled proportion of serious bleeding (random-effects generalized linear mixed model [GLMM]).

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from 12.9 to 26.0 days. The pooled mean ECMO duration was 17.8 days (95% CI 12.8-22.9), with high heterogeneity (I^2 = 79.8%) (**Figure 4**). The GRADE certainty was very low (**Table 4**).

ICU Length of Stay

A total of 4 studies (n = 287) were included in the analysis of ICU length of stay. Individual study means ranged from 15.8 to 40.0 days. The pooled mean ICU length of stay was 23.6 days (95% CI 7.5-39.7), with high heterogeneity (I^2 = 92.6%) (**Figure 4**). The GRADE certainty was very low (**Table 4**).

Major Complications

Serious bleeding was reported in 5 studies (n = 366), with 158 events observed. Individual study estimates for this outcome ranged from 16% to 55%. The pooled proportion of patients experiencing serious bleeding was 40% (95% CI 22%-61%), with high heterogeneity (I^2 = 85.7%) (**Figure 4**). The GRADE certainty was very low (**Table 4**).

Given the high heterogeneity for mortality, severity scores, ECMO duration, ICU length of stay, and serious bleeding, these pooled estimates should be interpreted as descriptive and potentially unstable.

The remaining predefined complication endpoints were reported too infrequently to support meta-analysis. Sepsis, pneumothorax, deep venous thrombosis, intracranial hemorrhage or stroke, and oxygenator failure were each reported in 2 studies. Multiorgan failure, barotrauma, and limb ischemia were each reported in a single study. Delirium was not reported in any included study.

Quality Assessment

Item-level JBI assessments are presented in **Table 5**. The pattern of "Yes", "No", "Unclear", and "Not applicable" ratings showed concerns regarding confounding, selection, and incomplete reporting in several studies. No numerical summary score or overall quality category was assigned. These item-level findings should be considered alongside the very low GRADE certainty for all pooled outcomes.

Certainty of Evidence Assessment

The overall certainty for each outcome was evaluated using the GRADE framework adapted for single-arm observational meta-analyses (**Table 4**). The evidence started at low certainty, because all included studies were observational, and was downgraded for serious risk of bias. Additional downgrading was applied for inconsistency and imprecision where appropriate. Consequently, the certainty of evidence for all 8 pooled outcomes was rated as very low.

Publication Bias

Assessment of publication bias was performed using visual inspection of the funnel plot and Egger's regression test for the primary outcome (in-hospital mortality) only, as the remaining meta-analyses included fewer than 10 studies each, precluding reliable assessment of publication bias.

The funnel plot showed no clear visual asymmetry (**Figure 2**), and Egger's regression test did not indicate significant asymmetry (t = -0.31, df = 8, P = 0.76). However, because only 10 studies contributed to this analysis, the absence of detectable asymmetry should not be interpreted as excluding publication bias.

Discussion

Primary Outcome: Mortality

The pooled in-hospital mortality in this CEE cohort was 65% (95% CI 0.57-0.72) based on 10 studies (n = 691). This estimate is higher than that of other early international ECMO reports, which reported mortality around 37% to 40% [1,2], a range comparable to historical ECMO-treated ARDS mortality before COVID-19 [36], and higher than later registry and meta-analytic estimates [3-5,37-39].

The similarity to high mortality reported in the SepsEast registry among mechanically ventilated COVID-19 patients supports the need for regional benchmarking but does not establish an ECMO-specific regional effect [9]. The highly heterogeneous outcome of ECMO has been extensively described in Europe during the COVID-19 pandemic. An exceptionally high mortality was described in Germany, reaching 65.9% and 72% in veno-venous and veno-arterial ECMO, respectively, in a large cohort of nearly 4300 patients [40]. Smaller regional studies yielded even higher mortality rates of 80% in a multicentric report from Middle Ruhr [41].

Substantial heterogeneity was observed for in-hospital mortality (I^2 = 70.6%). Country-level estimates, including those for the Czech Republic and Poland, were descriptive and should be interpreted cautiously because of the small number of studies and wide CIs. Referral timing, ECMO center volume, resource availability, and patient selection were not systematically measured; therefore, their role can only be considered hypothesis-generating.

Secondary Outcomes

Acuity and Procedural Timing: Pre-ECMO Patient Profile

Four studies (n = 170) reported SOFA scores, yielding a pooled mean of 8.1 (95% CI 1.1-15.0), and 3 studies (n = 106) reported

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Table 5. Risk of bias evaluation using the JBI checklist.

Study	Cohort studies										
	Question no.										
	1	2	3	4	5	6	7	8	9	10	11
Balik 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes
Barbura 2025	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Burša 2025	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes
Drmić 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes
Genzor 2023	NA	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Golicnik 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes
Kutleša 2023	Yes	NA	Yes	UC	No	Yes	Yes	Yes	Yes	NA	No
Sitina 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes
Trejnowska 2022	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ulakcsai 2023	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes

Study	Case series									
	Question no.									
	1	2	3	4	5	6	7	8	9	10
Rypulak 2024	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zöllei 2024	Yes	Yes	Yes	UC	Yes	Yes	Yes	Yes	Yes	Yes

Yes, criterion met; No, criterion not met; UC, insufficient information to determine whether the criterion was met; NA, criterion not applicable to the study design. No numerical summary score or overall quality category was assigned.

Cohort studies questions:

1. Were the two groups similar and recruited from the same population?
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?
3. Was the exposure measured in a valid and reliable way?
4. Were confounding factors identified?
5. Were strategies to deal with confounding factors stated?
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
7. Were the outcomes measured in a valid and reliable way?
8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?
9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?
10. Were strategies to address incomplete follow up utilized?
11. Was appropriate statistical analysis used?

Case series questions:

1. Were there clear criteria for inclusion in the case series?
2. Was the condition measured in a standard, reliable way for all participants included in the case series?
3. Were valid methods used for identification of the condition for all participants included in the case series?
4. Did the case series have consecutive inclusion of participants?
5. Did the case series have complete inclusion of participants?
6. Was there clear reporting of the demographics of the participants in the study?
7. Was there clear reporting of clinical information of the participants?
8. Were the outcomes or follow up results of cases clearly reported?
9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?
10. Was statistical analysis appropriate?

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APACHE II scores, yielding a pooled mean of 24.2 (95% CI -0.7 to 49.1). The negative lower CI limit for APACHE II is clinically implausible, and both severity score outcomes showed very high heterogeneity (I^2 = 99.4% for SOFA, and I^2 = 98.9% for APACHE II). These pooled severity estimates should therefore be interpreted as descriptive only. Differences in score timing, illness trajectory, chronic disease burden, and cannulation timing may have contributed to heterogeneity, but these factors were not consistently measured.

Duration of ECMO Therapy

The pooled mean ECMO duration in our CEE cohort was 17.8 days (95% CI 12.8-22.9; I^2 = 79.8%) based on 6 studies (n = 378), with individual study means ranging from 12.9 to 26.0 days. This estimate is comparable to the pooled ECMO duration of 15.1 days (95% CI 13.4-18.7) reported by Ramanathan et al (18 studies, 1844 patients) in their global meta-analysis of early pandemic data [1]. The updated and larger meta-analysis by Ling et al (52 studies, 18 211 patients) reported a pooled ECMO duration of approximately 16 days (95% CI 14.9-17.9) [5]. The slightly longer ECMO duration observed in our CEE cohort may reflect several factors, including more advanced disease at cannulation (as suggested by the elevated APACHE II scores) and prolonged viral courses in later pandemic waves. Whether lower center volume or less procedural experience contributed to slower weaning cannot be determined from the available data, because these variables were not systematically reported.

The high heterogeneity (I^2 = 79.8%) across the CEE studies may reflect inter-center variability in weaning protocols, patient case-mix, and definitions of ECMO run completion. The meta-analysis by Tan et al demonstrated that ECMO duration was significantly shorter in survivors than in non-survivors (standardized mean difference = -0.18; 95% CI -0.30 to -0.06; P = 0.003) [42], suggesting that prolonged ECMO runs may serve as a marker of treatment futility or irreversible organ damage rather than a modifiable risk factor per se. In the Ramanathan et al meta-analysis, meta-regression confirmed that ECMO duration was significantly associated with increased mortality [1]. These observations indicate that future prospective studies should evaluate whether standardized weaning criteria and futility benchmarks could improve consistency in decisions regarding treatment continuation or withdrawal.

ICU Length of Stay

The pooled mean ICU length of stay in our CEE cohort was 23.6 days (95% CI 7.5-39.7; I^2 = 92.6%) based on 4 studies (n = 287), with individual study means ranging from 15.8 to 40.0 days. This estimate is notably shorter than the pooled ICU length of stay of 33.5 days (95% CI 29.4-37.6) reported by Ling et al in their comprehensive meta-analysis of 14 studies [5]. This discrepancy may be partly explained by the higher mortality rate in the CEE cohort (65% vs 48.8% in the Ling et al analysis), as non-survivors typically have shorter ICU stays than survivors, who undergo prolonged weaning and rehabilitation. Indeed, in the EuroECMO-COVID study, the median ICU length of stay was substantially longer in survivors than in non-survivors [4,11].

The exceptionally high heterogeneity (I^2 = 92.6%) in our analysis limits the reliability of the pooled estimate and may reflect profound differences in ICU management practices, discharge criteria, and the availability of step-down and rehabilitation facilities across the CEE countries. The wide CI (7.5-39.7 days) further underscores this variability. These findings indicate that ICU resource utilization for patients on ECMO in the CEE region is highly variable. Whether standardization of post-ECMO care pathways could reduce this variability remains to be tested in prospective comparative studies.

Complications

Serious bleeding was observed in 40.2% (95% CI 22.2%-61.3%) of patients across 5 studies (n = 366) in our analysis. This rate is broadly consistent with, although slightly higher than, rates reported in the international literature. A large systematic review and meta-analysis by Jin et al, of 23 studies and 6878 patients with COVID-19 on ECMO, reported a pooled major hemorrhage rate of 37.4% (95% CI 28.1%-46.8%) [43]. In a French nationwide cohort of 620 patients with COVID-19 on ECMO (ECMOSARS registry), Mansour et al reported that 29% of patients experienced bleeding events alone, 16% had thrombotic events alone, and 20% had both [44]. Critically, bleeding was independently associated with in-hospital mortality (adjusted OR 2.91; 95% CI 1.94-4.4), whereas thrombotic events were not (adjusted OR 1.02; 95% CI 0.68-1.53) [44]. These data support future evaluation of standardized anticoagulation, hemostasis monitoring, and multidisciplinary coagulation management during ECMO support in CEE cohorts.

Strengths and Limitations

This study provides, to our knowledge, the first region-focused aggregation of ECMO outcomes in adult patients with COVID-19 from the CEE region. By pooling data from a geographically defined population that has been underrepresented in international registries, it offers contextual benchmarking, descriptive estimates of between-study heterogeneity, and country-level variation that can inform the design of future prospective studies. The methodology included comprehensive database searches, independent dual-reviewer screening and data extraction, and risk-of-bias assessment using validated JBI tools. The subgroup analysis by country describes inter-country variability, although the small number of studies per country and

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very low certainty of evidence limit definitive interpretation of these differences.

Additionally, the certainty of evidence for each pooled outcome was formally assessed using the GRADE framework (**Table 4**), providing a transparent evaluation of the reliability of the synthesized estimates. All pooled outcomes were rated as evidence of very low certainty. Therefore, the findings should be interpreted as hypothesis-generating and should not be used to support definitive clinical or organizational recommendations.

Several limitations must be acknowledged. The inclusion of exclusively observational studies introduces inherent selection and reporting biases, and the retrospective design of most included studies does not preclude the possibility that a substantial proportion of ECMO-treated patients were missing from the analysis. The total population of 802 patients, while the largest CEE-specific ECMO cohort assembled to date, remains relatively small compared with registry data from individual Western European countries; for instance, Germany alone reported 4279 ECMO procedures for COVID-19 [40], despite having a comparable total population to the analyzed region.

The high heterogeneity observed for mortality, SOFA, APACHE II, ECMO duration, ICU length of stay, and serious bleeding limits the reliability of pooled estimates. These results should therefore be interpreted mainly as descriptive benchmarks rather than stable summary measures.

A post hoc item-based sensitivity analysis produced a similar estimate of in-hospital mortality after studies with at least 1 "No" or "Unclear" JBI rating were excluded. However, heterogeneity remained substantial, and the exclusion rule was not a validated overall JBI score; the analysis should therefore be viewed as a robustness check rather than a reclassification of study quality.

Additionally, post-discharge and long-term mortality data were rarely reported across the included studies, precluding assessment of outcomes beyond the index hospitalization.

The EuroECMO-COVID study demonstrated that among hospital survivors, 35% experienced residual dyspnea and only 24% returned to full-time work at 6-month follow-up [4,11], suggesting that future CEE studies should incorporate longer-term outcome assessment.

Further limitations relate to language restriction, data transformation, and publication-bias assessment. Restricting inclusion to English, Polish, and Czech articles may have introduced selection bias. In addition, conversion of medians and IQRs to means and SDs may have increased uncertainty in pooled continuous outcomes. Moreover, funnel plots and Egger's test were used only when at least 10 studies were available and should be interpreted cautiously because of limited power in small meta-analyses. The use of affiliation fields and the restriction to the terms "prospective" or "retrospective" may have reduced search sensitivity and missed eligible multicenter or observational reports not indexed with these terms.

Finally, data on ECMO center volume, annual procedural experience, and the presence of formalized ECMO referral networks were not systematically reported, limiting our ability to directly quantify the contribution of institutional experience to the observed inter-country mortality differences.

Conclusions

In this CEE cohort, pooled in-hospital mortality among COVID-19 patients treated with ECMO was 65%, and serious bleeding occurred in 40% of cases. These estimates appear higher than several international benchmarks, but direct comparison is limited by differences in pandemic periods, case mix, patient selection and ECMO eligibility, and outcome definitions. Country-level mortality estimates, including those for the Czech Republic and Poland, were exploratory and based on few studies with wide CIs; they should not be interpreted as evidence of a true country-level difference. The GRADE certainty of evidence was very low for all pooled outcomes.

The possible roles of ECMO center experience, referral infrastructure, patient selection, and severity at cannulation should be treated as hypothesis-generating, as these factors were not directly measured or tested in this single-arm observational synthesis. These findings support the need for standardized regional ECMO registries, prospective multicenter data collection, harmonized complication reporting, and long-term functional and quality-of-life outcome assessment. Future studies should collect data on referral pathways, center volume, ECMO capacity, patient selection, and severity at cannulation to test the hypotheses generated by this review.

Data Availability Statement

The data supporting the conclusions of this article are included within the article and its supplementary materials. Additional data are available from the corresponding author upon reasonable request.

Presentation

Preliminary results of this work were presented as a poster (P076) at the 45th International Symposium on Intensive Care & Emergency Medicine (ISICEM), Brussels, Belgium, 17-20 March 2026.

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Declaration of Generative AI and AI-Assisted Technologies in the Manuscript Preparation Process

During the preparation of this work the author(s) used Google Gemini 2.5 Pro to improve the language, grammar, and overall clarity of the manuscript. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Ramanathan K, Shekar K, Ling RR, et al. Extracorporeal membrane oxygenation for COVID-19: A systematic review and meta-analysis. Crit Care. 2021;25(1):211
2. Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation support in COVID-19: An international cohort study of the Extracorporeal Life Support Organization registry. Lancet. 2020;396(10257):1071-78
3. Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation for COVID-19: Evolving outcomes from the international Extracorporeal Life Support Organization Registry. Lancet. 2021;398(10307):1230-38
4. De Piero ME, Mariani S, van Bussel BCT, et al. In-hospital outcomes and 6-month follow-up results of patients supported with extracorporeal membrane oxygenation for COVID-19 from the second wave to the end of the pandemic (EuroECMO-COVID): A prospective, international, multicenter, observational study. Lancet Respir Med. 2025;13(4):307-17
5. Ling RR, Ramanathan K, Sim JJL, et al. Evolving outcomes of extracorporeal membrane oxygenation during the first 2 years of the COVID-19 pandemic: A systematic review and meta-analysis. Crit Care. 2022;26(1):147
6. Molnar Z. SepsEast: Bridging between East and West. J Crit Care. 2017;40:323
7. Islam N, Shkolnikov VM, Acosta RJ, et al. Excess deaths associated with COVID-19 pandemic in 2020: Age and sex disaggregated time series analysis in 29 high income countries. BMJ. 2021;373:n1137
8. Lainscak M, Sustic A, Benes J, et al. SepsEast and COVID-19: Time to make a difference. Signa Vitae. 2020;16(1):1-4
9. Benes J, Jankowski M, Szułdrzynski K, et al. SepsEast Registry indicates high mortality associated with COVID-19 caused acute respiratory failure in Central-Eastern European intensive care units. Sci Rep. 2022;12(1):14906
10. Trejnowska E, Drobiński D, Knapik P, et al. Extracorporeal membrane oxygenation for severe COVID-19-associated acute respiratory distress syndrome in Poland: A multicenter cohort study. Crit Care. 2022;26(1):97
11. Lorusso R, De Piero ME, Mariani S, et al. In-hospital and 6-month outcomes in patients with COVID-19 supported with extracorporeal membrane oxygenation (EuroECMO-COVID): A multicenter, prospective observational study. Lancet Respir Med. 2023;11(2):151-62
12. Supady A, Combes A, Barbaro RP, et al. Respiratory indications for ECMO: Focus on COVID-19. Intensive Care Med. 2022;48(10):1326-37
13. Urner M, Barnett AG, Bassi GL, et al. Venovenous extracorporeal membrane oxygenation in patients with acute COVID-19 associated respiratory failure: Comparative effectiveness study. BMJ. 2022;377:e068723
14. Hajage D, Combes A, Guervilly C, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: An emulated target trial analysis. Am J Respir Crit Care Med. 2022;206(3):281-94
15. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:n71
16. Higgins JPT, Thomas J, Chandler J, et al, Editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 6.5 (Updated August 2024). Cochrane, 2024. Available from www.Cochrane.Org/Handbook
17. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: A practical tutorial. Evid Based Ment Health. 2019;22(4):153-60
18. McGrath S, Zhao X, Steele R, et al.; DEPRESsion Screening Data (DEPRESSD) Collaboration. Estimating the sample mean and standard deviation from commonly reported quantiles in meta-analysis. Stat Methods Med Res. 2020;29(9):2520-37
19. Moola S, Munn Z, Tufanaru C, et al. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z (Editors). Joanna Briggs Institute Reviewer's Manual The Joanna Briggs Institute, 2017. Available from: https://synthesismanual.jbi.global/
20. Munn Z, Barker TH, Moola S, et al. Methodological quality of case series studies: An introduction to the JBI critical appraisal tool. JBI Evidence Synthesis. 2020;18(10):2127
21. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-26
22. Schünemann HJ, Cuello C, Akl EA, et al. GRADE Guidelines: 18. How ROBINS-I and other tools to assess risk of bias in non-randomized studies should be used to rate the certainty of a body of evidence. J Clin Epidemiol. 2019;111:105-14
23. Burša F, Máca J, Sagan J, et al. A safety comparison of heparin and argatroban anticoagulation in veno-venous extracorporeal membrane oxygenation with a focus on bleeding. Transfusion Medicine. 2025;35(1):75-81
24. Genzor S, Pobeha P, Šimek M, et al. Long-term follow-up of patients needing extracorporeal membrane oxygenation following a critical course of COVID-19. Life. 2023;13(4):1054
25. Kutleša M, Santini M, Krajinović V, et al. Extracorporeal membrane oxygenation in COVID-19: Results of the Croatian Extracorporeal Membrane Oxygenation Referral Center. Int J Artif Organs. 2023;46(4):248-51
26. Zöllei É, Rudas L, Hankovszky P, et al. Venovenous extracorporeal membrane oxygenation for COVID-19 associated severe respiratory failure: Case series from a Hungarian tertiary center. Perfusion (United Kingdom). 2024;39(4):790-96
27. Sterne JAC, Sutton AJ, Ioannidis JPA, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ. 2011;343:d4002
28. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-34
29. Rypulak E, Szczukocka M, Czarnik T. Utilisation and outcomes of a mobile (ambulance and air transport) venovenous extracorporeal membrane oxygenation (VV-ECMO) program in Poland during the COVID-19 pandemic – A retrospective, two-centers, case-series study. Anaesthesiology Intensive Therapy. 2024;56(2):141-45
30. Golicnik A, Zivanovic I, Gorjup V, Berden J. Same but different—ECMO in COVID-19 and ARDS of other etiologies. Comparison of survival outcomes and management in different ARDS groups. J Intensive Care Med. 2023;38(7):635-42
31. Barbura N, Porosnicu TM, Oancea C, et al. Extracorporeal membrane oxygenation modulates the inflammatory milieu and organ failure trajectory in severe COVID-19 and sepsis. JCM. 2025;14(12):4224
32. Ulakcsai Z, Szabo L, Szabo Z, et al. T cell immune response predicts survival in severely ill COVID-19 patients requiring venovenous extracorporeal membrane oxygenation support. Front Immunol. 2023;14:1179620
33. Balik M, Svobodova E, Porizka M, et al. The impact of obesity on the outcome of severe SARS-CoV-2 ARDS in a high volume ECMO center: ECMO and corticosteroids support the obesity paradox. J Crit Care. 2022;72:154162
34. Sitina M, Sramek V, Helan M, Suk P. Prognostic significance of early acute kidney injury in COVID-19 patients requiring mechanical ventilation: A single-center retrospective analysis. Renal Failure. 2023;45(1):2205954
35. Drmić Ž, Bandić I, Hleb S, et al. Inflammatory biomarkers affecting survival prognosis in patients receiving veno-venous ECMO for severe COVID-19 pneumonia. Diagnostics. 2023;13(13):13132203

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36. Combes A, Hajage D, Capellier G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. N Engl J Med. 2018;378(21):1965-75
37. Chandel A, Puri N, Damuth E, et al. Extracorporeal membrane oxygenation for COVID-19: Comparison of outcomes to non-COVID-19-related viral acute respiratory distress syndrome from the extracorporeal life support organization registry. Crit Care Explor. 2023;5(2):e0861
38. Supady A, Taccone FS, Lepper PM, et al.; COVEC-Study Group. Survival after extracorporeal membrane oxygenation in severe COVID-19 ARDS: Results from an international multicenter registry. Crit Care. 2021;25(1):90
39. Schmidt M, Hajage D, Landoll M, et al. Comparative outcomes of extracorporeal membrane oxygenation for COVID-19 delivered in experienced European centers during successive SARS-CoV-2 variant outbreaks (ECMO-SURGES): An international, multicenter, retrospective cohort study. Lancet Respir Med. 2023;11(2):163-75
40. Friedrichson B, Kloka JA, Neef V, et al. Extracorporeal membrane oxygenation in coronavirus disease 2019: A nationwide cohort analysis of 4279 runs from Germany. Eur J Anaesthesiol. 2022;39(5):445-51
41. Aweimer A, Petschulat L, Jettkant B, et al. Mortality rates of severe COVID-19-related respiratory failure with and without extracorporeal membrane oxygenation in the Middle Ruhr Region of Germany. Sci Rep. 2023;13(1):5143
42. Tan Z, Su L, Chen X, et al. Relationship between the pre-ECMO and ECMO time and survival of severe COVID-19 patients: A systematic review and meta-analysis. J Clin Med. 2024;13(3):868
43. Jin Y, Zhang Y, Liu J, Zhou Z. Thrombosis and bleeding in patients with COVID-19 requiring extracorporeal membrane oxygenation: A systematic review and meta-analysis. Res Pract Thromb Haemost. 2023;7(2):100103
44. Mansour A, Flecher E, Schmidt M, et al. Bleeding and thrombotic events in patients with severe COVID-19 supported with extracorporeal membrane oxygenation: A nationwide cohort study. Intensive Care Med. 2022;48(8):1039-52

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