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Mechanical left ventricular unloading in cardiogenic shock treated with venoarterial extracorporeal membrane oxygenation: a systematic review and meta-analysis

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Abstract

Objective:

To evaluate if mechanical left ventricular unloading could reduce mortality in patients with cardiogenic shock undergoing venoarterial extracorporeal membrane oxygenation (VA-ECMO).

Methods

We searched MEDLINE, Embase, and the Cochrane Library for randomized controlled trials and propensity score-matched studies published until December 20, 2023. The primary outcome was mortality at the longest follow-up. We used a Mantel-Haenszel random effects meta-analysis and reported the pooled results with a risk ratio (RR) and 95% confidence interval (CI). The review protocol was registered on PROSPERO International prospective register of systematic review (CRD42024498665).

Results

We identified two randomized controlled trials and eleven propensity score-matched studies, totaling 9858 patients. Mechanical left ventricular unloading was significantly associated with reduced mortality at the longest follow-up (RR, 0.89; 95% CI, 0.84–0.94; P = 0.0001; moderate certainty of evidence), which was confirmed in studies using intraaortic ballon pump (IABP). Benefits of mechanical unloading were also observed in terms of successful VA-ECMO weaning (RR, 1.15; 95% CI, 1.02–1.29; P = 0.02; low certainty of evidence) and favorable neurological outcome (two studies; RR, 2.45; 95% CI, 1.62–3.69; P < 0.0001; low certainty of evidence), although we observed an increased incidence of major bleeding (RR, 1.27; 95% CI, 1.02–1.59; P = 0.03; low certainty of evidence) and hemolysis (RR, 1.49; 95% CI, 1.10–2.02; P = 0.01; moderate certainty of evidence).

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Conclusions

Among adult patients with cardiogenic shock treated with VA-ECMO, mechanical left ventricular unloading was associated with reduced mortality, which was confirmed in studies using IABP as an unloading device.

Keywords: meta-analysis; extracorporeal membrane oxygenation; cardiogenic shock; intra-aortic balloon pumping; heart-assist devices

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Introduction

Cardiogenic shock occurs in 15% of patients admitted to the cardiac intensive care units (1). For severe cardiogenic shock and cardiac arrest with persistent hypotension and hypoperfusion unresponsive to optimal pharmacological therapy, peripheral venoarterial extracorporeal membrane oxygenation (VA-ECMO) is an option to provide adequate extracorporeal blood flow and gas exchange (2, 3). Despite advances in management, mortality remains high in cardiogenic shock patients treated with VA-ECMO (4).

Increased left ventricular (LV) afterload is a hemodynamic drawback of peripheral VA-ECMO due to its retrograde blood flow. The subsequent LV distention is associated with pulmonary edema, thrombus formation, and myocardial ischemia, thereby impairing the recovery of LV function (5–8). Of note, LV distention occurs in 22% of patients undergoing VA-ECMO, with one-third of them requiring immediate decompression (6). Thus, in patients with increased afterload (e.g., lack of aortic valve opening), LV unloading to prevent or treat LV distention can reduce LV workload and myocardial oxygen consumption, and potentially improve clinical outcomes (9).

A previous meta-analysis suggested survival benefits from mechanical LV unloading in cardiogenic shock patients treated with VA-ECMO (10). However, this promising result requires cautious evaluation because all the included studies were observational and the authors did not adjust for relevant confounders (10). Furthermore, there has been accumulating evidence regarding the effectiveness of mechanical LV unloading. Of note, a large, international registry-based study recently reported a significant mortality reduction with mechanical LV unloading using propensity matching techniques (11). Furthermore, a recent randomized controlled trial (RCT) showed that adding percutaneous left ventricular

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assist device to standard care reduces mortality in patients with infarct-related cardiogenic shock (12). Despite its potential benefits, mechanical LV unloading may carry risks of complications. Previous literature suggests that mechanical LV unloading was associated with a higher incidence of bleeding (11, 13), limb ischemia (13), and hemolysis (10).

Accordingly, we systematically reviewed RCTs and propensity score-matched studies and performed an updated meta-analysis to test the hypothesis that adding mechanical LV unloading to VA-ECMO, compared to VA-ECMO alone, would reduce mortality in patients with cardiogenic shock.

Materials and Methods

We performed a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (14) and registered the review protocol with PROSPERO International prospective register of systematic review on January 15, 2024 (CRD42024498665). Our review question was built using the PICOS (Population, Intervention, Comparison, Outcome, Study design) framework: adult patients with cardiogenic shock treated with VA-ECMO (P); mechanical LV unloading (I); no mechanical LV unloading (C); mortality at the longest follow-up (O); RCTs and propensity score-matched studies (S).

Search strategy and selection criteria

We searched MEDLINE, Embase, and Cochrane Library for relevant studies published until December 20th, 2023. We considered eligible RCTs and propensity score-matched studies comparing mechanical LV unloading with no mechanical LV unloading among adult patients

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with cardiogenic shock undergoing VA-ECMO. We excluded observational studies without propensity score matching, systematic reviews, commentaries/editorials, narrative reviews, and studies not addressing our review question. Two investigators independently screened eligibility based on study titles and abstracts after removing duplicates. Then, we selected eligible studies based on full-text assessment. Disagreements were resolved through discussion with another senior investigator.

Data collection and risk of bias assessment

We extracted data from included studies using a standardized data collection form. For RCTs, necessary data were extracted according to an intention-to-treat principle, while data after propensity score matching were used for propensity score-matched studies. We collected data on first author, year of publication, country, study design, setting, and primary and secondary outcomes. If mortality data were not reported, we contacted the first or corresponding author to request further information.

We assessed the risk of bias for RCTs by using the Cochrane risk-of-bias tool for RCTs version 2 (RoB 2) (15) and for propensity score-matched studies by using Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool (16). We assessed the overall certainty of the evidence based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (17). We created the GRADE evidence profile tables using the GRADEpro software (18). The presence of publication bias on the primary outcome was investigated by visual inspection of funnel plot and Egger's test using R 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

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Outcomes

The primary outcome was all-cause mortality at the longest follow-up available. The secondary outcomes were weaning from VA-ECMO, major bleeding, hemolysis, limb ischemia, stroke, receipt of renal replacement therapy, bridge to heart transplantation or durable ventricular assist device, and favorable neurological outcome. The definition of major bleeding was left to each study. If a study reported the incidence of major bleeding according to bleeding sites (or causes), we used the one with the highest incidence. We defined favorable neurological outcome as a Cerebral Performance Category score of 1 or 2 (19).

Data analysis

For the primary and secondary outcomes, frequentist analyses were conducted using Review Manager version 5.4 (20). We calculated a risk ratio (RR) and 95% confidence interval (CI) using a Mantel-Haenszel random-effects model. A p value less than 0.05 was considered statistically significant. We performed three subgroup analyses for the primary outcome: unloading strategies (intraaortic balloon pumping [IABP], microaxial flow pump [mAFP], either IABP or mAFP, and other), indication for VA-ECMO (cardiogenic shock and extracorporeal cardiopulmonary resuscitation [ECPR]), and low risk of bias studies.

A trial sequential analysis (TSA) (21) including only RCTs was performed for the primary outcome with a diversity-adjusted information size calculated using a two-sided alpha of 0.05, a power of 80%, an anticipated relative risk decrease of 10%, and the actual control event rate. We used the TSA Viewer software (Version 0.9.5.10 Beta. Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark).

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Results

Characteristics of included studies

Of 3954 studies, we identified two RCTs and eleven propensity score-matched studies totaling 9858 patients (Figure 1) (11, 13, 22–32). Major exclusions are summarized in Table S1.

The included studies were published between 2014 and 2023. VA-ECMO was used as ECPR in three studies (26, 29, 32). In one study, propensity score-matching was separately performed for patients with and without acute coronary syndrome (ACS) (26): we used the matched data separately when pooling results. The unloading method was IABP in seven studies (22, 23, 25–29), mAFP in three studies (13, 24, 32), transseptal left atrial cannulation in two studies (30, 31), and either IABP or mAFP in one study (11). The comparison was early routine unloading versus conventional (on-demand) unloading in two RCTs (30, 31). Table 1 summarizes the characteristics of the included studies.

The RoB 2 assessment deemed one RCT as low risk of bias (30) and the other study as having some concerns (31). The ROBINS-I assessment deemed ten propensity score-matched studies as low risk of bias (11, 13, 22–27, 29, 32) and the remaining one as moderate risk of bias (28) The complete risk of bias assessments are illustrated in Table S2.

Primary outcome

Mortality at the longest follow-up was reported by all 13 studies while eight reported mortality at hospital discharge (11, 22–24, 27, 30–32), four reported mortality at 30 days (13, 26, 28, 29), and one at ICU discharge (25) (Table 1). Mortality at the longest follow-up available was significantly reduced with mechanical LV unloading (13 studies; 2783/4852

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[57%] vs. 3137/5006 [63%]; RR, 0.89; 95% CI, 0.84 to 0.94; P = 0.0001; moderate certainty of evidence) (Table 2, Figure 2, and Table S3). No significant publication bias was detected on the funnel plot (Figure S1) and Egger's test (t = -1.14, df = 12, P = 0.28). Mortality reduction was confirmed in the subgroups of IABP, either IABP or mAFP, cardiogenic shock, ECPR, and low risk of bias studies (Table 2, Figure 2, and Figure S2–3). TSA showed a lack of the evidence from RCTs only (Figure S4).

Secondary outcomes

Successful weaning from VA-ECMO was significantly increased with mechanical LV unloading (7 studies; 631/873 [72%] vs. 615/1027 [60%]; RR, 1.15; 95% CI, 1.02 to 1.29; P = 0.03; low certainty of evidence) (Table 2 and Figure 3). On the other hand, major hemorrhage and hemolysis were more frequently observed in the mechanical LV unloading group (RR, 1.27 [95% CI, 1.02 to 1.59]; P = 0.03 and RR, 1.49 [95% CI, 1.10 to 2.02]; P = 0.01, respectively) (Table 2 and Figure S5–6). Other secondary outcomes were not significantly different between the two groups (Table 2 and Figure S7–10), except for an increase in favorable neurological outcome in the unloading group (2 studies; 71/455 [16%] vs. 29/455 [6.4%]; RR, 2.45; 95% CI, 1.62 to 3.69; P < 0.0001; low certainty of evidence) (Table 2 and Figure S11). Favorable neurological outcome was only reported in two propensity score-matched studies, while none of the RCTs addressed this outcome. GRADE assessment is shown in Table S3.

Discussion

Key findings

The present systematic review and meta-analysis identified two RCTs and eleven propensity score-matched studies that evaluated the effects of mechanical LV unloading on clinically

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relevant outcomes among patients with cardiogenic shock treated with VA-ECMO. Pooled results showed that mechanical LV unloading was associated with reduced mortality and increased successful weaning from VA-ECMO, although hemorrhagic events and hemolysis were increased.

Relationship with previous literature

Our meta-analysis describes a reduction of mortality in patients receiving mechanical LV unloading, in line with a previously study (10). While the previous meta-analysis included studies up to 2018 and used unmatched data from eligible studies, the present study updated the literature search and focused on RCTs and propensity score-matched studies only, which added recent evidence and precision to the pooled treatment effects. The mortality reduction in the overall analysis translated into favorable neurological outcome in two ECPR studies (29, 32). Furthermore, we found an increased rate of successful weaning from VA-ECMO in patients receiving unloading, thus supporting the favorable effects of the technique on a hemodynamic profile and implying a beneficial effect on native heart recovery.

Recent RCTs investigating mechanical circulatory support have reported mixed results regarding mortality, yet they consistently report increased incidences of vascular complications (i.e., major bleeding and limb ischemia). While several trials failed to improve mortality with VA-ECMO (33–36), another RCT examining mAFP showed reduced mortality (12). On the other hand, elevated risks of bleeding and limb ischemia were found across these studies (12, 35, 36). Our meta-analysis aligns with one study (12) regarding mortality reduction and several studies concerning the risk of complications (12, 35, 36). The two RCTs included in our meta-analysis evaluated the efficacy of early transseptal left atrial

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cannulation in patients with cardiogenic shock, rather than assessing the impact of additional mechanical circulatory support (30, 31).

Based on the subgroup analyses comparing different unloading strategies, IABP was associated with a reduced mortality risk, whereas mAFP did not show such association. These results align with previous findings (10). A large propensity score-matched study showed that mAFP, when compared to IABP, was associated with an increased risk of hospital mortality and major bleeding among patients with infarct-related cardiogenic shock (37). Although mAFP may have more powerful LV unloading effects than IABP (38), the high risks of hemolysis and bleeding complications might explain the observed heterogeneity in treatment effects between different unloading strategies. Furthermore, a recent network meta-analysis evaluating various mechanical circulatory supports for cardiogenic shock also found that, compared to conventional pharmacological management without mechanical support, only a combination of VA-ECMO and IABP, and not VA-ECMO with mAFP, was associated with reduced mortality (39). Nonetheless, the sample size of the mAFP subgroup was small. Moreover, one study presented combined data for patients using IABP or mAFP as an unloading strategy (11), preventing its inclusion in the subgroup analysis of each device.

In contrast to the findings of Russo et al. (10), the present meta-analysis observed a significantly increased risk of major bleeding in the unloading group. These differences in bleeding between the two groups likely result from the necessity of an additional large-bore arterial cannulation. It is worth mentioning that the present meta-analysis also includes a substantially large proportion of patients receiving a mAFP. In fact, while Russo et al. described the use of a mAFP only in 5.5% of patients receiving unloading, our meta-analysis

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included a substantially higher proportion (> 10%) of patients receiving mAFP. This is possibly due to the growing use of mAFP in the setting of cardiogenic shock worldwide, thanks to its minimally invasive nature, the broadening scope of its clinical indications, the accumulation of promising evidence, and continuous technological advancements (40, 41). However, the vascular access required for mAFP positioning is substantially larger than that of IABP (14 Fr vs. 8 Fr) and may partially explain the increased rate of bleeding in the unloading group. Coagulation derangements may also play a key role when dealing with bleeding during mechanical circulatory support. While profound cardiogenic shock may cause severe coagulopathy on its own, a number of patient-machine interactions may contribute (42). Hemodilution from the priming of the ECMO machine, reaction of the blood with extracorporeal circuits and acquired von Willebrand disease due to the pump shear stress (43) may all contribute to cause profound coagulopathy. The optimal anticoagulation therapy for mitigating the risks of both bleeding and thrombotic events in this critical population remains uncertain. Anticoagulation management was mentioned in only one of the included studies, with patients in the unloading and control groups receiving the same protocol management (24). Historically, these patients receive heparin anticoagulation. Novel interventions (e.g., factor XII/XI inhibition) and bivalirudin—a direct thrombin inhibitor—have been investigated (44, 45). Moreover, patients with acute myocardial infarction often require percutaneous coronary intervention and dual antiplatelet therapy, which may increase bleeding risks (46). Preliminary experiences reporting a beneficial effect of cangrelor and bivalirudin are encouraging (47). However, no RCT is available for these new agents in this setting.

Hemolysis is an interesting related issue. In fact, our meta-analysis observed an increased risk of hemolysis when adding a second pump, although much lower than previous reports by

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Russo et al. (10). In fact, the impact—especially of mAFP—on the occurrence of hemolysis is well-known and non-negligible (48). A recent RCT found that adding a mAFP increased the risk of hemolysis in patients with cardiogenic shock (12). Clinical diagnosis of hemolysis during mechanical support requires constant monitoring of urine color and lab examinations (plasma-free hemoglobin and lactate dehydrogenase), while optimization requires frequent check of pump position and reduction of speed whenever possible. Although hemolysis may worsen kidney function, our meta-analysis did not observe a higher rate of renal replacement therapy in the unloading group. The topic of prevention of acute kidney injury in these patients remains of paramount importance and new interventions have recently showed promising results (49, 50).

Implications for clinical practice and future research

From a clinical practice perspective, the significant association between the use of mechanical LV unloading and reduced mortality is promising for cardiogenic shock patients, given their devastating prognosis despite the improved care (51). Moreover, the positive impact on favorable neurological outcome after cardiac arrest implies that implementing unloading devices may protect cerebral and physical function. However, our results do not immediately translate into routine practice because most of the included studies were not RCTs.

In contrast to the previous meta-analysis (10), our meta-analysis indicated the increased incidence of major bleeding and hemolysis with mechanical LV unloading. These findings highlight the necessity for increased awareness of these complications when implementing additional mechanical support. Moreover, mechanical LV unloading may require additional human resources and economic costs. When considering candidates for adding mechanical

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LV unloading to VA-ECMO, these risks need to be balanced with potential survival benefits. Given the association of major bleeding and hemolysis with increased mortality (52, 53), patients with a low risk of such vascular complications might represent a target population.

Our meta-analysis suggests that adding mechanical LV unloading to VA-ECMO deserves further investigation, given that recent clinical trials failed to show a reduction in mortality for standalone VA-ECMO in cardiogenic shock (54). Research priorities should include establishing initiation criteria, selecting the appropriate modality, and determining the optimal timing for insertion (9). Of note, several ongoing clinical trials aim to assess the efficacy of adding mechanical unloading device to VA-ECMO in patients with cardiogenic shock (55, 56). The findings of our meta-analysis provide clinical rationale and fundamental information for designing future RCTs. As shown in the TSA, future RCTs are necessary to draw a definitive conclusion as to whether mechanical LV unloading carries survival advantages. Moreover, studies focusing on cardiac structure and function are necessary to identify which subgroups among heterogenous cardiogenic shock patients are most likely to benefit from mechanical LV unloading. Given the considerable risk of major bleeding, the optimal anticoagulation therapy should be investigated for this specific setting.

Strengths and limitations

The strengths of our meta-analysis include a pre-registered protocol, an updated comprehensive literature search, exclusive evaluation of RCTs and propensity score-matched studies, and various sensitivity analyses confirming the main analyses. Since literature on this research topic included only observational studies till recently, the identified studies and pooled data were inevitably prone to several biases (10). In contrast, our meta-analysis exclusively selected RCTs or propensity score-matched studies, improving the certainty of

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the aggregated evidence. Moreover, assessment of favorable neurological outcome added new perspectives to the potential benefits of mechanical unloading.

Our meta-analysis has limitations. First, most of the included studies were observational studies. Although we exclusively selected propensity score-matched studies to ensure the quality of the studies, such studies are not immune to unknown or unmeasured confounding factors. In studies where mechanical LV unloading was initiated after VA-ECMO, an immortal time bias might also be a concern. Second, since our meta-analysis focused on the effectiveness of adding mechanical LV unloading compared to VA-ECMO alone, no conclusion can be drawn regarding superiority among different unloading modalities. Third, structural and functional cardiac abnormalities are crucial information for hemodynamic management. However, due to the nature of study-level meta-analyses, such information was not available in most of the included studies and therefore could not be incorporated into our meta-analysis. Fourth, since our meta-analysis focused on patients undergoing VA-ECMO for cardiogenic shock, our results do not inform the efficacy or safety of mechanical unloading in other populations. Fifth, the primary outcome, mortality at the longest follow-up, was assessed at different timepoints in included studies. However, pooling mortality data from different timepoints in a meta-analysis did not seem to affect the aggregated effect estimates but could improve the precision of analysis (57).

Conclusions

Among patients with cardiogenic shock managed with VA-ECMO, the addition of mechanical LV unloading was associated with better survival, although major bleeding and hemolysis were more frequent. Such mortality reduction was confirmed in studies using IABP as an unloading device. Given that our findings were mostly driven by propensity

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score-matched studies, the efficacy of mechanical LV unloading needs to be confirmed by adequately powered RCTs.

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List of abbreviations

CI: confidence interval; IABP, intraaortic balloon pumping; LV: left ventricular; mAFP, microaxial flow pump; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT: randomized controlled trial; RR: risk ratio; TSA: trial sequential analysis; VA-ECMO: venoarterial extracorporeal membrane oxygenation

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

We collected the summary data from published manuscripts. The published article and its supplementary files include all the data generated or analyzed for this study. Further information is available from the corresponding authors upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YK, TYam, TKo, TYag, YN, MT, TKa, PN, GL, and YH conceived the study. YK and PN designed the search strategy. YK, TYam, TKo, TYag, YN, and PN did the literature search. YK, TYam, TKo, TYag, and YN did the statistical analysis. YK, PN, and GL wrote the initial protocol. All authors shared the study data, gave a critical appraisal of the protocol, provided crucial revisions, and approved the final manuscript.

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References

1. Berg DD, Bohula EA, van Diepen S, Katz JN, Alviar CL, Baird-Zars VM, Barnett CF, Barsness GW, Burke JA, Cremer PC, Cruz J, Daniels LB, DeFilippis AP, Haleem A, Hollenberg SM, Horowitz JM, Keller N, Kontos MC, Lawler PR, Menon V, Metkus TS, Ng J, Orgel R, Overgaard CB, Park J-G, Phreaner N, Roswell RO, Schulman SP, Jeffrey Snell R, Solomon MA, Ternus B, Tymchak W, Vikram F, Morrow DA: Epidemiology of Shock in Contemporary Cardiac Intensive Care Units. *Circ Cardiovasc Qual Outcomes* 12(3):e005618, 2019.
2. Becher PM, Schrage B, Sinning CR, Schmack B, Fluschnik N, Schwarzl M, Waldeyer C, Lindner D, Seiffert M, Neumann JT, Bernhardt AM, Zeymer U, Thiele H, Reichenspurner H, Blankenberg S, Twerenbold R, Westermann D: Venoarterial Extracorporeal Membrane Oxygenation for Cardiopulmonary Support. *Circulation* 138(20):2298–2300, 2018.
3. Lorusso R, Shekar K, MacLaren G, Schmidt M, Pellegrino V, Meyns B, Haft J, Vercaemst L, Pappalardo F, Bermudez C, Belohlavek J, Hou X, Boeken U, Castillo R, Donker DW, Abrams D, Ranucci M, Hryniewicz K, Chavez I, Chen Y-S, Salazar L, Whitman G: ELSO Interim Guidelines for Venoarterial Extracorporeal Membrane Oxygenation in Adult Cardiac Patients. *ASAIO J* 67(8):827–844, 2021.
4. Rajsic S, Treml B, Jadzic D, Breitkopf R, Oberleitner C, Popovic Krneta M, Bukumiric Z: Extracorporeal membrane oxygenation for cardiogenic shock: a meta-analysis of mortality and complications. *Ann Intensive Care* 12(1):93, 2022.
5. Cevasco M, Takayama H, Ando M, Garan AR, Naka Y, Takeda K: Left ventricular distension and venting strategies for patients on venoarterial extracorporeal membrane oxygenation. *J Thorac Dis* 11(4):1676–1683, 2019.

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6. Truby LK, Takeda K, Mauro C, Yuzefpolskaya M, Garan AR, Kirtane AJ, Topkara VK, Abrams D, Brodie D, Colombo PC, Naka Y, Takayama H: Incidence and Implications of Left Ventricular Distention During Venoarterial Extracorporeal Membrane Oxygenation Support. *ASAIO J* 63(3):257, 2017.
7. Combes A, Price S, Slutsky AS, Brodie D: Temporary circulatory support for cardiogenic shock. *Lancet* 396(10245):199–212, 2020.
8. Rao P, Khalpey Z, Smith R, Burkhoff D, Kociol RD: Venoarterial Extracorporeal Membrane Oxygenation for Cardiogenic Shock and Cardiac Arrest. *Circ Heart Fail* 11(9):e004905, 2018.
9. Ezad SM, Ryan M, Donker DW, Pappalardo F, Barrett N, Camporota L, Price S, Kapur NK, Perera D: Unloading the Left Ventricle in Venoarterial ECMO: In Whom, When, and How? *Circulation* 147(16):1237–1250, 2023.
10. Russo JJ, Aleksova N, Pitcher I, Couture E, Parlow S, Faraz M, Visintini S, Simard T, Di Santo P, Mathew R, So DY, Takeda K, Garan AR, Karmpaliotis D, Takayama H, Kirtane AJ, Hibbert B: Left Ventricular Unloading During Extracorporeal Membrane Oxygenation in Patients With Cardiogenic Shock. *J Am Coll Cardiol* 73(6):654‑662, 2019.
11. Grandin EW, Nunez JI, Willar B, Kennedy K, Rycus P, Tonna JE, Kapur NK, Shaefi S, Garan AR: Mechanical Left Ventricular Unloading in Patients Undergoing Venoarterial Extracorporeal Membrane Oxygenation. *J Am Coll Cardiol* 79(13):1239–1250, 2022.
12. Møller JE, Engstrøm T, Jensen LO, Eiskjær H, Mangner N, Polzin A, Schulze PC, Skurk C, Nordbeck P, Clemmensen P, Panoulas V, Zimmer S, Schäfer A, Werner N, Frydland M, Holmvang L, Kjærgaard J, Sørensen R, Lønborg J, Lindholm MG, Udesen NLJ, Junker A, Schmidt H, Terkelsen CJ, Christensen S, Christiansen EH, Linke A, Woitek FJ, Westenfeld R, Möbius-Winkler S, Wachtell K, Ravn HB, Lassen JF,

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Boesgaard S, Gerke O, Hassager C: Microaxial flow pump or standard care in infarct-related cardiogenic shock. *N Engl J Med*, 2024.

13. Schrage B, Becher PM, Bernhardt A, Bezerra H, Blankenberg S, Brunner S, Colson P, Cudemus Deseda G, Dabboura S, Eckner D, Eden M, Eitel I, Frank D, Frey N, Funamoto M, Goßling A, Graf T, Hagl C, Kirchhof P, Kupka D, Landmesser U, Lipinski J, Lopes M, Majunke N, Maniuc O, McGrath D, Möbius-Winkler S, Morrow DA, Mourad M, Noel C, Nordbeck P, Orban M, Pappalardo F, Patel SM, Pauschinger M, Pazzanese V, Reichenspurner H, Sandri M, Schulze PC, H G Schwinger R, Sinning J-M, Aksoy A, Skurk C, Szczanowicz L, Thiele H, Tietz F, Varshney A, Wechsler L, Westermann D: Left Ventricular Unloading Is Associated With Lower Mortality in Patients With Cardiogenic Shock Treated With Venoarterial Extracorporeal Membrane Oxygenation: Results From an International, Multicenter Cohort Study. *Circulation* 142(22):2095–2106, 2020.
14. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372:n71, 2021.
15. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT: RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 366:l4898, 2019.
16. Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan A-W, Churchill R, Deeks JJ,

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Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JPT: ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 355:i4919, 2016.

17. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ: GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 336(7650):924–926, 2008.
18. McMaster University (developed by Evidence Prime): *GRADEpro GDT 2015*.
19. Suverein MM, Delnoij TSR, Lorusso R, Brandon Bravo Bruinsma GJ, Otterspoor L, Elzo Kraemer CV, Vlaar APJ, van der Heijden JJ, Scholten E, den Uil C, Jansen T, van den Bogaard B, Kuijpers M, Lam KY, Montero Cabezas JM, Driessen AHG, Rittersma SZH, Heijnen BG, Dos Reis Miranda D, Bleeker G, de Metz J, Hermanides RS, Lopez Matta J, Eberl S, Donker DW, van Thiel RJ, Akin S, van Meer O, Henriques J, Bokhoven KC, Mandigers L, Bunge JJH, Bol ME, Winkens B, Essers B, Weerwind PW, Maessen JG, van de Poll MCG: Early extracorporeal CPR for refractory out-of-hospital cardiac arrest. *N Engl J Med* 388(4):299–309, 2023.
20. The Cochrane Collaboration: *Review Manager (RevMan) version 5.4*. 2020.
21. Brok J, Thorlund K, Gluud C, Wetterslev J: Trial sequential analysis reveals insufficient information size and potentially false positive results in many meta-analyses. *J Clin Epidemiol* 61(8):763–769, 2008.
22. Ro SK, Kim JB, Jung SH, Choo SJ, Chung CH, Lee JW: Extracorporeal life support for cardiogenic shock: influence of concomitant intra-aortic balloon counterpulsation. *Eur J Cardiothorac Surg* 46(2):186–92; discussion 192, 2014.

Copyright © 2024 by the Shock Society. Unauthorized reproduction of this article is prohibited.

23. Aso S, Matsui H, Fushimi K, Yasunaga H: The effect of intraaortic balloon pumping under venoarterial extracorporeal membrane oxygenation on mortality of cardiogenic patients: An analysis using a nationwide inpatient database. *Crit Care Med* 44(11):1974–1979, 2016.

24. Pappalardo F, Schulte C, Pieri M, Schrage B, Contri R, Soeffker G, Greco T, Lembo R, Müllerleile K, Colombo A, Sydow K, De Bonis M, Wagner F, Reichenspurner H, Blankenberg S, Zangrillo A, Westermann D: Concomitant implantation of Impella® on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock. *Eur J Heart Fail* 19(3):404–412, 2017.

25. Bréchot N, Demondion P, Santi F, Lebreton G, Pham T, Dalakidis A, Gambotti L, Luyt C-E, Schmidt M, Hekimian G, Cluzel P, Chastre J, Leprince P, Combes A: Intra-aortic balloon pump protects against hydrostatic pulmonary oedema during peripheral venoarterial-extracorporeal membrane oxygenation. *Eur Heart J Acute Cardiovasc Care* 7(1):62–69, 2018.

26. Kuroki N, Nagao K, Otsuka T, Kuwabara M, Nakata J, Takayama T, Hosokawa Y, Ashida T, Suzuki K, Yamamoto T, Takayama M: Combined use of venoarterial extracorporeal membrane oxygenation and intra-aortic balloon pump after cardiac arrest. *Resuscitation* 167:345–354, 2021.

27. Björnsdóttir B, Biancari F, Dalén M, Dell'Aquila AM, Jónsson K, Fiore A, Mariscalco G, El-Dean Z, Gatti G, Zipfel S, Perrotti A, Bounader K, Alkhamees K, Loforte A, Lechiancole A, Pol M, Spadaccio C, Pettinari M, De Keyzer D, Welp H, Speziale G, Lichtenberg A, Ruggieri VG, Yusuf H, Ragnarsson S: Postcardiotomy Venoarterial Extracorporeal Membrane Oxygenation With and Without Intra-Aortic Balloon Pump. *J Cardiothorac Vasc Anesth* 36(8 Pt B):2876–2883, 2022.

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28. Radakovic D, Penov K, Hamouda K, Madrahimov N, Radakovic D, Bening C, Leyh RG, Aleksic I: Benefits of Intra-Aortic Balloon Pump Support in Patients with Postcardiotomy Shock Requiring Venoarterial Extracorporeal Membrane Oxygenation. *Life* 12(8), 2022.

29. Kashiura M, Kishihara Y, Ozawa H, Amagasa S, Yasuda H, Moriya T: Intra-aortic balloon pump use in out-of-hospital cardiac arrest patients who underwent extracorporeal cardiopulmonary resuscitation. *Resuscitation* 182:109660, 2023.

30. Kim MC, Lim Y, Lee SH, Shin Y, Ahn JH, Hyun DY, Cho KH, Sim DS, Hong YJ, Kim JH, Jeong MH, Jung YH, Jeong I-S, Ahn Y: Early Left Ventricular Unloading or Conventional Approach After Venoarterial Extracorporeal Membrane Oxygenation: The EARLY-UNLOAD Randomized Clinical Trial. *Circulation* 148(20):1570–1581, 2023.

31. Park H, Yang JH, Ahn J-M, Kang D-Y, Lee PH, Kim TO, Choi KH, Kang PJ, Jung S-H, Yun S-C, Park D-W, Lee S-W, Park S-J, Kim M-S: Early left atrial venting versus conventional treatment for left ventricular decompression during venoarterial extracorporeal membrane oxygenation support: The EVOLVE-ECMO randomized clinical trial. *Eur J Heart Fail* 25(11):2037–2046, 2023.

32. Thevathasan T, Kenny MA, Krause FJ, Paul J, Wurster T, Boie SD, Friebel J, Knie W, Girke G, Haghikia A, Reinthaler M, Rauch-Kröhnert U, Leistner DM, Sinning D, Fröhlich G, Heidecker B, Spillmann F, Praeger D, Pieske B, Stangl K, Landmesser U, Balzer F, Skurk C: Left-ventricular unloading in extracorporeal cardiopulmonary resuscitation due to acute myocardial infarction - A multicenter study. *Resuscitation* 186:109775, 2023.

33. Brunner S, Guenther SPW, Lackermair K, Peterss S, Orban M, Boulesteix A-L, Michel S, Hausleiter J, Massberg S, Hagl C: Extracorporeal Life Support in Cardiogenic Shock Complicating Acute Myocardial Infarction. *J Am Coll Cardiol* 73(18):2355–2357, 2019.

ACCEPTED

Copyright © 2024 by the Shock Society. Unauthorized reproduction of this article is prohibited.

34. Ostadal P, Rokyta R, Karasek J, Kruger A, Vondrakova D, Janotka M, Naar J, Smalcova J, Hubatova M, Hromadka M, Volovar S, Seyfrydova M, Jarkovsky J, Svoboda M, Linhart A, Belohlavek J, ECMO-CS Investigators: Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock: Results of the ECMO-CS Randomized Clinical Trial. *Circulation* 147(6):454–464, 2023.

35. Banning AS, Sabaté M, Orban M, Gracey J, López-Sobrino T, Massberg S, Kastrati A, Bogaerts K, Adriaenssens T, Berry C, Erglis A, Haine S, Myrmel T, Patel S, Buera I, Sionis A, Vilalta V, Yusuff H, Vrints C, Adlam D, Flather M, Gershlick AH: Venoarterial extracorporeal membrane oxygenation or standard care in patients with cardiogenic shock complicating acute myocardial infarction: the multicentre, randomised EURO SHOCK trial. *EuroIntervention* 19(6):482–492, 2023.

36. Thiele H, Zeymer U, Akin I, Behnes M, Rassaf T, Mahabadi AA, Lehmann R, Eitel I, Graf T, Seidler T, Schuster A, Skurk C, Duerschmied D, Clemmensen P, Hennersdorf M, Fichtlscherer S, Voigt I, Seyfarth M, John S, Ewen S, Linke A, Tigges E, Nordbeck P, Bruch L, Jung C, Franz J, Lauten P, Goslar T, Feistritzer H-J, Pöss J, Kirchhof E, Ouarrak T, Schneider S, Desch S, Freund A: Extracorporeal Life Support in Infarct-Related Cardiogenic Shock. *N Engl J Med* 389(14):1286–1297, 2023.

37. Dhruva SS, Ross JS, Mortazavi BJ, Hurley NC, Krumholz HM, Curtis JP, Berkowitz A, Masoudi FA, Messenger JC, Parzynski CS, Ngufor C, Girotra S, Amin AP, Shah ND, Desai NR: Association of Use of an Intravascular Microaxial Left Ventricular Assist Device vs Intra-aortic Balloon Pump With In-Hospital Mortality and Major Bleeding Among Patients With Acute Myocardial Infarction Complicated by Cardiogenic Shock. *JAMA* 323(8):734–745, 2020.

38. Seyfarth M, Sibbing D, Bauer I, Fröhlich G, Bott-Flügel L, Byrne R, Dirschinger J, Kastrati A, Schömig A: A randomized clinical trial to evaluate the safety and efficacy of

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a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. *J Am Coll Cardiol* 52(19):1584–1588, 2008.

39. Low CJW, Ling RR, Lau MPXL, Liu NSH, Tan M, Tan CS, Lim SL, Rochwerg B, Combes A, Brodie D, Shekar K, Price S, MacLaren G, Ramanathan K: Mechanical circulatory support for cardiogenic shock: a network meta-analysis of randomized controlled trials and propensity score-matched studies. *Intensive Care Med*, 2024.
40. Basir MB, Kapur NK, Patel K, Salam MA, Schreiber T, Kaki A, Hanson I, Almany S, Timmis S, Dixon S, Kolski B, Todd J, Senter S, Marso S, Lasorda D, Wilkins C, Lalonde T, Attallah A, Larkin T, Dupont A, Marshall J, Patel N, Overly T, Green M, Tehrani B, Truesdell AG, Sharma R, Akhtar Y, McRae T 3rd, O'Neill B, Finley J, Rahman A, Foster M, Askari R, Goldsweig A, Martin S, Bharadwaj A, Khuddus M, Caputo C, Korpas D, Cawich I, McAllister D, Blank N, Alraies MC, Fisher R, Khandelwal A, Alaswad K, Lemor A, Johnson T, Hacala M, O'Neill WW, National Cardiogenic Shock Initiative Investigators: Improved outcomes associated with the use of shock protocols: Updates from the National Cardiogenic Shock Initiative. *Catheter Cardiovasc Interv* 93(7):1173–1183, 2019.
41. Ikeda Y, Ako J, Toda K, Hirayama A, Kinugawa K, Kobayashi Y, Ono M, Nishimura T, Sato N, Shindo T, Takayama M, Yasukochi S, Shiose A, Sawa Y, J-PVAD Investigators: Short-term outcomes of Impella support in Japanese patients with cardiogenic shock due to acute myocardial infarction - Japanese registry for Percutaneous Ventricular Assist Device (J-PVAD). *Circ J* 87(5):588–597, 2023.
42. Masi P, Gendreau S, Moyon Q, Leguyader M, Lebreton G, Ropers J, Dangers L, Sitruk S, Bréchot N, Pineton de Chambrun M, Chommeloux J, Schmidt M, Luyt CE, Leprince P, Combes A, Frere C, Hékimian G: Bleeding complications, coagulation disorders, and

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their management in acute myocardial infarction-related cardiogenic shock rescued by veno-arterial ECMO: A retrospective cohort study. *J Crit Care* 82(154771):154771, 2024.

43. Tamura T, Horiuchi H, Obayashi Y, Fuki M, Imanaka M, Kuroda M, Nishimura S, Amano M, Sakamoto J, Tamaki Y, Enomoto S, Miyake M, Kondo H, Izumi C, Nakagawa Y: Acquired von Willebrand syndrome in patients treated with veno-arterial extracorporeal membrane oxygenation. *Cardiovasc Interv Ther* 34(4):358–363, 2019.
44. Vandenbriele C, Vanassche T, Price S: Why we need safer anticoagulant strategies for patients on short-term percutaneous mechanical circulatory support. *Intensive Care Med* 46(4):771–774, 2020.
45. Navaei A, Kostousov V, Teruya J: Is it time to switch to bivalirudin for ECMO anticoagulation? *Front Med (Lausanne)* 10:1237601, 2023.
46. Staudacher DL, Biever PM, Benk C, Ahrens I, Bode C, Wengenmayer T: Dual antiplatelet therapy (DAPT) versus no antiplatelet therapy and incidence of major bleeding in patients on venoarterial extracorporeal membrane oxygenation. *PLoS One* 11(7):e0159973, 2016.
47. Baldetti L, Nardelli P, Ajello S, Melisurgo G, Calabrò MG, Pieri M, Scandroglio AM: Anti-thrombotic therapy with cangrelor and bivalirudin in venoarterial extracorporeal membrane oxygenation patients undergoing percutaneous coronary intervention: A single-center experience. *ASAIO J* 69(7):e346–e350, 2023.
48. Van Edom CJ, Gramegna M, Baldetti L, Beneduce A, Castelein T, Dauwe D, Frederiks P, Giustino G, Jacquemin M, Janssens SP, Panoulas VF, Pöss J, Rosenberg A, Schaubroeck HAI, Schrage B, Tavazzi G, Vanassche T, Vercaemst L, Vlasselaers D, Vranckx P, Belohlavek J, Gorog DA, Huber K, Mebazaa A, Meyns B, Pappalardo F, Scandroglio AM, Stone GW, Westermann D, Chieffo A, Price S, Vandenbriele C:

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Management of bleeding and hemolysis during percutaneous microaxial flow pump support: A practical approach. *JACC Cardiovasc Interv* 16(14):1707–1720, 2023.

49. Landoni G, Monaco F, Ti LK, Baiardo Redaelli M, Bradic N, Comis M, Kotani Y, Brambillasca C, Garofalo E, Scandroglio AM, Viscido C, Paternoster G, Franco A, Porta S, Ferrod F, Calabrò MG, Pisano A, Vendramin I, Barucco G, Federici F, Severi L, Belletti A, Cortegiani A, Bruni A, Galbiati C, Covino A, Baryshnikova E, Giardina G, Venditto M, Kroeller D, Nakhnoukh C, Mantovani L, Silvetti S, Licheri M, Guarracino F, Lobreglio R, Di Prima AL, Fresilli S, Labanca R, Mucchetti M, Lembo R, Losiggio R, Bove T, Ranucci M, Fominskiy E, Longhini F, Zangrillo A, Bellomo R, PROTECTION Study Group: A Randomized Trial of Intravenous Amino Acids for Kidney Protection. *N Engl J Med*, 2024.
50. Losiggio R, Redaelli MB, Pruna A, Landoni G, Bellomo R: The renal effects of amino acids infusion. *Signa Vitae-Journal of Anesthesiology, Intensive Care Journal, Emergency Medical Journal* 20(7):1–4, 2024.
51. Laimoud M, Qureshi R: The value of clinical scores in predicting mortality of adult patients on veno-arterial extracorporeal membrane oxygenation. *Signa Vitae* 18(4):5–7, 2022.
52. Mazzeffi M, Greenwood J, Tanaka K, Menaker J, Rector R, Herr D, Kon Z, Lee J, Griffith B, Rajagopal K, Pham S: Bleeding, Transfusion, and Mortality on Extracorporeal Life Support: ECLS Working Group on Thrombosis and Hemostasis. *Ann Thorac Surg* 101(2):682–689, 2016.
53. Dufour N, Radjou A, Thuong M: Hemolysis and Plasma Free Hemoglobin During Extracorporeal Membrane Oxygenation Support: From Clinical Implications to Laboratory Details. *ASAIO J* 66(3):239–246, 2020.

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54. Zeymer U, Freund A, Hochadel M, Ostadal P, Belohlavek J, Rokyta R, Massberg S, Brunner S, Lüsebrink E, Flather M, Adlam D, Bogaerts K, Banning A, Sabaté M, Akin I, Jobs A, Schneider S, Desch S, Thiele H: Venoarterial extracorporeal membrane oxygenation in patients with infarct-related cardiogenic shock: an individual patient data meta-analysis of randomised trials. *Lancet* 402(10410):1338–1346, 2023.

55. NCT03431467. https://clinicaltrials.gov/study/NCT03431467. March 31, 2024.

56. ISRCTN82431978. https://trialsearch.who.int/Trial2.aspx?TrialID=ISRCTN82431978. January 24, 2024.

57. Roth D, Heidinger B, Havel C, Herkner H: Different Mortality Time Points in Critical Care Trials: Current Practice and Influence on Effect Estimates in Meta-Analyses. *Crit Care Med* 44(8):e737-41, 2016.

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Figure legends

Fig. 1. Flow chart of study selection

RCT, randomized controlled trial

Fig. 2. Forest plot for mortality at the longest follow-up available

ACS, acute coronary syndrome; IABP, intraaortic balloon pumping; mAFP, microaxial flow pump

Fig. 3. Forest plot for successful weaning from venoarterial extracorporeal membrane oxygenation

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Supplemental Digital Content

Search strategy for systematic literature review, PRISMA 2020 checklist, supplemental figures (Fig. S1–S11), supplemental tables (Table S1–S3), and supplemental references

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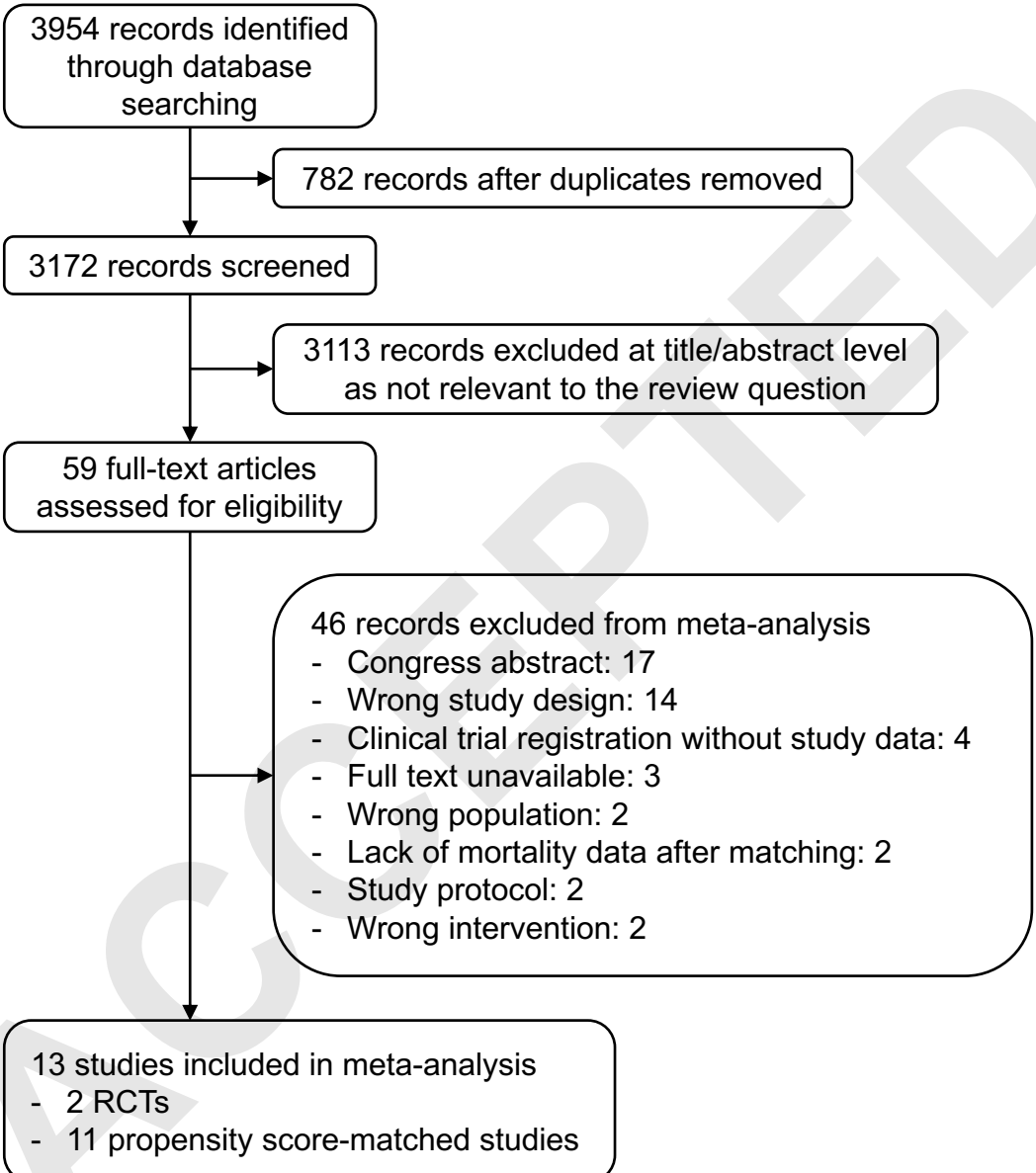

FIGURE 1

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FIGURE 2

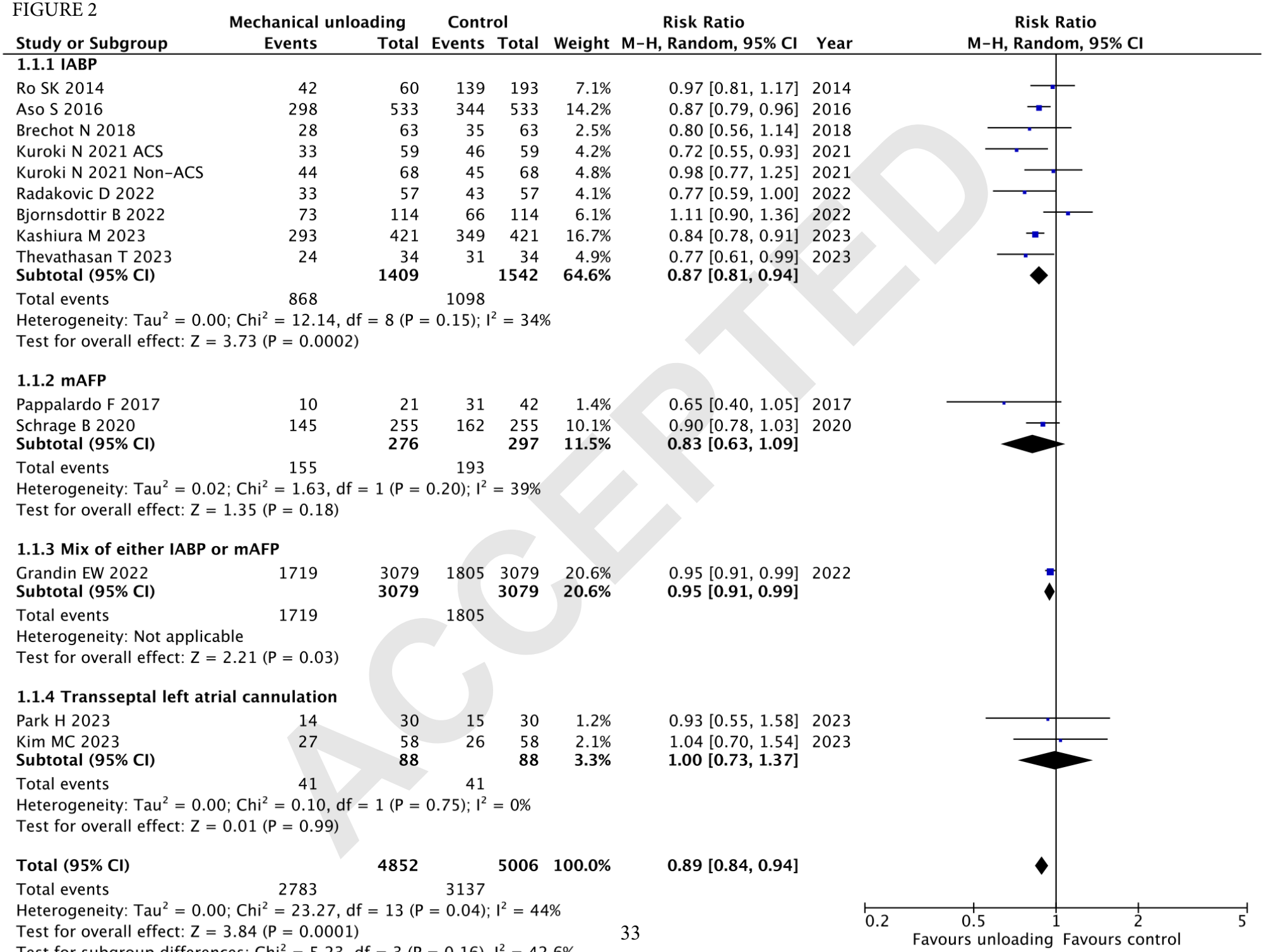

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FIGURE 3

Study or Subgroup	Mechanical unloading Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Ro SK 2014	34	60	79	193	13.0%	1.38 [1.05, 1.83]	2014
Aso S 2016	440	533	391	533	40.8%	1.13 [1.06, 1.20]	2016
Pappalardo F 2017	10	21	16	42	3.7%	1.25 [0.69, 2.26]	2017
Bjornsdottir B 2022	65	114	60	114	16.3%	1.08 [0.86, 1.37]	2022
Radakovic D 2022	29	57	15	57	4.9%	1.93 [1.17, 3.20]	2022
Kim MC 2023	32	58	31	58	9.9%	1.03 [0.74, 1.44]	2023
Park H 2023	21	30	23	30	11.3%	0.91 [0.67, 1.24]	2023
Total (95% CI)		**873**		**1027**	**100.0%**	**1.15 [1.02, 1.29]**	
Total events	631		615				

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 9.06$, df = 6 (P = 0.17); $I^2 = 34\%$

Test for overall effect: Z = 2.27 (P = 0.02)

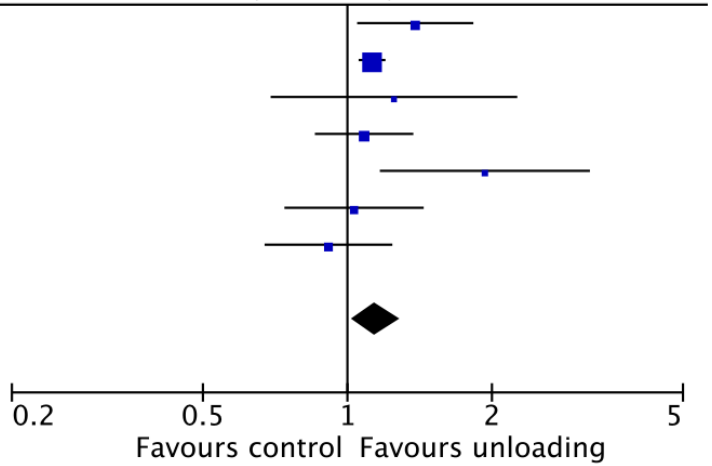

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Table 1. Characteristics of the included studies

First author, publication year	Setting	No. of patients[a]	Study design	Mechanical unloading strategy	Comparator	Timepoint of mortality assessment
Ro SK, 2014 (22)	Cardiogenic shock	253	Propensity score-matched study	IABP	ECMO alone	Hospital discharge
Aso S, 2016 (23)	Cardiogenic shock	1066	Propensity score-matched study	IABP	ECMO alone	Hospital discharge
Pappalardo F, 2017 (24)	Cardiogenic shock	63	Propensity score-matched study	Microaxial flow pump	ECMO alone	Hospital discharge
Brechot N, 2018 (25)	Cardiogenic shock	126	Propensity score-matched study	IABP	ECMO alone	ICU discharge
Schrage B, 2020 (13)	Cardiogenic shock	510	Propensity score-matched study	Microaxial flow pump	ECMO alone	30 days
Kuroki N, 2021 (26)	ECPR	254	Propensity score-matched study	IABP	ECMO alone	30 days
Björnsdóttir B, 2022 (27)	Cardiogenic shock	228	Propensity score-matched	IABP	ECMO alone	Hospital discharge

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			study			
Grandin EW, 2022 (11)	Cardiogenic shock	6158	Propensity score-matched study	IABP or microaxial flow pump	ECMO alone	Hospital discharge
Radakovic D, 2022 (28)	Cardiogenic shock	114	Propensity score-matched study	IABP	ECMO alone	30 days
Kashiura M, 2023 (29)	ECPR	842	Propensity score-matched study	IABP	ECMO alone	30 days
Kim MC, 2023 (30)	Cardiogenic shock	116	RCT	Transseptal left atrial cannulation	Conventional unloading strategy	Hospital discharge
Park H, 2023 (31)	Cardiogenic shock	60	RCT	Transseptal left atrial cannulation	Conventional unloading strategy	Hospital discharge
Thevathasan T, 2023 (32)	ECPR	68	Propensity score-matched study	Microaxial flow pump	ECMO alone	Hospital discharge

[a] For the randomized trial, we present the data according to the intention-to-treat principle. For propensity score matched studies, we present the number of patients included in the propensity score-matched analysis. In a study by Kuroki et al. (26), propensity score-matching was separately performed for patients with and without acute coronary syndrome (N = 118 and 136, respectively).

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Abbreviations: ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; IABP, intraaortic balloon; ICU, intensive care unit; RCT, randomized controlled trial

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Table 2. Effects of mechanical left ventricular unloading on the primary and secondary outcomes

Outcome	No. of studies	Mechanical LV unloading	Control	Risk ratio (95% CI)	P value	I^2
Primary outcome						
Mortality at the longest follow-up	13	2783/4852 (57%)	3137/5006 (63%)	0.89 (0.84 to 0.94)	0.0001	44%
Unloading strategy						
IABP	8	868/1409 (62%)	1098/1542 (71%)	0.87 (0.81 to 0.94)	0.0002	34%
mAFP	2	155/276 (56%)	193/297 (65%)	0.83 (0.63 to 1.09)	0.18	39%
Either IABP or mAFP	1	1719/3079 (56%)	1805/3079 (59%)	0.95 (0.91 to 0.99)	0.03	NA
Transseptal left atrial cannulation	2	41/88 (47%)	41/88 (47%)	1.00 (0.73 to 1.37)	0.99	0%
Indication of VA-ECMO						
Cardiogenic shock	10	2389/4270 (56%)	2666/4424 (60%)	0.92 (0.87 to 0.98)	0.005	21%
ECPR	3	394/582 (68%)	471/582 (81%)	0.83 (0.77 to 0.90)	<0.0001	8%
Low risk of bias studies	11	2736/4765 (57%)	3079/4919 (63%)	0.89 (0.84 to 0.95)	0.0005	49%
Secondary outcomes						
Successful VA-ECMO weaning	7	631/873 (72%)	615/1027 (60%)	1.15 (1.02 to 1.29)	0.02	34%
Major bleeding	7	747/3591 (21%)	565/3609 (16%)	1.27 (1.02 to 1.59)	0.03	70%
Hemolysis	4	235/3369 (7.0%)	176/3347 (5.3%)	1.49 (1.10 to 2.02)	0.01	53%
Renal replacement therapy	9	469/1163 (40%)	451/1184 (38%)	1.03 (0.83 to 1.27)	0.81	75%
Limb ischemia	7	362/3627 (10%)	326/3624 (9.0%)	1.20 (0.91 to 1.60)	0.20	27%
Stroke	5	170/3431 (5.0%)	156/3443 (4.5%)	1.10 (0.89 to 1.35)	0.40	0%
Bridge to heart transplant or durable VAD	5	35/286 (12%)	36/307 (12%)	1.04 (0.69 to 1.57)	0.84	0%

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Favorable neurological outcome	2	71/455 (16%)	29/455 (6.4%)	2.45 (1.62 to 3.69)	< 0.0001	0%

Abbreviations: CI, confidence interval; ECPR, extracorporeal cardiopulmonary resuscitation; IABP, intraaortic balloon pumping; LV, left ventricular; mAFP, microaxial flow pump; NA, not applicable; VAD, ventricular assist device; VA-ECMO, venoarterial extracorporeal membrane oxygenation

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Supplemental Digital Content

Mechanical left ventricular unloading in cardiogenic shock treated with venoarterial extracorporeal membrane: a systematic review and meta-analysis

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Table of contents

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Search strategy for systematic literature review

PubMed
(Propensity score [mh] OR Propensity score matching [tiab] OR Propensity score analysis [tiab] OR Propensity-matched [tiab] OR Propensity-adjusted [tiab] OR Matching score [tiab] OR Matched group [tiab] OR Matched sample [tiab] OR Matched case-control [tiab] OR Case-control matching [tiab] OR Matched-pair [tiab] OR Pair-matching [tiab] OR Pair-matched [tiab] OR Matched-Pair Analysis [mh] OR Matched Groups [mh] OR Matched Case-Control Studies [MeSH] OR score matc* [tiab] OR score-matc* [tiab] OR propensity-score [tiab] OR propensity-score [tiab] OR multivariable modeling [tiab] OR randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR clinical trial[tw] OR latin square[tw] OR random*[tw] OR research design[mh] OR follow-up studies[mh] OR prospective studies[mh] OR cross-over studies[mh] OR control*[tw] OR prospectiv*[tw] OR randomized [tiab] OR randomization [TIAB] OR randomly [tiab] OR randomised prospective study [tiab] OR random number table[tiab] OR cluster-randomized [tiab]) AND
(impella[tiab] OR axial[tiab] OR abiomed[tiab] OR percutaneous ventricular assist device[tiab] OR percutaneous left ventricular assist device[tiab] OR unloading[tiab] OR intra aortic balloon[tiab] OR intraaortic balloon[tiab] OR intra-aortic balloon pump[tiab] OR iabp[tiab] OR Counterpulsation[mh] OR counterpulsat*[tiab] OR counter pulsat*[tiab] OR transaortic catheter*[tiab] OR tacv[tiab] OR Decompression, Surgical[mh] OR Shock, Cardiogenic [mh] OR decompress*[tiab]) AND
(ECMO[tiab] OR extracorporeal life support[tiab] OR extracorporeal circulation[tiab] OR circulatory support[tiab] OR extracorporeal membrane oxygenation[tiab] OR venoarterial extracorporeal membrane oxygenation [tiab] OR Extracorporeal Membrane Oxygenation[mh] OR Extracorporeal Circulation[mh] OR ECLS[tiab])

Cochrane Library
#1 mh “Propensity score” or “propensity score”:ti,ab,kw or "propensity score matching":ti,ab,kw or "propensity score analysis":ti,ab,kw or "propensity-matched":ti,ab,kw or "propensity-adjusted":ti,ab,kw or "matching score":ti,ab,kw or "matched group":ti,ab,kw or "matched sample":ti,ab,kw or "matched case-control":ti,ab,kw or "case-control matching":ti,ab,kw or "matched-pair":ti,ab,kw or "pair-matching":ti,ab,kw or "pair-matched":ti,ab,kw or mh "matched-pair analysis" or mh "matched groups" or "matched case-control studies":ti,ab,kw or (score NEXT matc*):ti,ab,kw or (NEXT score-matc*):ti,ab,kw or "propensity-score":ti,ab,kw or "multivariable modeling":ti,ab,kw or "randomized controlled trial":ti,ab,kw or "controlled clinical trial":ti,ab,kw or mh "randomized controlled trials" or mh "random allocation" or mh "double-blind method" or mh "single-blind method" or "clinical trial":ti,ab,kw or mh "clinical trials" or "clinical trial":ti,ab,kw or "latin square":ti,ab,kw or (NEXT random*):ti,ab,kw or mh "research design" or mh "follow-up studies" or mh "prospective studies" or mh "cross-over studies" or (NEXT control*):ti,ab,kw or (NEXT prospectiv*):ti,ab,kw or "randomized":ti,ab,kw or "randomization":ti,ab,kw or "randomly":ti,ab,kw or "randomised prospective study":ti,ab,kw or "random number table":ti,ab,kw or "cluster-randomized":ti,ab,kw

#2 "impella":ti,ab,kw or "axial":ti,ab,kw or "abiomed":ti,ab,kw or "percutaneous ventricular assist device":ti,ab,kw or "percutaneous left ventricular assist device":ti,ab,kw or "unloading":ti,ab,kw or "intra aortic balloon":ti,ab,kw or "intraaortic balloon":ti,ab,kw or "intra-aortic balloon pump":ti,ab,kw or "iabp":ti,ab,kw or mh "Counterpulsation" or (NEXT

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counterpulsat*):ti,ab,kw or (counter NEXT pulsat*):ti,ab,kw or (transaortic NEXT catheter*):ti,ab,kw or "tacv":ti,ab,kw or mh "Decompression, Surgical" or mh "Shock, Cardiogenic" or (NEXT decompress*):ti,ab,kw

#3 "ECMO":ti,ab,kw or "extracorporeal life support":ti,ab,kw or "extracorporeal circulation":ti,ab,kw or "circulatory support":ti,ab,kw or "extracorporeal membrane oxygenation":ti,ab,kw or "venoarterial extracorporeal membrane oxygenation":ti,ab,kw or mh "Extracorporeal Membrane Oxygenation" or mh "Extracorporeal Circulation" or "ECLS":ti,ab,kw

#4 #1 and #2 and #3

Embase

(propensity score:de OR "propensity score matching":ti,ab,kw OR "propensity score analysis":ti,ab,kw OR "propensity-matched":ti,ab,kw OR "propensity-adjusted":ti,ab,kw OR "matching score":ti,ab,kw OR "matched group":ti,ab,kw OR "matched sample":ti,ab,kw OR "matched case-control":ti,ab,kw OR "case-control matching":ti,ab,kw OR "matched-pair":ti,ab,kw OR "pair-matching":ti,ab,kw OR "pair-matched":ti,ab,kw OR "matched-pair analysis":de OR "matched groups":de OR "matched case-control studies":de OR "score matc*":ti,ab,kw OR "score-matc*":ti,ab,kw OR "propensity-score":ti,ab,kw OR "propensity-score":ti,ab,kw OR "randomized controlled trial":it OR "controlled clinical trial":it OR "randomized controlled trials":de OR "random allocation":de OR "double-blind method":de OR "single-blind method":de OR "clinical trial":it OR "clinical trials":de OR "clinical trial":ti,ab,kw OR "latin square":ti,ab,kw OR "random*":ti,ab,kw OR "research design":de NOT "exp" OR "follow-up studies":de OR "prospective studies":de OR "cross-over studies":de OR "control*":ti,ab,kw OR "prospectiv*":ti,ab,kw OR "volunteer*":ti,ab,kw OR "randomized":ti,ab,kw OR "randomization":ti,ab,kw OR "randomly":ti,ab,kw OR "randomised prospective study":ti,ab,kw OR "post hoc analysis":ti,ab,kw OR "post hoc analyses":ti,ab,kw OR "random number table":ti,ab,kw OR "cluster-randomized":ti,ab,kw)
AND ("impella":ti,ab,kw OR "axial":ti,ab,kw OR "abiomed":ti,ab,kw OR "percutaneous ventricular assist device":ti,ab,kw OR "percutaneous left ventricular assist device":ti,ab,kw OR "unloading":ti,ab,kw OR "intra aortic balloon":ti,ab,kw OR "intraaortic balloon":ti,ab,kw OR "intra-aortic balloon pump":ti,ab,kw OR "iabp":ti,ab,kw OR "Counterpulsation":de OR “counterpulsat*”:ti,ab,kw OR “counter pulsat*”:ti,ab,kw OR “transaortic catheter*”:ti,ab,kw OR "tacv":ti,ab,kw OR "Decompression, Surgical":de OR "Shock, Cardiogenic":de OR “decompress*”:de)
AND ("ECMO":ti,ab,kw OR "extracorporeal life support":ti,ab,kw OR "extracorporeal circulation":ti,ab,kw OR "circulatory support":ti,ab,kw OR "extracorporeal membrane oxygenation":ti,ab,kw OR "venoarterial extracorporeal membrane ozygenation":ti,ab,kw OR "Extracorporeal Membrane Oxygenation":de OR "Extracorporeal Circulation":de OR "ECLS":ti,ab,kw)

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PRISMA 2020 checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4–5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplemental Material
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	7

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Section and Topic	Item #	Checklist item	Location where item is reported
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	7, Fig. 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	7
Study characteristics	17	Cite each included study and present its characteristics.	7–8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	8, Supplemental material
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	7, Table 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	8, Table 1, Additional file 1
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	8, Table 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	8, Table 2
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	8, Supplemental material
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Supplemental material
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supplemental material
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	9–10
	23b	Discuss any limitations of the evidence included in the review.	12
	23c	Discuss any limitations of the review processes used.	12
	23d	Discuss implications of the results for practice, policy, and future research.	11
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	13
Competing interests	26	Declare any competing interests of review authors.	13

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Section and Topic	Item #	Checklist item	Location where item is reported
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	13

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Fig. S1. Funnel plot for mortality at the longest follow-up available

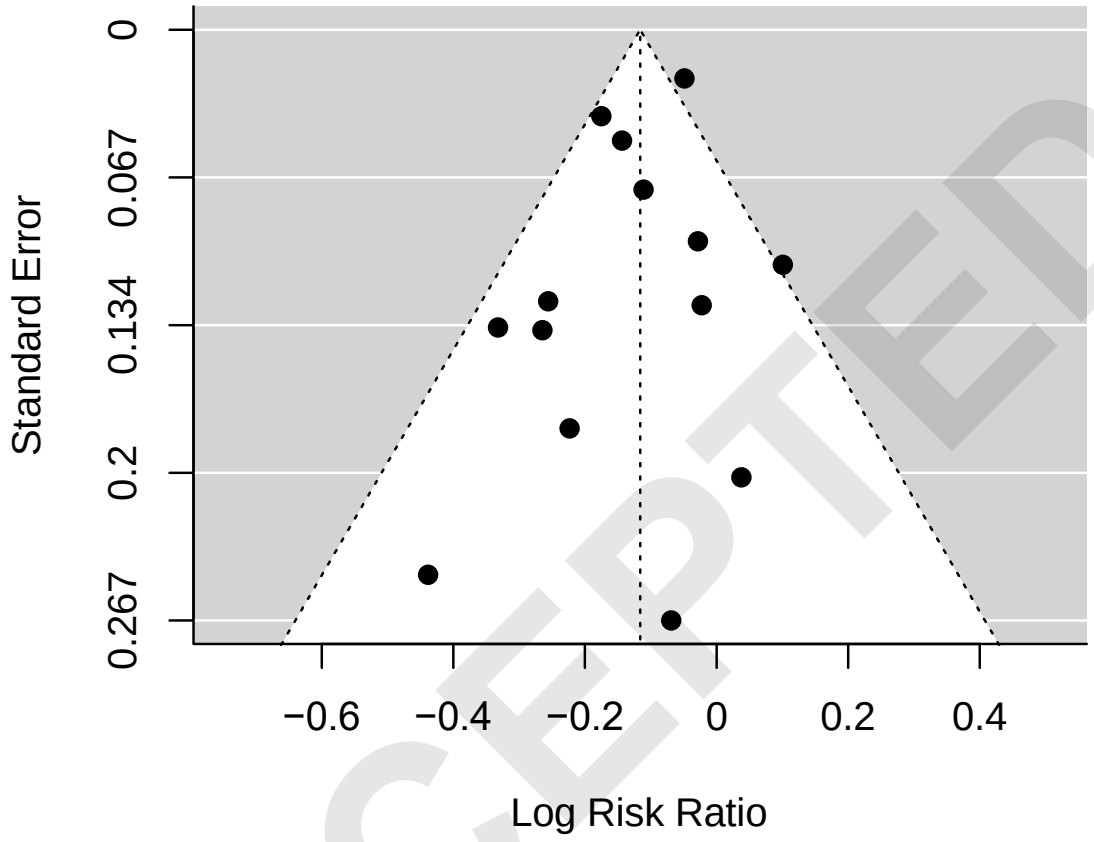

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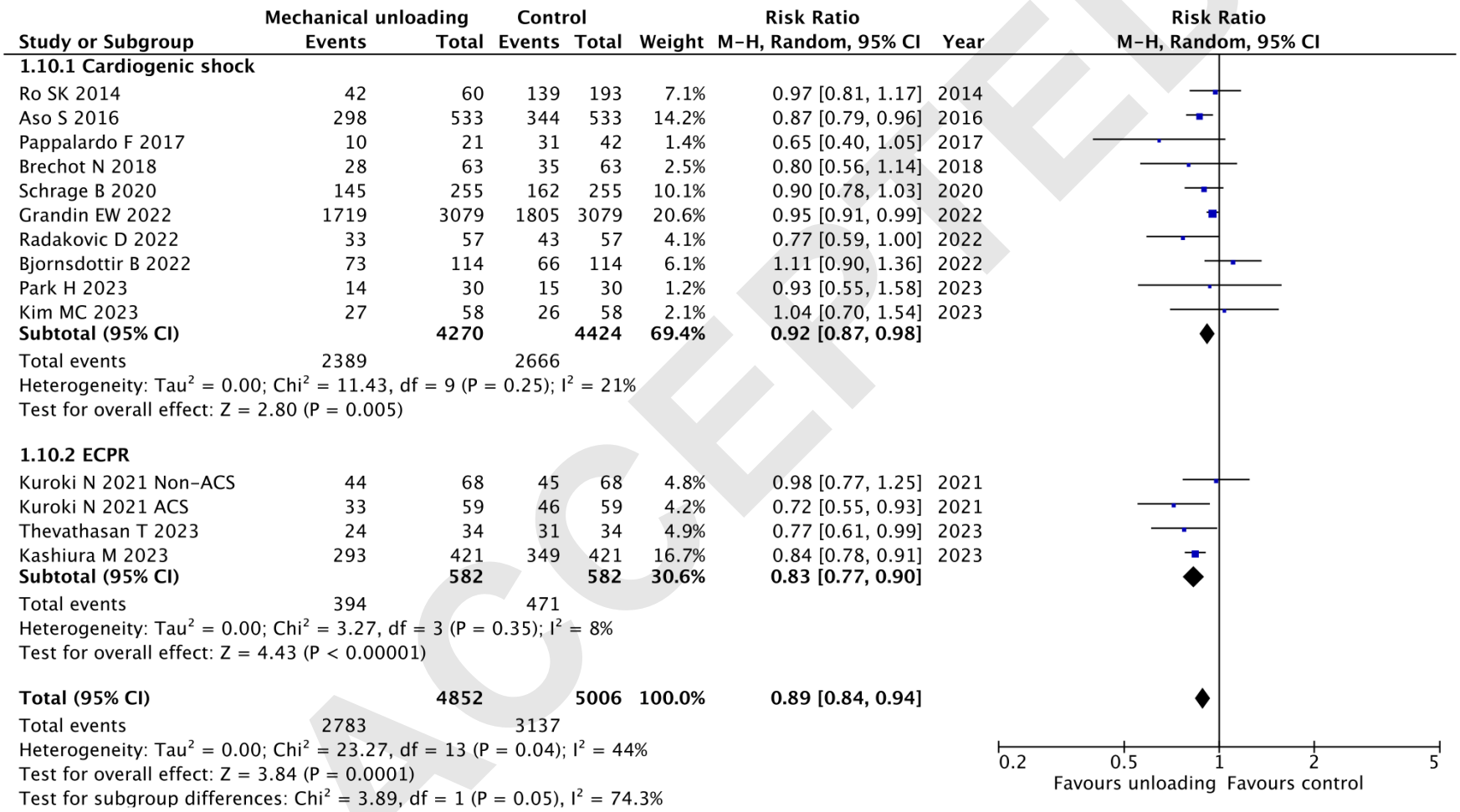
Fig. S2. Forest plot for mortality at the longest follow-up according to the indication of venoarterial extracorporeal membrane oxygenation



ACS, acute coronary syndrome; ECPR, extracorporeal cardiopulmonary resuscitation

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Fig. S3. Forest plot for mortality at the longest follow-up in studies with low risk of bias

Study or Subgroup	Mechanical unloading Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Ro SK 2014	42	60	139	193	7.6%	0.97 [0.81, 1.17]	2014
Aso S 2016	298	533	344	533	14.9%	0.87 [0.79, 0.96]	2016
Pappalardo F 2017	10	21	31	42	1.6%	0.65 [0.40, 1.05]	2017
Brechot N 2018	28	63	35	63	2.8%	0.80 [0.56, 1.14]	2018
Schrage B 2020	145	255	162	255	10.7%	0.90 [0.78, 1.03]	2020
Kuroki N 2021 ACS	33	59	46	59	4.5%	0.72 [0.55, 0.93]	2021
Kuroki N 2021 Non-ACS	44	68	45	68	5.1%	0.98 [0.77, 1.25]	2021
Bjornsdottir B 2022	73	114	66	114	6.5%	1.11 [0.90, 1.36]	2022
Grandin EW 2022	1719	3079	1805	3079	21.2%	0.95 [0.91, 0.99]	2022
Kashiura M 2023	293	421	349	421	17.5%	0.84 [0.78, 0.91]	2023
Thevathasan T 2023	24	34	31	34	5.3%	0.77 [0.61, 0.99]	2023
Kim MC 2023	27	58	26	58	2.3%	1.04 [0.70, 1.54]	2023
Total (95% CI)		**4765**		**4919**	**100.0%**	**0.89 [0.84, 0.95]**	
Total events	2736		3079				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 21.62$, df = 11 (P = 0.03); $I^2 = 49\%$

Test for overall effect: Z = 3.49 (P = 0.0005)

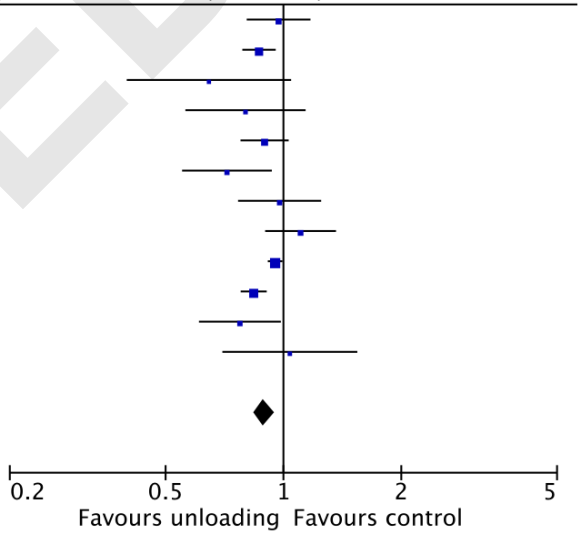

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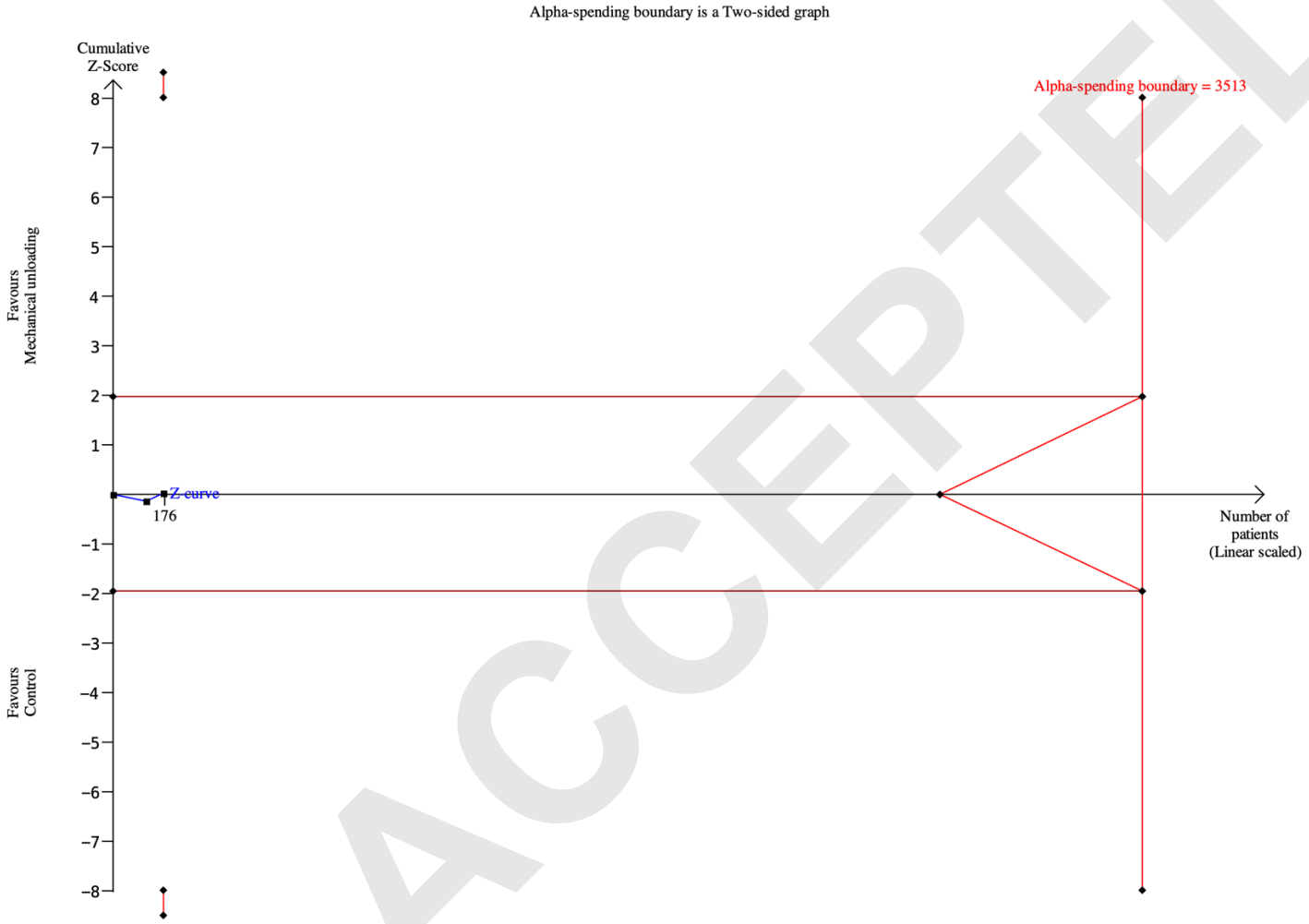
Fig. S4. Trial sequential analysis for mortality at the longest follow-up



Alpha error = 5%, power = 80%, relative risk decrease = 10%, diversity = 0%

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Fig. S5. Forest plot for major hemorrhage

Study or Subgroup	Mechanical unloading Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Pappalardo F 2017	8	21	12	42	6.9%	1.33 [0.65, 2.75]	2017
Schrage B 2020	98	255	45	252	18.0%	2.15 [1.58, 2.93]	2020
Bjornsdottir B 2022	47	114	46	114	17.8%	1.02 [0.75, 1.40]	2022
Grandin EW 2022	551	3079	420	3079	25.8%	1.31 [1.17, 1.47]	2022
Thevathasan T 2023	31	34	29	34	23.7%	1.07 [0.90, 1.27]	2023
Kim MC 2023	6	58	8	58	4.1%	0.75 [0.28, 2.03]	2023
Park H 2023	6	30	5	30	3.6%	1.20 [0.41, 3.51]	2023
Total (95% CI)		**3591**		**3609**	**100.0%**	**1.27 [1.02, 1.59]**	
Total events	747		565				

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 19.74$, df = 6 (P = 0.003); $I^2 = 70\%$

Test for overall effect: Z = 2.17 (P = 0.03)

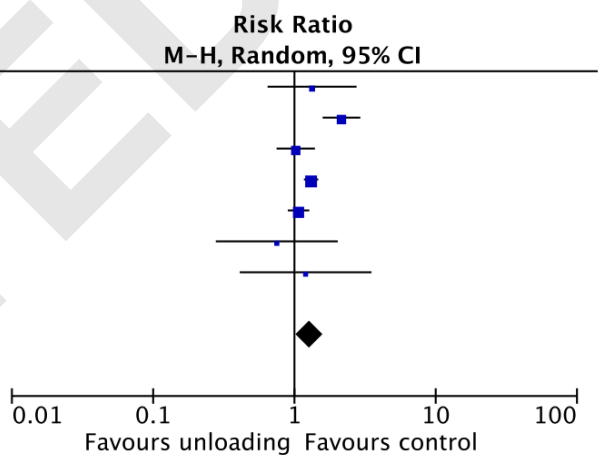

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Fig. S6. Forest plot for hemolysis

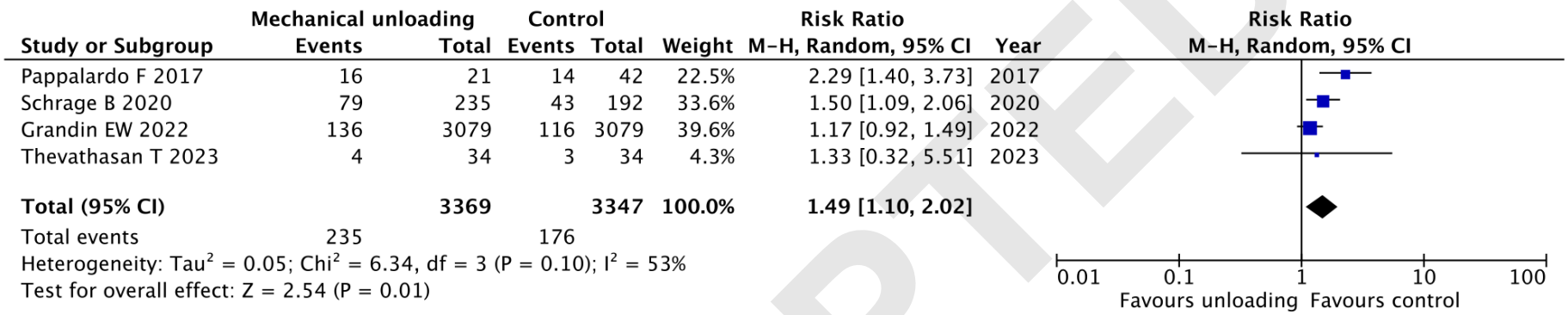

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Fig. S7. Forest plot for renal replacement therapy

Study or Subgroup	Mechanical unloading Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Aso S 2016	141	533	150	533	14.8%	0.94 [0.77, 1.14]	2016
Pappalardo F 2017	10	21	8	42	5.2%	2.50 [1.16, 5.39]	2017
Brechot N 2018	41	63	45	63	13.9%	0.91 [0.72, 1.16]	2018
Schrage B 2020	148	253	99	253	15.0%	1.49 [1.24, 1.80]	2020
Radakovic D 2022	16	57	29	57	8.9%	0.55 [0.34, 0.90]	2022
Bjornsdottir B 2022	53	114	64	114	13.6%	0.83 [0.64, 1.07]	2022
Kim MC 2023	27	58	24	58	10.3%	1.13 [0.74, 1.70]	2023
Thevathasan T 2023	14	34	14	34	7.6%	1.00 [0.57, 1.77]	2023
Park H 2023	19	30	18	30	10.6%	1.06 [0.71, 1.57]	2023
Total (95% CI)		**1163**		**1184**	**100.0%**	**1.03 [0.83, 1.27]**	
Total events	469		451				

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 31.57$, df = 8 (P = 0.0001); $I^2 = 75\%$

Test for overall effect: Z = 0.24 (P = 0.81)

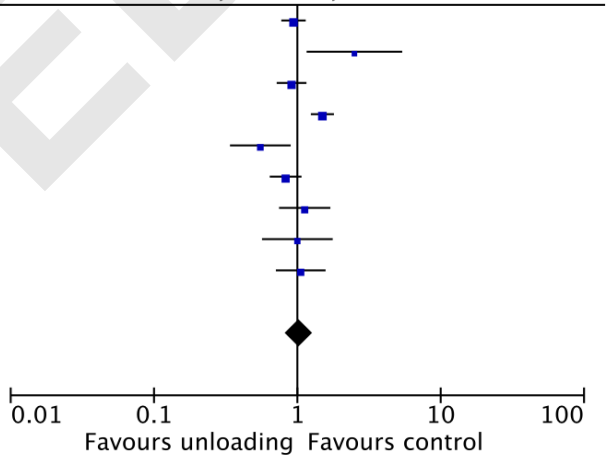

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Fig. S8. Forest plot for limb ischemia

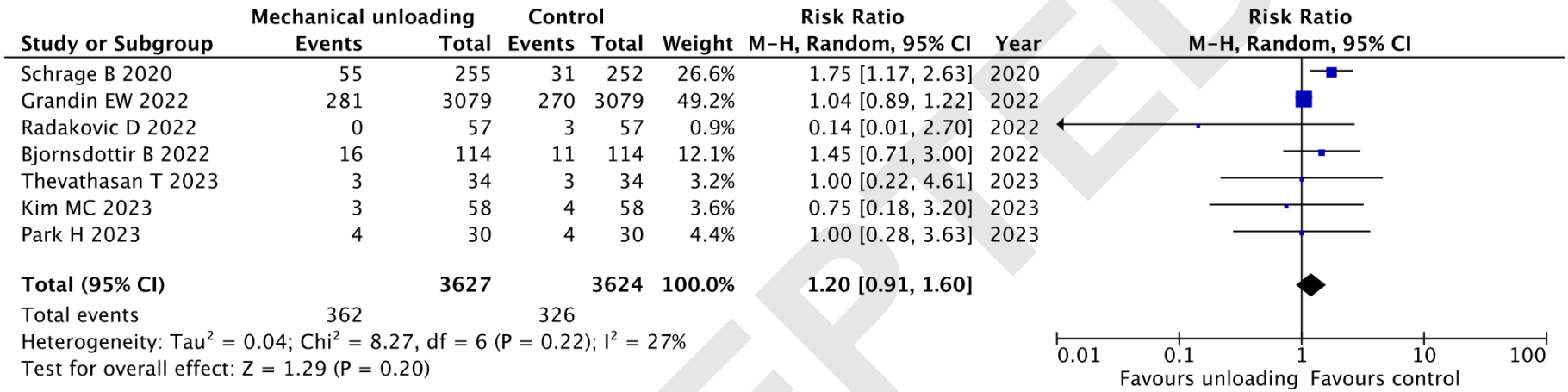

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Fig. S9. Forest plot for stroke

Study or Subgroup	Mechanical unloading Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Schrage B 2020	16	230	22	242	11.8%	0.77 [0.41, 1.42]	2020
Grandin EW 2022	137	3079	124	3079	79.9%	1.10 [0.87, 1.40]	2022
Park H 2023	8	30	4	30	3.8%	2.00 [0.67, 5.94]	2023
Thevathasan T 2023	3	34	1	34	0.9%	3.00 [0.33, 27.42]	2023
Kim MC 2023	6	58	5	58	3.5%	1.20 [0.39, 3.71]	2023
Total (95% CI)		**3431**		**3443**	**100.0%**	**1.10 [0.89, 1.35]**	
Total events	170		156				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.30$, df = 4 (P = 0.51); $I^2 = 0\%$

Test for overall effect: Z = 0.84 (P = 0.40)

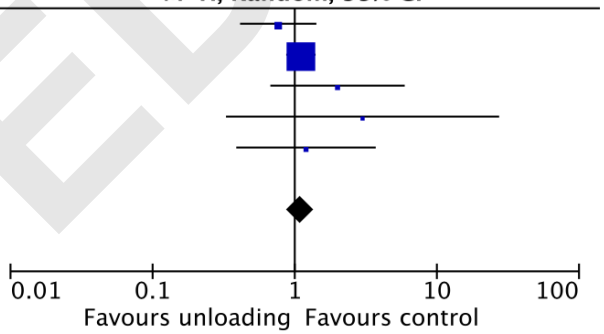

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Fig. S10 Forest plot for bridge to heart transplant or durable ventricular assist device

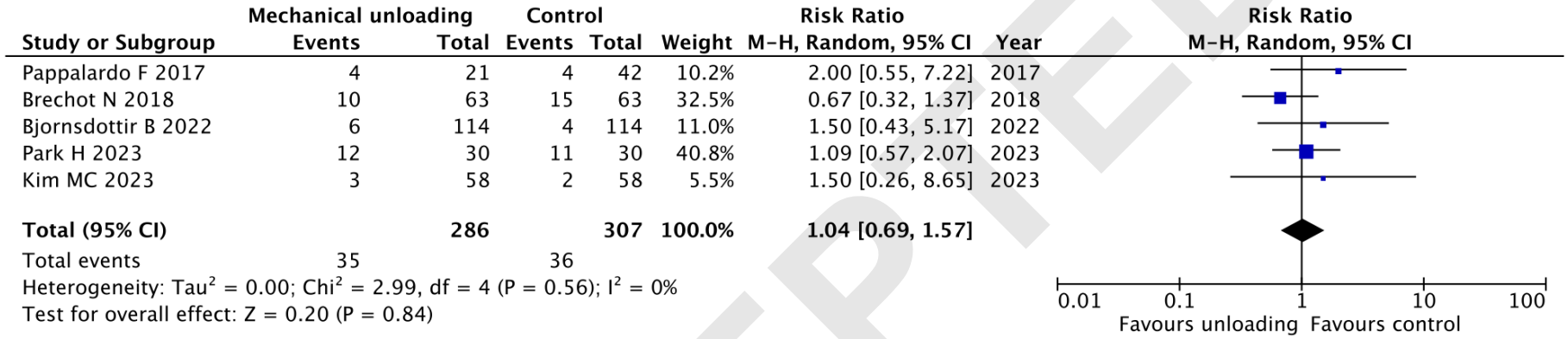

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Fig. S11 Forest plot for favorable neurological outcome

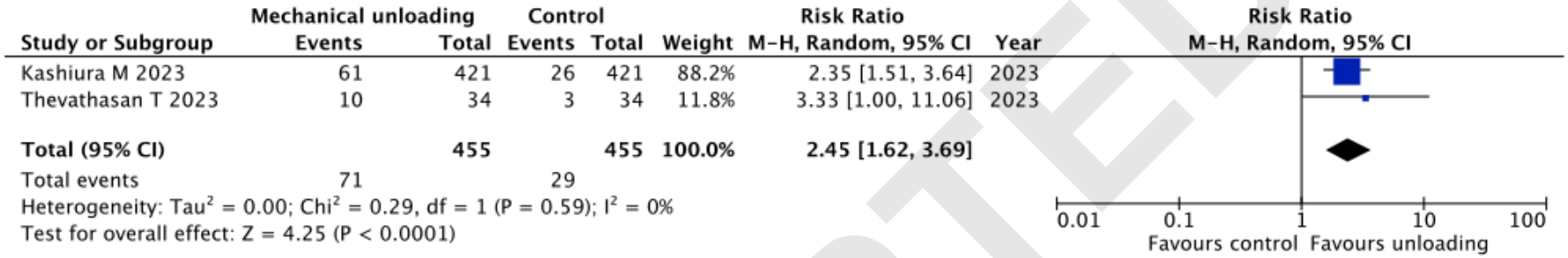

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Table S1. Major exclusions and reasons for exclusion, in order of year of publication

Author, year	Reason for exclusion
Schrage B, 2016 (1)	Congress abstract
Lee H, 2016 (2)	Congress abstract
Lin LY, 2016 (3)	Lack of mortality data after matching
Hou G, 2016 (4)	Wrong population
Ostadal P, 2017 (5)	Wrong population
Rivera M, 2017 (6)	Congress abstract
Zipfel S, 2018 (7)	Congress abstract
Kuroki N, 2018 (8)	Congress abstract
Reichenspurner H, 2018 (9)	Congress abstract
Scatola A, 2019A (10)	Congress abstract
Scatola A, 2019B (11)	Congress abstract
Singh A, 2019A (12)	Congress abstract
Zaid S, 2019 (13)	Congress abstract
Ok YJ, 2019 (14)	Wrong study design
Patel SM, 2019 (15)	Wrong study design
Singh A, 2019B (16)	Wrong study design
Tepper S, 2019 (17)	Wrong study design
Akanni O, 2019 (18)	Wrong study design
Barge-Caballero, 2019 (19)	Wrong study design
Ye FM, 2021 (20)	Full text unavailable
Thevathasan T, 2021 (21)	Congress abstract
Ibrahim M, 2021 (22)	Study protocol
Djordjevic I, 2021 (23)	Wrong study design
Kim AR, 2021 (24)	Wrong study design
Hasde Aİ, 2021 (25)	Wrong study design
Udongwo N, 2022 (26)	Congress abstract
Chen X, 2022 (27)	Full text unavailable
Hendrickson MJ, 2022 (28)	Wrong study design
Kida H, 2022 (29)	Wrong study design
Gaisendrees C, 2022 (30)	Wrong study design

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Denisenko A, 2022 (31)	Lack of mortality data after matching
Unoki T, 2022 (32)	Wrong intervention
Bogerd M, 2023 (33)	Congress abstract
Pan CL, 2023 (34)	Full text unavailable
Ginder K, 2023 (35)	Congress abstract
Girish A, 2023 (36)	Congress abstract
Kieserman J, 2023 (37)	Congress abstract
Yeo I, 2023 (38)	Congress abstract
Char S, 2023 (39)	Wrong study design
Kim MC, 2023 (40)	Study protocol
Radakovic D, 2023 (41)	Wrong intervention
Arafat AA, 2023 (42)	Wrong study design
ISRCTN82431978 (43)	Clinical trial registration without study data
NCT05577195 (44)	Clinical trial registration without study data
NCT05913622 (45)	Clinical trial registration without study data
NCT03431467 (46)	Clinical trial registration without study data

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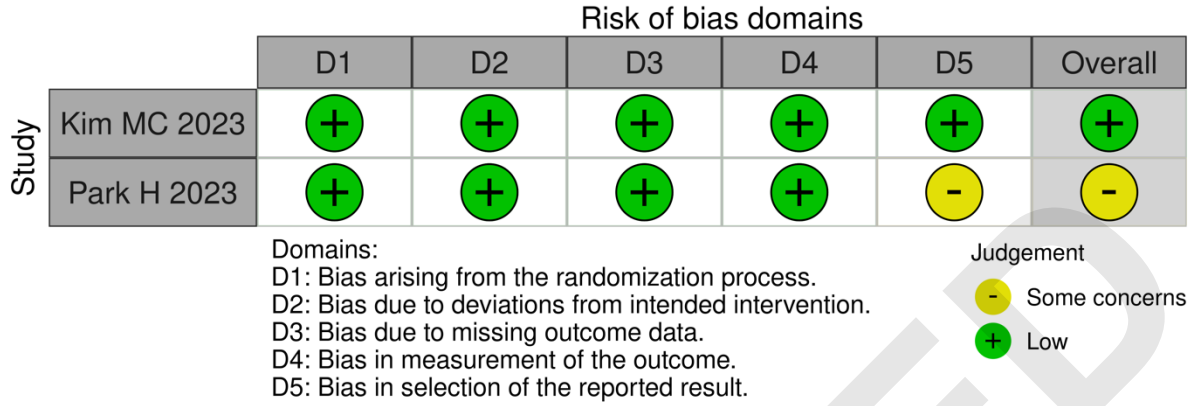
Table S2. Risk of bias assessment of included studies

ROB-2 tool for randomized controlled trials



ROBINS-I tool for non-randomized studies

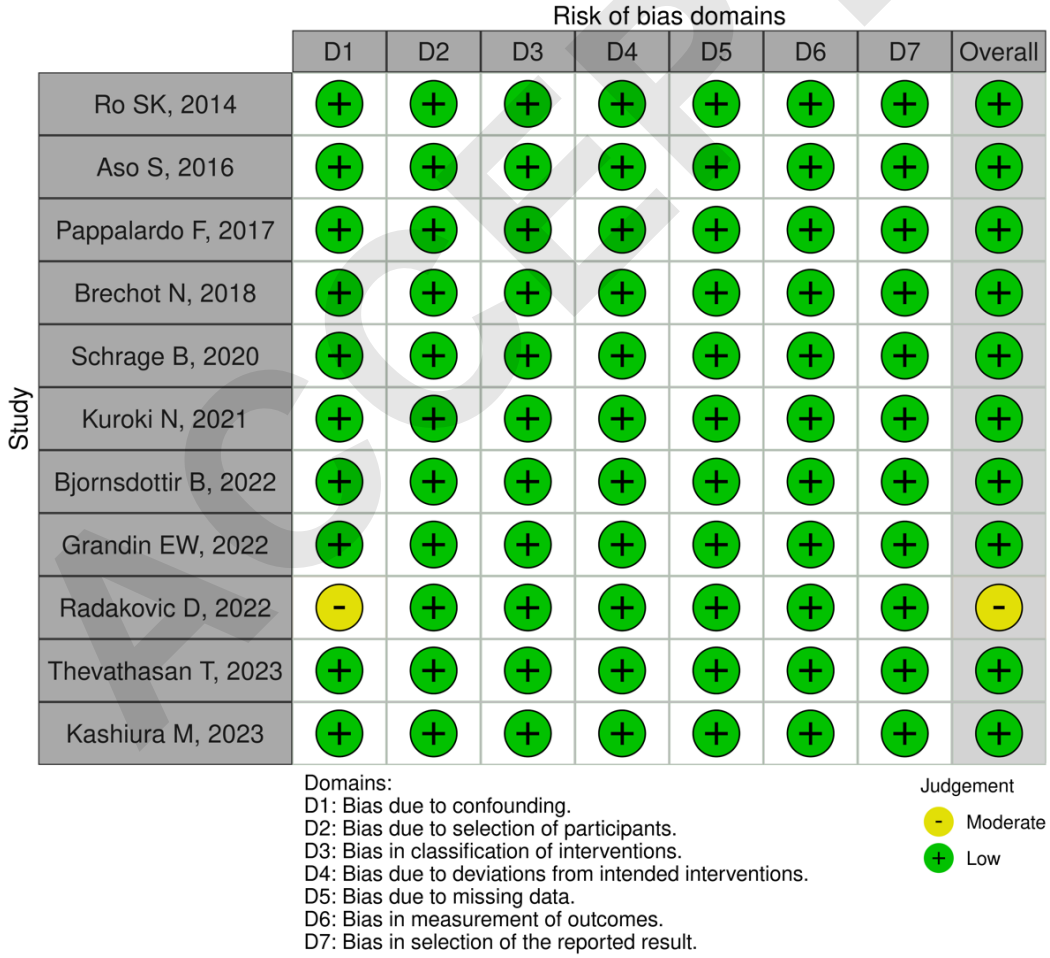


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Table S3. GRADE evaluation

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mechanical LV loading	control	Relative (95% CI)	Absolute (95% CI)		
Mortality at the longest follow-up												
13	randomised trials and non-randomized studies	serious[a]	not serious	not serious	not serious	none	2783/4852 (57.4%)	3137/5006 (62.7%)	**RR 0.89** (0.84 to 0.94)	**69 fewer per 1,000** (from 100 fewer to 38 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
Successful VA-ECMO weaning												
7	randomised trials and non-randomized studies	serious[a]	serious[b]	not serious	not serious	none	631/873 (72.3%)	615/1027 (59.9%)	**RR 1.15** (1.02 to 1.29)	**90 more per 1,000** (from 12 more to 174 more)	⨁⨁◯◯ Low	CRITICAL
Major hemorrhage												
7	randomised trials and observational studies	serious[a]	serious[c]	not serious	not serious	none	747/3591 (20.8%)	565/3609 (15.7%)	**RR 1.27** (1.02 to 1.59)	**42 more per 1,000** (from 3 more to 92 more)	⨁⨁◯◯ Low	CRITICAL
Hemolysis												
4	non-randomised studies	not serious	serious[d]	not serious	not serious	none	235/3369 (7.0%)	176/3347 (5.3%)	**RR 1.49** (1.10 to 2.02)	**26 more per 1,000** (from 5 more to 54 more)	⨁⨁⨁◯ Moderate	IMPORTANT
Renal replacement therapy												
9	randomised trials and non-randomized studies	serious[a]	serious[e]	not serious	serious[f]	none	469/1163 (40.3%)	451/1184 (38.1%)	**RR 1.03** (0.83 to 1.27)	**11 more per 1,000** (from 65 fewer to 103 more)	⨁◯◯◯ Very low	IMPORTANT
Limb ischemia												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mechanical LV loading	control	Relative (95% CI)	Absolute (95% CI)		
7	randomised trials and non-randomized studies	serious[a]	serious[g]	not serious	not serious	none	362/3627 (10.0%)	326/3624 (9.0%)	**RR 1.20** (0.91 to 1.60)	**18 more per 1,000** (from 8 fewer to 54 more)	⨁⨁◯◯ Low	IMPORTANT
Stroke												
5	randomised trials and non-randomized studies	serious[a]	not serious	not serious	not serious	none	170/3431 (5.0%)	156/3443 (4.5%)	**RR 1.10** (0.89 to 1.35)	**5 more per 1,000** (from 5 fewer to 16 more)	⨁⨁⨁◯ Moderate	IMPORTANT
Bridge to heart transplant or durable VAD												
5	randomised trials and non-randomized studies	serious[a]	not serious	not serious	serious[h]	none	35/286 (12.2%)	36/307 (11.7%)	**RR 1.04** (0.69 to 1.57)	**5 more per 1,000** (from 36 fewer to 67 more)	⨁⨁◯◯ Low	IMPORTANT
Favorable neurological outcome												
2	Non-randomized studies	serious[a]	not serious	not serious	serious[h]	none	71/455 (15.6%)	29/455 (6.4%)	**RR 2.45** (1.62 to 3.69)	**92 more per 1,000** (from 40 more to 172 more)	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **RR:** risk ratio; **VA-ECMO:** venoarterial extracorporeal membrane oxygenation; **VAD:** ventricular assist device

Explanations

a. Non-randomised studies were included.
b. Criteria to wean VA-ECMO were not standardized across studies.
c. Considerable heterogeneity
d. Diagnosis of hemolysis was not standardized across studies.
e. Criteria to initiate renal replacement therapy were not standardized across studies.
f. Criteria to initiate renal replacement therapy were not defined.
g. Diagnosis of limb ischemia was not standardized across studies.
h. The sample size was small.

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Supplemental references

1. Acute Cardiovascular Care 2016. *Eur Heart J Acute Cardiovasc Care* 5(1_suppl):4–440, 2016.
2. Lee H, Song S, Kim S, Oh S, Kim N, Kim J, Lee S, Park J, Oh J, Choi J, Lee H, Cha K, Hong T: Role of ECMO in Acute Myocardial Infarction Complicating Cardiogenic Shock. *J Heart Lung Transplant* 35(4):S377–S378, 2016.
3. Lin L-Y, Liao C-W, Wang C-H, Chi N-H, Yu H-Y, Chou N-K, Hwang J-J, Lin J-L, Chiang F-T, Chen Y-S: Effects of Additional Intra-aortic Balloon Counter-Pulsation Therapy to Cardiogenic Shock Patients Supported by Extra-corporeal Membranous Oxygenation. *Sci Rep* 6:23838, 2016.
4. Hou G, Yu K, Yin X, Wang H, Xu W, Du Z, Hou X, Long Y, Chen H, Xu L, Liu S: Safety research of extracorporeal membrane oxygenation treatment on cardiogenic shock: a multicenter clinical study. *Minerva Cardioangiol* 64(2):121–126, 2016.
5. Ostadal P, Rokyta R, Kruger A, Vondrakova D, Janotka M, Smíd O, Smalcova J, Hromadka M, Linhart A, Bělohlávek J: Extra corporeal membrane oxygenation in the therapy of cardiogenic shock (ECMO-CS): rationale and design of the multicenter randomized trial. *Eur J Heart Fail* 19 Suppl 2:124–127, 2017.
6. Rivera M, Patel N, Fernandes G, Cardoso R, Kumar V, Badiye A, Cohen M: Abstract 17578: Impact of the Adjunct Use of Intra-Aortic Counter Pulsation Devices to Extracorporeal Membrane Oxygenation for Cardiogenic Shock. *Circulation* 136(suppl_1):A17578–A17578, 2017.
7. Zipfel S, Reiter B, Yildirim Y, Hakmi S, Barten M, Rybczinski M, Westermann D, Reichenspurner H, Bernhardt A: Secondary LV Unloading after Out-of-hospital ECLS Implantation and Transportation Improved Survival and Probability of Successful Weaning. In *47th Annual Meeting of the German Society for Thoracic and*

ACCEPTED

Copyright © 2024 by the Shock Society. Unauthorized reproduction of this article is prohibited.

Cardiovascular Surgery (DGTHG). vol. 66Georg Thieme Verlag KG, 2018, p DGTHG-V80.

8. Kuroki N, Nagao K, Takayama T, Hosokawa Y, Tachibana E, Ashida T, Abe D, Yamamoto T, Takayama M, Tokyo CCU network: 2994Impact of extracorporeal membrane oxygenation (ECMO) and intra-aortic balloon pump (IABP) for cardiac arrest. *Eur Heart J* 39(suppl_1), 2018.
9. Abstracts of the 2017 A-CURE Symposium. *J Cardiovasc Transl Res* 11(1):58–70, 2018.
10. Featuring abstracts from the Society for Cardiovascular Angiography & Interventions 2019 Scientific Sessions May 19-22, 2019. *Catheter Cardiovasc Interv* 93(S2):S1–S250, 2019.
11. Scatola A, Singh A, Singh K, Singh N, Meraj P: Effect of Time from Cardiogenic Shock to Initiation of Complete Cardiovascular Support on Survival: "Shock to Support Time." *J Heart Lung Transplant* 38(4, Supplement):S177, 2019.
12. Singh A: Impact of left ventricular decompression with Impella during venoarterial extracorporeal membrane oxygenation support in acute myocardial infarction complicated by cardiogenic shock. In *2019 Scientific Sessions*. Scai, 2019.
13. Zaid Syed, Malik Aaqib, Undemir Cenap, Goldberg Joshua, Ahmad Hasan: TCT-815 Does Addition of Percutaneous Left Ventricular Decompression Therapy With Impella Affect Clinical Outcomes in Cardiogenic Shock Patients on Venoarterial Extracorporeal Membrane Oxygenation? A Nationwide Analysis. *J Am Coll Cardiol* 74(13_Supplement):B798–B798, 2019.
14. Ok YJ, Jung S-H, Lee S-W, Ahn J-M, Lim JY: Efficacy of left heart decompression during extracorporeal membrane oxygenation: a case-control study. *J Thorac Dis* 11(3):865–872, 2019.

Copyright © 2024 by the Shock Society. Unauthorized reproduction of this article is prohibited.

15. Patel SM, Lipinski J, Al-Kindi SG, Patel T, Saric P, Li J, Nadeem F, Ladas T, Alaiti A, Phillips A, Medalion B, Deo S, Elgudin Y, Costa MA, Osman MN, Attizzani GF, Oliveira GH, Sareyyupoglu B, Bezerra HG: Simultaneous Venoarterial Extracorporeal Membrane Oxygenation and Percutaneous Left Ventricular Decompression Therapy with Impella Is Associated with Improved Outcomes in Refractory Cardiogenic Shock. *ASAIO J* 65(1):21–28, 2019.
16. Singh A: Impact on mortality by presenting lactate level and lactate clearance in patients with acute myocardial infarction complicated by cardiogenic shock supported by VA-ECMO and ECPELLA. *Catheter Cardiovasc Interv* 93:S3–S4, 2019.
17. Tepper S, Garcia MB, Fischer I, Ahmed A, Khan A, Balsara KR, Masood MF, Itoh A: Clinical Outcomes and Reduced Pulmonary Artery Pressure With Intra-Aortic Balloon Pump During Central Extracorporeal Life Support. *ASAIO J* 65(2):173–179, 2019.
18. Akanni OJ, Takeda K, Truby LK, Kurlansky PA, Chiuzan C, Han J, Topkara VK, Yuzefpolskaya M, Colombo PC, Karmpaliotis D, Moses JW, Naka Y, Garan AR, Kirtane AJ, Takayama H: EC-VAD: Combined Use of Extracorporeal Membrane Oxygenation and Percutaneous Microaxial Pump Left Ventricular Assist Device. *ASAIO J* 65(3):219–226, 2019.
19. Barge-Caballero G, Castel-Lavilla MA, Almenar-Bonet L, Garrido-Bravo IP, Delgado JF, Rangel-Sousa D, González-Costello J, Segovia-Cubero J, Farrero-Torres M, Lambert-Rodríguez JL, Crespo-Leiro MG, Hervás-Sotomayor D, Portolés-Ocampo A, Martínez-Sellés M, De la Fuente-Galán L, Rábago-Juan-Aracil G, González-Vílchez F, Mirabet-Pérez S, Muñiz J, Barge-Caballero E: Venoarterial extracorporeal membrane oxygenation with or without simultaneous intra-aortic balloon pump support as a direct bridge to heart transplantation: results from a nationwide Spanish registry. *Interact Cardiovasc Thorac Surg* 29(5):670–677, 2019.

ACCEPTED

Copyright © 2024 by the Shock Society. Unauthorized reproduction of this article is prohibited.

20. Ye FM, Zhang JJ, Wang BB, Zhang J: [Efficacy of combined treatment with mechanical circulation support devices and immunomodulation therapy for patients with fulminant myocarditis]. *Zhonghua Xin Xue Guan Bing Za Zhi* 49(9):894–899, 2021.
21. Thevathasan T, Kenny M, Boie S, Wurster T, Last J, Kalinowsky R, Landmesser U, Balzer F, Skurk C: Abstract 12405: Treatment With Impella and Veno-Arterial Extracorporeal Membrane Oxygenation During Extracorporeal Cardiopulmonary Resuscitation Improves Survival - A Multicenter Cohort Study. *Circulation* 144(Suppl_1):A12405–A12405, 2021.
22. Ibrahim M, Acker MA, Szeto W, Gutsche J, Williams M, Atluri P, Woods M, Richards T, Gardner TJ, McGarvey J, Epler M, Wald J, Rame E, Birati E, Bermudez C: Proposal for a trial of early left ventricular venting during venoarterial extracorporeal membrane oxygenation for cardiogenic shock. *JTCVS Open* 8:393–400, 2021.
23. Djordjevic I, Deppe A-C, Sabashnikov A, Kuhn E, Eghbalzadeh K, Merkle J, Gerfer S, Gaisendrees C, Ivanov B, Moellenbeck L, Adler C, Rustenbach C, Rahmanian P, Mader N, Kuhn-Regnier F, Wahlers T: Concomitant ECMO And IABP Support in Postcardiotomy Cardiogenic Shock Patients. *Heart Lung Circ* 30(10):1533–1539, 2021.
24. Kim A-R, Park H, Lee S-E, Ahn J-M, Park D-W, Lee S-W, Kim J-J, Park S-J, Hong JA, Kang P-J, Jung S-H, Kim M-S: Outcomes of left ventricular unloading with a transseptal cannula during extracorporeal membrane oxygenation in adults. *Artif Organs* 45(4):390–398, 2021.
25. Hasde Aİ, Sarıcaoğlu MC, Dikmen Yaman N, Baran Ç, Özçınar E, Çakıcı M, İnan MB, Akar AR: Comparison of left ventricular unloading strategies on venoarterial extracorporeal life support. *Interact Cardiovasc Thorac Surg* 32(3):467–475, 2021.
26. Udongwo N, Narra L, Mararenko A, Alshami A, Fatuyi M, Abe T, Olanipekun T, Upadhyaya VD, Dhulipala V, Dominic J, Kurtz J, Kossack A, Saybolt M, Selan J,

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Sealove B, Singh D, Almendral J: Abstract 332: Does Concomitant Left Ventricular Unloading Improve Outcomes Of Cardiogenic Shock Managed By Venoarterial Extracorporeal Membrane Oxygenation? Analysis Of National Inpatient Sample Database 2019. *Circulation* 146(Suppl_1):A332–A332, 2022.

27. Chen X, Chen J, Wang R, Zheng J, Yang Q, Chen J, Wen D, Xiong X: [Relationship of in-hospital mortality and using intra-aortic balloon pump with extracorporeal cardiopulmonary resuscitation in patients with cardiac arrest: a secondary analysis based on literature data]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 34(3):269–273, 2022.
28. Hendrickson MJ, Jain V, Bhatia K, Chew C, Arora S, Rossi JS, Villablanca P, Kapur NK, Joshi AA, Fox A, Mahmood K, Birati EY, Ricciardi MJ, Qamar A: Trends in Veno-Arterial Extracorporeal Life Support With and Without an Impella or Intra-Aortic Balloon Pump for Cardiogenic Shock. *J Am Heart Assoc* 11(23):e025216, 2022.
29. Kida H, Sotomi Y, Hikoso S, Nakatani D, Mizuno H, Suna S, Okada K, Kitamura T, Komukai S, Dohi T, Kojima T, Oeun B, Sunaga A, Sato T, Sakata Y, Sato H, Hori M, Komuro I, Sakata Y, Osaka Acute Coronary Insufficiency Study (OACIS) Investigators: Prognostic significance of intra-aortic balloon pumping support in patients with acute myocardial infarction and veno-arterial extracorporeal membrane oxygenation therapy. *J Cardiol* 79(2):179–185, 2022.
30. Gaisendrees C, Djordjevic I, Sabashnikov A, Adler C, Eghbalzadeh K, Ivanov B, Walter S, Schlachtenberger G, Merkle-Storms J, Gerfer S, Carstens H, Deppe A-C, Kuhn E, Wahlers T: Impact of left ventricular unloading using a peripheral Impella®-pump in eCPR patients. *Artif Organs* 46(3):451–459, 2022.
31. Denisenko A, Ouattara A, Guinot P-G, Briant A, Fischer M-O, ICAEN group: Left ventricular unloading did not decrease mortality in cardiogenic shocks patients

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supported with VA-ECMO: A propensity score matching study. *Anaesth Crit Care Pain Med* 41(2):101042, 2022.

32. Unoki T, Kamentani M, Nakayama T, Tamura Y, Konami Y, Suzuyama H, Inoue M, Yamamuro M, Taguchi E, Sawamura T, Nakao K, Sakamoto T: Impact of extracorporeal CPR with transcatheter heart pump support (ECPELLA) on improvement of short-term survival and neurological outcome in patients with refractory cardiac arrest - A single-site retrospective cohort study. *Resusc Plus* 10:100244, 2022.
33. Bogerd Margriet, Peters Elma, Berg Sanne ten, Timmermans Marijke, Engström Annemarie, Otterspoor Luuk, Bunge Jeroen, Griffioen Alexander, Van Geuns Robert-Jan, Vlaar Alexander, Henriques Jose: TCT-479 A Propensity-Matched Analysis of Mechanical Circulatory Support in Cardiogenic Shock Complicating Acute Myocardial Infarction: Insights From the Netherlands. *J Am Coll Cardiol* 82(17_Supplement):B192–B192, 2023.
34. Pan CL, Zhao J, Hu SX, Lei P, Zhao CR, Su YR, Cai WT, Zhang SS, Yan ZJ, Lu AD, Zhang B, Bai M: [Impact of VA-ECMO combined with IABP and timing on outcome of patients with acute myocardial infarction complicated with cardiogenic shock]. *Zhonghua Xin Xue Guan Bing Za Zhi* 51(8):851–858, 2023.
35. Ginder K, Riddle C, Cox J, Amin A, Mammen P, Araj F: (799) Impact of Lv Venting During Va-Ecmo Support on Survival Outcomes: A Contemporary 5-Year Analysis of a Single Center Experience. *J Heart Lung Transplant* 42(4, Supplement):S350, 2023.
36. Girish A, Brown MA, Cevasco M, Wald JW, Olia S, Molina M, Senker R, Bermudez C: P54: Early mortality associated with combination Impella 5.5 and extracorporeal membrane oxygenation support as bridge to cardiac replacement therapy. *ASAIO J* 69(Supplement 2):136, 2023.

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37. Kieserman J, Park JH, Schurr J, Wald JW: SHOCK3: Comparing Veno-arterial Extracorpeal Membrane Oxygenation (VA-ECMO) vs. VA-ECMO plus Impella (ECPELLA) on Mortality in Patients with Cardiac Arrest After an Acute Myocardial Infarction (AMI). *ASAIO J* 69(Supplement 2):10, 2023.
38. Yeo I, Axman R, Lu DY, Feldman DN, Cheung JW, Minutello RM, Karas MG, Iannacone EM, Srivastava A, Girardi NI, Naka Y, Wong S-C, Kim LK: Abstract 11322: Comparative Outcomes of Impella and Intra-Aortic Balloon Pump for Left Ventricular Unloading Among Patients With Cardiogenic Shock on Veno-Arterial Extracorporeal Membrane Oxygenation. *Circulation* 148(Suppl_1):A11322–A11322, 2023.
39. Char S, Fried J, Melehy A, Mehta S, Ning Y, Kurlansky P, Takeda K: Clinical efficacy of direct or indirect left ventricular unloading during venoarterial extracorporeal membrane oxygenation for primary cardiogenic shock. *J Thorac Cardiovasc Surg* 165(2):699-707.e5, 2023.
40. Kim MC, Lim Y, Lee SH, Shin Y, Ahn JH, Hyun DY, Cho KH, Sim DS, Hong YJ, Kim JH, Jeong MH, Jung YH, Jeong I-S, Ahn Y: Early left ventricular unloading after extracorporeal membrane oxygenation: rationale and design of EARLY-UNLOAD trial. *ESC Heart Fail* 10(4):2672–2679, 2023.
41. Radakovic D, Zittermann A, Rojas SV, Opacic D, Razumov A, Prashovikj E, Fox H, Schramm R, Morshuis M, Rudolph V, Gummert J, Flottmann C, Deutsch M-A: Left Ventricular Unloading in Patients on Venoarterial Extracorporeal Membrane Oxygenation Therapy in Cardiogenic Shock: Prophylactic Versus Bail-Out Strategy. *Life* 13(2), 2023.
42. Arafat AA, Almedimigh AA, Algarni KD, Ismail HH, Pragliola C, Adam AI, AlBarrak M, Osman A, Albabtain MA, Tantawy TM: Concomitant intra-aortic balloon pump and

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veno-arterial extracorporeal membrane oxygenation for postcardiotomy cardiogenic shock. *Int J Artif Organs* 46(6):384–389, 2023.

43. ISRCTN82431978. https://trialsearch.who.int/Trial2.aspx?TrialID=ISRCTN82431978. January 24, 2024.
44. NCT05577195. https://clinicaltrials.gov/study/NCT05577195?term=NCT05577195&rank=1. January 24, 2024.
45. NCT05913622. https://clinicaltrials.gov/study/NCT05913622?term=NCT05913622&limit=10&rank=1. January 24, 2024.
46. NCT03431467. https://clinicaltrials.gov/study/NCT03431467?term=NCT03431467&limit=10&rank=1. February 19, 2024.

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