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ORIGINAL ARTICLE

Prognostic effect of sex according to shock severity in patients with acute myocardial infarction complicated by cardiogenic shock

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ABSTRACT

BACKGROUND Sex disparities in cardiogenic shock (CS) treatment are controversial, and the prognostic implications of sex remain unclear in CS caused by acute myocardial infarction (AMI).

OBJECTIVES This study aimed to evaluate the prognostic effect of sex according to the severity of CS in patients undergoing percutaneous coronary intervention (PCI) for AMI complicated by CS.

METHODS We assessed 695 patients from 12 tertiary centers in South Korea who underwent PCI for AMI complicated by CS, and analyzed outcomes by sex (female [n = 184] vs. male [n = 511]). We compared a 12-month patient-oriented composite endpoint (POCE, defined as a composite of all-cause mortality, myocardial infarction, re-hospitalization due to heart failure, and repeat revascularization) between the sexes, respective of SCAI shock stage C&D or E. Propensity score-matched analysis was performed to reduce bias.

RESULTS We found that the female group was older and had higher vasoactive-inotropic and IABP-SHOCK II scores than the male group, with findings consistent across SCAI shock stages. During the 12-month follow-up period, multivariate analysis revealed no significant differences in POCE (HR 1.01, 95% CI 0.67-1.53, $p = 0.963$ for SCAI stage C&D, HR 1.24, 95% CI 0.84-1.84, $p = 0.286$ for SCAI stage E) between females and males. After propensity score matching, the

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ABBREVIATIONS

AMI = acute myocardial infarction

CS = cardiogenic shock

MCS = mechanical circulatory support

POCE = patient-oriented composite endpoint

PCI = percutaneous coronary intervention

SCAI = the Society for Cardiovascular Angiography and Interventions

STEMI = ST-segment elevation myocardial infarction

VIS = vasoactive-inotropic score

incidence of POCE (HR 1.47, 95% CI 0.79-2.72, $p = 0.220$ for SCAI stage C&D, HR 0.88, 95% CI 0.49-1.57, $p = 0.665$ for SCAI stage E) was similar between sexes.

CONCLUSIONS Sex does not appear to influence the risk of 12-month POCE in patients treated with PCI for CS caused by AMI, irrespective of shock severity.

CLINICAL TRIAL REGISTRATION ClinicalTrials.gov NCT02985008. RESCUE (REtrospective and prospective observational Study to investigate Clinical oUtcomes and Efficacy of left ventricular assist device for Korean patients with cardiogenic shock), NCT02985008, Registered December 5, 2016 - retrospectively and prospectively.

IRB INFORMATION This study was approved by the institutional review board of Samsung Medical Center (Reference number: 2016-03-130). (Hellenic Journal of Cardiology 2025;82:3-14)

1. INTRODUCTION

Cardiogenic shock (CS) caused by acute myocardial infarction (AMI) is associated with high mortality despite advances in cardiovascular acute and intensive care[1-3]. Moreover, various mechanical circulatory support (MCS) approaches have been developed, but currently available MCS devices have not been demonstrated to improve survival in CS noticeably[4,5]. Previous studies demonstrated differences in clinical characteristics according to sex in patients with CS. Rathod et al. reported that female patients were older, less likely to smoke, and had a lower incidence of previous myocardial infarction than male patients with CS, and several other studies showed that female sex was predictive of mortality risk score and was associated with in-ICU death[3,6]. There exists a perspective positing that the variance in Acute Myocardial Infarction with Cardiogenic Shock (AMI-CS) outcomes between genders stems from dissimilarities in the treatment protocols administered to these two cohorts[7-10]. Notably, females often do not promptly receive medical treatment in accordance with established guidelines within the initial 24 hours. Moreover, they exhibit a reduced likelihood of receiving MCS compared to their male counterparts. Additionally, females tend to undergo less aggressive revascularization procedures than males, consequently contributing to higher in-hospital mortality rates compared to males[8]. In a study conducted by Schmitt et al., however, there were notable differences in 30-day all-cause mortality when comparing patients with AMI-CS[11]. However, sex disparities in CS treatment remain controversial because the available data are scarce and heterogeneous. Moreover, limited research exists on potential sex-related differences within the context of SCAI shock classification in cases of AMI-CS with a single etiology. Therefore, prognostic implications of sex according to CS severity remain unclear in CS caused by AMI. We investigated the impact of sex on mid-term clinical outcomes and clinical characteristics according to shock severity in patients who underwent percutaneous coronary intervention (PCI) for AMI complicated by CS.

2. METHODS

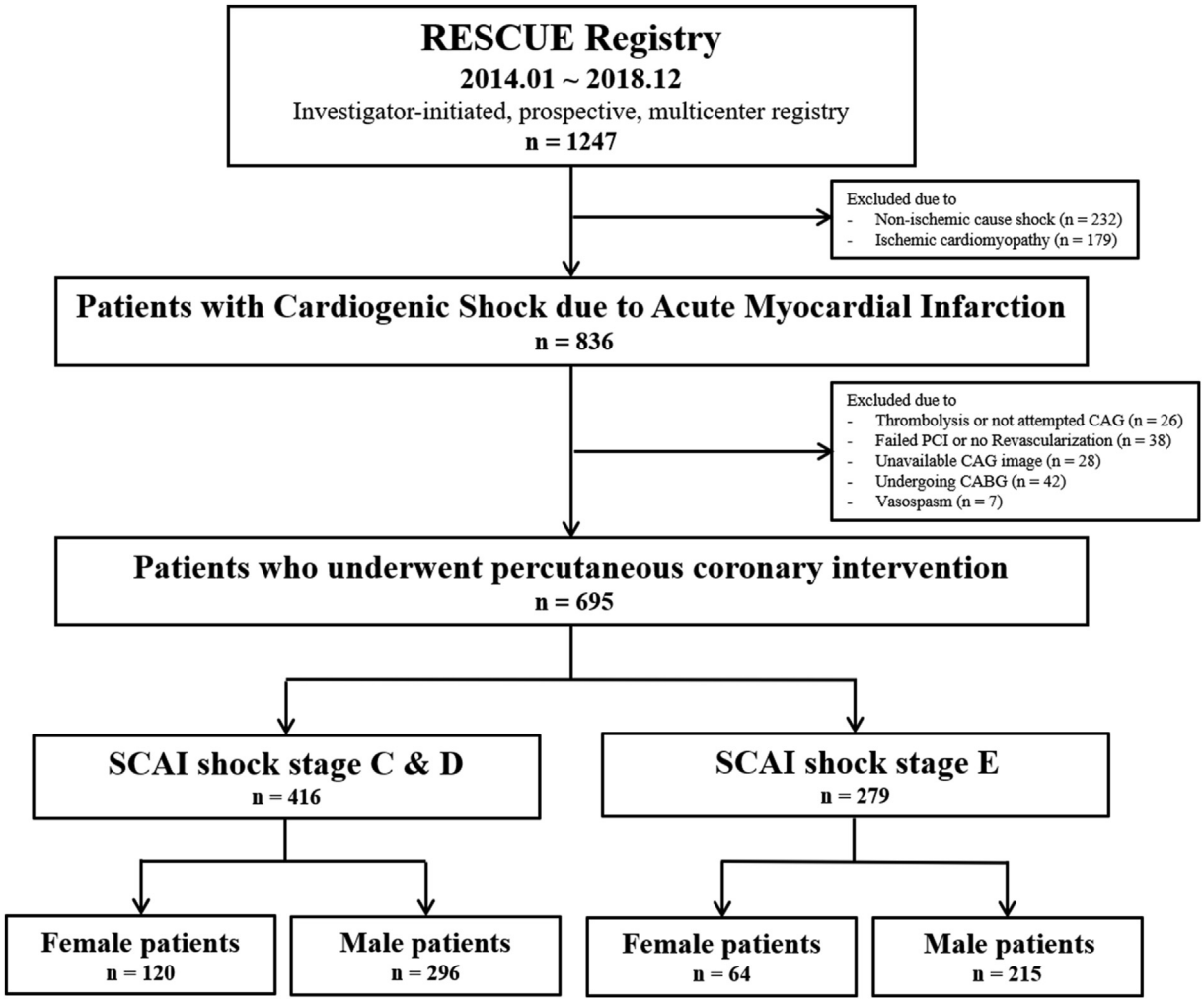
2.1. STUDY POPULATION. Study subjects were recruited from the REtrospective and prospective observational Study to investigate Clinical oUtcomes and Efficacy of left ventricular assist device for Korean patients with cardiogenic shock (RESCUE) registry, which is a multicenter, retrospective and prospective database of patients with CS[12]. Between January 2014 and December 2018, a total of 1,247 patients with CS were recruited from 12 tertiary centers in South Korea. The inclusion criteria were as follows:[1] older than 19 years,[2] systolic blood pressure under 90 mmHg for 30 minutes or need for inotrope or vasopressor support to achieve a systolic blood pressure over 90 mmHg, and[3] presence of pulmonary congestion and signs of impaired organ perfusion (altered mental status, cold peripherals, urine output under 0.5 mL/kg/h for the previous six hours, or blood lactate over 2.0 mmol/L). Exclusion criteria were[1] patients with out-of-hospital cardiac arrest,[2] other causes of shock, and[3] those who refused active treatment. For this study, among the 836 patients who presented with CS caused by AMI, data from 695 patients who underwent PCI were included in the final analysis. Reasons for exclusion are as

follows: 26 patients who did not undergo coronary angiography, 38 patients who did not undergo revascularization or who failed culprit lesion PCI, 28 patients who did not have images of coronary angiography, 42 patients who underwent coronary artery bypass grafting, and 7 patients with vasospasm. For this study, we divided the 695 CS patients into male and female groups and compared their clinical outcomes according to the Society for Cardiovascular Angiography and Interventions (SCAI) shock classification (SCAI shock stage C&D or stage E)[13] (Fig. 1).

2.2. DATA COLLECTION. Clinical patient demographics, in-hospital management, laboratory data, procedural data, and outcome data were collected by independent clinical research coordinators using web-based case report forms. All baseline data were measured upon admission of patients. Additional information was obtained from medical records or telephone contact if necessary. Institutional review board (IRB) approval was obtained at each of the participating sites, and the IRBs of the participating centers waived the requirement for informed consent from retrospectively enrolled patients. Informed consent was obtained before enrollment in all prospectively enrolled patients.

2.3. PCI AND PHARMACOLOGIC THERAPY. PCI was performed according to standard techniques[14]. Unfractionated heparin or low molecular weight heparin was used for anticoagulation during the procedure. The decision to perform thrombus

FIGURE 1 Schematic illustration of study cohort selection



CAG = coronary angiography; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; SCAI = the Society for Cardiovascular Angiography and Interventions.

aspiration, pre-dilation or post-dilation, or to use glycoprotein IIb/IIIa inhibitors was determined by the operator. Intravascular imaging or fractional flow reserve was also performed at the operator's discretion. Stent length and diameter were not restricted. All patients who were not taking aspirin or a P2Y12 inhibitor were administered a loading dose of aspirin (300 mg) or P2Y12 inhibitor (clopidogrel 600 mg, ticagrelor 180 mg, or prasugrel 60 mg). After the procedure, aspirin (100 mg orally once daily) was used indefinitely; clopidogrel (75 mg orally once daily), ticagrelor (90 mg orally twice daily), or prasugrel (10 mg orally once daily) was maintained. Anticoagulation was performed during PCI using low-molecular-weight heparin or unfractionated heparin to achieve an activated clotting time of 250 to 300 seconds. Optimal pharmacological therapy, including statins, beta-blockers, or renin-angiotensin system blockade if indicated, was recommended for all patients. The responsible clinicians determined the duration of dual antiplatelet therapy[15,16].

2.4. STUDY OUTCOMES AND DEFINITIONS. The primary outcome of this study was a patient-oriented composite event (POCE), defined as a composite of all-cause mortality, myocardial infarction, rehospitalization due to heart failure, and repeat revascularization. Secondary outcomes were consistent with the individual components of the primary outcome and cardiac mortality. The RESCUE registry consistently defined outcome criteria in accordance with the parameters outlined by The Academic Research Consortium-2 (ARC-2) consensus, so the definitions of clinical events and outcomes herein were also defined based on the ARC-2 consensus[17]. Analyses were truncated at 12 months of follow-up due to differences in follow-up duration.

2.5. STATISTICAL ANALYSIS. Categorical variables are presented as count and percentage and were compared using the χ^2 test or Fisher's exact test as appropriate. Continuous variables are presented as mean ± standard deviation or as median (25th percentile to 75th percentile) for variables lacking a normal distribution. Analysis of continuous variables was performed using Student's t-test or Wilcoxon rank-sum test. Survival curves were generated using Kaplan-Meier estimates and compared with the log-rank test. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using Cox proportional hazard models. The proportional hazards assumptions of the HRs were graphically inspected in the "log minus log" plot in the Cox proportional hazards models and were tested by Schoenfeld residuals. To mitigate selection bias and control for confounding factors, propensity score-matched analysis was also performed using a Greedy nearest neighbor matching method. The covariate balance after propensity score matching was assessed by calculating absolute standardized mean differences. Standardized mean differences after propensity score matching were within ±10% across all matched covariates with variance ratios near 1.0, suggesting achievement of balance between the female and male groups for each SCAI shock classification (SCAI stage C&D or stage E). Stratified Cox proportional hazard models were used to compare the outcomes of the matched groups. All probability values were two-sided, and $p < 0.05$ was considered to be statistically significant. Statistical analyses were performed using R Statistical Software (version 3.6.0; R Foundation for Statistical Computing, Vienna, Austria).

3. RESULTS

3.1. BASELINE CLINICAL CHARACTERISTICS. A total of 695 patients enrolled in this study, and they were divided into a female group (n = 184) and a male group (n = 511). Among them, 416 patients (59.9%) were included in SCAI shock stage C&D, whereas 279 patients (40.1%) were included in SCAI shock stage E. The female group was older than the male group, consistent across SCAI shock stages (64.04 ± 12.26 vs. 72.78 ± 11.05 years, $p < 0.001$, 63.84 ± 11.96 vs. 76.28 ± 9.53 years, $p < 0.001$). A lower incidence of hypertension was observed in the female group ($p < 0.001$) as well as fewer smokers ($p < 0.001$) regardless of SCAI shock stage. There were no significant differences in left ventricular ejection fraction (LVEF), initial blood pressure, heart rate, and emergent in-hospital management between the two sex groups. There was also no disparity between the sexes concerning in-hospital management, particularly in relation to the proportion of patients who underwent invasive interventions such as intra-aortic balloon pump (IABP) and extracorporeal membrane oxygenation (ECMO). Similar percentages of male and female patients underwent CPR in the SCAI stage E subgroup, but female patients tended to have higher vasoactive-inotropic scores (VIS) (153.28 ± 192.01 vs. 218.61 ± 278.13, $p = 0.033$) and higher IABP-SHOCK II scores (3.02 ± 1.68 vs. 3.77 ± 1.67, $p = 0.002$). Higher VIS (19.32 ± 18.61 vs. 24.51 ± 22.39, $p = 0.026$) and higher IABP-SHOCK II scores (1.43 ± 1.41 vs. 2.13 ± 1.54, $p < 0.001$) were also observed in the SCAI shock stage C&D subgroup (Table 1).

3.2. CLINICAL OUTCOMES. 3.2.1. Overall population. Among the study population, 229 POCEs occurred during the initial 30 days after PCI for

TABLE 1 Baseline characteristics

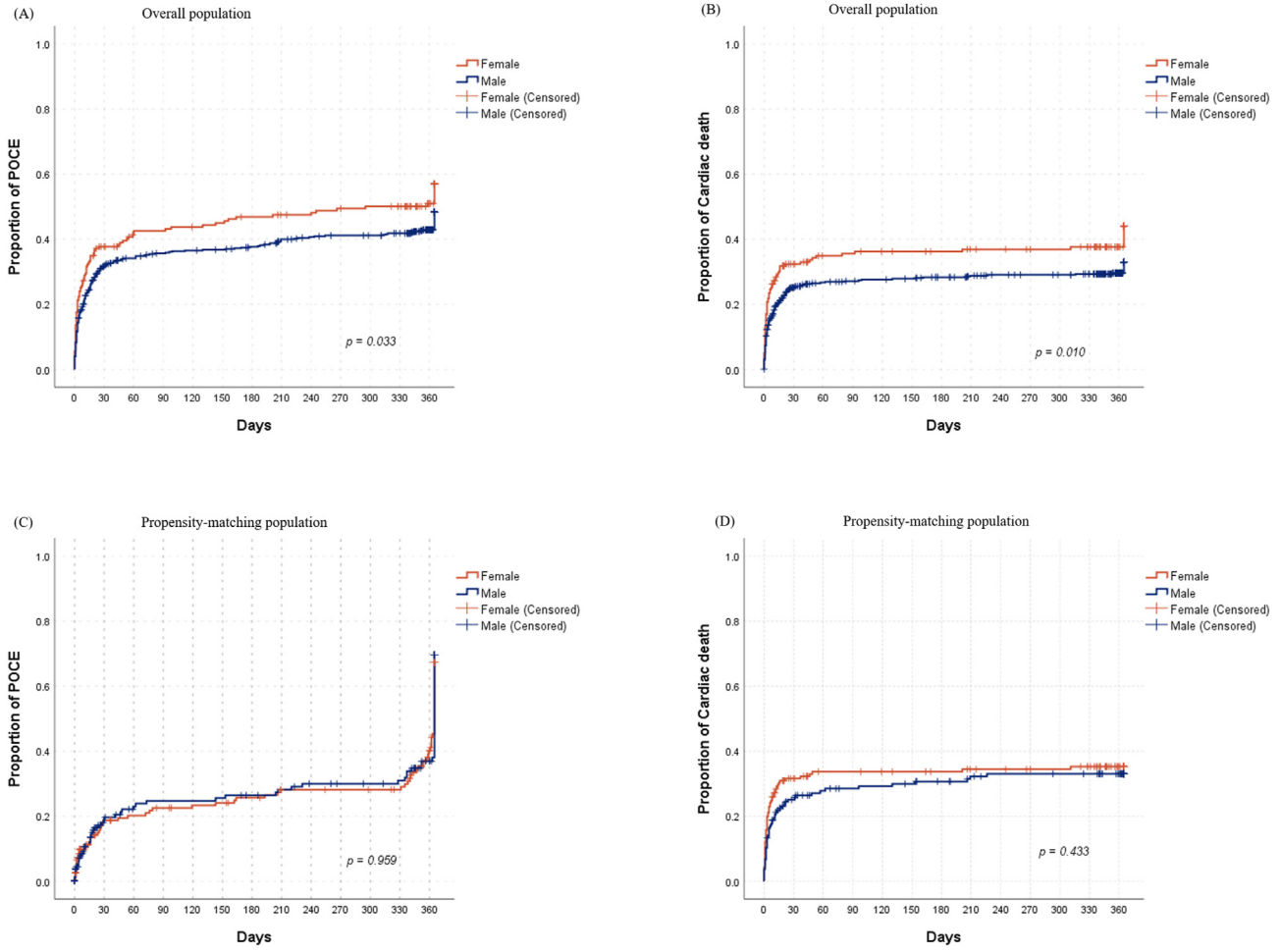
	Class C&D			Class E		
	Female (n = 120)	Male (n = 296)	*P value*	Female (n = 64)	Male (n = 215)	*P value*
Age, years	72.78 ± 11.05	64.04 ± 12.26	<0.001	76.28 ± 9.53	63.84 ± 11.96	<0.001
BMI, kg/m2	23.44 ± 3.70	24.35 ± 3.24	0.013	22.25 ± 3.43	23.67 ± 3.17	0.002
Cardiovascular risk factors						
Hypertension	86 (71.7)	155 (52.4)	<0.001	48 (75.0)	93 (43.3)	<0.001
Diabetes mellitus	48 (40.0)	104 (35.1)	0.351	25 (39.1)	72 (33.5)	0.411
Chronic kidney disease	13 (10.8)	27 (9.1)	0.592	3 (4.7)	15 (7.0)	0.772
Current smoking	12 (10.0)	134 (45.3)	<0.001	2 (3.1)	99 (46.0)	<0.001
Previous PCI	12 (10.0)	34 (11.5)	0.661	4 (6.2)	36 (16.7)	0.041
Previous myocardial infarction	14 (11.7)	38 (12.8)	0.743	1 (1.6)	35 (16.3)	0.001
Peripheral artery disease	3 (2.5)	9 (3.0)	1.000	3 (4.7)	6 (2.8)	0.433
Previous history of stroke	11 (9.2)	14 (4.7)	0.085	7 (10.9)	23 (10.7)	0.957
Reason for administration						
NSTEMI	48 (40.0)	86 (29.1)	0.030	22 (34.4)	46 (21.4)	0.034
STEMI	72 (60.0)	210 (70.9)		42 (65.6)	169 (78.6)	
Clinical manifestation						
LVEF, %	40.49 ± 13.81	41.13 ± 14.04	0.692	29.31 ± 14.73	29.11 ± 14.56	0.934
Systolic blood pressure, mmHg	80.71 ± 26.69	80.84 ± 23.21	0.960	65.70 ± 33.35	65.02 ± 34.20	0.888
Diastolic blood pressure, mmHg	50.40 ± 16.54	51.50 ± 16.64	0.540	41.78 ± 22.85	41.97 ± 23.37	0.954
Heart rate, beats/min	81.44 ± 28.83	80.03 ± 27.11	0.641	72.11 ± 39.70	76.89 ± 38.79	0.391
Culprit lesion						
Left main coronary artery	54 (45.0)	129 (43.6)	0.888	21 (32.8)	87 (40.5)	0.465
Left anterior descending artery	29 (24.2)	66 (23.3)		18 (28.1)	66 (30.7)	
Left circumflex artery	9 (23.3)	21 (7.1)		7 (10.9)	16 (7.4)	
Right coronary artery	28 (23.3)	80 (27.0)		18 (28.1)	46 (21.4)	
Laboratory findings						
Hemoglobin, g/dL	11.82 ± 1.95	13.84 ± 2.03	<0.001	11.26 ± 2.03	13.42 ± 2.47	<0.001
Creatinine, mg/dL	1.36 ± 1.04	1.42 ± 1.36	0.671	1.61 ± 1.55	1.58 ± 1.26	0.874
Glucose, mg/dL	215.25 ± 107.86	205.83 ± 93.33	0.386	269.08 ± 165.41	266.26 ± 130.86	0.891
Lactic acid, mmol/L	3.74 ± 2.09	3.65 ± 1.66	0.750	9.28 ± 4.92	9.43 ± 4.59	0.852
Peak troponin I, ng/mL	60.57 ± 127.25	67.40 ± 157.89	0.682	129.44 ± 247.61	99.65 ± 176.04	0.299
Shock characteristics						
Undergoing CPR	0	0	N/A	32 (50)	116 (54.0)	0.578
Vasoactive-Inotropic Score	24.51 ± 22.39	19.32 ± 18.61	0.026	218.61 ± 278.13	153.28 ± 192.01	0.033
IABP-SHOCK 2 score	2.13 ± 1.54	1.43 ± 1.41	<0.001	3.77 ± 1.67	3.02 ± 1.68	0.002
In-hospital management						
Mechanical ventilation	47 (39.2)	97 (32.8)	0.214	53 (82.8)	183 (85.1)	0.654
Requiring CRRT	13 (10.8)	29 (9.8)	0.751	13 (20.3)	68 (31.6)	0.080
Requiring IABP	47 (39.2)	94 (31.8)	0.148	11 (17.2)	58 (27.0)	0.111
Requiring ECMO	18 (15.0)	41 (13.9)	0.761	41 (64.1)	138 (64.2)	1.986

*Values are means ± standard deviations or n (%). SCAI shock classification "E" was defined as patients who requiring ECMO, undergoing CPR, lactate > 8 mmol/L, or vasoactive-inotropic score >90. Abbreviations: SCAI, the Society for Cardiovascular Angiography and Intervention; BMI, body mass index; PCI, percutaneous coronary intervention; NSTEMI, Non ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; CPR, cardio-pulmonary resuscitation; CRRT, continuous renal replacement therapy; IABP, Intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation.

AMI complicated by CS, and 30-day mortality was not significantly different between the groups (65 patients, 35.3% in the female group vs. 139 patients, 27.2% in the male group, adjusted HR 1.18, 95% CI 0.72-1.95; $p = 0.511$).

Kaplan-Meier survival curves for cumulative 12-month POCE and 12-month cardiac death showed significant differences between female and male groups ($p = 0.033$ and $p = 0.010$, respectively) (Fig. 2A and B). By 12 months after the index procedure, the primary outcome had occurred in 96 patients (52.2%) in the female group and 225 patients (44.0%) in the male group (adjusted HR 1.08, 95% CI 0.82-1.43; $p = 0.575$). There were no significant differences in individual components of the primary outcome (all-cause death 36.4% in the female group vs. 46.7% in the male group, adjusted HR 1.08, 95% CI 0.80-1.45; $p = 0.627$, myocardial infarction 2.2% vs. 2.7%, adjusted HR 1.14, 95% CI 0.35-3.79; $p = 0.826$, re-hospitalization due to heart failure 4.9% vs. 7.6%,

FIGURE 2 **Time-to-event Kaplan-Meier survival curves according to sex in patients with acute myocardial infarction complicated by cardiogenic shock**



(A) Kaplan-Meier curves for 12-month POCE in the overall study population. (B) Kaplan-Meier curves for 12-month POCE in the overall study population. (C) Kaplan-Meier curves for 12-month cardiac mortality in the PS-matched population. (D) Kaplan-Meier curves for 12-month cardiac mortality in the PS-matched population. POCE = patient-oriented composite endpoint; PS = propensity score.

adjusted HR 1.06, 95% CI 0.47-2.40; $p = 0.883$ and repeat revascularization 4.1% vs. 1.1%, adjusted HR 0.359, 95% CI 0.08-1.63; $p = 0.184$), or cardiac death (29.9% vs. 39.7%, adjusted HR 1.09, 95% CI 0.79-1.52; $p = 0.602$) at 12 months (Table 2).

3.2.2. Subgroup analysis of shock severity. There was no significant difference in the primary outcome after subgroup analysis according to shock severity across the SCAI stage C&D and SCAI stage E subgroups. Multivariate analysis revealed no significant differences in 12-month POCE (adjusted HR 1.01, 95% CI 0.67-1.53; $p = 0.963$ for SCAI stage C&D subgroup, adjusted HR 1.24, 95% CI 0.84-1.84; $p = 0.286$ for SCAI stage E subgroup). Adjusted variables included age, BMI >25, smoking, IABP-SHOCK II score, VIS, severe left ventricular systolic dysfunction (EF <30%), CRRT, mechanical ventilation, left main or left anterior descending artery as a culprit vessel, and pre-PCI ECMO insertion (Table 2). Cumulative 12-month POCE events in the SCAI stage C&D subgroup were not significantly different between female and male patients ($p = 0.057$) (Fig. 3A), whereas that measure in the SCAI stage E subgroup ($p = 0.005$) and 12-month cardiac death in each SCAI shock stage ($p = 0.034$ and $p = 0.001$, respectively) showed significant differences between the two sex groups (Fig. 3B-D).

3.2.3. Propensity score-matched population. - After performing propensity score matching, a total of 166 pairs were generated. There were no significant differences in Kaplan-Meier survival curves for

TABLE 2 12-month follow-up outcomes between male and female patients with acute myocardial infarction complicated by cardiogenic shock

					Univariate Analysis			Multivariable Analysis		
		Male (=296)	Female (=120)	P value	HR	95% CI	P value	HR	95% CI	P value
SCAI shock Class C&D	POCE† (per 12 months)	85 (28.7)	46 (38.3)	0.056	1.412	0.986-2.021	0.059	1.01	0.666-1.531	0.963
	All-cause mortality	59 (19.9)	38 (31.7)	0.01	1.678	1.116-2.523	0.013	1.017	0.627-1.648	0.947
	Cardiac mortality	44 (14.9)	28 (23.3)	0.039	1.653	1.029-2.655	0.038	0.958	0.536-1.715	0.886
	Myocardial infarction	6 (2.0)	4 (3.3)	0.483	1.739	0.491-6.163	0.391	1.024	0.260-4.035	0.973
	Re-hospitalization due to heart failure	18 (6.1)	12 (10.0)	0.162	1.787	0.861-3.711	0.119	0.915	0.373-2.242	0.845
	Revascularization	15 (5.1)	2 (1.7)	0.17	0.341	0.078-1.491	0.153	0.38	0.080-1.814	0.225
		Male (=215)	**Female (=64)**							
SCAI shock Class E	POCE† (per 12 months)	140 (65.1)	50 (78.1)	0.05	1.57	1.134-2.172	0.007	1.241	0.835-1.843	0.286
	All-cause mortality	127 (59.1)	48 (75.0)	0.021	1.629	1.167-2.274	0.004	1.288	0.861-1.927	0.218
	Cardiac mortality	109 (50.7)	45 (70.3)	0.006	1.732	1.222-2.454	0.002	1.379	0.904-2.105	0.136
	Myocardial infarction	5 (2.3)	1 (1.6)	1	0.866	0.099-7.542	0.896	1.122	0.084-15.069	0.931
	Re-hospitalization due to heart failure	7 (3.30	2 (3.1)	1	1.854	0.384-8.958	0.442	0.697	0.066-7.362	0.764
	Revascularization	6 (2.8)	0	0.342	0.037	0.000-409.208	0.487	0	N/A	N/A
		Male (=511)	**Female (=184)**							
SCAI shock Class C&D&E	POCE† (per 12 months)	225 (44.0)	96 (52.2)	0.057	1.291	1.017-1.640	0.036	1.083	0.820-1.429	0.575
	All-cause mortality	186 (36.4)	86 (46.7)	0.014	1.397	1.082-1.804	0.01	1.077	0.799-1.450	0.627
	Cardiac mortality	153 (29.9)	73 (39.7)	0.016	1.433	1.084-1.894	0.011	1.091	0.786-1.515	0.602
	Myocardial infarction	11 (2.2)	5 (2.7)	0.774	1.405	0.488-4.045	0.529	1.143	0.345-3.785	0.826
	Re-hospitalization due to heart failure	25 (4.9)	14 (7.6)	0.17	1.818	0.945-3.497	0.074	1.063	0.471-2.399	0.883
	Revascularization	21 (4.1)	2 (1.1)	0.054	0.294	0.069-1.255	0.098	0.359	0.079-1.630	0.184

The cumulative incidence of outcomes is presented as event number. Kaplan-Meier estimates at 12 months from the index procedure. †POCE was defined as a composite of all-cause mortality, myocardial infarction, re-hospitalization due to heart *Adjusted variables included age, BMI>25, smoking, IABP_SHOCK2 score, VIS score, severe left ventricular systolic dysfunction (ejection fraction <30%), CRRT, mechanical ventilation, left main or left anterior descending artery as a culprit vessel, and pre-PCI ECMO insertion. Abbreviations: SCAI, the Society for Cardiovascular Angiography and Intervention; POCE, patient-oriented composite endpoint; HR, hazard ratio; CI, confidence interval.

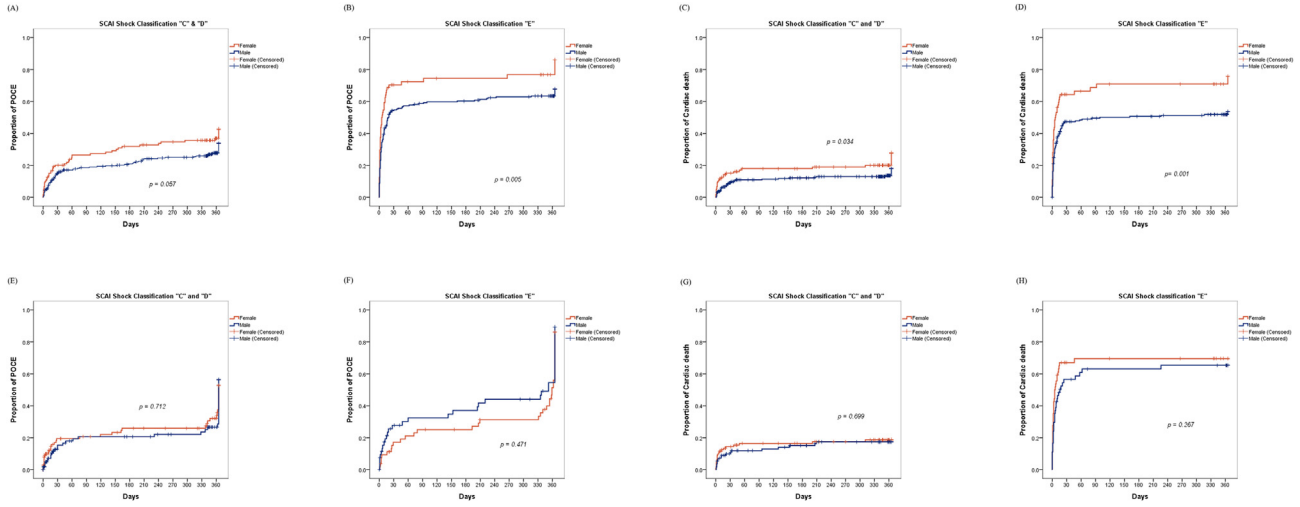
cumulative 12-month POCE or 12-month cardiac death ($p = 0.959$ and $p = 0.433$, respectively) (Fig. 2C and D). A total of 153 POCEs occurred during follow-up in matched patients. There were 112 pairs in SCAI stage C&D with no significant difference in the incidence of POCEs at 12 months between the female and male groups (matched HR 1.47, 95% CI 0.79-2.72; $p = 0.220$). The risk of all-cause death (matched HR 1.19, 95% CI 0.67-2.13; $p = 0.556$), myocardial infarction (3.6% vs. 3.6%, matched HR 1.00, 95% CI 0.20-4.96; $p = 1.000$), re-hospitalization due to heart failure (7.1% vs. 8.0%, matched HR 1.17, 95% CI 0.39-3.47; $p = 0.782$), repeat revascularization (2.7% vs. 1.8%, matched HR 0.50, 95% CI 0.05-5.51; $p = 0.571$), and cardiac death (matched HR 1.20, 95% CI 0.67-2.13; $p = 0.857$) were also similar between the two groups (Table 3). In the SCAI stage E subgroup, which had 54 pairs, there was no significant difference in the incidence of POCEs at 12 months (matched HR 0.88, 95% CI 0.49-1.57; $p = 0.665$) between the female and the male groups. The risk of all-cause death (matched HR 1.43, 95% CI 0.82-2.50; $p = 0.210$), myocardial infarction (0% vs. 1.9%, $p = 0.610$), repeat revascularization (1.9% vs. 0%, $p = 0.610$), and cardiac death (matched HR 1.50, 95% CI 0.85-2.64; $p = 0.160$) was also similar between the two groups (Table 3).

3.2.4. Analysis of various clinical subgroups. To investigate the relationship between sex and CS caused by AMI in various clinical situations, we additionally performed clinical subgroup analyses. The prognostic effects of sex did not differ significantly across subgroups regardless of age (<65 years vs. ≥65 years), body mass index (<25.0 vs. ≥25.0), type of AMI (STEMI vs. NSTEMI), mechanical ventilation, requiring renal replacement therapy (RRT) or ECMO, or VIS (<80.0 vs. ≥80.0), or IABP-Shock II score (<3.0 vs. ≥3.0) (Fig. 4). Nonetheless, the impact of sex on outcome demonstrated a divergent pattern based on LVEF (p for interaction = 0.041). When EF was below 30%, the sex effect exhibited a value less than 1, whereas for EF levels of 30% or higher, the sex effect surpassed 1. Although a distinct influence was observed, statistical significance was not established.

4. DISCUSSION

We investigated the prognostic effects of sex on clinical outcomes in patients with CS caused by AMI using a large, multicenter, real-world CS registry. Our main finding was the lack of significant difference in the risk of POCE at 12 months between female and

FIGURE 3 **Time-to-event Kaplan-Meier survival curves according to sex in shock severity subgroups (SCAI stage C&D and SCAI stage D)**



(A) Kaplan-Meier curves for 12-month POCE in SCAI shock stage C&D (overall study population). (B) Kaplan-Meier curves for 12-month POCE in SCAI shock stage E (overall study population). (C) Kaplan-Meier curves for 12-month cardiac mortality in SCAI shock stage C&D (overall study population). (D) Kaplan-Meier curves for 12-month cardiac mortality in SCAI shock E (overall study population). (E) Kaplan-Meier curves for 12-month POCE in SCAI shock stage C&D (PS-matched population). (F) Kaplan-Meier curves for 12-month POCE in SCAI shock stage E (PS-matched population). (G) Kaplan-Meier curves for 12-month cardiac mortality in SCAI shock stage C&D (PS-matched population). (H) Kaplan-Meier curves for 12-month cardiac mortality in SCAI shock E (PS-matched population). POCE = patient-oriented composite endpoint; PS = propensity score; SCAI = the Society for Cardiovascular Angiography and Interventions.

male patients undergoing PCI for AMI complicated by CS, irrespective of SCAI shock stage (stage C&D or stage E). The lack of association between sex and the mid-term prognosis was maintained after propensity score matching and was consistent across subgroups by age as well as various clinical factors.

CS still has a mortality rate of 50-60% despite advances in treatment methods[1]. The incidence of CS has

TABLE 3 **12-month follow-up outcomes between male and female patients with acute myocardial infarction complicated by cardiogenic shock after propensity-matching adjustment**

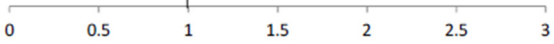
				Univariate Analysis		
		Male (=112)	**Female (=112)**	**HR**	**95% CI**	**P value**
SCAI shock Class C&D	POCE† (per 12 months)	37 (33.0)	38 (33.9)	1.47	0.79-2.72	0.220
	All-cause mortality	27 (24.1)	30 (26.8)	1.19	0.67-2.13	0.556
	Cardiac mortality	18 (16.1)	20 (17.9)	1.07	0.53-2.16	0.857
	Myocardial infarction	4 (3.6)	4 (3.6)	1	0.20-4.96	1.000
	Re-hospitalization due to heart failure	8 (7.1)	9 (8.0)	1.17	0.39-3.47	0.782
	Revascularization	3 (2.7)	2 (1.8)	0.5	0.05-5.51	0.571
		Male (=54)	**Female (=54)**			
SCAI shock Class E	POCE† (per 12 months)	38 (70.4)	40 (74.1)	0.88	0.49-1.57	0.665
	All-cause mortality	36 (66.7)	39 (72.2)	1.43	0.82-2.50	0.210
	Cardiac mortality	34 (63.0)	37 (68.5)	1.5	0.85-2.64	0.160
	Myocardial infarction	0	1 (1.9)	65.29	0. 00-628084630.4	0.610
	Re-hospitalization due to heart failure	2 (3.7)	0	N/A	N/A	N/A
	Revascularization	1 (1.9)	0	0.015	0.00-147346.84	0.610

The cumulative incidence of outcomes is presented as event number. Kaplan-Meier estimates at 12 months †POCE was defined as a composite of all-cause mortality, myocardial infarction, re-hospitalization due to heart failure, and repeat revascularization. Abbreviations: POCE, patient-oriented composite endpoint; HR, hazard ratio; CI, confidence interval.

FIGURE 4 Comparative adjusted subgroup hazard ratios for primary outcome at 12 months for various subgroups

Figure 4. Comparative adjusted subgroup hazard ratios for primary outcome at 12-months for various subgroups.

Subgroup	No of patients	Hazard ratio	95% CI	*P value*	*P for interaction*
Age					0.057
<65	305	0.57	0.26 - 1.22	0.145	
≥65	390	1.17	0.87 - 1.57	0.292	
BMI, kg/m2					0.988
< 25.0	220	1.28	0.71 - 2.30	0.409	
≥ 25.0	464	1.06	0.78 - 1.45	0.711	
Type of AMI					0.870
STEMI	493	1.10	0.79 - 1.52	0.582	
NSTEMI	202	1.18	0.71 - 1.96	0.519	
LVEF, %					0.041
≥30	395	1.30	0.84 - 2.01	0.235	
<30	300	0.90	0.63 - 1.28	0.543	
Mechanical ventilation					0.909
No	315	0.99	0.57 - 1.72	0.963	
Yes	380	1.11	0.81 - 1.51	0.520	
Requiring CRRT					0.488
No	572	0.99	0.72 - 1.36	0.960	
Yes	123	1.02	0.60 - 1.73	0.949	
Requiring ECMO					0.216
No	457	1.20	0.84 - 1.72	0.326	
Yes	238	0.96	0.64 - 1.46	0.856	
Vasoactive Inotropic Score					0.315
<80	518	0.94	0.67 - 1.32	0.716	
≥ 80	177	1.57	1.00 - 2.47	0.051	
SCAI Shock Classification					0.418
C & D	416	0.99	0.67 - 1.47	0.956	
E	279	1.29	0.88 - 1.90	0.198	



*Adjusted variables included age, BMI >25, smoking, IABP-SHOCK2 score, vasoactive-inotropic score, severe LVEF (ejection fraction <30%), RRT, mechanical ventilation, left main or left anterior descending artery as a culprit vessel, and prePCI ECMO insertion. AMI = acute myocardial infarction; BMI = body mass index; CI = confidence interval; RRT = renal replacement therapy; ECMO = extracorporeal membrane oxygenation; IABP = intraaortic balloon pump; LVEF = left ventricular systolic dysfunction; NSTEMI = non ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; SCAI = the Society for Cardiovascular Angiography and Interventions; STEMI= ST-segment elevation myocardial infarction.

been reported to be up to 13% recently, with approximately 40,000-50,000 cases per year in the United States and approximately 60,000-70,000 cases in Europe treated for CS[3,18]. AMI accompanied by left ventricular dysfunction continues to be the predominant etiology underlying CS[19]. The one-year survival rate among patients with AMI-CS who have undergone PCI has been documented to exceed 50%[20]. A surveillance study published in 2019 reported that female patients with AMI were typically older, had a greater burden of comorbidities, had a lower probability of receiving lipid-lowering therapies or non-aspirin antiplatelets, were less likely to have beta blockers, and were less likely to exhibit coronary revascularization[21]. Basir MB et al. showed that female sex was an independent predictor of higher in-hospital mortality, especially in older (≥75 years) adults with AMI[22]. Some studies reported no significant differences in in-hospital mortality between female and male patients with AMI[21,23]. However, there are limited data about sex disparities in CS caused by AMI because most previous studies did not identify CS patients or

specifically excluded them from analysis. To date, whether sex is an effective prognostic predictor in patients with CS remains controversial and the prognostic implications of sex according to shock severity remain unclear. Prior research conducted based on the existing ICD-10 coding system confirmed a higher mortality rate among females in cases of AMI-CS. Additionally, females received less frequent invasive treatments and GDMT, for reasons that remained unspecified[24,25]. While active revascularization, right heart catheterization, and MCS may mitigate outcome disparities between sexes in patients with AMI-CS, studies substantiating this remain sparse. The current study demonstrated that in patients with AMI-CS who underwent PCI, there were no differences between sexes in terms of all-cause mortality, revascularization, or cardiac mortality when in-hospital management did not vary. In cases of severe CS according to SCAI shock classification, promptly administering GDMT can reduce female mortality. The 2019 SCAI shock classification is a method of stratifying CS according to severity, and follow-up studies examining its clinical applications are ongoing. SCAI shock classification is an effective tool for risk stratification showing correlations with in-hospital mortality. Currently, in the era of SCAI shock classification, the treatment of CS has become more standardized[26]. Previous investigations centered around SCAI shock classification have demonstrated its efficacy as a reliable tool for categorizing patients and forecasting prognosis, in terms of both in-hospital mortality and long-term mortality outcomes[27,28]. In our study of a large, recent, dedicated CS dataset, we found no significant sex-related differences in mid-term POCE irrespective of indicators of shock severity such as SCAI shock stage C&D or E. 12-month cardiac mortality also did not vary by sex, and trends were similar for 6-month follow-up. Gimenez et al.[29] reported that when there is no difference in treatment revascularization strategies between the two sexes, there is no difference in 30-day mortality, indicating that the sexes should not be treated with different strategies; and our results are also in line with a substudy of the CUPRIT-SHOCK trial, which found that there is no difference in the prognosis of CS caused by AMI between sexes when standardized treatment is performed, although there are obvious differences in age, underlying cardiovascular risk factors, and vasopressor dose. SCAI shock classification objectively and systematically reflects critical CS status; therefore, the results of our study according to SCAI classification are valuable. Within the context of this present study, even among patients with AMI-CS who underwent PCI, one-year outcomes stratified by SCAI shock classification revealed discernible differences in SCAI shock C & D and E groups, consistent with previously observed mortality differences. This study's findings provide evidence that SCAI shock classification enjoys widespread confidence and can be employed for patient assessment irrespective of sex. Moreover, we analyzed short-term as well as mid-term outcomes in female and male patients with CS, unlike previous studies using older data during periods when more inotropes, vasopressors, or MCS were administered and subjective data without systematic shock classifications were used. In addition, most previous studies about sex differences in AMI complicated by CS[21,22,29] only evaluated a small number of female patients with CS and were limited by sex imbalance. In the present study, female patients with CS accounted for about 30% of the overall study population. As distinct differences in baseline characteristics between the two sexes may have acted as confounding variables, we performed propensity score-matched analysis and found that the similarities between the two sexes were consistent across different CS severities. Through subgroup analysis, we also found no significant differences in clinical outcomes between the two sexes according to age, initial heart function, or AMI clinical type.

Interestingly, there were no differences in outcomes even in terms of treatment options, which were consistent across mechanical ventilation, RRT, or ECMO support. However, there was a tendency toward differences in 12-month POCE between male and female patients with CS with high vasopressor use. In a previous study, increasing vasopressor requirements were independently associated with increasing mortality[30]. There was insufficient evidence that routine use of vasopressors and inotropics was associated with reduced mortality in patients with AMI complicated by CS in a previous meta-analysis, in addition to a previous study that showed lower mortality for patients who underwent invasive management compared with those managed conservatively[31,32]. The use of high-dose vasopressors in females might lead to poorer outcomes compared to males, which suggests that more aggressive interventions or alterations of treatment strategy might be required for females with high VIS in AMI complicated by CS. For female patients with CS caused by AMI, the higher the use of inotropes/vasopressors was, the poorer mid-term outcomes seemed to be compared to male patients with CS. However, relatively few female patients were enrolled, and only a quarter of patients were classified as having a high VIS for subgroup analysis, so the absolute number of high VIS females in this study was small. Consequently, it will be necessary to verify whether there is a significant difference in a larger cohort.

4.1. STUDY LIMITATIONS. Despite the strengths of this study as a large, multicenter, and dedicated study using a recent real-world CS registry with minimal exclusion criteria, our study has some limitations. First, this was a nonrandomized, retrospective, and observational study, and unmeasured confounding factors or selection bias may have significantly affected our results. In particular, the selection of revascularization and shock treatment strategies including MCS was at the operator's discretion, possibly introducing selection bias. In order to handle selection bias, we performed sensitivity analyses including multivariable Cox regression and propensity score matching to reduce the effects of potential confounders. However, we could not adjust for unmeasured variables. Second, because of the retrospective nature of our registry, we could not thoroughly identify any alterations in treatment strategies such as peri-procedural treatment or medical therapy in our overall study sample during follow-up. Moreover, we did not have any information on socioeconomic variables, menopausal or reproductive history, or behavioral and psychosocial characteristics and were unable to determine whether these factors play a role in the prognostic differences observed. Third, although our registry is the largest to date, the cohort was still relatively small; moreover, we evaluated patients with CS who were treated only with PCI. Patients with CS treated with thrombolysis or CABG are not reflected in our results. The lack of significant interactions in certain subgroup analyses may have been due to this limited study sample. Therefore, the current results should be interpreted as hypothesis-generating and should be confirmed in future, well-designed randomized trials. Fourth, the rate of nonfatal events was low relative to that of death during follow-up. Although we performed active follow-up, periodic site monitoring, and source document auditing in each center to ensure that all information was properly entered in the electronic case report form, we cannot rule out the possibility of missed events. Fifth, the generalizability of the findings from this study may be limited, primarily due to the restriction of study participants to South Korea. Nevertheless, we meticulously chose tertiary medical institutions, and this process was aimed at ensuring these institutions possessed the capacity to align with current guidelines and expert consensus pertaining to the appropriate management of CS. It is important to highlight that these chosen centers demonstrated proficiency in implementing Guideline-Directed Medical Therapy (GDMT) for the patients enrolled in the study. Due to the absence of available data regarding medical treatment after discharge, additional data collection or further GDMT analysis needs to be considered in future studies. Sixth, our analysis was limited to 12 months of follow-up and the true difference in prognostic effect of sex might not be apparent at 12 months. A longer follow-up duration may be necessary to confirm the clinical impact of sex on adverse outcomes in AMI complicated by CS. Finally, this study is constrained by the limited number of participants in relation to statistical power analysis. If we consider only the prospective aspect of the study, it is estimated that a minimum of 7,514 participants for POCE and 8,641 participants for all-cause mortality would be necessary to achieve 80% power according to a priori power analysis. However, it is important to note that this study is designed with both prospective and retrospective observational methodologies. Furthermore, anticipated outcomes from the subsequent investigation through the RESCUE II registry suggest that the study's findings will possess a broader scope due to its incorporation of a multicenter and multinational registry approach.

5. CONCLUSIONS

There was no significant difference in the 12-month risk of POCE and secondary outcomes between female and male patients who underwent PCI for AMI complicated by CS, irrespective of CS severity. The similarity of 12-month POCEs between the two sexes was consistent across various subgroups. Based on our results, sex does not seem to influence mid-term clinical outcomes in patients with CS caused by AMI. Further investigations regarding the potential therapeutic implications of these findings to narrow sex-related prognoses and identify disparities should be considered.

CONFLICTS OF INTEREST

All authors declare that there is no conflict of interest relevant to the submitted work.

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REFERENCES

1. Buerke M, Lemm H, Dietz S, Werdan K. Pathophysiology, diagnosis, and treatment of infarction-related cardiogenic shock. *Herz*. 2011;36(2):73.

2. Thiele H, Akin I, Sandri M, et al. PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock. *N Engl J Med*. 2017;377(25):2419-2432.

3. Rathod KS, Koganti S, Iqbal MB, et al. Contemporary trends in cardiogenic shock: Incidence, intra-aortic balloon pump utilisation and outcomes from the London Heart Attack Group. *Eur Heart J Acute Cardiovasc Care*. 2018;7(1):16-27.

4. Ouweneel DM, Eriksen E, Sjauw KD, et al. Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction. *J Am Coll Cardiol*. 2017;69(3):278-287.

5. Rob D, Belohlavek J. The mechanical support of cardiogenic shock. *Curr Opin Crit Care*. 2021;27(4):440-446.

6. Yan I, Schrage B, Weimann J, et al. Sex differences in patients with cardiogenic shock. *ESC Heart Fail*. 2021;8(3):1775-1783.

7. Muller G, Flecher E, Lebreton G, et al. The ENCOURAGE mortality risk score and analysis of long-term outcomes after VA-ECMO for acute myocardial infarction with cardiogenic shock. *Intensive Care Med*. 2016;42(3):370-378.

8. Vallabhajosyula S, Ya'Qoub L, Singh M, et al. Sex Disparities in the Management and Outcomes of Cardiogenic Shock Complicating Acute Myocardial Infarction in the Young. *Circ Heart Fail*. 2020;13(10):e007154.

9. Osman M, Syed M, Kheiri B, et al. Age stratified sex-related differences in incidence, management, and outcomes of cardiogenic shock. *Cathet Cardiovasc Interv*. 2022;99(7):1984-1995.

10. Lozano-Jiménez S, Iranzo-Valero R, Segovia-Cubero J, et al. Gender differences in cardiogenic shock patients: clinical features, risk prediction, and outcomes in a hub center. *Front Cardiovasc Med*. 2022;9:912802.

11. Schmitt A, Schupp T, Rusnak J, et al. Does sex affect the risk of 30-day all-cause mortality in cardiogenic shock? *Int J Cardiol*. 2023;381:105-111.

12. Yang JH, Choi KH, Ko YG, et al. Clinical Characteristics and Predictors of In-Hospital Mortality in Patients With Cardiogenic Shock: Results From the RESCUE Registry. *Circ Heart Fail*. 2021;14(6):e008141.

13. Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. *Cathet Cardiovasc Interv*. 2019;94(1):29-37.

14. Song YB, Hahn JY, Choi SH, et al. Sirolimus-versus paclitaxel-eluting stents for the treatment of coronary bifurcations results: from the COBIS (Coronary Bifurcation Stenting) Registry. *J Am Coll Cardiol*. 2010;55(16):1743-1750.

15. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2016;68(10):1082-1115.

16. Valgimigli M, Bueno H, Byrne RA, et al. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2018;39(3):213-260.

17. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115(17):2344-2351.

18. Thiele H, Allam B, Chatellier G, Schuler G, Lafont A. Shock in acute myocardial infarction: the Cape Horn for trials? *Eur Heart J*. 2010;31(15):1828-1835.

19. Thiele H, Zeymer U, Neumann F-J, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367(14):1287-1296.

20. Thiele H, Akin I, Sandri M, et al. One-year outcomes after PCI strategies in cardiogenic shock. *N Engl J Med*. 2018;379(18):1699-1710.

21. Arora S, Stouffer GA, Kucharska-Newton AM, et al. Twenty Year Trends and Sex Differences in Young Adults Hospitalized With Acute Myocardial Infarction. *Circulation*. 2019;139(8):1047-1056.

22. Basir MB, Lemor A, Gorgis S, et al. Vasopressors independently associated with mortality in acute myocardial infarction and cardiogenic shock. *Cathet Cardiovasc Interv*. 2022;99(3):650-657.

23. Jentzer JC, van Diepen S, Barsness GW, et al. Cardiogenic Shock Classification to Predict Mortality in the Cardiac Intensive Care Unit. *J Am Coll Cardiol*. 2019;74(17):2117-2128.

24. Ya'qoub L, Lemor A, Dabbagh M, et al. Racial, ethnic, and sex disparities in patients with STEMI and cardiogenic shock. *Cardiovasc Intervent*. 2021;14(6):653-660.

25. Elgendy IY, Wegermann ZK, Li S, et al. Sex differences in management and outcomes of acute myocardial infarction patients presenting with cardiogenic shock. *Cardiovasc Intervent*. 2022;15(6):642-652.

26. Jentzer JC, van Diepen S, Barsness GW, et al. Cardiogenic shock classification to predict mortality in the cardiac intensive care unit. *J Am Coll Cardiol*. 2019;74(17):2117-2128.

27. Naidu SS, Baran DA, Jentzer JC, et al. SCAI SHOCK Stage Classification Expert Consensus Update: A Review and Incorporation of Validation Studies: This statement was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS) in December 2021. *J Am Coll Cardiol*. 2022;79(9):933-946.

28. Burgos LM, Vila RCB, Botto F, Diez M. SCAI Cardiogenic Shock Classification for Predicting In-Hospital and Long-Term Mortality in Acute Heart Failure. *J Soc Cardiovasc Angiography Intervent*. 2022;1(6):100496.

29. Rubini Gimenez M, Zeymer U, Desch S, et al. Sex-specific management in patients with acute myocardial infarction and cardiogenic shock: a substudy of the CULPRIT-SHOCK trial. *Circulat Cardiovasc Intervent*. 2020;13(3):e008537.

30. Vallabhajosyula S, Vallabhajosyula S, Dunlay SM, et al., eds. *Sex and gender disparities in the management and outcomes of acute myocardial infarction-cardiogenic shock in older adults. Mayo Clinic Proceedings*. Elsevier; 2020.

31. Karami M, Hemradj VV, Ouweneel DM, et al. Vasopressors and inotropes in acute myocardial infarction related cardiogenic shock: a systematic review and meta-analysis. *J Clin Med*. 2020;9(7):2051.

32. Bangalore S, Gupta N, Guo Y, et al. Outcomes with invasive vs conservative management of cardiogenic shock complicating acute myocardial infarction. *Am J Med*. 2015;128(6):601-608.

KEYWORDS Sex, SCAI shock classification, Cardiogenic shock, Acute myocardial infarction

APPENDIX A. SUPPLEMENTARY DATA Supplementary data to this article can be found online at https://doi.org/10.1016/j.hjc.2023.11.007.