

Sex Differences in Systolic Heart Failure in Patients with Acute ST-Elevation Myocardial Infarction Undergoing Primary Percutaneous Intervention

Basant Zahid ^a, Tarek H. Abou-El Azm ^a,
Hamed G. Zaghloul ^{b*} and Amro Elnagar ^a

^a Cardiology Department, Faculty of Medicine, Benha University, AlQalyubia, Egypt.

^b Cardiology Department, Sheikh Zayed Specialized Hospital, Giza, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. Authors BZ, THAEA, HGZ and AE designed the study. Authors BZ and AE performed the experiments and analyzed the data. Authors AE and THAEA provided critical reagents. Authors HGZ and BZ supervised the experiments. Authors THAEA, HGZ and BZ wrote the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: <https://doi.org/10.9734/ca/2025/v14i1474>

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://pr.sdiarticle5.com/review-history/131171>

Original Research Article

Received: 15/12/2024
Accepted: 17/02/2025
Published: 21/02/2025

ABSTRACT

Aims: Sex differences refer to the biological and physiological variations in the cardiovascular system that arise from distinct gene expressions associated with sex chromosomes. Notable and well-documented sex differences in ST-elevation myocardial infarction (STEMI) indicate that women

*Corresponding author: E-mail: hamedgamal282@gmail.com;

tend to be elderly and present with a more significant number of comorbidities in comparison to men. The aim is to investigate sex-specific differences in systolic heart failure (SHF) among patients with acute STEMI who are undergoing primary percutaneous coronary intervention (PCI). This study also included a follow-up period of three months to assess the occurrence of major adverse cardiovascular events (MACE) and to conduct a conventional echocardiographic evaluation.

Study Design: This investigation is a prospective cohort study.

Place and Duration of Study: Department of Cardiology, Faculty of Medicine, Benha University, AlQalyubia, Egypt, between October 2023 and October 2024.

Methods: We included 116 adult patients with SHF following STEMI undergoing primary PCI. The subjects were divided into two equal groups: male (58 cases) and female (58 cases).

Results: Females exhibited significantly higher NT-proBNP levels and lower left ventricular ejection fraction (LVEF) than males ($P < 0.001$, $P = 0.02$, respectively). Readmission with acute heart failure (AHF) at three months was significantly increased in females compared to males ($P = < 0.001$). Cardiovascular death and AHF at three months were significantly higher in females compared to males ($P = 0.031$). Females showed significantly higher MACE compared to males ($P = 0.016$).

Conclusions: Female patients with SHF following STEMI who undergo primary PCI have a higher risk of cardiovascular mortality within the first three months compared to males. The observed difference in mortality suggests that female patients may require different clinical approaches and closer follow-up to improve outcomes.

Keywords: Sex differences; systolic heart failure; acute st-elevation myocardial infarction; percutaneous coronary intervention.

1. INTRODUCTION

Acute coronary syndromes (ACS) comprise a range of clinical manifestations, primarily distinguished by the characteristics of the presenting electrocardiogram, which may indicate either ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation acute coronary syndrome (NSTEMI) (Collet, et al., 2021).

Primary percutaneous coronary intervention (PCI) is the optimal reperfusion method for patients presenting with STEMI within 12 hours of symptom onset, provided that it is performed promptly within 120 minutes of the STEMI diagnosis by a skilled medical team. PCI demonstrates superior efficacy compared to fibrinolysis in reducing mortality rates, the incidence of reinfarction, and the occurrence of stroke (Jortveit, et al., 2022).

Heart failure (HF) is a clinical condition defined by multiple symptoms, including dyspnea, tiredness, and exertional intolerance, as well as indicators including edema, gallop rhythm, and rales, all of which are linked with cardiac issues (Fudim et al., 2018). HF may also be characterized hemodynamically as the inability to deliver sufficient cardiac output to the body, whether at rest, during physical exertion, or solely in the presence of elevated cardiac filling pressures (Selvaraj et al., 2019).

The maintained left ventricular ejection fraction (LVEF) exceeds 50% of the total blood volume. An LVEF of 40% or below signifies a significant left ventricular systolic function deterioration. This condition is categorized as heart failure with reduced ejection fraction (HFrEF). Patients presenting with an LVEF between 41% and 49% manifest a mild impairment in left ventricular systolic function, which is categorized as heart failure with mid-range ejection fraction (HFmrEF) (Bozkurt et al., 2021; Masip et al., 2022).

We aimed to investigate sex-specific differences in systolic heart failure (SHF) among patients experiencing acute STEMI who underwent primary PCI and followed up after three months to evaluate the occurrence of major adverse cardiovascular events (MACE) and to perform a conventional echocardiographic study.

2. MATERIALS AND METHODS

This prospective cohort study was carried out on 116 adult patients with SHF (with ejection fraction less than 50%) following STEMI undergoing primary PCI at Benha University Hospital and El Sheikh Zayed Specialized Hospital during the period from October 2023 to October 2024.

Inclusion criteria were male and female genders, ages older than 18 years old, undergoing primary PCI due to STEMI, and with SHF (LVEF less than 50%) classified to reduced LVEF is defined

as equal or less than 40%. This is classified as HFrEF. Patients with an LVEF ranging from 41% to 49% have mildly reduced LVSF, classified as HFmrEF.

Exclusion criteria were severe chronic renal and liver failure, complete or incomplete bundle branch block, atrial fibrillation, moderate-severe valvular pathology, moderate to severe anemia, pulmonary hypertension (HTN) or pulmonary embolism, thyroid dysfunction, active cancer, and chronic pulmonary diseases.

2.1 Patient Grouping

(Male Group): 58 male patients with SHF following STEMI undergoing primary PCI.

(Female Group): 58 female patients with SHF following STEMI undergoing primary PCI.

All patients underwent the following procedures: History Acquisition, Clinical Assessment, Echocardiographic Evaluation, and quantification of N-terminal pro-b-type Natriuretic Peptide (NT-proBNP).

2.1.1 History taking

- **Personal History:** Age, sex, residence, occupation, and smoking habits were recorded.
- **Medical History:** HTN, diabetes, hyperlipidemia, CAD, and cardiac events (stable angina, MI, PCI, CABG, PAD, stroke) were examined.
- **Present illness:** Symptoms related to heart failure (e.g., dyspnea, orthopnea, paroxysmal nocturnal dyspnea) were documented.

2.1.2 Clinical examination

Upon admission, all patients underwent a comprehensive clinical examination to assess their overall condition, focusing on cardiovascular health and signs of heart failure. The following findings were recorded:

2.1.3 General examination

- **Vital Signs,** including heart rate and blood pressure.

2.1.4 Systemic Examination

Cardiovascular System: Signs of HF, such as jugular vein distension, hepatomegaly,

hepatojugular reflux, and the presence of an S3 gallop, were evaluated. (Selvaraj et al., 2019).

2.1.5 Killip Classification

- The Killip classification was used to stratify the severity of heart failure in patients following acute STEMI based on clinical signs observed during admission (Mello, et al., 2014, Del, et al., 2021).

Killip Class I patients have no HF signs such as rales, S3 gallop, or jugular venous distension. Killip Class II is mild heart failure with lung rales, an S3 gallop, and elevated jugular venous pressure but no pulmonary edema. Killip Class III patients exhibit acute pulmonary edema with substantial pulmonary rales and respiratory distress. Cardiogenic shock patients with hypotension (systolic blood pressure < 90 mmHg), peripheral vasoconstriction generating cold extremities, oliguria, and mental confusion are in Killip Class IV.

2.2 Echocardiographic Study

According to the most recent guidelines, a baseline echocardiographic assessment was conducted upon admission, followed by a subsequent evaluation three months later. This study aimed to assess LVEF, left ventricular end-diastolic volume (LVEDV), and left ventricular end-systolic volume (LVESV). All patients underwent an initial transthoracic echocardiogram. LVEF was quantified utilizing the biplane Simpson's method, with patients categorized as having SHF if their LVEF was below 50%. Additional echocardiographic parameters, including LVEDV and LVESV, were documented to corroborate the diagnosis and evaluate the extent of systolic dysfunction. A normal LVEF is defined as exceeding 50% of the total blood volume, while a reduced LVEF is characterized as being equal to or less than 40%, which is classified as HFrEF. Patients exhibiting an LVEF ranging from 41% to 49% are identified as having mildly reduced left ventricular systolic function, referred to as HFmrEF (Bozkurt B, Coats AJS, 2021).

2.3 N-terminal Pro-B-type Natriuretic Peptide (NT-proBNP) Measurement

NT-proBNP levels were measured for all patients upon admission to evaluate the severity of HF. Blood samples were obtained in the emergency

department within the initial 24 hours following admission before the commencement of any interventions. Serum concentrations of NT-proBNP were quantified using an automated electrochemiluminescence immunoassay (ECLIA) on a Cobas e411 analyzer (Roche Diagnostics), per the manufacturer's guidelines. The findings were presented in picograms per milliliter (pg/mL). An elevated level of NT-proBNP was deemed indicative of a more severe manifestation of HF. The reference ranges were established utilizing age and gender-specific thresholds, with elevated levels delineated as exceeding 300 pg/mL for patients under the age of 50 years and exceeding 900 pg/mL for individuals aged 50 years and older. (Sarak & Karadeniz, 2019).

2.4 Study Interventions

Patients with STEMI complicated by acute HF require urgent and coordinated management of both conditions. All patients received standard medical treatment according to the latest STEMI and heart failure guidelines (Lee, et al., 2023), Including dual antiplatelet therapy, statins, Beta-blockers, ACE inhibitors or ARBs, diuretics when needed, and spironolactone when indicated. All patients received the same drugs, excluding patients who received different drugs or doses. All patients underwent primary PCI within the window.

Angiography: Coronary angiography was conducted utilizing either the femoral or radial approach, employing the standard technique with a 6Fr arterial sheath. The objective of PCI was to achieve thrombolysis in myocardial infarction (TIMI) grade 3 flow, which was evaluated according to established criteria. A successful procedure was defined as having a residual stenosis of less than 30% based on visual estimation. Complete procedural success was characterized by less than 30% residual stenosis and TIMI grade 3 flow in all treated lesions. In comparison, partial success was indicated by residual stenosis exceeding 30% or TIMI flow of less than 3 in non-infarct-related artery lesions (La, et al., 2023). The no-reflow phenomenon was defined as a TIMI myocardial perfusion grade of less than 3, assessed according to standard criteria and duly reported. Complete revascularization was defined as the absence of total occlusion and/or residual stenosis greater than 70% in any significant coronary artery or its principal branches at discharge (Ndrepepa, et al., 2018).

Follow-Up: Three months follow-up was done for both echocardiographic data and for detection of MACE, defined as non-fatal stroke, non-fatal MI, rehospitalization due to acute heart failure (AHF), and cardiovascular death. (Okkonen, et al., 2021).

Statistical analysis: The statistical analysis and administration of the data were carried out using the SPSS version 28 software crafted by IBM (Armonk, New York, United States of America). Using the Shapiro-Wilk test and direct data visualization tools, we ensured that the quantitative data was high quality. Following a description of the quantitative data, which included the means and standard deviations, we compared the data using the independent t-test, considering the normalcy assumption. To describe the categorical data, percentages, and numbers were used, and the Chi-square test was utilized to make comparisons. The use of multivariate logistic regression analysis estimated the likelihood of dying from cardiovascular disease. In cases where the p-value was lower than 0.05, the findings were deemed statistically significant.

3. RESULTS

Males and females exhibited significant differences in several variables. Females were older than males, with a mean age of 64.5 ± 5.2 years compared to 56.4 ± 5.3 years ($P < 0.001$). A higher proportion of females had a family history of CAD ($P < 0.001$) and diabetes ($P < 0.001$). Similarly, HTN was more prevalent in females ($P < 0.001$). Current smoking was significantly more common in males ($P < 0.001$). Prior stable angina was also more frequent in females ($P = .04$). Other variables, including hypercholesterolemia, prior MI, prior PCI, prior CABG, peripheral artery disease, and prior stroke, were not significant ($P = 1.0$). Females had a lower admission heart rate than males ($P = .03$). Killip class distribution also differed significantly; males were more likely to present in Killip I, while females had higher rates of Killip II and Killip III. Additionally, females exhibited higher NT-proBNP levels than males ($P < 0.001$). Other variables, including systolic blood pressure, serum creatinine, and the STEMI type at admission, were insignificant Table 1.

Females exhibited significantly lower LVEF (40.8 ± 5.9) than males (43 ± 4), with a P value of 0.02. males and females had comparable LVEDV,

LVESV, LA diameter, tricuspid annular plane pressure ($P = .41$, $P = .27$, $P = .83$, $P = .57$, and systolic excursion, or pulmonary artery systolic $P = .42$, respectively) Table 2.

Table 1. General characteristics and baseline clinical characteristics according to gender

	Males (n = 58)	Females (n = 58)	P
Age (years)	56.4 ± 5.3	64.5 ± 5.2	<0.001*
Family history of CAD	9 (15.5)	37 (63.8)	<0.001*
Diabetes	8 (13.8)	36 (62.1)	<0.001*
Hypertension	38 (65.5)	53 (91.4)	<0.001*
Hypercholesterolemia	23 (39.7)	30 (51.7)	0.192
Current smokers	32 (55.2)	4 (6.9)	<0.001*
Prior stable angina	26 (44.8)	37 (63.8)	0.04*
Prior myocardial infarction	17 (29.3)	12 (20.7)	0.284
Prior PCI	6 (10.3)	4 (6.9)	0.508
Prior CABG	0 (0)	1 (1.7)	1.0
Peripheral artery disease	2 (3.4)	2 (3.4)	1.0
Prior stroke	4 (6.9)	3 (5.2)	1.0
Clinical characteristics			
Admission SBP (mm Hg)	130 ± 16	135 ± 12	0.058
Admission heart rate (beats/min)	86 ± 11	82 ± 10	0.034*
Admission serum creatinine (mg/dL)	1.2 ± 0.4	1.2 ± 0.3	0.41
Killip Class			
Killip I	43 (74.1)	20 (34.5)	<0.001*
Killip II	15 (25.9)	28 (48.3)	
Killip III	0 (0.0)	10 (17.2)	
Type of STEMI			
Anterior	19 (32.8)	15 (25.9)	0.948
Anterior-inferior	2 (3.4)	3 (5.2)	
Antro-lateral	2 (3.4)	2 (3.4)	
Inferior	23 (39.7)	24 (41.4)	
Lateral	6 (10.3)	9 (15.5)	
Septal	2 (3.4)	3 (5.2)	
Posterior	4 (6.8)	2 (3.4)	
NT-proBNP (pg/mL)	730(350 – 2041)	1303.5 (350 – 3373)	<0.001*

Data are represented as Mean + SD, Range or frequency (%), Median (IQR), CAD: Coronary artery disease; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft. SBP: Systolic blood pressure; SD: Standard deviation; STEMI: ST-elevation myocardial infarction; NT-proBNP: N-terminal pro-b-type natriuretic peptide. *: significant P value

Table 2. Baseline Echocardiography findings according to gender

	Males (n = 58)	Females (n = 58)	P
LVEF (%)	43 ± 4	40.8 ± 5.9	0.02*
LVEDV (mL)	5.4 ± 0.6	5.5 ± 0.7	0.407
LVESV (mL)	3.8 ± 0.5	4 ± 0.6	0.273
LA Diameter (cm)	3.9 ± 0.5	3.9 ± 0.5	0.833
TAPSE	18.3 ± 2.2	18 ± 2.7	0.565
PASP (mmHg)	19.3 ± 1.5	19.5 ± 1.2	0.418

Data are represented as Mean + SD, LVEF: Left ventricular ejection fraction; SD: Standard deviation; LVEDV: Left ventricular end-diastolic volume; LVESV: Left ventricular end-systolic volume; LA: Left atrial; TAPSE: Tricuspid annular plane systolic excursion; PASP: Pulmonary artery systolic pressure. *: significant P value

In hospital outcome: No in-hospital MACEs were reported in both genders.

Three-month follow-up for MACE and Echocardiography: Echocardiography- No significant differences were observed between males and females in LVEF, LVEDV, LVESV, left atrial diameter,

tricuspid annular plane systolic excursion, or pulmonary artery systolic pressure ($P = .47$, $P = .47$, $P = .25$, $P = .49$, $P = .91$ and $P = .21$ respectively) Table 3.

Table 3. Three-month Echocardiography findings according to gender

	Males (n = 58)	Females (n = 58)	P
LVEF%	43.8 ±4.6	43.1 ±4.7	0.465
LVEDV (mL)	5.4 ±0.6	5.5 ±0.7	0.467
LVESV (mL)	3.9 ±0.5	4 ±0.6	0.249
LA Diameter (cm)	4 ±0.5	4 ±0.5	0.491
TAPSE (mm)	18.3 ±2.3	18.4 ±2.8	0.906
PASP	19.5 ±1.5	19.8 ±1.2	0.211

Data are represented as Mean ±SD, LVEF: Left ventricular ejection fraction; LVEDV: Left ventricular end-diastolic volume; LVESV: Left ventricular end-systolic volume; LA: Left atrial; TAPSE: Tricuspid annular plane systolic excursion; PASP: Pulmonary artery systolic pressure

Cardiovascular mortality and readmission due to AHF at three months were markedly elevated in females in comparison to males ($P = .03$, $P < 0.001$, respectively). The incidence of non-fatal stroke and non-fatal MI was found to be comparable between males and females, with $p = 1.0$ and 0.47 , respectively.

Females showed significantly higher MACE than males (60.3% vs. 37.9%), with a P-value of 0.016. Fig. 1.

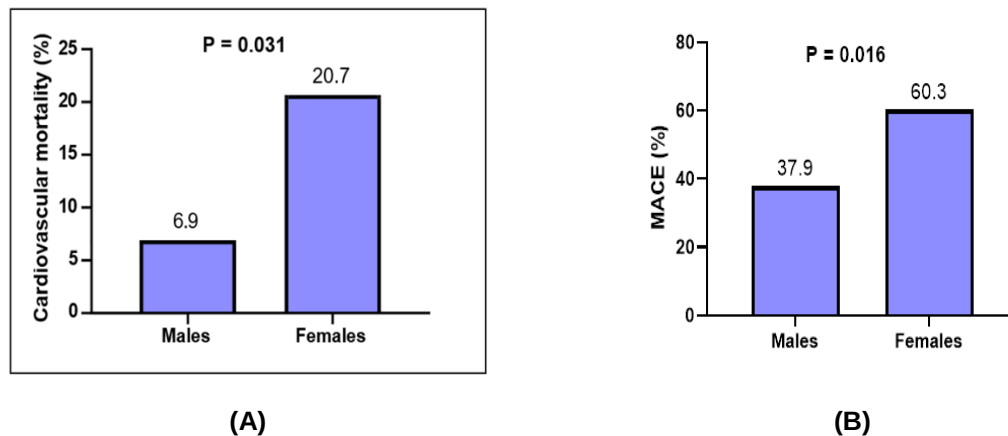


Fig. 1. Three-month outcome (A) Cardiovascular mortality and (B) MACE according to gender
MACE: major adverse cardiovascular events

Multivariate logistic regression analysis was done to predict MACE. Gender was a significant predictor, with females having a higher odds ratio for MACE than males (OR: 7.4, 95% CI: 1.835 - 29.849, $P = .01$); other variables, including age, family history of CAD, diabetes, HTN, smoking status, and hypercholesterolemia ($P = 0.35$), were not statistically significant predictors ($P = .01$, $P = .32$, $P = .903$, $P = 0.97$ and $P = .19$ respectively) Table 4.

Table 4. Multivariate logistic regression analysis to predict mortality

	OR (95% CI)	P
Age (years)	0.939 (0.87 - 1.012)	0.099
Female gender	7.4 (1.835 - 29.849)	0.005*
Family history of CAD (%)	0.619 (0.241 - 1.59)	0.319
Diabetes (%)	0.945 (0.379 - 2.352)	0.903
Hypertension (%)	1.02 (0.38 - 2.737)	0.969
Current smokers (%)	1.961 (0.724 - 5.309)	0.185
Hypercholesterolemia (%)	1.453 (0.667 - 3.168)	0.347

OR: Odds ratio; CI: Confidence interval; CAD: Coronary artery disease, *: significant P value

4. DISCUSSION

ACS are categorized based on ECG findings into STEMI and NSTEMI-ACS. The study aims to determine sex-specific differences in SHF in patients with acute STEMI undergoing primary PCI and follow-up after 3 months for MACE and conventional echocardiographic study.

In our study, males and females exhibited significant differences in several variables. Females were older than males, with a mean age of 64.5 ± 5.2 years compared to 56.4 ± 5.3 years ($P < 0.001$). A higher proportion of females had a family history of CAD ($P < 0.001$) and diabetes ($P < 0.001$). Similarly, HTN was more prevalent in females ($P < 0.001$). Current smoking was significantly more common in males ($P < 0.001$). Prior stable angina was also more frequent in females ($P = .04$). Other variables, including hypercholesterolemia ($P = .19$), prior MI ($P = .28$), prior PCI ($P = .51$), prior CABG ($P = 1.0$), peripheral artery disease ($P = 1.0$), and previous stroke ($P = 1.0$), were not significant.

Women tend to experience cardiovascular events at an older age due to the protective effects of estrogen before menopause. (Ryczkowska, et al., 2023). A higher prevalence of family history of CAD, diabetes, and HTN in females suggests a more significant burden of predisposing risk factors. (Garcia, et al., 2016). Conversely, current smoking was significantly more common in males, reflecting gender-based differences in lifestyle behaviors. (Branstetter, et al., 2012).

The study by Savage et al., which aimed to assess sex differences in treatment and outcomes in STEMI patients treated with primary PCI, including 1244 patients treated with primary PCI, found a significantly higher smoking history among males compared to females (64.9% vs 55.1%, P value=0.002). Contrasting our results, they found no significant differences regarding risk factors such as diabetes, HTN, dyslipidemia, and a history of CAD.

Cenko et al., on the other hand, conducted a study to evaluate and investigate sex-specific differences in 30-day mortality in patients with ACS and acute HF at the time of presentation. Of the 87,812 patients, 30,922 (35.2%) were female. The study found no significant differences between men and women in age or family history of CAD, diabetes, HTN, or hypercholesterolemia. These differences may be

attributed to the differences in population and methodology. While parallel to our results regarding smoking, they found a relatively similar percentage of current smokers.

Females had a lower admission heart rate than males (82 ± 10 vs. 86 ± 11 beats/min, $P = .03$). Killip class distribution also differed significantly; males were more likely to present in Killip I ($P < 0.001$), while females had higher rates of Killip II and Killip III. Additionally, females exhibited higher NT-proBNP levels than males ($P < 0.001$). Other variables, including admission systolic blood pressure ($P = .06$), admission serum creatinine ($P = .41$), and the type of STEMI ($P = .95$), did not differ significantly between groups.

Gevaert and colleagues aimed to compare the predictive effectiveness of the TIMI risk score and in-hospital mortality between Belgian women and men undergoing primary PCI among 8,073 consecutive primary PCI-treated STEMI patients. They discovered significant differences between males and females regarding blood pressure, Killip class, and heart rate, which agreed with our findings (P values were <0.001). (Gevaert, et al., 2014).

Males tend to exhibit higher sympathetic nervous system activity, which can increase heart rate, particularly during acute conditions like STEMI (Kasahara, et al., 2021). Smoking, more common among males, further elevates heart rate by stimulating the sympathetic system (Price & Martinez, 2019). Gender differences in physiological responses to ischemia and acute stress may also play a role, with males potentially experiencing greater heart rate increases due to higher baseline physical stress levels or variations in autonomic cardiovascular regulation (Vaccarino, et al., 2014). Additionally, testosterone's influence on cardiovascular responses during acute events like STEMI may contribute to these differences (Kaur & Werstuck, 2021).

The Killip class distribution shows that males were more likely to present with milder heart failure symptoms (Killip I). At the same time, females had higher rates of moderate to severe heart failure (Killip II and III), indicating a more critical clinical presentation, which was further supported by significantly elevated NT-proBNP levels in females, a marker of cardiac stress and worse heart failure severity. Similar results were reported by Murat et al., who looked at the angiographic findings, risk factors, and clinical

features of patients under 40, as well as the in-hospital and one-year death rates, taking gender differences into account.

Their study included a cohort of 244 patients and revealed that males were more frequently classified as Killip class 1, whereas females were more commonly classified as Killip class 2 (P value = 0.02) (Murat, et al., 2021). Women were shown to present with more atypical symptoms, which led to delayed or incorrect diagnosis in previous studies such as NRMI (National Registry of MI) and VIRGO (Variation in Recovery, Role of Gender on Outcome of Young AMI Patients).

Females exhibited significantly lower LVEF (40.8 ± 5.9) than males (43 ± 4), with a P value of .02. LVEDV ($P = .41$), LVESV ($P = .27$), left atrial diameter ($P = .83$), tricuspid annular plane systolic excursion ($P = .57$), and pulmonary artery systolic pressure ($P = .42$) did not vary significantly between men and females.

In accordance with this, Murat et al. observed that LVEF measured via transthoracic echocardiography was substantially reduced in women compared to men prior to discharge (P value = 0.02) (Murat, et al., 2021). This may be due to their older age, higher prevalence of comorbidities such as HTN and diabetes, and delayed presentation or diagnosis, leading to more extensive myocardial damage. Hormonal changes post-menopause, smaller coronary artery size, and higher myocardial stress (evidenced by elevated NT-proBNP levels) further contribute to impaired systolic function. Additionally, women may experience distinct adverse ventricular remodeling following STEMI, exacerbating LVEF reduction. (Schamroth, et al., 2021).

Leboube et al. conducted a study involving 791 patients to evaluate the prevalence of heart failure subsequent to primary PCI for STEMI across genders. Their findings indicated no significant difference in the increase of LV volumes or the proportion of adverse LV remodeling between male and female patients, with rates of 44.4% and 48.5%, respectively ($P = .64$). The p -value was 0.74, indicating that the LVEF was similar between the two groups both at baseline and after one year of follow-up, with values of $45.4 \pm 9.5\%$ in women compared to $46.4 \pm 8.8\%$ in men ($p = 0.55$; $p = 0.55$). (Leboube, et al., 2024).

At 3-month follow-up, AHF was significantly higher in females (48.3%) compared to males (15.5%), with a P value of < 0.001 . Cardiovascular death at three months was significantly higher in females compared to males (20.7% vs. 6.9%, $P = .03$). Other variables, including non-fatal stroke ($P = 1.0$) and non-fatal MI ($P = .47$), showed no significant differences between males and females.

Women were also more likely than males to have 30-day mortality (29.8% vs 25.5%; RR: 1.24; 95% CI: 1.17–1.31). The sample of ACS patients without clinical acute HF on presentation helped to lower the fatality rates. Still, the sex variations in 30-day mortality remained. Following PCI, the death rate steadily dropped in both sexes but remained higher in women than in men (24.0% vs 20.1%; RR: 1.25; 95% CI: 1.12–1.39) (Cenko, et al., 2019).

Females showed significantly higher MACE than males (60.3% vs. 37.9%), with a P -value of 0.016.

Martinho also conducted a retrospective observational analysis from 2010 to 2015 with 884 consecutive patients hospitalized with STEMI who received PCI within 48 hours of symptom start. By comparison to 4.6% of males, the results showed that 11.8% of women had died at the 30-day point, producing a hazard ratio (HR) of 2.76. Unlike 16.9% of men (hazard ratio 2.33), over one-third of women (32.1%) had given up at the five-year milestone. Comparatively to 19.8% of males (HR 2.10), more than one-third of women (34.2%) reported MACE within five years. (Martinho, 2023).

Multivariate logistic regression analysis was done to predict mortality. Gender was a significant predictor, with females having a higher odds ratio for the outcome than males (OR: 4.62, 95% CI: 1.004 - 21.259, $P = .05$). Other variables, including age ($P = .94$), family history of CAD ($P = .46$), diabetes ($P = .43$), HTN ($P = .58$), smoking status ($P = .43$), and hypercholesterolemia ($P = .85$), were not statistically significant predictors.

A multivariable model was developed in the Cenko et al. research to investigate further the impact of sex on AHF and 30-day mortality. AHF (OR: 1.14; 95% CI: 1.11-1.18) and 30-day mortality (OR: 1.27; 95% CI: 1.20-1.34) were independently correlated with female sex. Additionally, the multivariable analysis revealed an independent relationship between AHF and

30-day mortality (OR: 6.60; 95% CI: 6.25-6.98) (Cenko, et al., 2019).

In addition, Izadnegahdar et al. produced a 10-year descriptive study of mortality risk in a Canadian context using 70,628 AMI hospitalizations in people aged ≥ 20 years in British Columbia, Canada, with 17.1% of the cohort being younger individuals ≤ 55 years. Men (13.0% to 9.3%) and women (19.4% to 13.9%) saw comparable declining 30-day mortality rates (sex-year interaction $p = .33$). Even in the most recent period; however, younger women still had a greater risk of mortality than younger men [odds ratio: (2008-09) = 1.61 (95% CI: 1.25, 2.08)] (Izadnegahdar, et al., 2014).

Study limitation: Our investigation has limitations. First, the research was carried out at two relatively small institutions, which may not fairly reflect the larger community of STEMI patients of both sexes. Furthermore, the three-month follow-up period may not have been sufficient to record the long-term effects of SHF on STEMI sufferers.

5. CONCLUSION

Female patients with SHF following STEMI who undergo primary PCI have a higher risk of cardiovascular mortality and readmission with AHF within the first three months compared to males. The observed difference in mortality suggests that female patients may require different clinical approaches and closer follow-up to improve outcomes. This study points to the necessity of further research to understand the underlying factors contributing to these sex-specific disparities in prognosis, aiming to develop more effective and individualized treatment strategies for female patients post-PCI.

CONSENT

An informed written consent obtained from all patients or first-degree relatives before participation was obtained.

ETHICAL APPROVAL

It is not applicable.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image

generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Bozkurt, B., Coats, A. J., Tsutsui, H., Abdelhamid, C. M., Adamopoulos, S., Albert, N., Anker, S. D., Gomez-Mesa, J. E., Heidenreich, P., Imamura, T., & Jankowska, E. A. (2021). Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. *European Journal of Heart Failure*, 23, 352-380.
- Branstetter, S. A., Blosnich, J., Dino, G., Nolan, J., & Horn, K. (2012). Gender differences in cigarette smoking, social correlates, and cessation among adolescents. *Addictive Behaviors*, 37, 739-742.
- Cenko, E., van der Schaar, M., Yoon, J., Manfrini, O., Vasiljevic, Z., Vavlukis, M., et al. (2019). Sex-related differences in heart failure after ST-segment elevation myocardial infarction. *Journal of the American College of Cardiology*, 74, 2379-2389.
- Collet, J. P., Thiele, H., Barbato, E., Barthélémy, O., Bauersachs, J., Bhatt, D. L., et al. (2021). 2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *European Heart Journal*, 42, 1289-1367.
- Del Buono, M. G., Montone, R. A., Rinaldi, R., Gurgoglione, F. L., Meucci, M. C., Camilli, M., et al. (2021). Clinical predictors and prognostic role of high Killip class in patients with a first episode of anterior ST-segment elevation acute myocardial infarction. *Journal of Cardiovascular Medicine*, 22, 530-538.
- Fudim, M., Parikh, K. S., Dunning, A., et al. (2018). Relation of volume overload to clinical outcomes in acute heart failure (from ASCEND-HF). *American Journal of Cardiology*, 122, 1506-1512.
- Garcia, M., Mulvagh, S. L., Merz, C. N., Buring, J. E., & Manson, J. E. (2016). Cardiovascular disease in women: Clinical perspectives. *Circulation Research*, 118, 1273-1293.

- Gevaert, S. A., De Bacquer, D., Evrard, P., Convens, C., Dubois, P., Boland, J., et al. (2014). Gender, TIMI risk score, and in-hospital mortality in STEMI patients undergoing primary PCI: Results from the Belgian STEMI registry. *EuroIntervention*, 9, 1095-1101.
- Izadnegahdar, M., Singer, J., Lee, M. K., Gao, M., Thompson, C. R., Kopec, J., et al. (2014). Do younger women fare worse? Sex differences in acute myocardial infarction hospitalization and early mortality rates over ten years. *Journal of Women's Health (Larchmt)*, 23, 10-17.
- Jortveit, J., Pripp, A. H., & Halvorsen, S. (2022). Outcomes after delayed primary percutaneous coronary intervention vs. pharmaco-invasive strategy in ST-segment elevation myocardial infarction in Norway. *European Heart Journal – Cardiovascular Pharmacotherapy*, 8, 442-451.
- Kasahara, Y., Yoshida, C., Saito, M., & Kimura, Y. (2021). Assessments of heart rate and sympathetic and parasympathetic nervous activities of normal mouse fetuses at different stages of fetal development using fetal electrocardiography. *Frontiers in Physiology*, 12, 652828.
- Kaur, H., & Werstuck, G. H. (2021). The effect of testosterone on cardiovascular disease and cardiovascular risk factors in men: A review of clinical and preclinical data. *CJC Open*, 3, 1238-1248.
- La Scala, E., Peyre, J. P., & Maupas, E. (2023). Effect of preoperative coronary CT for planning of percutaneous coronary intervention for complex chronic total occlusion (CTS-C-CTOPCI): Study protocol for an open-label randomized controlled trial. *Trials*, 24, 560.
- Leboube, S., Camboulives, L., Bochaton, T., Amaz, C., Bergerot, C., Altman, M., et al. (2024). What underlies sex differences in heart failure onset within the first year after a first myocardial infarction? *Frontiers in Cardiovascular Medicine*, 10, 1290375.
- Lee, D. S., Straus, S. E., Farkouh, M. E., Austin, P. C., Taljaard, M., Chong, A., Fahim, C., Poon, S., Cram, P., Smith, S., & McKelvie, R. S. (2023). Trial of an intervention to improve acute heart failure outcomes. *New England Journal of Medicine*, 388(1), 22-32.
- Martinho, M. (2023). Women more likely to die after heart attack than men. *Proceedings in Heart Failure, Congress of European Society of Cardiology, Topics Heart Failure*.
- Masip, J., Peacock, W. F., Arrigo, M., Rossello, X., Platz, E., Cullen, L., et al. (2022). Acute heart failure in the 2021 ESC Heart Failure Guidelines: A scientific statement from the Association for Acute Cardiovascular Care (ACVC) of the European Society of Cardiology. *European Heart Journal – Acute Cardiovascular Care*, 11, 173-185.
- Mello, B. H., Oliveira, G. B., Ramos, R. F., Lopes, B. B., Barros, C. B., Carvalho Ede, O., et al. (2014). Validation of the Killip-Kimball classification and late mortality after acute myocardial infarction. *Arquivos Brasileiros de Cardiologia*, 103, 107-117.
- Murat, B., Kivanc, E., Dizman, R., Mert, G. O., & Murat, S. (2021). Gender differences in clinical characteristics and in-hospital and one-year outcomes of young patients with ST-segment elevation myocardial infarction under the age of 40. *Journal of Cardiovascular and Thoracic Research*, 13, 116.
- Ndrepepa, G., Colleran, R., & Kastrati, A. (2018). No-reflow after percutaneous coronary intervention: A correlate of poor outcome in both persistent and transient forms. *EuroIntervention*, 14, 139-141.
- Okkonen, M., Havulinna, A. S., Ukkola, O., Huikuri, H., Pietilä, A., Koukkunen, H., et al. (2021). Risk factors for major adverse cardiovascular events after the first acute coronary syndrome. *Annals of Medicine*, 53, 817-823.
- Price, L. R., & Martinez, J. (2019). Cardiovascular, carcinogenic, and reproductive effects of nicotine exposure: A narrative review of the scientific literature. *F1000Research*, 8, 1586.
- Rydzkowska, K., Adach, W., Janikowski, K., Banach, M., & Bielecka-Dabrowa, A. (2023). Menopause and women's cardiovascular health: Is it really an obvious relationship? *Archives of Medical Science*, 19, 458-466.
- Sarak, T., & Karadeniz, M. (2019). The relationship between serum NT-proBNP levels and severity of coronary artery disease assessed by SYNTAX score in patients with acute myocardial infarction. *Turkish Journal of Medical Sciences*, 49, 1366-1373.
- Schamroth Pravda, N., Karny-Rahkovich, O., Shiyovich, A., Schamroth Pravda, M., Rapeport, N., Vaknin-Assa, H., et al. (2021). Coronary artery disease in women:

- A comprehensive appraisal. *Journal of Clinical Medicine*, 10, 347.
- Selvaraj, S., Claggett, B., Pozzi, A., McMurray, J. J., Jhund, P. S., Packer, M., Desai, A. S., Lewis, E. F., Vaduganathan, M., Lefkowitz, M. P., & Rouleau, J. L. (2019). Prognostic implications of congestion on physical examination among contemporary patients with heart failure and reduced ejection fraction: PARADIGM-HF. *Circulation*, 140(17), 1369-1379.
- Vaccarino, V., Shah, A. J., Rooks, C., Ibeanu, I., Nye, J. A., Pimple, P., et al. (2014). Sex differences in mental stress-induced myocardial ischemia in young survivors of an acute myocardial infarction. *Psychosomatic Medicine*, 76, 171-180.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of the publisher and/or the editor(s). This publisher and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© Copyright (2025): Author(s). The licensee is the journal publisher. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:

<https://pr.sdiarticle5.com/review-history/131171>