Original Article

Sex-Related Differences in the Presentation and Management of Acute Coronary Syndrome and Stable Angina in Iranian Patients

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ABSTRACT

Background: Little is known about the impact of sex-related differences on clinical presentation, treatment adherence, and outcomes in patients with acute coronary syndrome (ACS) in developing countries, such as Iran.

Methods: This observational cross-sectional study used the Coronary Angiography and Angioplasty Registry (CAAR) data. We included all adults who underwent coronary angiography or angioplasty within 1 year, analyzing data from 1548 cases.

Results: A total of 1548 patients were included in the analysis. Women were older than men when experiencing ACS and had a higher prevalence of atypical symptoms. Women were also more likely to have comorbid conditions such as hypertension, diabetes, obesity, dyslipidemia, and depression. Still, men were more likely to have a history of smoking and previous myocardial infarction (MI). Investigation of differences regarding invasive therapeutic procedures, culprit arteries, and numbers of diseased vessels showed no significant differences between women and men in the ST-elevation myocardial infarction (STEMI) and non-STEMI groups. However, there was a significant difference between women and men in these factors in patients with unstable angina and stable angina. Men in these groups were more likely to have the involvement of 2 or 3 coronary arteries and were more likely to be recommended for percutaneous coronary intervention and coronary artery bypass graft surgery. Nonetheless, there was no significant difference in acceptance rates of recommended treatment in these groups between men and women.

Conclusions: The study findings provide insight into the differences between male and female ACS patients in the Iranian population, highlighting the need for sex-specific approaches in treatment. ***(Iranian Heart Journal 2024; 25(3): 58-71)***

KEYWORDS: Acute coronary syndrome, STEMI, Sex differences, Iran, Stable angina, Ischemic heart disease

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Received: December 31, 2023 **Accepted:** April 26, 2024

Acute coronary syndrome (ACS) is a common and life-threatening condition that arises from coronary artery disease (CAD) and is a leading cause of mortality globally.[1] According to the World Health Organization report, about 4 out of 5 deaths caused by cardiovascular diseases are due to heart attacks and strokes. One-third of premature deaths caused by these diseases occur in people under the age of 70.[2]

Although research on ACS has improved our understanding of this condition, it is still unclear how sex influences the prevalence, presentation, and prognosis of ACS. A better understanding of sex-related differences in ACS can help inform personalized treatment and management strategies for affected patients.[3, 4] Several studies have identified significant differences in ACS incidence, presentation, and outcomes between men and women. Women are known to experience ACS later in life, present with atypical symptoms, and have a higher incidence of in-hospital mortality than men.[5] Moreover, traditional risk factors, such as hypertension, diabetes, and smoking, have stronger associations with ACS in women than men.[6] Furthermore, emerging evidence suggests that sociocultural factors such as gender roles, access to healthcare, and socioeconomic status may also influence the presentation and outcomes of ACS in both men and women.[7, 8] For instance, women are more likely to delay seeking medical attention due to caregiving responsibilities and societal norms that prioritize others' needs above their own.[9]

Despite these sex-related differences, earlier studies on ACS were mostly conducted on men, with little or no attention given to women. Nonetheless, in recent years, there has been a growing recognition of the need to address such shortcomings in research and clinical practice.[10] Sex-related differences in ACS are an important area of research, as they may inform tailored prevention and management approaches for this deadly disease. Indeed, studies suggest that when explicitly considered in clinical practice, sex-related differences in ACS can lead to better risk management and treatment outcomes.[11]

Although these studies have been conducted in different parts of the world, there is a lack of such studies in Iran despite its distinct cultural and social conditions. Therefore, the objective of this study was to evaluate sex-related differences in demographic features, clinical presentations, and outcomes in patients with ACS at our hospital. By conducting this study, we aim to provide a comprehensive analysis of these differences, identify crucial knowledge gaps, and establish future research directions to guide clinical practice and enhance patient outcomes.

METHODS

Study Design and Participants

This single-center, registry-based, observational, cross-sectional study utilized Coronary Angiography and Angioplasty Registry (CAAR) data. The CAAR contains demographic features, clinical data, and follow-up information of patients who undergo coronary angiography at Imam Hossein Hospital, a major educational hospital in Tehran, Iran. We included all adult patients (age ≥18 y) who underwent coronary angiography or angioplasty within 1 year (July 2021 through July 2022) at Imam Hossein Hospital. Data from 1548 cases recorded by the CAAR between July 2021 and July 2022 were extracted for analysis.

Variables and Data Extraction

Patient data were extracted using a comprehensive checklist from the CAAR registry database with a complete enumeration method. The checklist includes various sections such as patient demographic characteristics, comorbidities, habits, medical history, family history of cardiovascular diseases, cardiac presentations on admission, ECG results, echocardiography results,

coronary angiography results, treatment recommendations, prescribed medications at discharge, and 1-month follow-up after discharge.
All patients underwent a follow-up during hospital admission and for 30 days after discharge through a telephone interview. Information on underlying diseases or habits was obtained from patients' self-reporting, medical records, and medication history. This study categorized information based on ACS and stable angina as cardiac presentations. Patients with ACS were defined as those who presented with ST-elevation myocardial infarction (STEMI), non–ST-elevation myocardial infarction (NSTEMI), and unstable angina at the time of hospital admission. Coronary angiography of patients at Imam Hossein Hospital was performed using the Siemens Zee Pure machine, with at least 4 views from the left coronary system and 2 views from the right coronary system.
All the mentioned information was extracted from the CAAR database in Excel format. The checklist analysis was performed using STATA software, version 14. To prevent selection bias, we included all patients who underwent angiography or angioplasty at this hospital during a specified 1-year period in the study.

Ethical Approval

The study protocol was approved and registered by the Ethics Committee of Shahid Beheshti University of Medical Sciences and the Vice-Chancellor for Research and Technology (IR.SBMU.RETECH.REC.1400.256). Written consent from all participants was obtained and recorded in the registry database.

Sampling Method and Sample Size Estimation

In this study, all patients who underwent coronary angiography and angioplasty between July 2021 and July 2022 and were registered in the CAAR database were considered using a convenience sampling method. Thus, information on all 1548 eligible patients during the specified period was extracted from the database.

Statistical Analysis

Continuous variables were described using means and standard deviations, while categorical variables were reported as frequencies and percentages. The Student *T* or Mann-Whitney *U* test was used to compare the means of continuous variables between the 2 groups. The Fisher exact or χ^2 test was performed to compare the frequency of the categorical variables between groups. Initially, a general comparison of information was conducted based on sex groups. Then, the study population was divided into patients with stable angina and those with ACS (STEMI, NSTEMI, and unstable angina), and the differences between the demographic and clinical information of women and men in each of these groups were separately examined. All statistical tests were 2-sided with a significance level of less than 0.05 using STATA software, version 14.

RESULTS

A total of 1548 adult patients (44.40% women and 55.60% men) met the inclusion criteria and were included in the analysis. The mean age of male patients was 59.45±12.41 years, while the mean age of female patients was 61.64±11.47 years (P<0.001).
The average age and body mass index (BMI) (29.37±5.54 in women vs 26.95±5.22 in men; *P*<0.001) and the prevalence rates of traditional cardiovascular risk factors, such as hypertension (52.90% vs 47.10%; *P*<0.001), diabetes (55.40% vs 44.60%; *P*<0.001), and dyslipidemia (53% vs 47%; *P*<0.001), were higher among women. However, in this study, the prevalence rates of smoking, drinking alcohol, and opium use were

significantly higher in men than in women (89.80% vs 10.20%; *P*<0.001, 83.30% vs 16.70%; *P*<0.001, and 87.30% vs 12.7; *P*<0.001, respectively). Additionally, the history of previous MI and heart failure was higher in men (74.20% vs 25.80%; *P*<0.001 and 65.3% vs 34.70%; *P*=0.003, respectively).
There was also a significant difference in the family history of diseases. Among those who had a family history of cerebrovascular accident/transient ischemic attack, ischemic heart disease (IHD), or sudden cardiac death in at least a first-degree relative, a higher percentage were women (Table 1).
Based on Table 2, women tended to have more atypical symptoms of ACS, such as shortness of breath and palpitation, than men, who were more likely to experience chest pain (*P*<0.001). In our study, more women were recommended for guideline-directed medical therapy (53.40%), and more men were recommended for percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) (*P*<0.05). Nonetheless, there was no significant difference in the final treatment adherence between men and women (49.80% vs 50.20%; *P*=0.118). In other words, sex exerted no significant impact on treatment adherence. In this study, 18 patients (0.01%) died during hospitalization, and 9 patients died in the 30-day follow-up period after discharge. Death occurred more often among male patients than among female ones, but this difference was not statistically significant (*P*>0.05) (Table 2).
Table 3 showcases the traditional risk factors and clinical presentation of patients who underwent coronary angiography or angioplasty based on ACS and IHD groups. The mean BMI was higher among women than among men, but only this sex-related difference was statistically significant among patients with stable angina and unstable angina (*P*<0.001). Moreover, the prevalence of unhealthy behaviors, such as smoking and drinking alcohol, in men was higher than that in women (*P*<0.005). In addition, the prevalence of past medical history of heart failure and IHD was higher among men than among women in the ACS and stable angina groups. More details are reported in Table 3.
Based on Table 4, when we compared women and men in separate analyses of different ACS and IHD groups, there was no significant difference in treatment selection in the STEMI, NSTEMI, and stable angina groups. Nevertheless, in the unstable angina group, medical therapy was more frequently recommended for women (55%), and PCI and CABG were more often recommended for men. In this group, men were more likely to refuse PCI (*P*=0.02). Regarding the results of coronary angiography in patients, there was a significant difference between men and women overall, with a higher percentage of women having normal/mild CAD, while men were more likely to have double- or triple-vessel disease (Table 2). This study also compared the results between men and women in different ACS and IHD groups separately and found no significant difference between the STEMI and NSTEMI groups. Still, in the unstable angina and stable angina groups, the results were as mentioned above (Table 4).
Women remained less likely to receive aspirin, clopidogrel, angiotensin-converting enzyme inhibitors, and anti-arrhythmic drugs. However, anti-anxiety drugs and calcium channel blockers were more frequently prescribed for women than for men. This finding may be explained by the different patterns of coronary artery involvement in women. In-hospital mortality was higher in the STEMI group than in the other groups (4 female and 3 male patients). The follow-up of male and female patients concerning prognosis was compared both overall and separately in different ACS groups, but no significant difference was observed between men and women in this study.

Table 1: Baseline Characteristics and Cardiac Risk Factors

Variable	Women N=688 (44.40%)	Men N=860 (55.60%)	*P* value
Age, y	61.64 ± 11.47	59.45 ± 12.41	<0.001*
Body mass index, kg/m^2	29.37 ± 5.54	26.95 ± 5.22	<0.001*
Habits and Underlying Diseases (Yes)			
Current smoker	41(10.20)	362(89.80)	<0.001*
Drinking alcohol	13(16.70)	65(83.30)	<0.001*
Opium addiction	37(12.70)	255(87.30)	<0.001*
Myocardial infarction	48(25.80)	138(74.20)	<0.001*
Ischemic heart disease	233(43.60)	301(56.40)	0.641
Heart failure	68(34.70)	128(65.30)	0.003*
Syncope	25(37.90)	41(62.10)	0.273
Cerebrovascular accident/transient ischemic attack	49(46.20)	57(53.80)	0.702
Hypertension	440(52.90)	391(47.10)	<0.001*
Dyslipidemia	408(53.0)	362(47.0)	<0.001*
Diabetes	280(55.40)	225(44.60)	<0.001*
Family history (Yes)			
Cerebrovascular accident/transient ischemic attack in the mother	67(58.80)	47(41.20)	0.001*
Cerebrovascular accident/transient ischemic attack in the father	61(41.20)	87(58.80)	0.406
Cerebrovascular accident/transient ischemic attack in the brother	31(50.0)	31(50.0)	0.369
Cerebrovascular accident/transient ischemic attack in the sister	25(65.80)	13(34.20)	0.007*
Ischemic heart disease in the mother	163(51.90)	151(48.10)	0.003*
Ischemic heart disease in the father	139(43.80)	178(56.20)	0.811
Ischemic heart disease in the brother	167(51.50)	157(48.50)	0.004*
Ischemic heart disease in the sister	123(66.50)	62(33.50)	<0.001*
Sudden cardiac death in the mother	44(54.30)	37(45.70)	0.066
Sudden cardiac death in the father	64(47.10)	72(52.90)	0.521
Sudden cardiac death in the brother	53(60.20)	35(39.80)	0.002*
Sudden cardiac death in the sister	16(59.30)	11(40.70)	0.118

Values are n (%) or mean ± SD.
*Statistically significant: *P*<0.05

Table 2: Clinical Presentations, Patterns of Coronary Artery Involvement, Treatment Recommendations, and Disease Outcomes

Variable	Women N=688 (44.40%)	Men N=860 (55.60%)	*P* value
Chief Complaint (Yes)			
Atypical chest pain	99(45.60)	118(54.40)	0.707
Non-anginal chest pain	49(36.80)	84(63.20)	0.065
Typical angina	359(44.30)	451(55.70)	0.918
Abdominal pain	4(40.0)	6(60.0)	0.777
Dyspnea	417(50.50)	409(49.50)	<0.001*
Palpitation	95(59.70)	64(40.30)	<0.001*
Pedal edema	13(43.30)	17(56.70)	0.902
Weakness	60(47.60)	66(52.40)	0.454
Syncope	7(41.20)	10(58.80)	0.785
Faint	1(20.0)	4(80.0)	0.271
No symptom	39(37.50)	65(62.50)	0.140

CAD presentation (Yes)			
Stable angina	177(48.80)	186(51.20)	0.059
Unstable angina	371(47.70)	407(52.30)	0.010
NSTEMI	22(33.80)	43(66.20)	0.079
STEMI	27(23.90)	86(76.10)	<0.001*
Cardiac arrest	3(33.30)	6(66.70)	0.501
Heart failure	16(39.0)	25(61.0)	0.479
Cardiogenic shock	1(25.0)	3(75.0)	0.433
No cardiac presentation	21(36.20)	37(63.80)	0.198
Coronary Artery Involvement			
Normal or mild CAD	281 (60.43)	184 (39.57)	<0.001*
Ectasia	68(36.80)	117(63.20)	0.025*
Muscle bridge	6(37.50)	10(62.50)	0.574
Slow flow	25(39.70)	38(60.30)	0.437
SVD	108(41.40)	153(58.60)	0.274
2VD	86(33.0)	175(67.0)	<0.001*
3VD	130(34.10)	251(65.90)	<0.001*
Recommendation			
MT	422(53.40)	369(46.60)	<0.001*
PCI	114(34.90)	213(65.10)	<0.001*
PPCI or PPCI and staging	21 (31.34)	46 (68.66)	0.027*
CABG or Re-CABG	66 (36.67)	114 (63.33)	0.025*
Final clinical decision			
MT	462(50.20)	458(49.80)	<0.001*
PCI	132(34.10)	255(65.90)	<0.001*
CABG	61(33.30)	122(66.70)	0.001*
CIED	2(22.20)	7(77.80)	0.178
Patient Decision			
Accepted clinical decision	622(45.10)	756(54.90)	0.118
Refused PCI	3(11.10)	24(88.90)	<0.001*
Refused CABG	19(29.70)	45(70.30)	0.015*
PCI instead of CABG	4(44.40)	5(55.60)	1.000
Outcomes			
In-hospital mortality	8 (44.44)	10 (55.56)	1.000
30-day all-cause mortality	2 (22.22)	7 (77.78)	0.183

Values are n (%).
*Statistically significant: $P<0.05$
CAD: coronary artery disease, STEMI: ST-elevation myocardial infarction, NSTEMI: non–ST-elevation myocardial infarction, SVD: single-vessel disease, 2VD: double-vessel disease, 3VD: triple-vessel disease, MT: medical treatment, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, PPCI: primary percutaneous coronary intervention, CIED: cardiac implantable electronic device

Table 3: The Baseline Characteristics and Clinical Presentations of Patients With Ischemic Heart Disease

Variable	NSTEMI (n=65)			Stable Angina (n=363)			STEMI (n=113)			Unstable Angina (n=778)		
	Women (n = 22, 33.85%)	Men (n=43, 66.15%)	P-value	Women (n=177, 48.76%)	Men (n=186, 51.24%)	P-value	Women (n= 27, 23.89%)	Men (n=86, 76.11%)	P-value	Women (n=371, 47.69%)	Men (n=407, 52.31%)	P-value
BMI, kg/cm^2	27.90 ±7.00	27.91 ± 7.31	0.988	30.08 ±5.86	27.36 ±6.07	<0.001*	27.50 ±4.19	26.50 ±3.93	0.878	29.05 ± 5.19	27.01 ±4.63	<0.001*
Age, y	65.42 ± 14.56	59.50 ±12.21	0.088	60.70 ±11.59	60.63 ±12.10	0.951	67.36 ±11.43	56.62 ±10.85	0.562	60.78 ±11.11	58.43 ±12.08	0.005*
Habits and Medical History (Yes)												
Current smoker	2(8.70)	21(91.30)	0.002*	7(9.0)	71(91.0)	<0.001*	3(5.90)	48(94.10)	<0.001*	23(11.70)	174(88.30)	<0.001*
Opium addiction	1(5.30)	18(94.70)	0.002*	9(15.0)	51(85.0)	<0.001*	3(10.0)	27(90.0)	0.037	17(12.10)	123(87.90)	<0.001*
Drinking alcohol	0(0.0)	1(100.0)	0.184	3(17.60)	14(82.40)	0.005*	0(0.0)	4(100.0)	0.153	9(22.50)	31(77.50)	<0.001*
MI	5(38.50)	8(61.50)	0.749	9(29.0)	22(71.0)	0.022*	6(24.0)	19(76.0)	0.989	23(25.60)	67(74.40)	<0.001*
IHD	10(41.70)	14(58.30)	0.308	45(42.90)	60(57.10)	0.151	12(32.40)	25(67.6)	0.138	132(46.0)	155(54.0)	0.470
Previous PCI	6(37.50)	10(62.50)	0.722	17 (43.59)	22 (56.41)	0.494	8(40.0)	12(60.0)	0.083	56(39.40)	86(60.60)	0.029*
Heart failure	4(26.70)	11(73.30)	0.503	12(28.60)	30(71.40)	0.005*	6(28.60)	15(71.40)	0.577	35(40.70)	51(59.30)	0.169
Syncope	1(50.0)	1(50.0)	1.000	10(52.60)	9(47.40)	0.729	1(25.0)	3(75.0)	1.000	8(29.60)	19(70.40)	0.056
PVD	0(0.0)	3(100.0)	0.545	3(30.0)	7(70.0)	0.338	0 (0.0)	0 (0.0)	N/A	2(18.20)	9(81.80)	0.048*
CVA/TIA	4(66.70)	2(33.30)	0.168	15(46.90)	17(53.10)	0.823	2(50.0)	2(50.0)	0.241	22(47.80)	24(52.20)	0.984
Hypertension	13(41.90)	18(58.10)	0.188	108(57.80)	79(42.20)	<0.001*	15(29.40)	36(71.60)	0.212	239(56.60)	183(43.40)	<0.001*
Dyslipidemia	13(46.40)	15(53.60)	0.062	103(54.80)	85(45.20)	0.017*	20(43.50)	26(56.50)	<0.001*	224(56.0)	176(44.0)	<0.001*
DM	10(40.0)	15(60.0)	0.407	67(55.40)	54(44.60)	0.075	14(38.90)	22(61.10)	0.011*	155(62.20)	94(37.80)	<0.001*
Family History[1]												
CVA/TIA	7 (41.20)	10 (58.80)	0.457	34 (53.10)	30 (46.90)	0.441	15(39.47)	23(60.53)	0.009*	92(54.10)	78 (45.90)	0.058
IHD/MI	13 (39.40)	20 (60.60)	0.337	93 (55.03)	76 (44.97)	0.028*	21(31.30)	46(68.70)	0.025*	224(51.90)	208 (48.10)	0.009*
SCD	6 (46.20)	7 (53.80)	0.336	34 (59.60)	23 (40.40)	0.084	9(30.0)	21(70.0)	0.360	91 (54.80)	75 (45.20)	0.038*
Chief Complaint												
Non-anginal CP	2(33.30)	4(66.7)	1.000	22(35.50)	40(64.50)	0.022*	1(33.30)	2(66.70)	0.563	20(41.70)	28(58.30)	0.389
Atypical CP	1(20.0)	4(80.0)	0.655	49(50.0)	49(50.0)	0.774	2(33.30)	4(66.70)	0.628	39(40.60)	57(59.40)	0.139
Typical angina	17(34.0)	33(66.0)	0.962	32(54.20)	27(45.80)	0.358	22(22.40)	76(77.60)	0.347	256(48.20)	275(51.80)	0.668
Abdominal pain	0(0.0)	1(100.0)	1.000	1(33.30)	2(66.70)	1.000	0 (0.0)	0 (0.0)	N/A	2(66.70)	1(33.30)	0.608
Dyspnea	15(48.40)	16(51.60)	0.018*	109(54.50)	91(45.50)	0.015*	13(25.0)	39(75.0)	0.799	232(52.70)	208(47.30)	0.001*
Palpitation	3(37.50)	5(62.50)	1.000	23(67.60)	11(32.40)	0.021*	3(37.50)	5(62.50)	0.394	59(60.80)	38(39.20)	0.006*
Pedal edema	0 (0.0)	0 (0.0)	N/A	1(12.50)	7(87.50)	0.068	0 (0.0)	0 (0.0)	N/A	7(50.0)	7(50.0)	0.861
Weakness	3(33.30)	6(66.70)	1.000	8(40.0)	12(60.0)	0.420	5(38.50)	8(61.50)	0.296	36(55.40)	29(44.60)	0.194
Syncope	0 (0.0)	0 (0.0)	N/A	0(0.0)	2(100.0)	0.499	1(100.0)	0(0.0)	0.239	5(62.50)	3(37.50)	0.489
Faint	0 (0.0)	0 (0.0)	N/A	1(100.0)	0(0.0)	0.488	0(0.0)	1(100.0)	1.000	0(0.0)	1(100.0)	1.000
No symptom	0(0.0)	1(100.0)	1.000	15(40.50)	22(59.50)	0.291	0 (0.0)	0 (0.0)	N/A	4(33.30)	8(66.70)	0.316

Values are n (%) or mean ± SD.
N/A: not applicable
*Statistically significant: *P*<0.05
BMI: body mass index, MI: myocardial infarction, IHD: ischemic heart disease, CVA: cerebrovascular accident, TIA: transient ischemic attack, FH: family history, SCD: sudden cardiac death, PVD: peripheral vascular disease, PCI: percutaneous coronary intervention

1 History of IHD/MI or CVA/TIA or SCD at least in 1 of the first relatives (mother, father, brother, or sister)

Table 4: Numbers of Diseased Vessels, Culprit Arteries, and Recommendations

	NSTEMI (n=65)			Stable Angina (n=363)			STEMI (n=113)			Unstable Angina (n=778)		
Variable	Women (n = 22, 33.85%)	Men (n=43, 66.15%)	P-value	Women (n=177, 48.76%)	Men (n=186, 51.24%)	P-value	Women (n= 27, 23.89%)	Men (n=86, 76.11%)	P-value	Women (n=371, 47.69%)	Men (n=407, 52.31%)	P-value
Coronary Artery Involvement												
Normal or mild CAD	0(0.0)	4(100.0)	0.291	93 (64.58)	51 (35.42)	<0.001*	0 (0.0)	3 (100.0)	1.000	152 (61.79)	94 (38.21)	<0.001*
Ectasia	2(25.0)	6(75.0)	0.706	18(36.0)	32(64.0)	0.052	1(16.70)	5(83.30)	1.000	36(38.30)	58(61.70)	0.052
Muscle bridge	0 (0.0)	0 (0.0)	N/A	1(33.30)	2(66.70)	1.000	0 (0.0)	0 (0.0)	N/A	4(40.0)	6(60.0)	0.755
Slow flow	0(0.0)	1(100.0)	1.000	7(53.80)	6(46.20)	0.709	1(25.0)	3(75.0)	1.000	12(38.70)	19(61.30)	0.307
SVD	6(54.50)	5(45.50)	0.162	19(35.80)	34(64.20)	0.042*	6(22.20)	21(77.80)	0.815	66(47.80)	72(52.20)	0.971
2VD	3(18.70)	13(81.30)	0.142	17(34.0)	33(66.0)	0.025*	7(29.20)	17(70.80)	0.495	51(36.70)	88(63.30)	0.004*
3VD	9(34.60)	17(65.40)	0.915	27(36.50)	47(63.50)	0.018*	14(26.40)	39(73.60)	0.555	61(35.90)	109(64.10)	<0.001*
Types of Involved Vessel												
Left main	1(50.0)	1(50.0)	1.000	5(35.70)	9(64.30)	0.319	2(50.0)	2(50.0)	0.241	7(41.20)	10(58.80)	0.632
Proximal LAD	2(33.30)	4(66.70)	1.000	6(35.30)	11(64.70)	0.255	1(11.10)	8(88.90)	0.684	16(32.70)	33(67.30)	0.030*
LAD	14(31.80)	30(68.20)	0.617	69(41.30)	98(58.70)	0.009*	24(27.90)	62(72.10)	0.074	156(41.90)	216(58.10)	0.002*
Diagonal	11(30.60)	25(69.40)	0.532	27(32.50)	56(67.50)	0.001*	9(18.0)	41(82.0)	0.191	76(34.10)	147(65.90)	<0.001*
LCX	9(26.50)	25(73.50)	0.188	38(38.0)	62(62.0)	0.011*	14(29.80)	33(70.20)	0.215	95(42.80)	127(57.20)	0.084
OM	11(37.90)	18(62.10)	0.532	31(35.60)	56(64.40)	0.005*	9(19.60)	37(80.40)	0.371	75(41.20)	107(58.80)	0.046*
Ramus	0(0.0)	3(100.0)	0.545	5(41.70)	7(58.30)	0.617	2(25.0)	6(75.0)	1.000	10(33.30)	20(66.70)	0.108
RCA	14(40.0)	21(60.0)	0.257	42(35.60)	76(64.40)	<0.001*	19(26.80)	52(73.20)	0.353	98(35.60)	177(64.40)	<0.001*
PDA	3(42.90)	4(57.10)	0.681	7(33.30)	14(66.70)	0.145	3(30.0)	7(70.0)	0.700	20(33.90)	39(66.10)	0.027*
PLV	1(50.0)	1(50.0)	1.000	0(0.0)	2(100.0)	0.499	2(33.30)	4(66.70)	0.628	4(20.0)	16(80.0)	0.012*
SVG	2(66.70)	1(33.30)	0.263	2(33.30)	4(66.70)	0.685	1(33.30)	2(66.70)	0.563	4(26.70)	11(73.30)	0.100
LIMA	1(100.0)	0(0.0)	0.338	2(66.70)	1(33.30)	0.615	1(100.0)	0(0.0)	0.239	2(40.0)	3(60.0)	0.730
Recommendation												
MT	4(30.80)	9(69.20)	1.000	127(24.70)	105(45.30)	0.002*	1(16.70)	5(83.30)	1.000	235(55.0)	192(45.0)	<0.001*
PCI	7(36.80)	12(63.20)	0.743	20(36.40)	35(63.60)	0.046*	5(15.20)	28(84.80)	0.162	69(39.20)	107(60.80)	0.010*
PPCI or PPCI and staging	1 (16.67)	5 (83.33)	0.655	0 (0.0)	0 (0.0)	N/A	15(31.25)	33(68.75)	0.115	1 (25.0)	3 (75.0)	0.626
CABG or Re-CABG	5(33.33)	10(66.67)	1.000	14 (38.89)	22 (61.11)	0.224	7 (31.82)	15 (68.18)	0.331	34 (40.0)	51 (60.0)	0.137
Patient Decision												
Accepted clinical decision	16(34.0)	31(66.0)	0.957	165(49.40)	169(50.60)	0.444	23(23.0)	77(77.0)	0.507	340(48.40)	362(51.60)	0.205
Refused PCI	0(0.0)	4(100.0)	0.291	1(20.0)	4(80.0)	0.372	0(0.0)	1(100.0)	1.000	1(10.0)	9(90.0)	0.022*
Refused CABG	3(50.0)	3(50.0)	0.398	2(20.0)	8(80.0)	0.106	4(36.40)	7(63.60)	0.291	9(31.0)	20(69.0)	0.067
PCI instead of CABG	1(33.30)	2(66.70)	1.000	0 (0.0)	0 (0.0)	N/A	0(0.0)	1(100.0)	1.000	2(40.0)	3(60.0)	1.000
Outcomes												
In-hospital mortality	1 (100.0)	0 (0.0)	0.328	2 (100.0)	0 (0.0)	0.232	4 (57.14)	3 (42.86)	0.062	0 (0.0)	2 (100.0)	0.500
30-day all-cause mortality	1 (100.0)	0 (0.0)	0.338	0 (0.0)	2 (100.0)	0.499	0 (0.0)	1 (100.0)	1.000	1 (50.0)	1 (50.0)	1.000

Values are n (%) or mean ± SD.
N/A: not applicable
*Statistically significant: *P*<0.05
CAD: coronary artery disease, SVD: single-vessel disease, 2VD: double-vessel disease, 3VD: triple-vessel disease, LAD: left anterior descending artery, LCX: circumflex artery, OM: obtuse marginal artery, RCA: right coronary artery, PDA: posterior descending artery, PLV: posterior left ventricular artery, SVG: saphenous vein grafts, LIMA: left internal mammary artery, MT: medical treatment, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, PPCI: primary percutaneous coronary intervention

DISCUSSION

Investigating the impact of sex differences on cardiovascular risk involves considering traditional and non-traditional risk factors, female-specific risk factors, and socio-cultural elements. The underlying causes of sex-related disparities in ACS outcomes are not entirely understood, but they likely result from a combination of physiological, psychological, and socio-cultural factors. Women's susceptibility to non-obstructive CAD and endothelial dysfunction, which may lead to adverse outcomes, might be influenced by their smaller coronary artery diameters and more extensive coronary microvascular disease.[11] Women are more likely to experience comorbid conditions that exacerbate underlying cardiac disease, while men may develop CAD more frequently due to modifiable risk factors such as smoking and unhealthy lifestyles.[12] Research focusing on the influence of social and cultural factors on the presentation and management of ACS in women is essential to develop targeted interventions and improve outcomes for female patients. There is a lack of comprehensive data regarding sex differences in patients with ACS in developing countries like Iran. To address this gap, we conducted this study using the coronary angiography and angioplasty registry in a Tehran hospital. Our findings revealed significant sex-related differences in demographic characteristics, clinical presentation, and comorbidities, echoing similar observations in other countries. While traditional risk factors are similar in both sexes, their prevalence and impact vary between men and women. Our study revealed that women were older, on average, than men when experiencing ACS. Additionally, women were more prone to comorbid conditions such as hypertension, diabetes, obesity, dyslipidemia, and depression, while men exhibited a higher prevalence of smoking history and previous MI. This finding aligns with previous research indicating an elevated cardiovascular risk profile in women, particularly those with type 2 diabetes.[12, 13] Smoking has a more pronounced impact on women, increasing their risk for cardiovascular events by 25%, independent of other risk factors, compared with men. This smoking-related cardiovascular risk is particularly elevated among young and middle-aged women.[14-16]

Diabetes is another risk factor that varies between sexes. Diabetic women face a significantly higher risk of developing CAD or heart failure with preserved ejection fraction (HFpEF) than men with similar conditions.[17] A maternal family history of MI in women under 65 years old is associated with a 4-fold increased risk of ACS when compared with age-matched men or older women.[18] Depression, psychological trauma, and stress are strong predictors of cardiovascular events in young and middle-aged women.[19] Lower socioeconomic status also poses a greater coronary risk for women compared with men.[20] In our study, women with ACS exhibited a high prevalence of atypical symptoms, such as shortness of breath and palpitation, compared with men. These findings are consistent with observations from other studies.[21]

Potential mechanisms and non-traditional risk factors that may influence the disease process differently in men and women include sexual differences in coronary biology, endothelial shear stress effects, α estrogen receptor-related effects, primary MI mechanisms, and socioeconomic conditions. Women have significantly smaller coronary arteries and higher baseline myocardial blood flow than men, resulting in a substantial increase in endothelial shear stress in women. Given that low endothelial shear stress is linked to focal lipid accumulation, pathological remodeling, and plaque instability, it is proposed that the higher shear stress conditions in women's coronary arteries may contribute to the sex-related differences in susceptibility to CAD.[22, 23] The sex-related difference, particularly during premenopausal years, can be attributed to the effects of estrogen on endothelial mediators such as nitric oxide, prostaglandins, and endothelium-derived hyperpolarizing factor. Vascular estrogenic activities are mainly regulated by the α estrogen receptor, promoting an anti-inflammatory low-vascular resistance phenotype that guards against cardiovascular diseases. The variance in vascular stiffness throughout women's lives is primarily due to estrogen-mediated effects through the alpha receptor.[24]

An increase in vascular stiffness is strongly linked to higher blood pressure, diastolic dysfunction, impaired ventricular coupling, and left ventricular remodeling, playing a significant role in conditions predominantly affecting postmenopausal women, such as HFpEF and isolated systolic hypertension.[25] Furthermore, women exhibit unique coronary plaque characteristics, including a more diffuse and non-obstructive disease pattern, reduced overall plaque burden and calcium content, and less evidence of necrosis in plaque cores. While the primary mechanism responsible for MI in men is plaque rupture, women are more likely to experience plaque erosion, the leading cause of coronary thrombosis, particularly in premenopausal women.[26] Although women generally have a lower plaque burden, coronary artery calcium scoring serves as a stronger predictor of future cardiovascular events in women than in men. Therefore, coronary artery calcium scoring is recommended for assessing asymptomatic women with a 10-year cardiovascular disease risk greater than 7.5%.[27] Female-specific risk factors encompass postmenopausal estrogen withdrawal, which adversely affects cardiovascular and metabolic function through changes in body fat distribution, endothelial dysfunction, vascular inflammation, sympathetic tone, and increased insulin resistance, contributing to hypertension.[28] Menopause is linked to a senility-dependent rise in peripheral and cardiac sympathetic activity. Altered iron status has been suggested as another mechanism contributing to the elevated risk in postmenopausal women, with higher plasma iron levels and iron metabolism changes following early-onset menopause, impacting the cardiovascular system via inflammatory cascade induction. Nevertheless, the iron hypothesis remains contentious, as several observations indicate that iron deficiency independently predicts adverse cardiovascular outcomes in both sexes.[29]

MINOCA (MI with Non-Obstructive Coronary Arteries) has a higher prevalence in women than in men, potentially due to multiple mechanisms, including differences in plaque composition. Women exhibit lower plaque burden but higher instances of plaque erosion and thin-cap fibroatheroma. Other contributing factors include coronary artery dissection, coronary vasospasm (including microvascular), Takotsubo cardiomyopathy, and myocarditis.[30] The incidence of microvascular angina is twice as high in women as in men.[31] Coronary microvascular disease may play a role in the development of HFpEF, which is more common in women.[32] Another noteworthy point is that although Takotsubo cardiomyopathy constitutes only 3% of all ACS cases, it is twice as prevalent in postmenopausal women.[33]

An examination of the differences between male and female patients concerning invasive therapeutic procedures, culprit arteries, and numbers of diseased vessels yielded interesting results. In the overall analysis of ACS patients, coronary angiography results showed normal/mild CAD more frequently in women, while double- and triple-vessel disease was more common in men. In general, medical therapy was more frequently recommended for women, whereas PCI and CABG were more often recommended for men. Although compliance with the recommended treatment did not significantly differ between women and men, comparing women and men in separate groups revealed no significant differences in coronary angiography results or recommended treatments for the NSTEMI and STEMI groups. However, in unstable angina and stable angina groups, the differences in coronary artery involvement patterns and recommended treatments between female and male patients were significant, mirroring the overall comparison. A study of patients with unstable angina and stable angina found significant differences between men and women in terms of coronary angiography results and treatment plans. These differences included a higher prevalence of normal/mild CAD in women, leading to guideline-directed medical therapy. Conversely, men in these groups showed a higher likelihood of stenosis in 2 or 3 coronary arteries, resulting in recommendations for PCI and CABG. Still, no significant differences were observed in the acceptance rate of the recommended treatments between men and women in these groups. Therefore, it can be inferred that the discrepancies observed in the overall comparison may stem from overlooking the pattern of coronary artery involvement and the clinical type of ACS and IHD. The results of the present study indicated that women, like men, received guideline-recommended treatments, which somewhat contradicts previous studies reporting that women received evidence-based treatments to a lesser extent.[21, 34, 35] No significant differences were reported concerning in-hospital mortality and 30-day follow-up between men and women, possibly due to the small sample size. To obtain a more accurate evaluation, increasing the sample size and standardizing conditions for male and female patients regarding clinical ACS patterns and types of coronary artery involvement could be helpful for a more efficient comparison. The study's findings shed light on the differences between male and female ACS patients, emphasizing the necessity of sex-specific approaches in treatment. Clinicians can utilize these insights to adapt their practice and optimize patient care.

Limitations

The present study derived its findings from a single-center registry in east Tehran, which could be strengthened by employing a multicenter approach. Furthermore, the 1-year duration of the study may have restricted the sample size and the accuracy of the results; a more extensive study period could have facilitated a more in-depth analysis. It is also important to consider that potential response bias from patients during data collection may have resulted in an overestimation of the percentage of treatment adherence post-discharge.

CONCLUSIONS

Women with ACS exhibit distinct demographic features, clinical presentations, and patterns of diseased vessels compared with men, with these disparities influenced by various factors such as age, comorbidities, physiological factors, socioeconomic status, and healthcare access. Healthcare providers must be cognizant of these differences to tailor management strategies and improve outcomes for both sexes with ACS. Moreover, healthcare systems should ensure equitable access to medical and interventional therapies for all eligible patients, irrespective of sex, race, or ethnicity. Further studies examining the impact of social and cultural factors on ACS presentation and management in women are essential for developing targeted interventions to enhance women's outcomes. Continued research is needed to better comprehend the underlying mechanisms of these differences and devise targeted interventions to address them.

Acknowledgments
The data presented in this article were derived from the disease registry titled "Coronary Angiography and Angioplasty Registry (CAAR)" (the ethics committee code number: "IR.SBMU.RETECH.REC.1400.256) (https://dregistry.sbmu.ac.ir/), supported by the Deputy of Research and Technology at Shahid Beheshti University of Medical Sciences. This work is affiliated with the Prevention of Cardiovascular Disease Research Center, Imam Hossein Hospital of Tehran. We express our gratitude to the CCU nursing staff at Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, for their contributions to data collection and their invaluable support in executing this project.

Availability of Data and Materials
The data utilized in this study are not publicly accessible, as they contain sensitive information that may potentially infringe on the privacy of research participants.

Conflicts of Interest
The authors affirm that there are no conflicts of interest to declare.

Research Funding
This research was supported by the Prevention of Cardiovascular Disease Research Center at Shahid Beheshti University of Medical Sciences (SBMU). No specific grants from funding agencies or commercial or non-profit sectors were obtained for the research, authorship, or publication of this article.

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