

Bias Risk Assessment Report

Combination of extracorporeal membrane oxygenation and continuous renal replacement therapy in critically ill patients: a systematic review of the past decade (2014--2023)

January 25, 2025

1. Background

This systematic review included 17 retrospective observational studies and 2 prospective studies. Due to the inherent potential bias risk in retrospective study designs, the Newcastle-Ottawa Scale (NOS) was used to assess the bias risk of the included studies. The 2 prospective studies were also evaluated using the NOS scale due to the lack of randomization and blinding.

2. Assessment Methods

2.1 Tool Selection

NOS Scale: Applicable to case-control/cohort studies. Quality is rated across three dimensions (selection of study populations, comparability between groups, and outcome assessment) using a star system (maximum 9 stars; 1–3, 4–6, and 7–9 stars indicate low, moderate, and high quality, respectively).

2.2 Assessment Process

Two independent reviewers (ZXY, GJH) conducted blinded evaluations. Discrepancies were resolved through discussion or adjudication by a third reviewer (ZL).

3. Assessment Results

3.1 Overall Study Quality Distribution (Details in Appendix 1)

Quality Grade	Number of Studies (Percentage)	Number of Patients Included (Percentage)	Reference Numbers
Low Quality	0 (0%)	0	/
Moderate Quality	9 (47%)	805 (45%)	7,8,9,10,12,13,18,20,24
High Quality	10 (53%)	981 (55%)	6,11,14,15,16,17,19,21,22,23

3.2 Main Sources of Bias (by NOS Dimensions)

- **Control of Confounding Factors:** Four studies ^[10,11,20,23] failed to adjust for key confounders (e.g., age, sex, comorbidities).
- **Selection Bias:** Five studies ^[10,11,15,20,23] exhibited mismatched baseline characteristics between study and control groups.
- **Outcome Measurement:** Most included studies (17/19) were retrospective, with fixed outcome indicators and varying time spans (up

to 10 years). This introduces potential heterogeneity in data collection and challenges in assessing objectivity and accuracy.

- **Data Completeness:** Retrospective studies rely on pre-existing records. Two studies ^[13,24] did not report mortality data, raising concerns about documentation completeness.

4. Sensitivity Analysis

1. Since no low-quality studies were included, the overall results remained consistent in direction.
2. The funnel plot showed approximate symmetry (Appendix 2).

5. Conclusions and Recommendations

1. Conclusions:

The findings of this systematic review rely heavily on retrospective studies. Despite the absence of low-quality studies, the inherent limitations of retrospective designs (e.g., data heterogeneity, time span variability) necessitate cautious interpretation of the conclusions.

2. Recommendations for Future Research:

Adopt randomized controlled trials or pragmatic designs to generate higher-quality evidence.

Clearly report methods for confounder adjustment.

Implement standardized blinded outcome assessments.

Appendix 1:

Author, publication year, reference	Study design	Age distribution of study population	Time frame for sample inclusion	Diseases included	Number of patients	S1	S2	S3	S4	C1	E1/O1	E2/O2	E3/O3	总 Ø
Shum, 2014 ^[6]	retrospective, single-center study	Adult	May,2009 to May 2013	ECMO with CRRT for various indications	37	1	1	-	1	1	1	1	1	7

Lin,2014 ^[7]	retrospective cohort study	Adult	January 2008 and December 2010.	ECMO+C RRT used to acute myocardia l infarction with cardiogeni c shock and out-of-hospital cardiac arrest	15	-	-	1	1	1	1	-	-	4
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Bijin,2015 ^[8]	Retrospective analysis	Adult	January 2007 to January 2012	patients who meets ECMO indications	40	1	-	1	-	1	1	1	1	6
Elio,2016 ^[9]	Retrospective cohort study	Adult	November 2008 to December 2013	patients who meets ECMO indications	135	1	-	-	1	1	1	-	-	4
Yetimakman,2017 ^[10]	retrospective study	Children	April 2013 to September 2016	ECMO with CRRT used to fluid	35	1	-	1-	-	1	1	-	-	5

				overload (FO)										
Zhou, 2018 ^[11]	Retrospective study	Children	December 2015 to November 2017	Cardiopul monary failure with acute kidney injury (AKI) or fluid overload	14	1	1	1	-	1	1	1	1	7

Richard, 2018 ^[12]	Retrospective study	Adult	August 2010 to May 2016	ARDS patients with ECMO+C RRT	54	1	-	1	-	1-	1	1	1	6
Ping, 2018 ^[13]	Retrospective study	Adult	January 2007 to December 2017	ECMO+C RRT used to fluid overload (FO) and electrolyte imbalance	32	1	-	1	-	1	1	1	1	6

[illegible]

			2018.	and heart failure										
Kuo,2019 ^[16]	Retrospective population-based cohort study	Adult	January 1, 2007 and December 31, 2013	patients who meets ECMO indications	2272	1	-	1	1	1	-	-	5	7
Dennis, 2020 ^[17]	single-center, prospective, observational study	Adult	October 1,2018 and December 31,2019.	Patients with ECMO+C RRT on β -lactam antibiotics and	30	1	1	1	-	1	1	1	1	7

				linezolid										
Gorga, 2020 ^[18]	Multicenter retrospective cohort study	children	January 1, 2007, to December 31, 2011	fluid overload (FO) at CRRT initiation and fluid removal during CRRT	367	1	-	1	1	-	1	1	-	5

Marco,2020 ^[19]	Retrospective study	Adult	June 2009 and May 2018	ECMO+C RRT used to ARDS	37	1	-	1	1	1	1	1	1	7
Thyagarajan,2021 ^[20]	A single-centre retrospective cohort study	Adult	January 2015 and June 2019	acute kidney injury due to ECMO	65(27 for VAECMO 、 28 for VVECMO)	1	-	1	1	1	1	-	-	5
Toshiki, 2022 ^[21]	single-center, Retrospective study	Adult	April 2015 - March 2018	ECMO with AKI	42	1	1	1	-	1	1	1	1	7
Thomas,2022 ^[22]	A retrospective	Adult	January 1, 2012, and	Burn injuries	19	1	1	1	-	1	1	1	1	7

	analysis		January 1, 2020	and Cardiovascular injuries										
Raja,2023 ^[23]	A prospective service evaluation	Adult	May–September 2019	patients who meets ECMO indications	20	1	1	1	-	1	1	1	1	7
Costantini,2023 ^[24]	retrospective single-center case series	Adult	April 2014 and February 2020	patients who meets ECMO indications	35	1	1	-	-	1	1	-	-	4

S1: the case definition is adequate ; S2 : Representativeness of cases ; S3: Selection of controls ; S4: Definition of controls.

C: Study controls for important factor or additional factor.

E1: Ascertainment of exposure; E2: Same method of ascertainment cases and controls; E3: Nonresponse rate.

Appendix 2:

- 附图 1：偏倚风险分布图

