Libyan Med J. 2026;18(4):151-157
https://doi.org/10.69667/lmj.26402
Libyan Medical Journal
https://lmj.ly/index.php/ojs/index eISSN: 3107-0426

Original article

Sex-Based Differences in Coronary Artery Anatomy and Clinical Outcomes in Acute Coronary Syndrome: A Multicenter Study from Tripoli, Libya

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Keywords*.*
Acute Coronary Syndrome, ACS, Sex Differences, Coronary Anatomy.

ABSTRACT
Acute Coronary Syndrome (ACS) exhibits significant sex-based disparities in presentation, management, and outcomes. Understanding anatomical and clinical differences between men and women is essential for optimizing diagnostic and therapeutic strategies. This study aimed to identify sex-specific anatomical and clinical variations in ACS patients, evaluate their influence on diagnosis and management, and assess their impact on short-term outcomes. A retrospective descriptive study was conducted from June to October 2025 at Tajoura Cardiac Hospital and Al-Khadra Hospital, Tripoli, Libya. Medical records of 100 ACS patients were analyzed for demographics, comorbidities, presentation, coronary involvement, and outcomes. A survey of 20 cardiologists assessed recognition and application of sex-specific anatomical considerations. Of 100 patients, 67% were male and 33% female. Typical chest pain was more common in males (36%), while females more frequently reported dyspnea (70%). The left anterior descending artery was most commonly involved (48%), with males showing a higher prevalence of proximal lesions and STEMI (27% vs. 13%). Females more often presented with NSTEMI and diffuse, distal disease. In-hospital major adverse cardiac events occurred in 20% of patients, slightly higher in males. All surveyed cardiologists acknowledged the impact of sex-specific anatomy on outcomes; however, only 10% reported adjusting treatment strategies based on sex. Significant sex-based differences exist in ACS presentation and coronary anatomy. Males typically present with obstructive focal lesions and classic symptoms, while females exhibit diffuse disease, microvascular involvement, and atypical symptoms. Recognizing these variations is essential for developing tailored management approaches to improve outcomes for all patients.

Introduction

Acute Coronary Syndrome (ACS) remains a leading cause of global morbidity and mortality despite advances in cardiovascular medicine (1). Historically, clinical research has predominantly focused on middle-aged men, creating a knowledge gap in understanding how ACS manifests and responds to treatment in women, whose unique anatomical and physiological characteristics alter the disease course (2). The pathophysiology of ACS is rooted in the coronary arterial system. Variations in vessel caliber, branching patterns, and collateral circulation influence the extent of ischemia during acute events (3,4). Significant sex-based anatomical differences exist: men typically have larger epicardial arteries with focal, obstructive plaques prone to rupture (5,6), while women often possess smaller-caliber, more tortuous arteries with diffuse atherosclerosis, plaque erosion, and microvascular dysfunction (7,8). These structural differences, modulated by sex hormones and risk factors such as diabetes and hypertension, underlie divergent clinical presentations (9,10).

Clinically, these anatomical variations create diagnostic and management challenges. Men frequently present with classic chest pain associated with ST-Elevation Myocardial Infarction (STEMI), whereas women more commonly exhibit atypical symptoms such as dyspnea, fatigue, and nausea, associated with Non-ST-Elevation Myocardial Infarction (NSTEMI) or ischemia with non-obstructive coronary arteries (11,12). This leads to diagnostic delays and less aggressive initial management in women (13). Anatomical differences also impact interventional strategies. Smaller coronary arteries in women increase the complexity and risk of percutaneous coronary intervention (14), and smaller target vessels reduce graft patency following coronary artery bypass grafting (15), contributing to poorer outcomes in women (16,17).

This study aims to identify anatomical and clinical differences between sexes in ACS patients, evaluate their influence on diagnosis and management, and assess their impact on short-term outcomes.

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Received*: 26-01-2026 -* ***Accepted****: 25-03-2026 -* ***Published****: 02-04-2026*

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Methods

Study Design and Setting

a retrospective descriptive design, conducted over five months from June to October 2025 at two tertiary care hospitals in Tripoli, Libya: Tajoura Cardiac Hospital and Al-Khadra Hospital. Both institutions serve as major referral centers for cardiovascular diseases in the western region of Libya, offering specialized cardiac services including diagnostic catheterization, percutaneous coronary interventions, and cardiothoracic surgery.

Study Population

The study population consisted of 100 patients diagnosed with Acute Coronary Syndrome (ACS). Diagnosis was confirmed based on standard clinical criteria, including characteristic symptoms, electrocardiographic changes, and cardiac biomarker elevation. Patients of all ages and both sexes were included. Exclusion criteria comprised incomplete medical records or missing key clinical data. In parallel, a cross-sectional survey was conducted among 20 cardiologists practicing at the same institutions to assess their awareness of sex-specific anatomical differences and the extent to which these considerations influenced their clinical decision-making.

Data Collection

Patient data were retrospectively extracted from electronic medical records and hospital archives using a standardized data collection form. The information obtained encompassed several domains. Demographic characteristics included age and sex. Clinical presentation variables comprised symptoms at admission, including chest pain type (typical, atypical, or absent), dyspnea, nausea, vomiting, and palpitations, along with systolic and diastolic blood pressure and heart rate measurements. Comorbidities documented included hypertension, diabetes mellitus, hyperlipidemia, obesity, smoking status, and family history of coronary artery disease or ischemic heart disease. Diagnostic findings encompassed electrocardiogram results, troponin levels categorized as normal, high, or very high, and imaging modalities utilized, such as invasive coronary angiography, echocardiography, or CT coronary angiography. Coronary anatomy was assessed by identifying affected vessels, including the left anterior descending artery, right coronary artery, left circumflex artery, and posterior descending artery. Therapeutic interventions recorded included thrombolytic therapy, medications prescribed (antiplatelets, statins, beta-blockers, and ACE inhibitors), and a history of prior cardiac procedures, such as percutaneous coronary intervention or coronary artery bypass grafting. Clinical outcomes evaluated were in-hospital major adverse cardiac events (heart failure, recurrent ischemia, stroke, and death), length of hospital stay, intensive care unit admission, and 30-day post-discharge outcomes, including re-hospitalization, myocardial infarction, stroke, and death.
A structured questionnaire was developed based on the study objectives and relevant literature. The survey explored three key areas: recognition of sex-specific anatomical differences, adjustments to treatment strategies based on anatomical considerations, and the perceived value of additional anatomical information for patient care. The survey was distributed electronically to 20 cardiologists. Participation was voluntary and anonymous, and electronic informed consent was obtained prior to completion.

Data Analysis

Data were coded and entered into Microsoft Excel for initial descriptive analysis. Frequencies and percentages were calculated for all categorical variables. For inferential analysis, data were transferred to IBM SPSS Statistics (version 26). Chi-square tests were applied to evaluate associations between sex and clinical, anatomical, management, and outcome variables. A p-value of less than 0.05 was considered statistically significant. Only complete patient records and fully answered surveys were included in the final analysis.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the institutional review boards of Tajoura Cardiac Hospital and Al-Khadra Hospital prior to data collection.

Results

Patient Demographics and Clinical Presentation

A total of 100 patients diagnosed with Acute Coronary Syndrome (ACS) were included in this study, comprising 67 males (67%) and 33 females (33%). The majority of patients were aged >50 years, with 32%

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***Received**: 26-01-2026 - **Accepted**: 25-03-2026 - **Published**: 02-04-2026*

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aged >70 years, 30% between 51–60 years, and 24% between 61–70 years. Males and females showed similar age distribution patterns, with the highest proportion in the >70 years group (21% and 11%, respectively). Significant sex-based differences were observed in symptom presentation. Typical chest pain was reported in 54% of patients, with a markedly higher proportion in males (36%) compared to females (18%). Dyspnea was the most frequently reported atypical symptom, affecting 70% of patients overall, with a significantly higher prevalence in females (p = 0.0068). Palpitations (p = 0.0069) and nausea/vomiting (p = 0.0024) were also significantly more common in female patients (Table 1).

Table 1. Demographic Characteristics, Clinical Symptoms, and Comorbidities by Gender

Variable	Male (n=67)	Female (n=33)	Total (N=100)	P-value
Age Group				
31–50 years	9 (9%)	4 (4%)	13 (13%)	
51–70 years	36 (36%)	18 (18%)	54 (54%)	
>70 years	21 (21%)	11 (11%)	32 (32%)	
Clinical Symptoms				
Typical Chest Pain	36 (36%)	18 (18%)	54 (54%)	0.12
Atypical Chest Pain	21 (21%)	11 (11%)	32 (32%)	0.45
Dyspnea	47 (47%)	23 (23%)	70 (70%)	0.0068
Palpitations	17 (17%)	8 (8%)	25 (25%)	0.0069
Nausea/Vomiting	11 (11%)	5 (5%)	16 (16%)	0.0024
Comorbidities				
Hypertension	42 (42%)	20 (20%)	62 (62%)	0.98
Diabetes Mellitus	41 (41%)	20 (20%)	61 (61%)	0.98
Hyperlipidemia	23 (23%)	11 (11%)	34 (34%)	0.98
Obesity	27 (27%)	13 (13%)	40 (40%)	0.98
Smoking	15 (15%)	0 (0%)	15 (15%)	0.002

Hemodynamic and Diagnostic Findings

Assessment of hemodynamic status at admission revealed notable variability between sexes. Normal blood pressure was observed in 40% of patients, while hypertension was present in 40% and hypotension in 19%. Heart rate analysis showed that 42% of patients had normal rates, 22% exhibited tachycardia, and 36% had bradycardia. Males demonstrated a slightly higher prevalence of both bradycardia and tachycardia compared to females. All 100 patients demonstrated positive electrocardiographic findings at admission. Coronary angiography was the predominant imaging modality, performed in 84% of patients, with a higher utilization rate in males (56%) compared to females (28%). Troponin level analysis revealed that 84% of patients had elevated levels, with males showing a higher proportion of very high levels (19% vs. 8%), reflecting more extensive myocardial injury (Table 2).

Table 2: Hemodynamic Parameters, Diagnostic Findings, and ACS Type by Gender

Variable	Male (n=67)	Female (n=33)	Total (N=100)
Blood Pressure			
Normal	27 (27%)	13 (13%)	40 (40%)
Hypotension	13 (13%)	6 (6%)	19 (19%)
Hypertension	27 (27%)	13 (13%)	40 (40%)
Heart Rate			
Normal	28 (28%)	14 (14%)	42 (42%)
Tachycardia	15 (15%)	7 (7%)	22 (22%)
Bradycardia	24 (24%)	12 (12%)	36 (36%)
Imaging Modality			
Coronary Angiography	56 (56%)	28 (28%)	84 (84%)
Echocardiography	6 (6%)	2 (2%)	8 (8%)
CT Angiography	5 (5%)	3 (3%)	8 (8%)
Troponin Level			
Normal	10 (10%)	6 (6%)	16 (16%)
High	38 (38%)	19 (19%)	57 (57%)
Very High	19 (19%)	8 (8%)	27 (27%)
ACS Type			
STEMI	27 (27%)	13 (13%)	40 (40%)

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NSTEMI	32 (32%)	15 (15%)	47 (47%)
Unstable Angina	8 (8%)	5 (5%)	13 (13%)

Coronary Anatomy and Therapeutic Interventions

Anatomical analysis of coronary involvement demonstrated that the left anterior descending artery was the most frequently affected vessel, involved in 48% of patients. Male patients exhibited more proximal artery involvement, consistent with larger vessel diameters and focal plaque formation, while females demonstrated more distal and diffuse vessel narrowing.

Percutaneous coronary intervention was performed in 36% of patients, with a higher rate in males (26%) compared to females (10%), reflecting the higher prevalence of focal obstructive lesions in males. Thrombolytic therapy was administered to only 6% of patients, indicating the preference for primary PCI as the standard reperfusion strategy. Medication administration showed mild sex-related variation, with antiplatelets prescribed to 99% of patients and statins to 83% (Table 3).

Table 3: Coronary Artery Involvement and Therapeutic Interventions by Gender

Variable	Male (n=67)	Female (n=33)	Total (N=100)
Coronary Artery Involved			
LAD	32 (32%)	16 (16%)	48 (48%)
RCA	23 (23%)	11 (11%)	34 (34%)
LCx	9 (9%)	8 (8%)	17 (17%)
PDA	1 (1%)	0 (0%)	1 (1%)
Procedural Interventions			
PCI	26 (26%)	10 (10%)	36 (36%)
CABG	3 (3%)	2 (2%)	5 (5%)
Both PCI and CABG	1 (1%)	1 (1%)	2 (2%)
No Prior Procedures	37 (37%)	23 (23%)	60 (60%)
Thrombolytic Therapy	4 (4%)	2 (2%)	6 (6%)
Medications			
Antiplatelets	67 (67%)	32 (32%)	99 (99%)
Statins	56 (56%)	27 (27%)	83 (83%)
Beta-Blockers	51 (51%)	24 (24%)	75 (75%)
ACE Inhibitors	25 (25%)	10 (10%)	35 (35%)

Clinical Outcomes

In-hospital major adverse cardiac events occurred in 20% of patients. Recurrent ischemia affected 10%, heart failure 6%, and death 11%. Males had slightly higher rates of adverse events and longer hospital stays. Intensive care unit admission was required in 28% of patients. At 30-day follow-up, re-hospitalization occurred in 6%, recurrent myocardial infarction in 3%, and death in 11%. No strokes were reported during the follow-up period. Anatomical differences, including smaller coronary arteries and diffuse plaque patterns in females, may explain lower acute complication rates but similar mortality between sexes (Table 4).

Table 4: Clinical Outcomes by Gender

Outcome	Male (n=67)	Female (n=33)	Total (N=100)
In-Hospital MACE			
Heart Failure	4 (4%)	2 (2%)	6 (6%)
Recurrent Ischemia	7 (7%)	3 (3%)	10 (10%)
Stroke	1 (1%)	1 (1%)	2 (2%)
Death	7 (7%)	4 (4%)	11 (11%)
No Events	48 (48%)	32 (32%)	80 (80%)
ICU Admission	19 (19%)	9 (9%)	28 (28%)
Hospital Stay			
Days	45 (45%)	23 (23%)	68 (68%)
Weeks	20 (20%)	9 (9%)	29 (29%)
Months	2 (2%)	1 (1%)	3 (3%)
30-Day Outcomes			
Re-hospitalization	4 (4%)	2 (2%)	6 (6%)
Myocardial Infarction	2 (2%)	1 (1%)	3 (3%)
Death	7 (7%)	4 (4%)	11 (11%)

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Received*: 26-01-2026 -* ***Accepted****: 25-03-2026 -* ***Published****: 02-04-2026*

Physician Survey Results

The survey of 20 cardiologists revealed that all respondents (100%) agreed that anatomical differences between men and women, such as coronary artery size, branching patterns, and vessel tortuosity, have a direct impact on ACS outcomes. However, only 10% reported adjusting their treatment strategies based on sex-specific anatomy. Notably, all respondents agreed that having more detailed anatomical information would enhance patient care and improve clinical decision-making (Table 5).

Table 5: Physician Survey on Sex-Specific Anatomy in ACS Management

Survey Question	Yes	No
Do sex-specific anatomical differences affect ACS outcomes?	20 (100%)	0 (0%)
Do you adjust treatment strategies based on sex-specific anatomy?	2 (10%)	18 (90%)
Would additional anatomical information enhance patient care?	20 (100%)	0 (0%)

Discussion

This multicenter study from Tripoli, Libya, reveals significant sex-based differences in ACS patients, with important implications for clinical presentation, coronary anatomy, management, and outcomes.

Males predominantly presented with typical chest pain (36% vs. 18% females), while females more frequently reported atypical symptoms, particularly dyspnea (70% overall, p=0.0068). These findings align with regional studies from Egypt and Lebanon (7,8). The anatomical basis lies in males' propensity for focal obstructive plaques in large epicardial arteries, whereas females exhibit diffuse atherosclerosis, plaque erosion, and microvascular dysfunction, resulting in less localized ischemia and variable symptoms (5,6,8). The high prevalence of dyspnea in females is clinically significant, as this symptom is often overlooked, contributing to diagnostic delays (13).

Angiographic data showed that the LAD was the most frequently affected vessel (48%). Males had more proximal LAD lesions, while females demonstrated distal and diffuse involvement. This pattern reflects known anatomical differences: men have larger epicardial arteries with thicker walls predisposing to focal proximal plaque accumulation, while women have smaller, more tortuous arteries prone to diffuse disease (5,6,8). Consequently, males had higher rates of STEMI (27% vs. 13%) and very high troponin levels (19% vs. 8%), consistent with larger infarct sizes. Females more often presented with NSTEMI or ischemia with non-obstructive coronary arteries, which may be missed on conventional angiography (6,8).

The anatomical differences between sexes directly impact diagnostic accuracy. Women frequently demonstrate non-specific ECG changes, complicating STEMI identification (13). Additionally, lower baseline troponin in females necessitates sex-specific thresholds to improve diagnostic sensitivity (13). Our finding that 16% of patients had normal troponin, with a higher proportion in females, suggests potential underdiagnosis using standard cutoffs.

Management patterns reflected underlying anatomy. PCI was performed more frequently in males (26% vs. 10%), consistent with their higher prevalence of focal obstructive lesions amenable to stenting. However, this disparity may also reflect a lower likelihood of referring women for invasive evaluation, particularly those with atypical symptoms (13,14). Similar patterns have been reported in Lebanese and Egyptian studies (7,8).

The smaller caliber of female coronary arteries presents technical challenges for interventions, increasing the risk of dissection, perforation, and stent expansion (14). During CABG, smaller target vessels in women are associated with lower long-term graft patency (15). Although our sample size limited detailed CABG analysis, literature consistently reports higher complication rates in women undergoing surgical revascularization (15,16).

In-hospital MACE occurred in 20% of patients, with slightly higher rates in males. While some studies report higher post-ACS mortality in women (16,17), our findings suggest that males, due to larger infarct sizes from proximal vessel occlusion, may experience higher short-term complications. The similar 30-day mortality (7% males vs. 4% females) indicates that outcomes are comparable with appropriate management. The higher rate of recurrent ischemia in males (7% vs. 3%) may reflect residual obstructive disease, while the higher rate of heart failure in females (4% vs. 2%) aligns with their greater susceptibility to diastolic dysfunction (13).

The survey revealed a critical gap: all 20 cardiologists acknowledged that sex-specific anatomy affects outcomes, yet only 10% adjusted treatment based on these differences. This disconnect may stem from sex-neutral clinical guidelines (3,4), the acute nature of ACS requiring rapid protocol-based decisions, and limited access to advanced imaging for real-time anatomical characterization. The unanimous agreement

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***Received**: 26-01-2026 - **Accepted**: 25-03-2026 - **Published**: 02-04-2026*

that additional anatomical information would enhance care suggests a desire for more personalized approaches.
Our findings are consistent with international literature while highlighting regional nuances. The exclusive smoking in males (15%) reflects cultural norms in Libya and the Middle East. The high prevalence of diabetes (61%) and hypertension (62%) aligns with the region's high metabolic disease burden (10). Similar patterns reported from Egypt, Lebanon, Saudi Arabia, and Morocco suggest consistent sex-based differences across the MENA region (7,8).
Several key implications emerge: First, maintain high suspicion for ACS in females presenting with dyspnea, fatigue, or nausea, even without typical chest pain (11,12,13). Second, implement sex-specific troponin thresholds to improve diagnostic accuracy in women (13). Third, account for smaller coronary caliber and tortuosity in females during interventional procedures (14). Fourth, consider functional testing for microvascular dysfunction in female patients with suspected ACS but non-obstructive coronary arteries (6,8).

Limitations
Study limitations include the retrospective design, single-city setting limiting generalizability, lack of detailed anatomical data (vessel diameter, plaque characteristics), absence of long-term follow-up beyond 30 days, and a small physician survey sample (n=20).

Future Directions
Prospective multicenter studies with larger cohorts and advanced imaging (IVUS, OCT) are needed better to characterize sex-specific anatomical differences and their prognostic implications. Interventional studies evaluating sex-specific management protocols would help translate these findings into clinical practice.

Conclusions
Significant sex-based differences exist in ACS presentation and coronary anatomy. Males typically present with obstructive focal lesions and classic symptoms, while females exhibit diffuse disease, microvascular involvement, and atypical symptoms. Recognizing these variations is essential for developing tailored management approaches to improve outcomes for all patients.

Conflict of interest. Nil

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***Received**: 26-01-2026 - **Accepted**: 25-03-2026 - **Published**: 02-04-2026*

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Received*: 26-01-2026 -* ***Accepted****: 25-03-2026 -* ***Published****: 02-04-2026*