

ORIGINAL RESEARCH

Mechanical Circulatory Support for Complex High-Risk Indicated Percutaneous Coronary Intervention: Network Meta-Analysis of Randomized Trials

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BACKGROUND: Mechanical circulatory support (MCS) is increasingly used during complex high-risk indicated percutaneous coronary intervention, yet whether different support strategies improve clinical outcomes remains uncertain. We sought to compare the efficacy and safety of individual MCS strategies with standard care and with each other at short- and long-term follow-up.

METHODS: This frequentist random-effects network meta-analysis included randomized trials of patients undergoing nonemergent complex high-risk indicated percutaneous coronary intervention and comparing percutaneous left ventricular assist devices, intra-aortic balloon pump, venoarterial extracorporeal membrane oxygenation, or standard care. The primary efficacy outcome was major adverse cardiovascular events. Secondary outcomes included death, myocardial infarction, stroke, or repeat revascularization, and periprocedural major adverse events.

RESULTS: Eight trials (n=1856) were included. At 30 days, no MCS was associated with lower major adverse cardiovascular events compared with standard care, though percutaneous left ventricular assist devices (risk ratio [RR] 0.30, 95% CI 0.10–0.90) and intra-aortic balloon pump (RR 0.26, 95% CI 0.07–0.90) reduced periprocedural major adverse events. At a weighted mean of 10.8 months, no significant differences in major adverse cardiovascular events were observed with percutaneous left ventricular assist devices (incidence rate ratio 0.79; 95% CI 0.47–1.35), intra-aortic balloon pump (incidence rate ratio 0.89, 95% CI 0.52–1.54), or venoarterial extracorporeal membrane oxygenation (incidence rate ratio 1.47, 95% CI 0.64–3.40) compared with standard care. Consistently, no MCS strategy reduced death, myocardial infarction, stroke, or repeat revascularization.

CONCLUSIONS: Among patients undergoing complex high-risk indicated percutaneous coronary intervention, MCS did not improve clinical outcomes, despite fewer periprocedural adverse events with percutaneous left ventricular assist devices and intra-aortic balloon pump. These findings do not support routine prophylactic use and suggest that MCS should be limited to selected patients.

Key Words: extracorporeal membrane oxygenation ■ intraaortic balloon pump ■ mechanical circulatory support ■ microaxial flow pump ■ percutaneous coronary intervention ■ percutaneous left ventricular assist device

Coronary artery disease involving the left main coronary artery and/or anatomically complex multivessel disease is associated with increased

morbidity and mortality, particularly among patients with severely reduced left ventricular systolic function.¹ In this population, coronary artery bypass grafting is

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CLINICAL PERSPECTIVE

What Is New?

- In this network meta-analysis of 8 randomized trials including 1856 patients undergoing non-emergent complex high-risk indicated percutaneous coronary intervention, prophylactic mechanical circulatory support with percutaneous left ventricular assist devices or intra-aortic balloon pump did not reduce short- or long-term ischemic clinical outcomes compared with standard care, despite fewer periprocedural hemodynamic adverse events. The effect of venoarterial extracorporeal membrane oxygenation remained unclear, with large CIs compatible with both benefit and harm, reflecting its more limited evidence base.

What Are the Clinical Implications?

- These findings do not support routine prophylactic mechanical circulatory support during complex high-risk indicated percutaneous coronary intervention, suggesting that mechanical circulatory support should be limited to highly selected patients based on anticipated hemodynamic vulnerability, procedural complexity, and bleeding or vascular access risk.
- The subgroup of patients undergoing complex high-risk indicated percutaneous coronary intervention who may derive the greatest clinical benefit from prophylactic mechanical circulatory support remains largely unknown and warrants further investigation in future randomized studies.

Nonstandard Abbreviations and Acronyms

CHIP	complex high-risk indicated percutaneous coronary intervention
IABP	intra-aortic balloon pump
IRR	incidence rate ratio
MACE	major adverse cardiovascular events
MCS	mechanical circulatory support
pLVAD	percutaneous left ventricular assist device
VA-ECMO	venoarterial extracorporeal membrane oxygenation

the preferred revascularization strategy.² However, many patients are not candidates for surgery because of advanced age, significant comorbidity burden, and poor distal targets, leading to high operative risk and frequent surgical turnaround.³

Percutaneous coronary intervention (PCI) may be considered in selected patients deemed unsuitable for coronary artery bypass grafting.² In this setting, PCI is often technically complex, frequently involving severe coronary calcification, bifurcation disease, and chronic total occlusions.^{1,4} These procedures, commonly referred to as complex high-risk indicated PCI (CHIP), are associated with an increased risk of intraprocedural ischemia, which may further impair left ventricular function, precipitate hemodynamic instability, and worsen periprocedural outcomes.^{1,4} Anticipation or actual occurrence of these complications may lead to deviation from the intended revascularization plan, suboptimal PCI, or incomplete revascularization, resulting in worse long-term outcomes.¹

Mechanical circulatory support (MCS) devices, including percutaneous left ventricular assist device (pLVAD), intra-aortic balloon pump (IABP), and venoarterial extracorporeal membrane oxygenation (VA-ECMO), have emerged as an adjunctive option in CHIP, aiming to provide hemodynamic assistance during procedure-related ischemia associated with transient vessel occlusion during balloon angioplasty and stenting, coronary blood flow reduction related to catheterization and intracoronary guidewires and devices, or in case of intraprocedural complications, which are more frequent in challenging coronary artery disease settings.^{3,4} By limiting myocardial ischemia and maintaining cardiac output and systemic perfusion, MCS may reduce periprocedural hemodynamic compromise and its sequelae and facilitate optimal procedural techniques and more complete revascularization, ultimately improving clinical short- and long-term outcomes.^{3,4}

Despite increasing use, individual randomized trials evaluating MCS in CHIP are most often characterized by modest sample sizes and a primary focus on surrogate or procedural outcomes, leaving uncertainty about their influence on clinically meaningful outcomes.^{5–14} Although the recent CHIP-BCIS3 (Controlled Trial of High-Risk Coronary Intervention with Percutaneous Left Ventricular Unloading) trial has expanded the contemporary randomized evidence base, comparative data among different MCS devices remains limited.¹⁴ Accordingly, we performed a systematic review and network meta-analysis of randomized trials to evaluate the relative effectiveness and safety of individual MCS devices and standard care during CHIP.

METHODS

This meta-analysis was prospectively registered in PROSPERO, the International Prospective Register of Systematic Reviews (registration number: CRD420261330062), and conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-Analyses (PRISMA-NMA)

recommendations.¹⁵ The PRISMA-NMA Checklist has been included in the [Supplemental Material](#). Ethics committee approval was not required because the study was based exclusively on aggregate data from previously published randomized trials.

Availability of Data

The database compiled for the present meta-analysis and the statistical analysis scripts used to generate the reported results are available from the corresponding author upon reasonable request.

Eligibility Criteria

Studies were considered eligible if they: (i) enrolled patients undergoing nonemergent CHIP, as defined by the individual trials, generally involving anatomically and procedurally complex coronary artery disease and/or severely impaired left ventricular systolic function; (ii) provided random allocation to MCS or standard care and/or to different MCS devices; (iii) reported at least one prespecified outcome of interest. Studies were excluded if: (i) they included patients with cardiogenic shock at randomization; (ii) and/or with acute ST-segment-elevation myocardial infarction. No language restrictions were applied.

Search Strategy, Data Selection, Extraction, and Qualitative Assessment

PubMed, Web of Science, and Cochrane Central Register of Controlled Trials were screened from their inception through March 31, 2026. The search strategy is presented in [Table S1](#). Additionally, websites of major cardiovascular societies and conference proceedings were screened, and backward citation chasing of previously identified studies was performed. After removing duplicates across databases, 2 co-authors (M.S.M., S.F.) independently screened articles at the title and abstract level. Then, full texts of the remaining reports that potentially met the inclusion criteria based on the titles and abstracts were assessed for eligibility. Discrepancies among reviewers were resolved by consensus under the supervision of a third author (K.B.). Reports belonging to the same trial were combined before inclusion in the meta-analysis. Key trial-level and arm-level data were extracted by 2 co-authors (K.B., C.L.). The included trials were independently assessed for bias by 2 co-authors (K.B., C.L.) using the Cochrane risk-of-bias tool for randomized trials, version 2 (RoB 2),¹⁶ and any discrepancies were resolved by consensus. Publication bias was examined through visual inspection of comparison-adjusted funnel plots. Formal testing of asymmetry with the Egger test had been prespecified if the number of included trials was greater than 10.

Outcomes

The primary efficacy outcome was a study-defined composite of major adverse cardiovascular events (MACE). When multiple definitions of MACE were reported, definitions that more closely aligned with the Academic Research Consortium definition (ie, a composite of all-cause death, any myocardial infarction, any stroke, or any repeat revascularization) were prioritized.¹⁷ Secondary outcomes included the following individual outcomes: all-cause death, myocardial infarction, stroke, repeat revascularization, and study-defined periprocedural major adverse events (prioritizing composite outcomes comprising prolonged hypotension, malignant arrhythmia, and cardiopulmonary resuscitation). Both primary and secondary outcomes were assessed at short-term (30 days or, if unavailable, hospital discharge) and at the longest available follow-up (except for periprocedural major adverse events). The safety outcomes included major bleeding, any bleeding, and vascular complications, all assessed short term.

Statistical Analysis

The analysis was performed in the intention-to-treat population. Risk ratios (RRs) and incidence rate ratios (IRRs) with corresponding 95% CIs were used as measures of relative treatment effect for short- and long-term outcomes, respectively, the latter accounting for variable follow-up duration across trials by expressing events as rates per person-time rather than proportions.

A frequentist random-effects network meta-analysis using both direct and indirect evidence on treatment effects was conducted to compare the following nodes: standard care, pLVAD, IABP, and VA-ECMO. A 0.5 continuity correction was used for trials with zero events in either arm.

Between-study heterogeneity was assumed to follow a single common variance (τ^2) across all comparisons within each outcome network, which is reasonable given the sparse number of trials informing most individual comparisons and the clinical comparability of the included trial populations; τ^2 was estimated using the DerSimonian-Laird method. Heterogeneity in the network meta-analysis was assessed using the Cochrane Q statistic, τ^2 , and I^2 , and categorized as low, moderate, or high based on I^2 values of <25%, 25% to 50%, and >50%, respectively. Because I^2 depends on trial precision as well as true heterogeneity, these categories served only as a descriptive reference; heterogeneity was interpreted primarily through τ^2 , the between-study variance on the log effect scale. Assuming normally distributed true effects, τ^2 implies an expected multiplicative difference of $\exp(\sqrt{2 \times \tau})$ between the true effects of any 2 individual trials, allowing comparison

against the pooled treatment effect to gauge clinical relevance.¹⁸

Network meta-analysis further assumes consistency between direct and indirect evidence, relying on transitivity across trials with respect to effect modifiers other than randomized treatment; given the comparability of trial populations and clinical context, transitivity was considered plausible. Local inconsistency was checked by splitting direct and indirect evidence (Separate Indirect from Direct Design Evidence [SIDDE] method) and formally testing the contrast.

To illustrate the network configuration, network plots were generated. Relative treatment effects were presented in forest plots, using standard care as the reference treatment, and league tables. Treatments were ranked using the surface under the cumulative ranking curve, which can be interpreted as the estimated fraction of competing treatments that a given treatment outperforms. Surface under the cumulative ranking curve values range from 0 to 1, with higher values indicating that a treatment is estimated to outperform a greater fraction of competing treatments.¹⁹

A prespecified sensitivity analysis was performed by limiting the studies to trials evaluating devices approved in the United States and Europe to reduce heterogeneity arising from differences in device type, availability, and regulatory status across trials. An additional sensitivity analysis was performed by restricting the trials to those that tested contemporary devices. Moreover, as a post hoc sensitivity analysis addressing potential bias from rare-event trials in the primary contrast-based frequentist 2-stage network meta-analysis, a one-stage, arm-based Bayesian network meta-analysis was fitted directly to observed event counts per person-years. Long-term outcomes were modeled with a Poisson likelihood (log link) using event counts and person-time to estimate IRRs; short-term outcomes were modeled analogously using a modified Poisson approach, with patients at risk as the exposure, to estimate RRs. Random-effects models used weakly informative priors and were fitted via Hamiltonian Monte Carlo sampling (4 chains, 4000 iterations, 2000 warm-up).

Finally, within trials directly comparing any MCS with standard care, an exploratory pairwise meta-analysis was performed after collapsing individual MCS device classes into a single group to assess the overall effect of MCS versus standard care.

A 2-tailed *P* value less than 0.05 was considered significant. All statistical analyses were conducted in R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Selection, Characteristics of Included Trials, and Bias Assessment

After removing duplicates, 690 unique records were identified and screened by title and abstract, and 13 were assessed for eligibility. Of them, 5 records were excluded, with ST-segment-elevation myocardial infarction presentation being the most common exclusion criterion (Table S2). Finally, 8 randomized trials were included in the meta-analysis.^{5–14} The flow diagram illustrating the study identification process is included in Figure S1. The inclusion and exclusion criteria of individual studies pooled in the meta-analysis are shown in Table S3. Briefly, the trials consistently included hemodynamically stable patients with reduced left ventricular ejection fraction undergoing elective CHIP. Two trials compared standard care with IABP,^{5,7,9} one with pLVAD,¹⁴ and another with VA-ECMO,¹⁰ while four compared different MCS devices.^{6,8,11–13} In the pLVAD arms, Impella 2.5 was the most tested device (30.8%), followed by Impella CP (20.9%). The main characteristics of the included trials are provided in Table. CHIP definitions, details on tested devices, and MCS characteristics are shown in Table S4.

A total of 1856 patients, with a weighted mean age of 66.0 years and 17.3% women, were included. Among them, 727 were randomized to pLVAD support, 512 to IABP, 273 to VA-ECMO, and 344 to standard care. The weighted mean Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery score was 35, indicating high angiographic complexity of coronary artery disease, and the average left ventricular ejection fraction was 28%. The baseline clinical, angiographic, and procedural characteristics were overall comparable across the trials, suggesting no major violations of the transitivity assumption underlying indirect comparisons (Tables S5 and S6).

Two trials were deemed at low risk of bias, whereas the other 6 raised some concerns, mostly because of potential bias in the selection of reported outcomes (Figure S2). The visual inspection of the comparison-adjusted funnel plots did not reveal asymmetry, suggesting the absence of publication bias (Figure S3).

Network Meta-Analysis

Available outcomes across the included studies, and the components of MACE and periprocedural major adverse events, are presented in Tables S7 and S8. The network configuration showed closed loops across all analyzed outcomes (Figure S4). The event rates across individual trials and per arm are shown in Tables S9 and S10.

Table. Characteristics of Included Trials

Trial	Year	Intervention	Control	Tested device	No. of patients (intervention/control)	Primary safety end point	Primary efficacy end point	Follow-up*
CHIP-BCIS3	2026	pLVAD	Standard care	Impella CP	148/151	NA	Hierarchical composite end point at minimum 12 mo	22 mo (median)
Pan et al	2025	VA-ECMO	Standard care	VA-ECMO	33/33	Life-threatening complications during PCI	Reduction in SYNTAX score after PCI	12 mo
SAVE-PCI	2025	pLVAD	IABP	NyokAssist	113/115	NA	MACCE at 30-d	1 mo
REC-CHIPMCS	2025	pLVAD	VA-ECMO	CorVad 4.0/6.0	133/127	MAE at 30 d	NA	3 mo
PERSIST III	2025	pLVAD	VA-ECMO	SynFlow 3.0	109/113	MAE at 30 d	NA	3 mo
Zelias et al	2020	IABP	Standard care	IABP	27/9	Composite hemodynamic end point	NA	12 mo
PROTECT II	2012	IABP	pLVAD	Impella 2.5	219/224	MAE at 30 d	NA	3 mo
BCIS-1	2010	IABP	Standard care	IABP	151/150	NA	MACCE at hospital discharge	1 mo (MACCE); 51 mo (death)

BCIS-1 indicates the Balloon Pump-Assisted Coronary Intervention Study; CHIP-BCIS3, Controlled Trial of High-Risk Coronary Intervention with Percutaneous Left Ventricular Unloading; IABP, intra-aortic balloon pump; MACCE, major adverse cardiac and cerebrovascular events; MAE, major adverse events; NA, not applicable; PCI, percutaneous coronary intervention; pLVAD, percutaneous left ventricular assist device; PERSIST III, Prospective Evaluation for Receiving SynFlow 3.0 Interventional Circulatory Support in High-Risk PCI; PROTECT II, Prospective, Randomised Clinical Trial of Haemodynamic Support With Impella 2.5 Versus IABP in Patients Undergoing High-Risk PCI; REC-CHIPMCS, Interventional Ventricular Assist System for PCI in Complex High-Risk Indicated PCI Patients; SAVE-PCI, NyokAssist Small-Bore pVAD versus IABP in Elective High-Risk PCI; SYNTAX, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; and VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

*Refers to the longest available follow-up.

Primary and Secondary Efficacy at Short-Term Follow-Up

At short term, no significant reduction in MACE was observed with pLVAD (RR 0.50; 95% CI 0.15–1.69; $P=0.27$), IABP (RR 0.61; 95% CI 0.25–1.51; $P=0.29$), or VA-ECMO (RR 0.92; 95% CI 0.19–4.39; $P=0.92$) compared with standard care (Figure 1). Similarly, no significant differences emerged across individual MCS devices in the network estimates (Table S11). Between-study heterogeneity was moderate ($I^2=43.9\%$; $\tau^2=0.26$; $P=0.15$), corresponding to an expected ~2-fold difference in true RR between individual trials, and no evidence of inconsistency between direct and indirect comparisons was identified (Table S12).

Both pLVAD (RR 0.30; 95% CI 0.10–0.90; $P=0.03$) and IABP (RR 0.26; 95% CI 0.07–0.90; $P=0.03$) were associated with lower rates of periprocedural major adverse events compared with standard care, whereas VA-ECMO was not (RR 0.45; 95% CI 0.12–1.69; $P=0.24$) (Figure 1). No significant differences were observed among individual devices (Table S11). Heterogeneity was high ($I^2=58.1\%$; $\tau^2=0.32$; $P=0.07$), corresponding to an expected ~2.2-fold difference in true RR between individual trials. Significant local inconsistency was observed for the comparison between pLVAD and standard care ($P_{\text{inconsistency}}=0.04$) (Table S12). In

ranking analyses, IABP had the highest surface under the cumulative ranking curve value (0.797), followed by pLVAD (0.722).

No individual MCS strategy was associated with a reduction in all-cause death, myocardial infarction, stroke, or repeat revascularization at short-term follow-up. Heterogeneity remained low across all secondary efficacy outcomes, with no evidence of local inconsistency (Figure 1; Tables S11 and S12).

Primary and Secondary Efficacy Outcomes at the Longest Available Follow-Up

At a weighted mean follow-up of 10.8 months, neither pLVAD (IRR 0.79; 95% CI 0.47–1.35; $P=0.40$), IABP (IRR 0.89; 95% CI 0.52–1.54; $P=0.68$), nor VA-ECMO (IRR 1.47; 95% CI 0.64–3.40; $P=0.36$) was associated with reduced MACE compared with standard care (Figure 2). No significant differences were observed among individual MCS devices in the network comparisons (Table S11). Heterogeneity was moderate ($I^2=39.4\%$; $\tau^2=0.09$; $P=0.14$), corresponding to an expected ~1.5-fold difference in true IRR between individual trials, and local inconsistency was found for the comparisons of VA-ECMO versus standard care ($P_{\text{inconsistency}}=0.03$) and VA-ECMO versus pLVAD

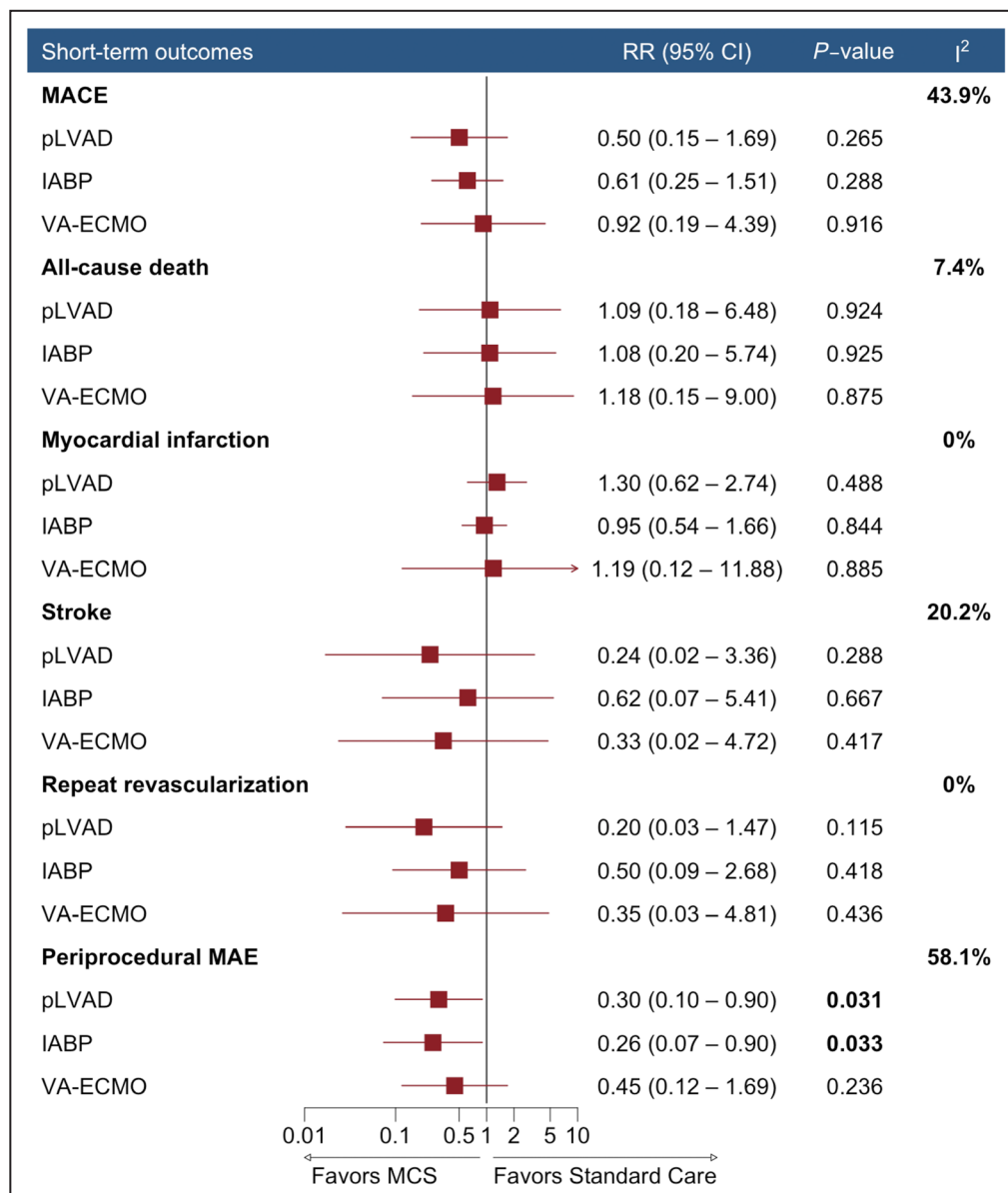


Figure 1. Forest plot presenting the results of network meta-analysis for the primary and secondary efficacy outcomes at short-term follow-up.

The forest plot presents network estimates for the comparisons of individual MCS devices with standard care. IABP indicates intra-aortic balloon pump; MACE, major adverse cardiovascular events; MAE, major adverse events; MCS, mechanical circulatory support; pLVAD, percutaneous left ventricular assist device; RR, risk ratio; and VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

($P_{\text{inconsistency}}=0.03$), with direct and indirect estimates going in different directions (Table S12).

For secondary efficacy outcomes, the weighted mean follow-up was 10.8 months, except for all-cause death (14.1 months). The risks of all-cause death, myocardial infarction, stroke, and repeat revascularization remained not significantly different across all MCS strategies and standard care, with low heterogeneity and no detectable local inconsistency (Figure 2; Tables S11 and S12).

Safety Outcomes

The rates of safety outcomes were low overall. No significant differences in major bleeding were observed, but there was a trend toward higher risk of any bleeding with IABP compared with standard care (RR 1.53; 95% CI 0.98–2.42; $P=0.06$). Similarly, vascular complications did not differ significantly across strategies, although pLVAD showed a trend toward higher risk versus standard care (RR 1.71; 95% CI 0.97–3.01; $P=0.07$).

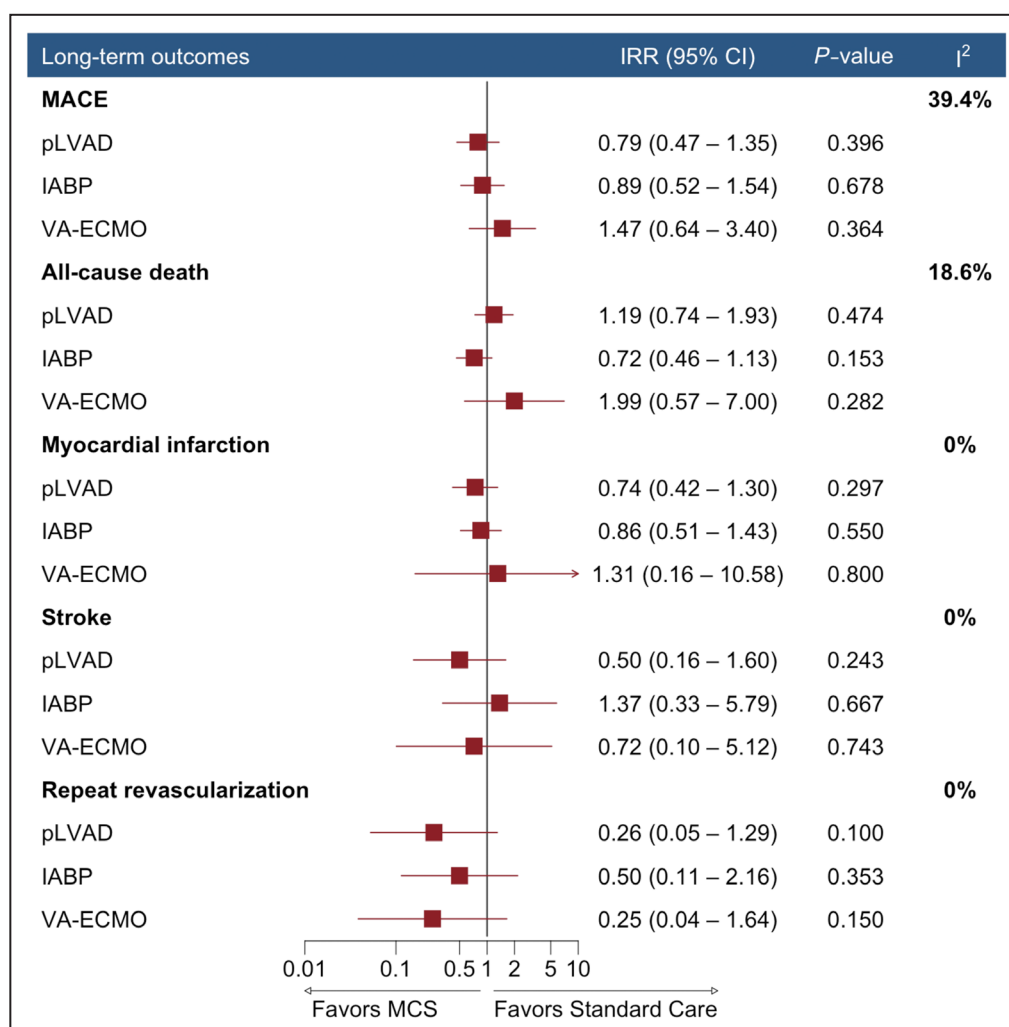


Figure 2. Forest plot presenting the results of network meta-analysis for primary and secondary efficacy outcomes at the longest available follow-up.

The forest plot presents network estimates for the comparisons of individual MCS devices with standard care. IABP indicates intra-aortic balloon pump; IRR, incidence rate ratio; MACE, major adverse cardiovascular events; MCS, mechanical circulatory support; pLVAD, percutaneous left ventricular assist device; and VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

No significant heterogeneity or inconsistency was observed for these outcomes (Figure 3; Tables S11 and S12).

Sensitivity and Exploratory Analyses

In sensitivity analyses restricted to MCS devices approved in the United States and Europe, pLVAD was associated with a higher incidence rate of long-term all-cause death compared with IABP (IRR 1.84; 95% CI 1.22–2.79; $P=0.004$), whereas no significant differences were observed among the remaining strategies. Conversely, pLVAD was associated with a lower incidence rate of long-term repeat revascularization compared with standard care (IRR 0.19; 95% CI 0.04–0.94; $P=0.04$).

All other findings were directionally consistent with the primary analysis, with only minor variations likely attributable to reduced statistical power after restricting the network, and no local inconsistency (Tables S13 through S16).

Similarly, the results of the repeated analysis, restricted to trials testing contemporary devices, were generally consistent with the main findings (Tables S17 through S20).

In a 1-stage Bayesian sensitivity analysis modeling arm-level event counts directly, effect estimates for the primary outcome were consistent in direction and magnitude with the primary analysis (Table S21). Across secondary and safety outcomes, point estimates were generally directionally concordant with the

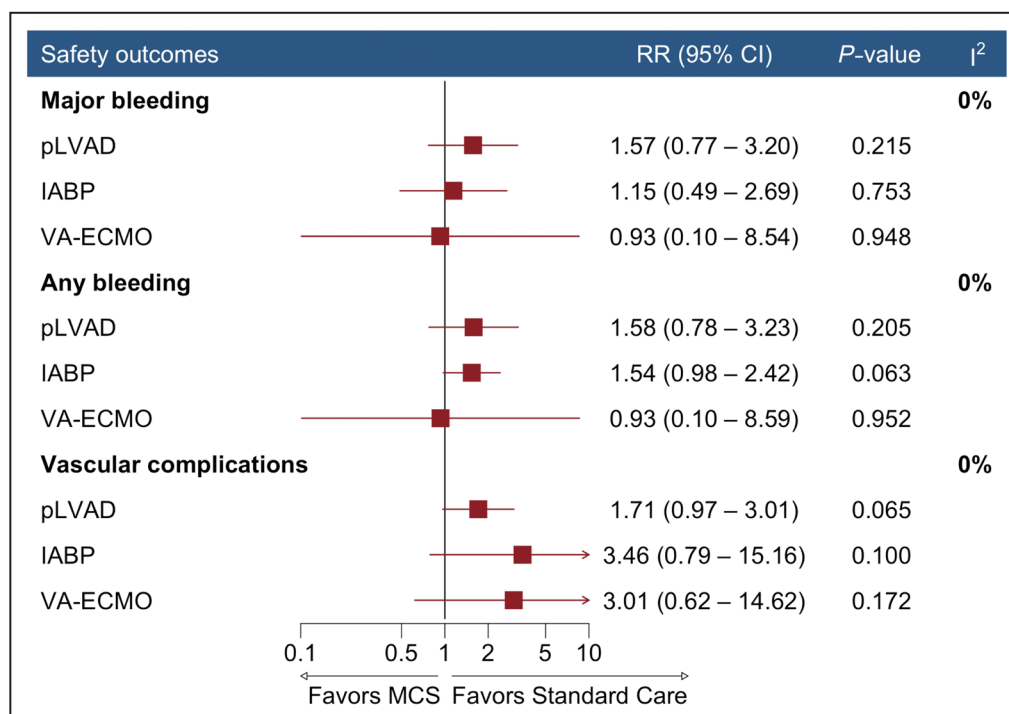


Figure 3. Forest plot presenting the results of network meta-analysis for the safety outcomes.

The forest plot presents network estimates for the comparisons of individual MCS devices with standard care. IABP indicates intra-aortic balloon pump; MCS, mechanical circulatory support; pLVAD, percutaneous left ventricular assist device; RR, risk ratio; and VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

primary 2-stage analysis; however, credible intervals were considerably wider for outcomes with few observed events, reflecting uncertainty in the estimates (Table S21).

In the exploratory pairwise meta-analysis, MCS increased the risk of any bleeding compared with standard care (RR 1.54; 95% CI 1.05–2.26; $P=0.03$), with no other significant differences in primary or secondary outcomes (Figure S5).

DISCUSSION

In this network meta-analysis of 8 randomized trials, including 1856 hemodynamically stable patients undergoing nonemergent CHIP, prophylactic MCS did not improve ischemic clinical outcomes compared with standard care, either in the early postprocedural phase or at the longest available follow-up. The absence of significant differences was consistent across MCS device classes for MACE and its major individual components, including death, myocardial infarction, stroke, and repeat revascularization. However, CIs for VA-ECMO were wide and compatible with both benefit and harm, such that only extreme effects could be excluded, reflecting its more limited evidence base. On the other hand, both pLVAD and IABP were associated with

fewer periprocedural major adverse events, comprising prolonged hypotension, malignant arrhythmia, and cardiopulmonary resuscitation, suggesting that temporary hemodynamic support may enhance hemodynamic stability during the procedure, although without translating into improved long-term clinical outcomes.

Unlike previous meta-analyses that incorporated both observational and randomized data, the present analysis was restricted to randomized trials to minimize confounding.^{20,21} Moreover, whereas prior evidence syntheses often combined cardiogenic shock and CHIP populations, we focused exclusively on hemodynamically stable patients undergoing nonemergent CHIP, a distinct clinical scenario in which MCS is used prophylactically during planned high-risk revascularization rather than as rescue therapy for overt hemodynamic collapse.²² In addition, by including the recent CHIP-BCIS3,¹⁴ the present analysis provides the most up-to-date overview of comparative evidence on preventive MCS use for CHIP. Importantly, the accrued sample size substantially exceeds that of the largest individual trial in this field,⁶ allowing a more precise and statistically robust assessment of clinically relevant outcomes.

The findings of the meta-analysis consistently reflect some important conclusions of landmark trials. In the

BCIS-1 (Balloon Pump-Assisted Coronary Intervention Study), elective IABP use did not improve early clinical outcomes, although a lower risk of death was later reported during long-term follow-up, but these results were based on administrative data rather than formal event adjudication.^{7,9} The mechanism underlying this late mortality finding remained unclear.^{7,9} Similarly, the PROTECT II (Prospective, Randomised Clinical Trial of Haemodynamic Support With Impella 2.5 Versus IABP in Patients Undergoing High-Risk PCI) showed no meaningful difference in early adverse events between Impella 2.5 and IABP, despite numerically favorable trends with pLVAD support at 90 days.^{6,8} More recently, the CHIP-BCIS3 trial extended these observations to Impella CP, again showing no reduction in major adverse clinical outcomes at a minimum follow-up of 12 months.¹⁴ Taken together, these trials suggest that the procedural hemodynamic advantages of MCS do not necessarily translate into fewer ischemic events in the long term.

The distinction between periprocedural hemodynamic stability and long-term prognosis remains clinically important. The reduction in periprocedural major adverse events observed with pLVAD and IABP is mechanistically plausible, as temporary support may attenuate the hemodynamic consequences of prolonged ischemia during complex procedural steps, including atherectomy, left main intervention, bifurcation treatment, or prolonged balloon inflations.³ However, long-term outcomes in CHIP are likely determined predominantly by factors extending beyond the procedure itself, including the severity of baseline ventricular dysfunction, residual coronary disease burden, completeness of revascularization, follow-on medication optimization, and non-cardiovascular comorbidities.¹ As a result, any procedural hemodynamic benefit may be diluted by these competing determinants of risk.

At the same time, any potential advantage must be interpreted alongside the possibility of device-related harm. Although no statistically significant differences in bleeding or vascular complications were observed, there were directional trends toward more vascular complications and more bleeding with MCS. Given that these outcomes were relatively infrequent and not uniformly reported across all trials, the absence of a significant difference should not be interpreted as evidence that excess harm is absent, particularly in the setting of large-bore support devices. Importantly, although there were directional trends toward more vascular and bleeding complications with MCS, these events did not necessarily translate into worse hard clinical outcomes in the present analysis. Nevertheless, it remains plausible that a reduction in procedure-related hemodynamic instability may, at least in part, be offset by access-site or bleeding complications, supporting careful patient selection for MCS based on procedural

complexity, anticipated hemodynamic vulnerability, and the risk of access-related complications. Whether future device and sheath miniaturization may mitigate these safety signals remains uncertain, although the development of lower-profile support systems, such as the 9 French Impella ECP, may potentially reduce access-site and vascular complications.⁴

Nonetheless, these data should not be interpreted as arguing against the selective use of MCS in all cases. Indeed, although the enrolled patients consistently represented a high-risk population with severely reduced left ventricular function and complex coronary anatomy, it remains possible that patients considered to be at the highest anticipated risk may have been underrepresented because prophylactic support was deemed necessary upfront. This is an inherent challenge in randomized CHIP studies and may reduce the ability to detect benefits in the subgroup most likely to derive them. In patients perceived to be at the highest procedural risk, the potential acute benefits of MCS, particularly avoiding severe hemodynamic compromise, may exert a greater influence than potential longer-term benefits related to more complete revascularization. However, previous large, randomized trials have not clearly identified such patients,¹⁴ and it remains uncertain whether ongoing studies will adequately clarify which specific clinical features, hemodynamic profiles, severity of left ventricular dysfunction, coronary anatomy, or a combination thereof define this population.

In addition, the recent CHIP-BCIS3 trial demonstrated similar rates of complete revascularization between study arms, although patients in the non-pLVAD arm more frequently underwent staged procedures.¹⁴ This observation raises the possibility that alternative strategies, including optimization of guideline-directed medical therapy before CHIP, intentional staging of procedures, improved preprocedural planning, and procedural techniques aimed at reducing ischemic time and burden, may reduce the need for prophylactic MCS in selected patients. Taken together, while the present analysis does not support routine prophylactic MCS use, a potential role in carefully selected patients cannot be excluded, particularly in the setting of limited hemodynamic reserve, poor tolerance to prolonged ischemia, or procedures in which the quality or completeness of revascularization might otherwise be compromised.⁴

An additional consideration relates to generalizability across device platforms. Although Impella CP is currently the most widely adopted support device in CHIP, it represented only a minority of supported patients in the present data set. Nevertheless, pLVADs not available in the United States or Europe that were included in the main analysis (and excluded in a pre-specified sensitivity analysis) shared a similar micro-axial design and provided comparable peak flow to

Impella CP,^{4,11–13} although direct randomized comparisons between those devices are lacking. Reassuringly, both sensitivity analyses, restricted to contemporarily available devices and to devices approved in the United States and Europe, remained generally directionally consistent with the primary findings. Within the latter restricted analysis, the isolated signal of lower repeat revascularization with pLVAD compared with standard care should be interpreted cautiously in an unblinded setting. Likewise, the apparent mortality excess in the pLVAD versus IABP comparison, but not relative to standard care, more likely reflects the difficult-to-interpret low mortality observed with IABP in the BCIS-1 trial, rather than a true adverse effect of pLVAD support.⁷

The ongoing PROTECT IV trial (NCT04763200), the largest randomized controlled trial in this field and the first adequately powered for long-term clinical outcomes, will provide important supplementary evidence.²³ By randomizing 1252 patients with complex coronary artery disease and reduced left ventricular ejection fraction who are deemed at excessive surgical risk, and by incorporating a 3-year composite end point including death, ischemic events, and heart failure hospitalizations, the trial is expected to clarify whether routine Impella CP support during high-risk PCI can improve long-term clinical outcomes.²³ Importantly, the trial also incorporates several mechanistic sub-studies, including an exploratory right heart catheterization hemodynamic sub-study designed to evaluate the prognostic utility of invasive hemodynamic assessment during high-risk PCI and its role in guiding MCS weaning, which may provide additional insights into patient selection and procedural management strategies.²³ Until those data become available, the present meta-analysis represents the most complete synthesis of randomized evidence in this setting.

This study has some limitations. First, as a trial-level meta-analysis, it was based on aggregate rather than patient-level data, limiting the ability to identify subgroups most likely to benefit from MCS. Similarly, the available data did not allow assessment of potential sex-, or race-related differences in the treatment effects of MCS among patients undergoing CHIP, although such disparities may influence outcomes in other high-risk settings, including acute myocardial infarction complicated by cardiogenic shock.²⁴ Second, definitions of MACE and periprocedural major adverse events varied across trials, although the consistency of findings across individual ischemic end points supports the robustness of the main conclusions. Third, local inconsistency was observed in selected network comparisons. However, the included trials applied broadly similar inclusion and exclusion criteria and enrolled clinically comparable CHIP populations, suggesting that these signals are more likely related to imprecision and sparse data than to a true violation

of transitivity. Fourth, although different devices were grouped within some MCS categories, their overall technical characteristics and hemodynamic support profiles were broadly similar. Finally, the evidence base remains limited for some device classes, particularly VA-ECMO, and CIs for several short-term outcomes, including safety end points, were wide, reflecting lower precision for these estimates despite synthesis of the total available randomized evidence.

CONCLUSIONS

In patients undergoing CHIP, prophylactic MCS with pLVAD or IABP was not associated with improved short- or long-term ischemic clinical outcomes, despite enhancing hemodynamic stability during the procedure. The effect of VA-ECMO remained unclear, with wide CIs reflecting limited evidence. Overall, these findings do not support routine prophylactic use and suggest that any potential role for MCS should be limited to highly selected patients.

ARTICLE INFORMATION

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Supplemental Material

PRISMA Checklist
Figures S1–S5
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REFERENCES

1. Protty M, Sharp ASP, Gallagher S, Farooq V, Spratt JC, Ludman P, Anderson R, McEntegart MM, Hanratty C, Walsh S, et al. Defining percutaneous coronary intervention complexity and risk: an analysis of the United Kingdom BCIS database 2006–2016. *JACC Cardiovasc Interv*. 2022;15:39–49. doi: [10.1016/j.jcin.2021.09.039](https://doi.org/10.1016/j.jcin.2021.09.039)
2. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, Banning AP, Budaj A, Buechel RR, Chiariello GA, et al. 2024 ESC guidelines for the management of chronic coronary syndromes. *Eur Heart J*. 2024;45:3415–3537. doi: [10.1093/eurheartj/ehae177](https://doi.org/10.1093/eurheartj/ehae177)

3. Schafer A, Alasnag M, Giaccoppo D, Collet C, Rudolph TK, Roguin A, Buszman PP, Collieran R, Stefanini G, Lefevre T, et al. High-risk percutaneous coronary intervention in patients with reduced left ventricular ejection fraction deemed not suitable for surgical revascularisation. A clinical consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) in collaboration with the ESC Working Group on Cardiovascular Surgery. *EuroIntervention*. 2025;21:22–34. doi: [10.4244/EIJ-D-23-01100](https://doi.org/10.4244/EIJ-D-23-01100)
4. Ferro EG, Kim JM, Lalani C, Abbott DJ, Yeh RW. Mechanical circulatory support for complex, high-risk percutaneous coronary intervention. *EuroIntervention*. 2025;21:e149–e160. doi: [10.4244/EIJ-D-24-00386](https://doi.org/10.4244/EIJ-D-24-00386)
5. Zelas A, Zajdel W, Malinowski K, Geremek J, Zmudka K. Circulatory support with larger volume intra-aortic balloon pump vs. standard volume or no-balloon pump during high-risk percutaneous coronary interventions. A randomised study. *Postępy Kardiologii Interwencyjnej*. 2020;16:30–40. doi: [10.5114/aic.2020.93910](https://doi.org/10.5114/aic.2020.93910)
6. Dangas GD, Kini AS, Sharma SK, Henriques JP, Claessen BE, Dixon SR, Massaro JM, Palacios I, Popma JJ, Ohman M, et al. Impact of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump on prognostically important clinical outcomes in patients undergoing high-risk percutaneous coronary intervention (from the PROTECT II randomized trial). *Am J Cardiol*. 2014;113:222–228. doi: [10.1016/j.amjcard.2013.09.008](https://doi.org/10.1016/j.amjcard.2013.09.008)
7. Perera D, Stables R, Clayton T, De Silva K, Lumley M, Clack L, Thomas M, Redwood S; Investigators B. Long-term mortality data from the balloon pump-assisted coronary intervention study (BCIS-1): a randomized, controlled trial of elective balloon counterpulsation during high-risk percutaneous coronary intervention. *Circulation*. 2013;127:207–212. doi: [10.1161/CIRCULATIONAHA.112.132209](https://doi.org/10.1161/CIRCULATIONAHA.112.132209)
8. O'Neill WW, Kleiman NS, Moses J, Henriques JP, Dixon S, Massaro J, Palacios I, Maini B, Mulukutla S, Dzavik V, et al. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. *Circulation*. 2012;126:1717–1727. doi: [10.1161/CIRCULATIONAHA.112.098194](https://doi.org/10.1161/CIRCULATIONAHA.112.098194)
9. Perera D, Stables R, Thomas M, Booth J, Pitt M, Blackman D, de Belder A, Redwood S; Investigators B. Elective intra-aortic balloon counterpulsation during high-risk percutaneous coronary intervention: a randomized controlled trial. *JAMA*. 2010;304:867–874. doi: [10.1001/jama.2010.1190](https://doi.org/10.1001/jama.2010.1190)
10. Pan C, Zhu Y, Zhao J, Zhang B, Hu S, Zhao C, Meng X, Zhou X, Su Y, Xing E, et al. Prophylactic VA-ECMO during complex high-risk PCI: a randomized controlled trial. *JACC Adv*. 2025;4:102095. doi: [10.1016/j.jaccadv.2025.102095](https://doi.org/10.1016/j.jaccadv.2025.102095)
11. Ge J. A novel microaxial flow pump versus VA-ECMO in high-risk PCI patients with severely reduced LVEF: a multicenter randomized controlled trial (PERSIST III Study). San Francisco, CA: TCT; 2025.
12. Wang R. SAVE-PCI: NyokAssist small-bore VAD vs. IABP in elective high-risk PCI. San Francisco, CA: TCT; 2025.
13. Gao C, Tao L. mAFF versus VA-ECMO for patients with high-risk PCI (REC-CHIPMCS): a multicenter, non-inferiority trial. San Francisco, CA: TCT; 2025.
14. Perera D, Ryan M, Ezad SM, Khan SQ, Webb I, O'Kane PD, Weerackody R, Dodd M, Kwok M, Laidlaw L, et al. Left ventricular unloading in high-risk percutaneous coronary intervention. *N Engl J Med*. 2026;394:1779–1789. doi: [10.1056/NEJMoa2515704](https://doi.org/10.1056/NEJMoa2515704)
15. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, Ioannidis JP, Straus S, Thorlund K, Jansen JP, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med*. 2015;162:777–784. doi: [10.7326/M14-2385](https://doi.org/10.7326/M14-2385)
16. Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898. doi: [10.1136/bmj.l4898](https://doi.org/10.1136/bmj.l4898)
17. Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, Onuma Y, Morel MA, van Es GA, Zuckerman B, et al. Standardized end point definitions for coronary intervention trials: the academic research Consortium-2 consensus document. *Eur Heart J*. 2018;39:2192–2207. doi: [10.1093/eurheartj/ehy223](https://doi.org/10.1093/eurheartj/ehy223)
18. Rucker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I(2) in assessing heterogeneity may mislead. *BMC Med Res Methodol*. 2008;8:79. doi: [10.1186/1471-2288-8-79](https://doi.org/10.1186/1471-2288-8-79)
19. Salanti G, Nikolakopoulou A, Efthimiou O, Mavridis D, Egger M, White IR. Introducing the treatment hierarchy question in network meta-analysis. *Am J Epidemiol*. 2022;191:930–938. doi: [10.1093/aje/kwab278](https://doi.org/10.1093/aje/kwab278)
20. Xu H, Guo W, Chou OHI, Tse G, Li G, Liu T, Fu H. Comparative effectiveness of mechanical circulatory support devices in patients undergoing complex high-risk percutaneous coronary interventions (CHIP): a systematic review and network meta-analysis. *Catheter Cardiovasc Interv*. 2025;106:1263–1272. doi: [10.1002/ccd.31678](https://doi.org/10.1002/ccd.31678)
21. Elbenawi H, Doma M, Cangut B, Abdelgalil MS, Khlidj Y, Thakurathi P, Hammad A, Mohammed F, Almaadawy O, Farhoud H, et al. Percutaneous micro-axial flow pump use during non-emergent high-risk PCI: systematic review and meta-analysis. *Cardiovasc Revasc Med*. 2025;85:104–112. doi: [10.1016/j.carrev.2025.10.019](https://doi.org/10.1016/j.carrev.2025.10.019)
22. Kuno T, Takagi H, Ando T, Kodaira M, Numasawa Y, Fox J, Bangalore S. Safety and efficacy of mechanical circulatory support with Impella or intra-aortic balloon pump for high-risk percutaneous coronary intervention and/or cardiogenic shock: insights from a network meta-analysis of randomized trials. *Catheter Cardiovasc Interv*. 2021;97:E636–E645. doi: [10.1002/ccd.29236](https://doi.org/10.1002/ccd.29236)
23. Mangner N, Sharma SK, O'Connor C, Kaki A, Dangas GD, Moses JW, Mahmud E, Tarantini G, Achenbach S, Pocock SJ, et al. Mechanical circulatory support in high-risk elective PCI: rationale and design of the PROTECT IV trial. *EuroIntervention*. 2025;21:e1244–e1258. doi: [10.4244/EIJ-D-25-00486](https://doi.org/10.4244/EIJ-D-25-00486)
24. Ya'qoub L, Lemor A, Dabbagh M, O'Neill W, Khandelwal A, Martinez SC, Ibrahim NE, Grines C, Voeltz M, Basir MB. Racial, ethnic, and sex disparities in patients with STEMI and cardiogenic shock. *JACC Cardiovasc Interv*. 2021;14:653–660. doi: [10.1016/j.jcin.2021.01.003](https://doi.org/10.1016/j.jcin.2021.01.003)