Clinical use and impact of mechanical circulatory support for myocardial infarction-related cardiogenic shock in the Netherlands: a registry-based propensity-matched analysis

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openheart

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► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/openhrt-2024-002846).

To cite: Bogerd M, Griffioen AM, Bunge JJH, *et al*. Clinical use and impact of mechanical circulatory support for myocardial infarction-related cardiogenic shock in the Netherlands: a registry-based propensity-matched analysis. *Open Heart* 2025;**12**:e002846. doi:10.1136/openhrt-2024-002846

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Received 15 July 2024
Accepted 25 July 2024

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ABSTRACT

Background Despite limited beneficial evidence, mechanical circulatory support (MCS) is commonly used in patients with acute myocardial infarction-related cardiogenic shock (AMI-CS). In this Dutch registry, we investigated MCS usage, associated patient characteristics and clinical outcomes.

Methods This real-world, multicentre registry included CS patients undergoing percutaneous coronary intervention between 2017 and 2021 in 14 Dutch hospitals. The impact on clinical outcomes was analysed after 1:1 average propensity-score (aPS) matching.

Results This AMI-CS registry included 2217 patients with a mean age of 66.4 (±12.3) years and predominantly male (72.8%, n=1613). MCS was deployed in 516 patients (23.3%), of which the intra-aortic balloon pump was used most frequently (n=253, 49.0%). Impella was used in 94 patients (18.2%), extracorporeal membrane oxygenation in 68 patients (13.2%) and 95 patients (18.4%) received multiple devices. Patients receiving MCS were younger (64.2 vs 67.0, p<0.01), presented with lower mean arterial pressures (74.7 vs 78.4 mm Hg, p<0.01), higher heart rates (88.3 vs 81.7 beats per minute, p<0.01) and higher initial lactate levels (6.4 vs 5.4 mmol/L, p<0.01). The percentage of resuscitated patients was comparable among MCS and non-MCS patients (38.6% vs 42.2%, p=0.17). The 30-day mortality rate was higher in MCS patients (55.0% vs 34.7%, p<0.01). After aPS-matching (n=970), 30-day mortality remained higher for MCS patients (53.8% vs 44.7%, p<0.01), with an associated OR of 1.44 (95% CI 1.12 to 1.85, p<0.01).

Conclusions Despite limited evidence, MCS was used in a fourth of all AMI-CS patients. MCS usage was associated with an increased 30-day mortality in this real-world setting, even after propensity-matching.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Mechanical circulatory support (MCS) usage is rising, despite limited evidence of benefit.
⇒ Only the recently published DanGer Shock trial demonstrated survival improvement with Impella in a highly selected, non-comatose cardiogenic shock (CS) population.

WHAT THIS STUDY ADDS

⇒ In the Netherlands, one in every four acute myocardial infarction-related CS patients received MCS. The intra-aortic balloon pump was used most often.
⇒ The present average propensity-score-matched analysis describes real-world data of an unselected cohort outside a trial setting. Here, MCS usage was associated with a higher 30-day mortality, even after extensive confounder control.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results of this study advocate a thorough risk–benefit assessment of MCS in every individual.
⇒ Identifying patients who have the potential to benefit from MCS remains a challenge and should be the focus of future research.

INTRODUCTION

Cardiogenic shock (CS) is described as a life-threatening condition of hypoxaemia and end-organ hypoperfusion and is caused by low-cardiac output.[1] Although acute myocardial infarction (AMI) is the primary cause of CS, the presence of CS is only observed in 3%–10% of all AMI patients.[2–5] Whereas mortality rates of AMI without CS have decreased over the years, mortality rates in

patients with CS due to AMI (AMI-CS) continue to linger around 40%–50%.[4–6]

Mechanical circulatory support (MCS) seems an intuitive manner to assist the endangered circulation in AMI-CS patients. Around 20%–25% of the AMI-CS patients in Europe are treated with MCS devices, including the intra-aortic balloon pump (IABP), Impella, venoarterial-extracorporeal membrane oxygenation (VA-ECMO) or a combination of the aforementioned devices.[7 8] In the USA, around 40% of the AMI-CS patients receive MCS.[9] Since the results of the IABP-SHOCK-II trial, the use of IABP has rapidly decreased in the setting of AMI-CS.[7 10 11] The use of Impella and VA-ECMO on the other hand has been increasing ever since.[11–14] The evidence from randomised studies supporting the usage of MCS devices in patients suffering from AMI-CS is, however, limited. In fact, randomised controlled trials (RCTs) evaluating routine use of MCS, including IABP and VA-ECMO, in AMI-CS patients have not shown any survival benefit.[12 15–17] Only the recently published, long-awaited, DanGer Shock trial demonstrated a survival benefit at 180 days of Impella over standard of care alone (SOC) in a highly selected ST-elevation myocardial infarction (STEMI) CS population.[18] This study is only recently published and various subanalyses will be needed to understand its implications for the overall field of CS.

Data on patient and procedural characteristics and clinical outcomes in patients receiving MCS in the Netherlands are scarce. Obtaining a better understanding of the treatment of AMI-CS patients, specifically the use of MCS, could aid clinical decision-making and create awareness for clinical outcomes. This large, real-world retrospective registry, therefore, has three objectives. First, to evaluate the extent of use of different MCS devices in AMI-CS patients in the Netherlands. Second, to identify patient characteristics associated with MCS usage and third, to evaluate and compare clinical outcomes of MCS and non-MCS patients in a real-world setting.

METHODS

Study design and population

Data on the baseline characteristics and outcomes of the overall AMI-CS cohort have previously been published.[19] In short, all patients undergoing percutaneous coronary intervention (PCI) in the Netherlands are prospectively registered in the National Netherlands Heart Registration (NHR), in which baseline, procedural and outcome data are collected.[20] Online supplemental table 1 includes all PCI centres participating in this NHR registration. To perform an observational retrospective study including patients with CS undergoing PCI, patients with CS undergoing PCI between January 2017 and September 2021 were identified through this registration. The CS diagnoses were made by local clinicians at the time of hospitalisation, based on the following definition: 'the presence of hypotension (systolic blood pressure (SBP) ≤90 mm Hg for ≥30 min or support to maintain SBP ≥90 mm Hg) and end-organ hypoperfusion (cold extremities and/or oliguria <30 mL/hour and/or heart rate ≥60 beats per minute)'. For the present NHR-CS registry, additional variables were retrospectively collected for the identified CS patients in 14 hospitals, including data on the use and type of MCS.

Patient and public involvement

This observational, retrospective study was conducted in collaboration with the NHR. Patients were not involved in the study design, conduct or result dissemination.

Statistical analysis

Normally distributed variables were displayed using mean and standard deviation (SD) and statistical differences were assessed using the two-samples t-test. Non-normally distributed variables were displayed as median and interquartile ranges (IQRs) and statistical differences were assessed using the Mann-Whitney U test. Binary and categorical variables were displayed as counts and percentages and statistical differences were assessed using the χ^2 test. Associations with 30-day mortality from any cause were assessed using univariate logistic regression analysis. Multivariable logistic regression and propensity-score matching analysis were used to assess the association between MCS and 30-day mortality while adjusting for measured confounders. To this end, missing data were imputed using multiple imputation by chained equation using the R-package mice V.3.15.0. Variables with low outflux (outflux <0.5) were removed before imputation. The Nelson-Aalen estimate was calculated and used as one of the standard predictors together with age, the event-indicator (30-day mortality) and device usage for all models. The average number of predictors was set to 25. Using predictive mean matching, 30 imputed datasets were generated.

Propensity scores for each record were calculated using the R-package MatchThem. Propensity-score calculations were based on the following variables: (1) demographic characteristics: age and sex, (2) characteristics regarding medical history: renal function, body mass index (BMI) and diabetes, (3) clinical presentation characteristics: duration of complaints, (non-)STEMI ((N)STEMI) aetiology, presence of out-of-hospital cardiac arrest (OHCA), whether it was witnessed and the duration of OHCA till the return of spontaneous circulation, mean arterial pressure, heart rate, haemoglobin levels, lactate levels, glucose levels and creatinine levels, the presence of in-hospital cardiac arrest (IHCA) prior to PCI and at the catheterisation laboratory, inotropes and vasopressors used before PCI and whether the patient was intubated before admission to the intensive care unit or cardiac care unit and (4) angiographic characteristics: the target vessel treated with PCI and whether Thrombolysis in Myocardial Infarction (TIMI) 3 flow was achieved. The propensity scores were then averaged across the imputed data sets.[21] The averaged propensity scores (aPSs) were used to match patients with MCS to patients without MCS in a 1:1 ratio

with a calliper of 0.10, using the R-package MatchIt. The balance of potential confounders was assessed using the absolute standardised mean difference (SMD). An SMD <0.1 indicates a negligible difference between the two groups.

For both the unmatched and aPS-matched cohorts, the Kaplan-Meier method was used to construct survival curves. The proportional hazards assumption was not met based on the Schoenfeld-residuals method. Therefore, no hazard ratios (HRs) are presented. The log-rank statistic is presented, indicating the presence of an overall difference, with a p<0.05 considered statistically significant.

Subgroup analysis in the aPS-matched cohort was performed for predefined subgroups including age (below or above 65 years old), sex, BMI (below or above 30 kg/m^2), history of diabetes, the presence of OHCA, NSTEMI or STEMI aetiology, admission lactate level (below or above 6.5 mmol/L), mechanical ventilation, the presence of multivessel disease and left main PCI, using logistic regression analyses including the interaction terms between MCS usage and the variables indicating the subgroup. The reported p values represent the p value of the interaction term. An interaction p<0.05 indicates that the association of MCS usage with 30-day mortality differs significantly between the subgroups.

Statistical analyses were performed by using the statistical software R V.4.1.3 (R Foundation for Statistical Computing, https://www.R-project.org)[22]

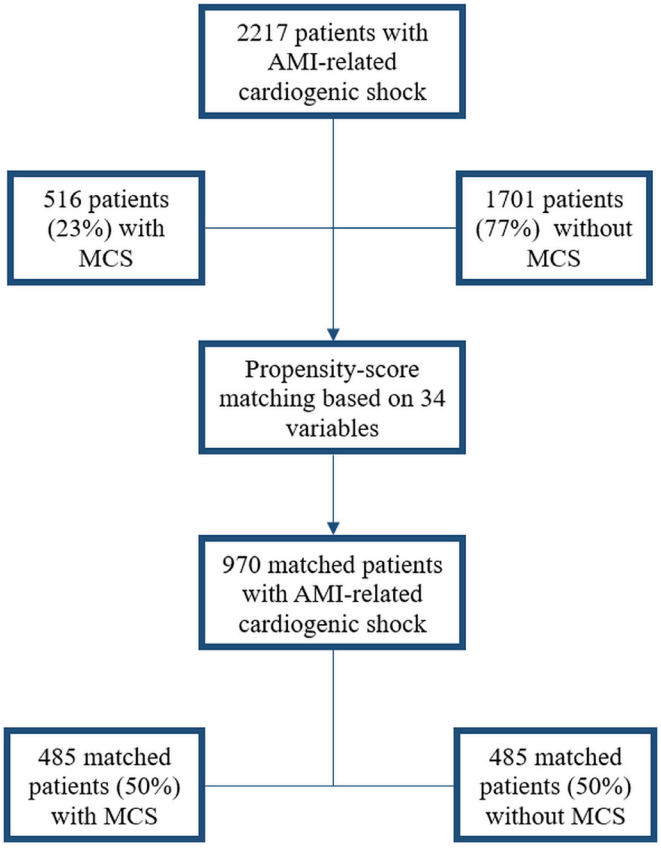

Figure 1 Study flow chart. AMI, acute myocardial infarction; MCS, mechanical circulatory support; (N)STEMI, (non-)ST-elevated myocardial infarction.

RESULTS

The cohort consists of 2217 AMI-CS patients with data on device status and 30-day mortality registered. Of these AMI-CS patients, 23.3% (n=516) received MCS (figure 1). In the overall cohort, AMI-CS patients had a mean age of 66.4 (±12.3) years and 72.8% (n=1613) were male ((Visual summary). Patients predominantly presented with STEMI (86.1%) and with a duration of symptoms less than 3 hours (59.1%). OHCA occurred in 914 patients (41.3%). The baseline lactate value was 5.6 (2.7–9.5) mmol/L (online supplemental table 2).

In the unmatched cohort, patients who received MCS were younger (64.2 vs 67.0, p<0.01), presented less often with a symptom duration of below 3 hours (49.4% vs 62.0%, p<0.01), presented with lower mean arterial pressures (74.7 vs 78.4 mm Hg, p<0.01), higher heart rates (88.3 vs 81.7 beats per minute, p<0.01) and a higher initial lactate levels (6.4 vs 5.4 mmol/L, p<0.01) (visual summary). The number of patients who presented after an OHCA was similar between MCS and non-MCS patients, namely 38.6% and 42.2%, respectively (p=0.17). Although there is a significant shift in usage of IABP towards Impella, ECMO or a combination of devices over the years (IABP: p<0.001) (figure 2), the majority of MCS patients in this cohort (n=253, 49.0%) received an IABP. The Impella device was used in 94 patients (18.2%) and ECMO was deployed in 68 patients (13.2%). A combination of multiple devices (simultaneously or consecutively) was used in 95 patients (18.4%) (table 1). The baseline characteristics per device category can be found in online supplemental table 3A.

Patients with MCS had significantly higher levels of peak troponin (9796 vs 3033 ng/L, p<0.01), CK-MB (454 vs 180 IU/I, p<0.01) and lactate levels after PCI (4.1 vs 2.7 mmol/L, p<0.01). Moreover, MCS patients had longer lengths of hospital stay (6.0 vs 5.0 days, p=0.05) and higher 30-day mortality rates (55.0% vs 34.7%, p<0.01) (visual summary, table 2 and figure 3A). The unadjusted odds ratio (OR) for 30-day mortality for patients with MCS compared with patients without MCS was 2.30 (95% CI 1.88 to 2.81). Moreover, 30-day mortality was highest in patients treated with multiple devices (66.3%), followed by VA-ECMO-supported patients (60.3%), Impella-supported patients (56.4%) and lastly IABP-supported patients (48.6%) (online supplemental table 4A). Online supplemental figure 1A illustrates Kaplan-Meier (KM) curves for each device, including the unadjusted ORs.

Multivariable analysis was performed to adjust for relevant confounders (online supplemental table 5). In adjustment for various confounders, the use of MCS in AMI-CS patients was associated with a 67% higher risk of 30-day mortality, compared with non-MCS patients (OR 1.67 (95% CI 1.19 to 2.35)).

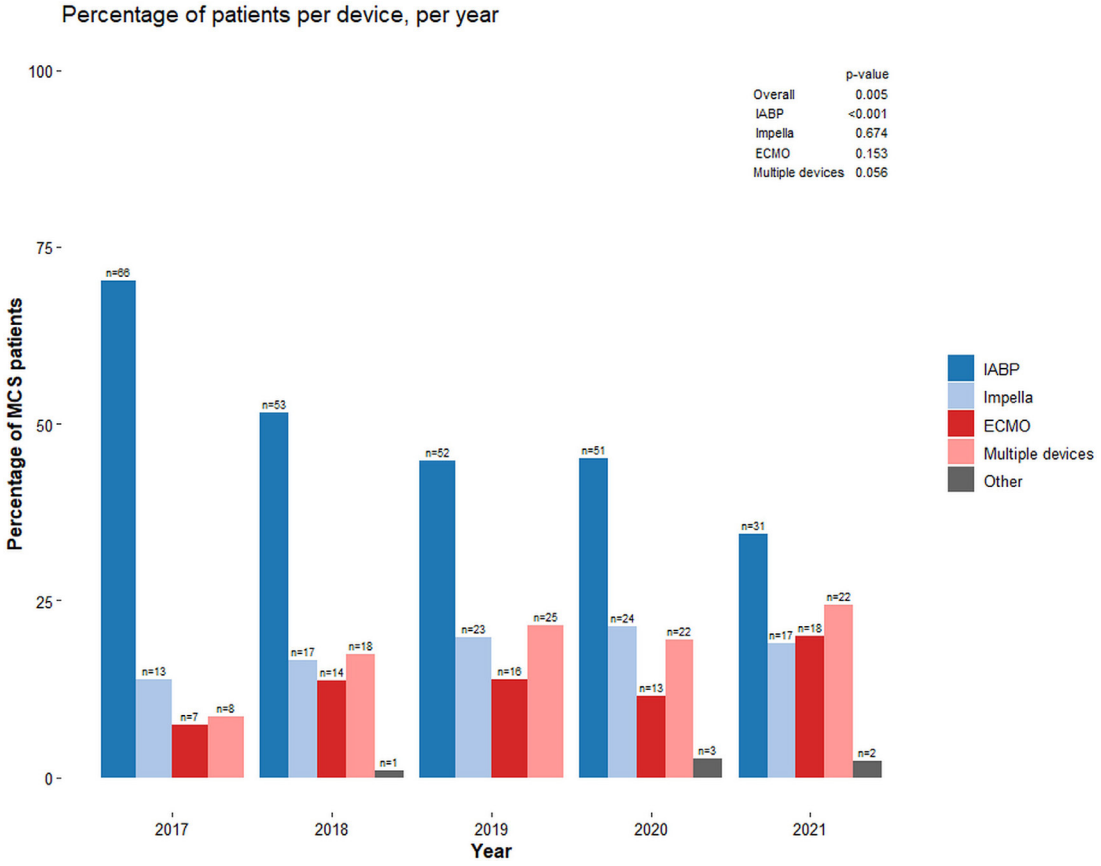

Figure 2 Use of MCS devices. ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support.

Propensity-score-matched analysis

aPS-matching resulted in 970 AMI-CS patients, of whom 485 patients received MCS and 485 patients did not. Baseline and angiographic characteristics were well distributed between MCS and non-MCS patients, as illustrated in table 1. The majority of patients with MCS received IABP (50.3%). Impella was used in 91 patients (18.8%) and VA-ECMO in 60 patients (12.4%). A combination of multiple devices was used in 17.3% of the MCS population. The baseline characteristics per device of the matched cohort can be found in online supplemental table 3B.

After aPS-matching, patients who received MCS showed significantly higher values of troponin (9390 vs 3715 ng/L, p<0.01), CK-MB (449 vs 205 IU/I, p<0.01) and lactate levels after PCI (4.0 vs 3.0 mmol/L, p<0.01). The difference in length of stay became more outspoken (7.0 vs 4.0 days, p<0.01). The 30-day mortality difference observed in the unmatched cohort persisted after aPS-matching, namely 53.8% in the MCS patients and 44.7% in the non-MCS patients (visual summary, table 2 and figure 3B). The 30-day mortality was still highest in patients treated with multiple devices (64.3%), followed by VA-ECMO-supported patients (60.3%), Impella-supported patients (56.0%) and lastly IABP-supported patients (47.5%) (online supplemental table 4B). In the matched cohort, the OR of MCS on 30-day mortality was 1.44 (95% CI 1.12 to 1.85, p<0.01). Compared with no device, the OR of IABP on 30-day mortality was 1.12 (95% CI 0.82 to 1.52), whereas the OR of Impella and ECMO were 1.57 (95% CI 1.00 to 2.48) and 1.85 (95% CI 1.08 to 3.23), respectively. Multiple devices exhibited an OR of 2.22 (95% CI 1.38 to 3.63) (online supplemental figure 1B—KM-curves per device).

Subgroup analyses

No significant subgroup differences in the association between MCS and 30-day mortality were found in the matched cohort, as apparent from the non-significant interaction terms (figure 4). The OR of MCS on 30-day mortality for each subgroup is illustrated in figure 4.

DISCUSSION

To our knowledge, this study describes the largest PS-matched (n=970) analysis of MCS versus non-MCS in the setting of AMI-CS in Europe. In addition, meticulous (measured) confounder control was used for this aPS-matched analysis. Beyond demographic factors, matching parameters encompassed indicators of shock severity, particular risk modifiers and angiographic measurements.

Table 1 Baseline characteristics

	Unmatched study cohort				Matched study cohort		
	No MCS (n=1701)	MCS (n=516)	P value	Missing data	No MCS (n=485)	MCS (n=485)	SMD
Demographics							
Age, years (±SD)	67.0 (±12.9)	64.2 (±12.5)	<0.01	0.0%	64.2 (±13.1)	64.6 (±12.2)	0.03
Male, n (%)	1228 (72.2)	385 (74.6)	0.305	0.0%	363 (74.8)	361 (74.4)	<0.01
Medical history							
Diabetes, n (%)	323 (19.8)	115 (23.6)	0.08	4.6%	120 (25.8)	110 (24.1)	0.04
eGFR<60 mL/min, n (%)	704 (45.2)	256 (53.8)	<0.01	8.2%	251 (57.2)	239 (53.3)	0.08
Prior coronary event*, n (%)	449 (28.4)	127 (27.1)	0.61	7.6%	124 (27.8)	119 (27.0)	0.02
BMI, kg/m^2 (± SD)	26.6 (±4.5)	27.0 (±4.7)	0.14	18.4%	27.1 (±4.8)	26.9 (±4.7)	0.03
Clinical presentation							
STEMI, n (%)	1466 (86.2)	443 (85.9)	0.91	0.0%	412 (84.9)	417 (86.0)	0.03
Duration of symptoms							
<3 hours	912 (62.0)	217 (49.4)	<0.01	13.8%	208 (49.6)	205 (49.8)	<0.01
≥12 hours	288 (19.6)	127 (28.9)	<0.01	13.8%	117 (27.9)	117 (28.4)	<0.01
OHCA, n (%)	716 (42.2)	198 (38.6)	0.17	0.3%	191 (39.4)	187 (38.8)	0.01
OHCA witnessed, n (%)			0.04	1.6%			0.01
Unwitnessed	111 (6.6)	26 (5.2)			26 (5.4)	25 (5.3)	
Witnessed	579 (34.5)	150 (29.8)			146 (30.5)	142 (30.1)	
OHCA duration, n (%)			<0.01	4.2%			0.06
<30 min	516 (31.5)	93 (19.1)			84 (18.3)	91 (20.0)	
≥30 min	150 (9.2)	75 (15.4)			78 (15.1)	68 (14.9)	
IHCA, n (%)	211 (12.5)	70 (13.6)	0.55	0.4%	73 (15.1)	65 (13.4)	0.05
MAP, mm Hg (± SD)	78.4 (±24.0)	74.7 (±24.2)	<0.01	12.9%	76.0 (±23.4)	75.4 (±24.3)	0.02
Heart rate, bpm (± SD)	81.7 (±28.8)	88.3 (±28.7)	<0.01	13.8%	90.0 (±30.9)	88.2 (±29.0)	0.06
Haemoglobin at admission, mmol/L (±SD)	8.3 (±1.4)	8.3 (±1.5)	0.91	4.9%	8.4 (±1.4)	8.3 (±1.4)	0.03
Glucose at admission, mmol/L (IQR)	11.8 (8.7–16.6)	13.5 (9.6–19.0)	<0.01	11.0%	13.9 (9.7–19.4)	13.5 (9.6–18.8)	0.08
Lactate at admission, mmol/L (IQR)	5.4 (2.5–9.0)	6.4 (3.4–11.4)	<0.01	34.2%	7.3 (3.2–11.2)	6.3 (3.2–10.5)	0.07
Creatinine at admission, mmol/L (IQR)	99.0 (81.0–121.0)	104.0 (84.0–128.0)	<0.01	9.0%	107.0 (87.3–128.8)	104.0 (84.5–127.0)	0.05
Mechanical ventilation, n (%)							
Intubated before PCI	762 (45.0)	239 (46.5)	0.587	0.5%	230 (47.6)	227 (47.0)	0.01
Intubated at cathlab	755 (44.7)	300 (58.4)	<0.01	0.7%	274 (57.3)	271 (56.1)	0.03
Inotropes before PCI, n (%)							
Norepinephrine	505 (30.2)	205 (40.4)	<0.01	1.7%	187 (39.5)	186 (39.0)	<0.01
Dobutamine	94 (5.6)	65 (12.8)	<0.01	1.4%	60 (12.7)	56 (11.8)	0.03
Enoximone/milrinone	70 (4.2)	55 (10.8)	<0.01	1.0%	52 (10.9)	46 (9.6)	0.04
Epinephrine	480 (29.1)	157 (31.4)	0.34	2.9%	160 (34.2)	147 (31.3)	0.06
Dopamine	11 (0.7)	2 (0.4)	0.74	1.0%	1 (0.2)	2 (0.4)	0.04
Periprocedural cardiac arrest, n (%)	294 (17.3)	151 (29.3)	<0.01	0.3%	143 (29.6)	133 (27.5)	0.05
LVEF†, % (± SD)	36.3 (± 11.1)	29.9 (± 10.9)	<0.01	46.7%	32.1 (± 10.7)	30.3 (± 10.96)	0.17
Angiographic characteristics							
Multivessel disease, n (%)	981 (58.2)	354 (68.7)	<0.01	0.7%	332 (69.5)	327 (67.6)	0.04
PCI performed, n (%)							
LM	169 (10.9)	110 (24.0)	<0.01	9.3%	94 (21.8)	94 (21.8)	<0.01
LAD	673 (43.4)	242 (52.7)	<0.01	9.3%	236 (54.8)	227 (52.7)	0.04
LCx	327 (21.1)	124 (27.0)	<0.01	9.3%	106 (24.6)	117 (27.1)	0.06

Continued

Table 1 Continued

	Unmatched study cohort				Matched study cohort		
	No MCS (n=1701)	MCS (n=516)	P value	Missing data	No MCS (n=485)	MCS (n=485)	SMD
RCA	623 (40.1)	135 (29.4)	<0.01	9.3%	115 (26.7)	132 (30.6)	0.09
Graft	23 (1.5)	6 (1.3)	0.96	9.3%	4 (0.9)	6 (1.4)	0.04
TIMI three flow after PCI, n (%)	1207 (81.6)	342 (78.8)	0.23	13.7%	325 (80.4)	317 (78.1)	0.06
Mechanical circulatory support devices							
Device type, n (%)			<0.01	3.0%			N/A
ECMO, n (%)	0 (0.0)	68 (13.2)			0 (0.0)	60 (12.4)	
IABP, n (%)	0 (0.0)	253 (49.0)			0 (0.0)	244 (50.3)	
Impella, n (%)	0 (0.0)	94 (18.2)			0 (0.0)	91 (18.8)	
Multiple devices, n (%)	0 (0.0)	95 (18.4)			0 (0.0)	84 (17.3)	
Other, n (%)	0 (0.0)	6 (1.2)			0 (0.0)	6 (1.2)	
No device, n (%)	1701 (100.0)	0 (0.0)			485 (100.0)	0 (0.0)	
Time of MCS implantation, n (%)			<0.01	2.0%			N/A
Before arrival at cathlab	0 (0.0)	76 (14.9)			0 (0.0)	71 (14.8)	
At cathlab	0 (0.0)	374 (73.2)			0 (0.0)	348 (72.6)	
After departure from cathlab	0 (0.0)	60 (11.7)			0 (0.0)	60 (12.5)	

*Prior coronary event includes prior myocardial infarction and/or prior coronary revascularisation with PCI or CABG.
†LVEF measured 2 hours before up to 24 hours after PCI.
BMI, body mass index; CABG, Coronary artery bypass grafing; ECMO, extracorporeal membrane oxygenation; eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pump; IHCA, in-hospital cardiac arrest; LAD, left anterior descending; LCx, left circumflex; LM, left main; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; MCS, mechanical circulatory support; NA, not applicable; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; RCA, right coronary artery; SMD, standardised mean difference; STEMI, ST-elevated myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

Overall, 23% of the AMI-CS patients in this cohort received a form of MCS. Patients who received MCS were younger, often had longer duration of complaints and had a worse haemodynamic profile including higher lactate levels on admission, compared with patients not receiving MCS. The number of resuscitated patients prior to admission was similar in the MCS and non-MCS cohort. Importantly, patients who received MCS had a higher 30-day mortality. After aPS-matching, MCS patients still had a 44% higher risk of mortality in the first 30 days after the onset of AMI-CS. Although the use of IABP was demonstrated to have no effect, more invasive devices such as Impella and ECMO imply even an harmful effect on 30-day mortality. Subgroup analyses in the matched cohort did not reveal significant interactions between various subgroups and 30-day mortality, indicating an overall association between MCS and a higher 30-day mortality.

Currently, the evidence from randomised studies supporting the usage of MCS devices in patients suffering from AMI-CS is limited. The IABP-SHOCK-II trial (n=600) evaluating IABP in AMI-CS patients and the ECLS-SHOCK (n=420) evaluating VA-ECMO in AMI-CS patients showed no clinical outcome improvements associated with device usage.[12 15 17] The recently published, long-awaited, DanGer Shock trial (n=360) demonstrated a survival benefit of Impella over SOC, although in a highly selected STEMI-CS population.[18]

Nonetheless, our study shows that MCS devices were used in 23% of the Dutch AMI-CS cases, which is comparable with other European countries[7 8] and slightly less compared with the USA.[9] Unlike several other European countries, the utilisation of the IABP in the Netherlands remains notably high as approximately 35%–70% of the MCS devices used were IABP, as illustrated in figure 2. This is in contrast to the widespread abandonment of IABP in other European nations following the publication of the IABP-SHOCK-II trial.[7 11 23] The enduring popularity of IABP in the Netherlands might be attributable to its relatively low costs, low complication rate and ease of use compared with Impella and VA-ECMO. In addition, it is mandatory for all Dutch PCI centres to have an IABP available. Noteworthy, the current ESC guidelines assign a class 3 indication for the use of IABP in the setting of AMI-CS, whereas Impella and VA-ECMO hold a class 2b recommendation in the same guideline. This guideline does, however, not yet incorporate the most recent RCTs evaluating VA-ECMO nor Impella in the setting of AMI-CS.[24]

In contrast to the neutral effect of IABP and VA-ECMO on 30-day mortality found in two well-powered RCTs and the observed benefit of Impella on 180-mortality in

Table 2 Clinical course

	Unmatched study cohort				Matched study cohort		
	No MCS (n=1701)	MCS (n=516)	P value	Missing data	No MCS (n=485)	MCS (n=485)	P value
Postprocedural treatment							
Inotropes after PCI, n (%)							
Norepinephrine	1080 (64.6)	425 (83.3)	<0.01	1.7%	352 (73.8)	396 (83.2)	<0.01
Dobutamine	396 (23.7)	251 (49.8)	<0.01	2.0%	128 (27.1)	232 (49.1)	<0.01
Enoximone/milrinone	215 (12.9)	192 (37.9)	<0.01	1.4%	95 (20.1)	174 (36.6)	<0.01
Epinephrine	183 (11.1)	128 (25.4)	<0.01	2.4%	93 (20.1)	115 (24.4)	0.04
Dopamine	36 (2.2)	10 (2.0)	0.45	1.5%	7 (1.5)	10 (2.1)	0.25
Laboratory values							
Troponin*, ng/L (IQR)	3033 (703–8350)	9796 (1996–20363)	<0.01	16.6%	3715 (1098–9178)	9390 (1981–20100)	<0.01
CK-MB*, IU/L (IQR)	180 (61–380)	454 (160–736)	<0.01	50.9%	205 (77–529)	449 (167–731)	<0.01
Lactate after PCI†, mmol/L (IQR)	2.7 (1.7–4.6)	4.1 (2.3–7.2)	<0.01	37.0%	3.0 (2.0–5.7)	4.0 (2.3–7.1)	<0.01
Clinical outcome							
Admission duration, days (IQR)	5.0 (2.0–11.0)	6.0 (1.0–15.3)	0.05	22.5%	4.0 (1.0–10.0)	7.0 (1.0–16.0)	<0.01
Permanent VAD, n (%)	4 (0.2)	13 (2.5)	<0.01	0.0%	4 (0.8)	12 (2.5)	0.08
HTx, n (%)	0 (0.0)	3 (0.6)	0.01	0.0%	0 (0.0)	3 (0.6)	0.25
Mortality after 30 days, n (%)	591 (34.7)	284 (55.0)	<0.01	0.0%	217 (44.7)	261 (53.8)	<0.01
Mortality after 365 days, n (%)	487 (40.6)	225 (56.1)	<0.01	27.8%	178 (51.3)	211 (55.5)	0.29

*Highest value within 1–3 days after admission.
†Highest value within 6–24 hours after PCI.
HTx, heart transplantation; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention; VAD, ventricular assist device.

the DanGer Shock trial,[12 15 17 18] this aPS-matched analysis demonstrated that MCS usage was associated with a higher 30-day mortality. This association appeared approximately 7 days after MCS device implantation. Possibly, these findings are due to residual unmeasured and, therefore, unmatched confounding. However, several other reasons might also explain these differences in outcome between the aforementioned RCTs and this aPS-matched analysis. The present aPS-matched analysis describes real-world data of an unselected cohort outside a trial setting. While the DanGer Shock trial handled very strict patient-selection criteria, MCS devices might be applied too often in patients unable to benefit from it in the real world. Perhaps, the increased mortality after 7 days is merely a reflection of the expanded survival in patients who were actually beyond survival from the start. In a trial setting, patients are often extensively monitored, which may result in lower adverse event rates compared with the 'actual' rates. High complication rates are not uncommon in patients receiving MCS.[8] Perhaps,

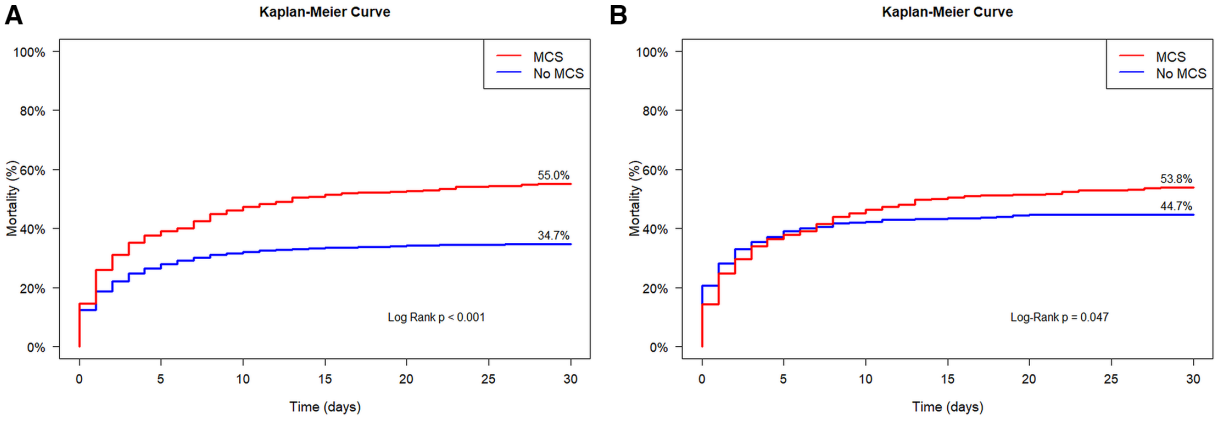

Figure 3 (A) Kaplan-Meier curve of the unmatched cohort. (B) Kaplan-Meier curve of the matched cohort. MCS, mechanical circulatory support.

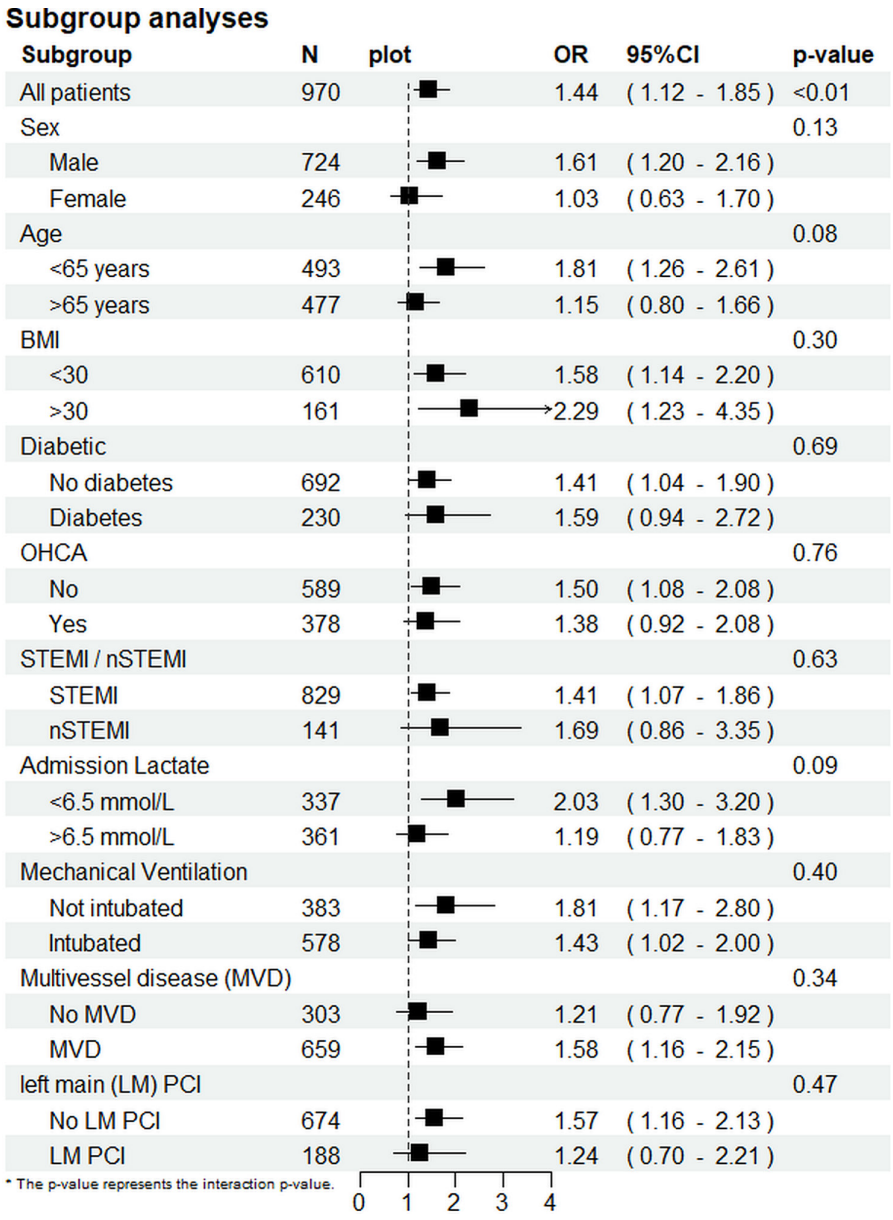

Figure 4 Association between mechanical circulatory support (MCS) use and 30-day mortality in subgroups of interest from the matched study. The p-value represents the interaction p-value. BMI, body mass index; LM, left main; MVD, multivessel disease; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; (N)STEMI, (non-)ST-elevated myocardial infarction.

the potential beneficial effects of MCS devices might not outweigh the negative effects of MCS devices outside a trial setting. The occurrence of fatal complications would also underscore the observed late increased mortality in the MCS cohort. Moreover, unblinded trials like the DanGer Shock trial risk treatment bias. As a matter of fact, as in the DanGer Shock trial, we also found that patients treated with MCS more often received permanent ventricular assist devices or heart transplantation. Therefore, it is still unclear whether MCS in itself is associated with better outcomes or with a more liberal use of permanent cardiac replacement therapy. Furthermore, higher peak troponin and CK-MB levels after PCI were observed in the MCS vs non-MCS patients from our matched cohort, indicating that these patients suffered larger myocardial damage, which is associated with a worse prognosis.[25] This could be attributable to residual confounding. However, MCS devices themselves might also negatively affect infarct size. The CRISP-AMI RCT trial revealed a trend towards larger infarct sizes after IABP-assisted PCI and preclinical studies also report an association between VA-ECMO and increased infarct size or increased LV oxygen demand.[26–28] On the contrary, preclinical animal studies have shown that Impella is associated with infarct-size reduction, probably due to a decreased myocardial oxygen demand through unloading of the left ventricle.[29] It is noteworthy, however, that there is currently no evidence confirming the existence of this association in humans. The primary publication of the DanGer Shock does not report infarct sizes unfortunately.[18]

A large proportion of patients in this NHR-CS received vasopressors and inotropes. MCS and non-MCS patients were matched on inotropes prior to PCI. After PCI, however, MCS patients were more frequently treated with inotropes and vasopressors. To date, no evidence exists of their beneficial effects. The NORSHOCK trial (NCT05168462) is evaluating the effect of lower dosages of noradrenalin. In line with this hypothesis, one could hypothesise that the potential beneficial effects of MCS usage in patients might have been more outspoken if patients had received fewer vasopressors prior to MCS.

Finally, more than 40% of the patients in our cohort presented after an OHCA and approximately 13% experienced an IHCA. The question remains whether these patients were able to benefit from the potential beneficial effects of MCS devices because of possible brain damage.[8 30] However, no significant interactions between various subgroups and MCS usage with 30-day mortality were found in our study.

In summary, this extensive, real-world registry revealed a higher 30-day mortality in patients who received MCS, even after meticulous (measured) confounder control through aPS matching. This observed higher 30-day mortality may be attributed to an overall limited or potentially harmful effect of (some) MCS devices. Alternatively, the potential clinical outcome benefits may be overshadowed by the adverse effects of associated complications. But for most, identifying the right patients who have the potential to benefit from MCS remains a challenge. This, along with the high associated costs and potential adverse effects, advocates a thorough risk–benefit assessment in every individual. The results of this study highlight the importance of patient selection and the caution that is required when extrapolating the findings from the DanGer shock beyond the enrolled population.

Limitations

This study has several limitations. Extensive aPS matching was performed to control for confounding. However, residual confounding cannot be excluded. Second, aPS matching was performed for MCS versus non-MCS and comparisons per device type should therefore be interpreted as hypothesis generating. In addition, the retrospective study design led to encountering missing data, thereby limiting the interpretability of some important variables. Missing percentages per variable are, however, reported to enhance transparency. Last, some important variables including clinical signs of shock and the SCAI Shock stages per patient are unknown. In addition, complication rates were not collected.

CONCLUSION

In this cohort of AMI-CS patients undergoing PCI in the Netherlands, MCS was used in 23% of all patients. IABP was used in approximately half of the MCS population. The MCS population was younger and presented with a worse haemodynamic profile compared with the non-MCS population. In this large, real-world, aPS-matched analysis, MCS usage was associated with an increased 30-day mortality.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval No ethical approval was required under the Medical Research Involving Human Subjects Act (WMO), confirmed by the Medical Research Ethics Committees United (MEC-U).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The data presented in this study were obtained from the Netherlands Heart Registration and are not openly available. Data may be provided upon reasonable request.

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REFERENCES

1 van Diepen S, Katz JN, Albert NM, *et al*. Contemporary Management of Cardiogenic Shock: A Scientific Statement From the American Heart Association. *Circulation* 2017;136:e232–68.
2 Harjola V-P, Lassus J, Sionis A, *et al*. Clinical picture and risk prediction of short-term mortality in cardiogenic shock. *Eur J Heart Fail* 2015;17:501–9.

3 Thiele H, Ohman EM, de Waha-Thiele S, *et al*. Management of cardiogenic shock complicating myocardial infarction: an update 2019. *Eur Heart J* 2019;40:2671–83.
4 Karami M, Peters EJ, Lagrand WK, *et al*. Outcome and Predictors for Mortality in Patients with Cardiogenic Shock: A Dutch Nationwide Registry-Based Study of 75,407 Patients with Acute Coronary Syndrome Treated by PCI. *J Clin Med* 2021;10:2047.
5 Kolte D, Khera S, Aronow WS, *et al*. Trends in incidence, management, and outcomes of cardiogenic shock complicating ST-elevation myocardial infarction in the United States. *J Am Heart Assoc* 2014;3:e000590.
6 Collet J-P, Thiele H, Barbato E, *et al*. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2021;42:1289–367.
7 Helgestad OKL, Josiassen J, Hassager C, *et al*. Contemporary trends in use of mechanical circulatory support in patients with acute MI and cardiogenic shock. *Open Heart* 2020;7:e001214.
8 Bogerd M, Ten Berg S, Peters EJ, *et al*. Impella and venoarterial extracorporeal membrane oxygenation in cardiogenic shock complicating acute myocardial infarction. *Eur J Heart Fail* 2023;25:2021–31.
9 Dhruva SS, Ross JS, Mortazavi BJ, *et al*. Use of Mechanical Circulatory Support Devices Among Patients With Acute Myocardial Infarction Complicated by Cardiogenic Shock. *JAMA Netw Open* 2021;4:e2037748.
10 Nan Tie E, Dinh D, Chan W, *et al*. Trends in Intra-Aortic Balloon Pump Use in Cardiogenic SHOCK After the SHOCK-II Trial. *Am J Cardiol* 2023;191:125–32.
11 Schrage B, Becher PM, Goßling A, *et al*. Temporal trends in incidence, causes, use of mechanical circulatory support and mortality in cardiogenic shock. *ESC Heart Fail* 2021;8:1295–303.
12 Thiele H, Zeymer U, Neumann F-J, *et al*. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med* 2012;367:1287–96.
13 Shah M, Patnaik S, Patel B, *et al*. Trends in mechanical circulatory support use and hospital mortality among patients with acute myocardial infarction and non-infarction related cardiogenic shock in the United States. *Clin Res Cardiol* 2018;107:287–303.
14 Eckman PM, Katz JN, El Banayosy A, *et al*. Veno-Arterial Extracorporeal Membrane Oxygenation for Cardiogenic Shock: An Introduction for the Busy Clinician. *Circulation* 2019;140:2019–37.
15 Thiele H, Zeymer U, Akin I, *et al*. Extracorporeal Life Support in Infarct-Related Cardiogenic Shock. *N Engl J Med* 2023;389:1286–97.
16 Ostadal P, Rokyta R, Karasek J, *et al*. Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock: Results of the ECMO-CS Randomized Clinical Trial. *Circulation* 2023;147:454–64.
17 Thiele H, Zeymer U, Thelemann N, *et al*. Intraaortic Balloon Pump in Cardiogenic SHOCK Complicating Acute Myocardial Infarction: Long-Term 6-Year Outcome of the Randomized IABP-SHOCK II Trial. *Circulation* 2019;139:395–403.
18 Møller JE, Engstrøm T, Jensen LO, *et al*. Microaxial Flow Pump or Standard Care in Infarct-Related Cardiogenic Shock. *N Engl J Med* 2024;390:1382–93.
19 Peters EJ, Berg ST, Bogerd M, *et al*. Characteristics, Treatment Strategies and Outcome in Cardiogenic Shock Complicating Acute Myocardial Infarction: A Contemporary Dutch Cohort. *J Clin Med* 2023;12:5221.
20 Timmermans MJC, Houterman S, Daeter ED, *et al*. Using real-world data to monitor and improve quality of care in coronary artery disease: results from the Netherlands Heart Registration. *Neth Heart J* 2022;30:546–56.
21 Mitra R, Reiter JP. A comparison of two methods of estimating propensity scores after multiple imputation. *Stat Methods Med Res* 2016;25:188–204.
22 Team RC. *R: A Language and Environment for Statistical Computing*. 2022.
23 Hunziker L, Radovanovic D, Jeger R, *et al*. Twenty-Year Trends in the Incidence and Outcome of Cardiogenic Shock in AMIS Plus Registry. *Circ Cardiovasc Interv* 2019;12:e007293.
24 Byrne RA, Rossello X, Coughlan JJ, *et al*. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J Acute Cardiovasc Care* 2023.
25 Stone GW, Selker HP, Thiele H, *et al*. Relationship Between Infarct Size and Outcomes Following Primary PCI: Patient-Level Analysis From 10 Randomized Trials. *J Am Coll Cardiol* 2016;67:1674–83.
26 Patel MR, Smalling RW, Thiele H, *et al*. Intra-aortic balloon counterpulsation and infarct size in patients with acute anterior myocardial infarction without shock: the CRISP AMI randomized trial. *JAMA* 2011;306:1329–37.
27 Everett KD, Swain L, Reyelt L, *et al*. Transvalvular Unloading Mitigates Ventricular Injury Due to Venoarterial Extracorporeal Membrane Oxygenation in Acute Myocardial Infarction. *JACC Basic Transl Sci* 2023;8:769–80.
28 Donker DW, Brodie D, Henriques JPS, *et al*. Left Ventricular Unloading During Veno-Arterial ECMO: A Simulation Study. *ASAIO J* 2019;65:11–20.
29 Miyashita S, Kariya T, Yamada KP, *et al*. Left Ventricular Assist Devices for Acute Myocardial Infarct Size Reduction: Meta-analysis. *J Cardiovasc Transl Res* 2021;14:467–75.
30 Ostenfeld S, Lindholm MG, Kjaergaard J, *et al*. Prognostic implication of out-of-hospital cardiac arrest in patients with cardiogenic shock and acute myocardial infarction. *Resuscitation* 2015;87:57–62.