

## Research Article

## Inequality in The Management of Acs in Women

Hassan Fadoum<sup>1</sup>, Manouri K<sup>2</sup>, Ibrahim Deka<sup>3</sup>, Zarzur Jamila<sup>4</sup>, Cherti Mohamed<sup>5</sup>

Cardiology B departement, Ibn Sina university Hospital, Mohamed V University, Rabat, Morocco

**Abstract:**

Coronary artery disease is the leading cause of death in women, yet it is considered a man's disease. Management is made difficult by an often non-specific clinical presentation, delaying myocardial revascularisation. To improve the care pathway, no diagnostic strategy has been developed in the management guidelines. The aim of our study is to analyse the clinical features of coronary artery disease in Moroccan women through a retrospective study including 191 patients and to compare these data with those in the literature. The average age of the patients in our study was 62 years, and the most frequently found risk factors were menopause and hypertension. A history of coronary artery disease was present in 16.2% of patients. Chest pain was the main symptom in 91% of cases. The average admission time was 24 hours. STEMI accounted for 40% of clinical presentations and IVA was the most common coronary artery lesion. We report gender disparities in pathophysiology and clinical presentation affecting time to treatment. The longer delays in treatment found in our study may be related to a lack of awareness, a lack of resources but also to a particular social environment.

**Keywords:** Woman - atypical chest pain - late management**Introduction**

Coronary heart disease is responsible for four to six times more deaths than breast cancer in the female population [1]. The non-specific clinical presentation in women results in a delay in diagnosis that has a significant impact on prognosis. The prevalence of coronary heart disease is the same for both sexes after the age of 70 [2]. It is estimated that 60% of coronary deaths in women were not preceded by symptoms of coronary artery disease, which implies the relatively high frequency of asymptomatic forms [3]. In addition, 40% of these asymptomatic forms are fatal.

More active research and the establishment of a diagnostic strategy are more than necessary in the management of coronary artery disease in women. With this in mind, the aim of this study was to analyse the clinical aspects of coronary artery disease in women and compare them with the data for men found in the literature.

**Methods-Results**

This is a retrospective study conducted in the Cardiology Department B of the Souissi Hospital in Rabat, Morocco. It included 191 patients hospitalized for acute coronary syndrome. The data were collected from the medical records using a similar data collection form for all cases. The exclusion criteria was male gender. The average age was 62 years. The main cardiovascular risk factors were menopause followed by hypertension.

Cardiovascular risk factors	N	Percentage
Menopause	178	93.2%
hypertension	116	60.7%
Diabete	108	56.5%
Age	75	39%
Dyslipidemia	59	30.9%
Depression	12	6.3%
smoking	9	4.7%

**Figure 1: Distribution of cardiovascular risk factors in our population**

A history of investigated coronary artery disease was recorded in 16% of cases and 34% had stress angina without medical investigation because it was neglected by the patients.

The average admission time was 24 hours. Chest pain was the main symptom motivating the consultation. Accompanying signs

such as nausea and vomiting that could direct the practitioner to another diagnosis were found in 35% of our patients. A STEMI was found on the ECG in 38.7% of our patients, with the inferior territory most frequently found. The proportion of NSTEMI was 61.3%. A normal ECG was found in 12% of cases.

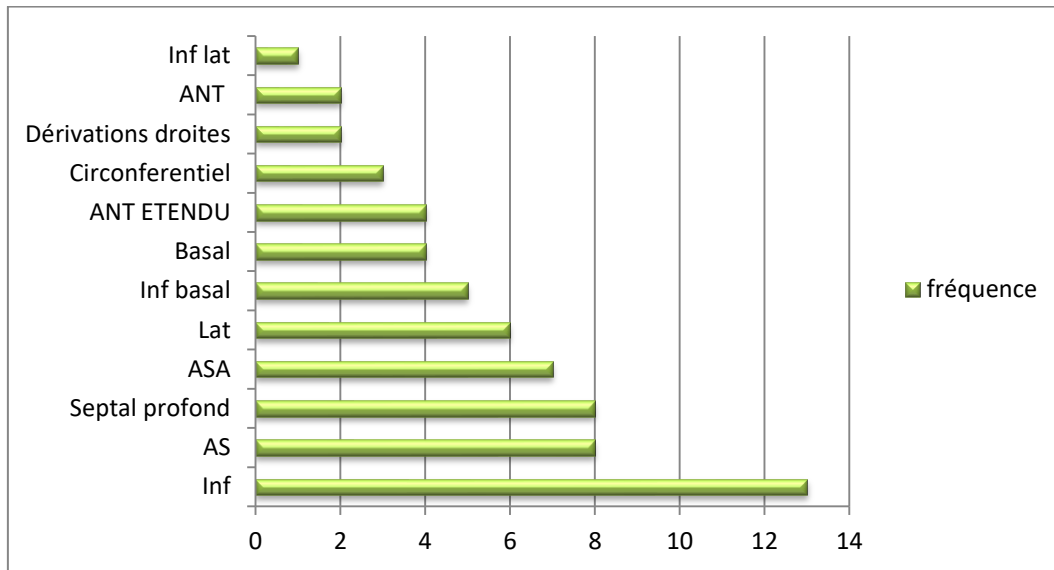


Figure 2: Distribution by territory of STEMI

The majority of our patients (90%) had no rhythmic complications. Severe left ventricular dysfunction prior to revascularisation was found in only 9% of cases. Atheromatous lesions accounted for 83% and dominated coronary angiography. Involvement of the LAI was the most common location. Monotruncal status was more prevalent in our study population and accounted for 45% of cases.

Localisation	Prevalence
TCG1	1.2%
TCG2	5%
IVAI	<b>25%</b>
IVAI	<b>32%</b>
IVAI	16%
CxI	14%
CxII	15%
CxIII	10%
CDI	11.5%
CDII	<b>18%</b>
CDIII	6.2%
Diag 1	10%
Diag 2	2.5%
Diag 3	0.6%
Marg 1	<b>13%</b>
Marg 2	2.5%
IVP	4.3%
BIFURCATION	5.6%
BISSECTRICE	1.2%
Pont Saphène	0.6%
G1	1.2%
Lésion ostiale	18%
Lésion étagée IVA	1.2%
Lésion étagée Cx	2.5%
Lésion étagée CD	2.5%

Figure 3: Distribution of coronary lesions in our population

Coronary angiography was normal in 17% of patients. Angioplasty was performed in 83 patients (43%) of whom 2.6% were primary angioplasty. Surgical treatment was indicated in 21% of our study sample. Medical treatment was indicated in 13.6% of cases.

There was a significant correlation between history of stress angina and the number of coronary events on multivariate analysis.

		history of exertional angina	dyspnea on admission	LVEF range	Number of coronary injuries
history of exertional angina	Pearson Correlation	1	-,163*	,006	-,249**
	Sig. (2-tailed)		,024	,938	,001
	N	191	191	191	180
dyspnea on admission	Pearson Correlation	-,163*	1	-,130	,170*
	Sig. (2-tailed)	,024		,073	,023
	N	191	191	191	180
LVEF range	Pearson Correlation	,006	-,130	1	,056
	Sig. (2-tailed)	,938	,073		,453
	N	191	191	191	180
Number of coronary injuries	Pearson Correlation	-,249**	,170*	,056	1
	Sig. (2-tailed)	,001	,023	,453	
	N	180	180	180	180

\*. Correlation is significant at the 0.05 level (2-tailed). **Figure 4: correlation between some parameters and coronary damage**

## Discussion

Coronary heart disease in women remains an underestimated public health problem. Women should be prioritised in the establishment of prevention programmes to improve screening for CHD as even young women (< 55 years) are not spared [4].

This evolution in young women is probably the consequence of profound changes in behaviour and lifestyle, contributing to the emergence of a new cardiovascular risk profile in women over the last 20 years [5].

Thus, there is an increase in the proportion of young women who develop coronary heart disease without hypertension, diabetes or dyslipidaemia but with smoking and obesity as the main classical cardiovascular risk factors [3-5]. In addition, there are specific hormonal risk and emerging risk factors (psychosocial factors, breast radiotherapy, polycystic ovary syndrome, early menarche) that are not included in conventional risk scores [3].

In our study, we reported a total number of 843 patients hospitalised for ACS who underwent coronary angiography, of whom 22.6% were women (191) versus 77.4% men (652). This male predominance was found in most of the studies carried out with a rate of 38% of women in sub-Saharan Africa and 27% in the study by T. SIMON in France [6]. The GRACE [7] and CRUSADE [8] registers included 28% and 41% of women respectively.

However, this prevalence in women increases progressively and reaches that of men around the age of 70, probably due to the absence of the protective effects of oestrogens as a result of the menopause [9]. However, the cardiovascular risk profile of young women is changing, marked mainly by increased exposure to smoking and increased psychosocial stress [10].

Apart from the common cardiovascular risk factors in women and men, it appears that menopause precipitates the onset of coronary heart disease in women [11].

Nevertheless, an important notion should be emphasised concerning young women who are not free of complications in cardiovascular events.

Their in-hospital mortality is 4.1 times higher, their cardiac and cerebrovascular complications at 30 days of hospitalisation are 2.1 times more frequent with a 5-year mortality risk multiplied by 1.96 [12]. The results of the VIRGO study indicate that these young women have a poorer quality of life and mental health compared to men of the same age [13].

This psychological and hormonal state in combination with other classical risk factors gives women an increased exposure to cardiovascular events. Risk stratification should take into account this overall assessment. Certain scores have been established for this purpose, such as that of the AHA, which, in addition to the usual risk factors, includes an assessment of lifestyle [14].

Chest pain, which is the main symptom in ACS, is found mainly in both sexes, as highlighted by the series by Canto et al [15].

Typical symptomatology (angina pain at rest) was described by 91% of our study sample.

The particularity in women is that they present many more accompanying symptoms such as neck pain, nausea, fatigue or dyspnoea with an average of 2.6 compared to 1.8 in men [16]. In our series, 35% of patients had accompanying signs and 32% had associated dyspnoea on admission.

Apart from signs associated with chest pain, atypical clinical manifestations may be found in women, delaying diagnosis. Signs such as anxiety, stress or gastroesophageal reflux are reported in the study by Canto et al, particularly in young women [15].

These symptoms may be influenced by ethnicity. The study by Eastwood et al analysing symptoms following ACS in women reported that black women had fewer chest symptoms compared to Caucasian women [17].

These atypicalities in clinical presentation are at the origin of the delay in the management of ACS in women.

Lack of awareness of the symptoms of myocardial infarction, underestimation of the prevalence of coronary artery disease in women, and asymptomatic forms of the disease have been reported to be factors in the delay in consultation in women [18,19]. The average consultation time in our series was 24 hours.

Consultation period	<6H	6-12H	> 12H
Frequency	17	10	164
Percentage	8.8%	5.4%	85%

While the clinic is almost always suggestive in men and the ECG conclusive, data from the CRUSADE registry suggest that women consulting for ACS had less ECG within 10 minutes of emergency admission compared to men [8].

Risk stratification in NSTEMI based primarily on electrical changes and troponin elevation is biased in women. Indeed, compared to men, a T-wave inversion without elevation of myocardial necrosis markers is common in the female group [8]. In our work, 44% of the women had negative T waves and of these, 30% had negative troponins.

Also 75% of our patients who had a normal ECG had angiographically significant lesions.

Women tend to have lower troponin levels compared to men, and this is mainly explained by the lower ventricular mass in women [20]. The adaptation of ultra-sensitive troponin thresholds to gender in troponin testing is related to this anatomical difference between the two sexes.

It is therefore logical to assume that women suspected of having MI on the basis of enzyme elevation data alone are less likely to be referred for appropriate care.

The series by Shah et al, investigated the sensitivity of ACS diagnosis by comparing an ultra-sensitive troponin assay with gender-specific cut-offs (male= 34ng/L; female= 16ng/L) to a routine laboratory test (50ng/L) [21].

The authors found that the troponin I test (high sensitivity) significantly increased the diagnosis of myocardial infarction in women (from 11% to 22%; P<0.001) but had a minimal effect in men (from 19% to 21%, P=0.002).

They also highlighted the fact that at 12 months, women with increases in troponin I concentration (17-49 ng/L) and those with myocardial infarction (≥50 ng/L) had the highest rate of death or reinfarction compared with women without myocardial infarction (≤16 ng/L).

It therefore appears that changes in the ultra-sensitive troponin threshold could in practice allow the recruitment of twice as many patients with ACS who would not normally be managed for a coronary event.

The apparent under-diagnosis of MI in women historically attributed to the atypical clinical presentation and low electrical changes, suggests an additional explanation which is the use of inappropriate troponin diagnostic thresholds [22].

The Apple and Morrow series, emphasise that contemporary laboratory troponin testing that sets a diagnostic threshold for the sexes has heavily disadvantaged women and contributed to the underdiagnosis of MI [23,24].

## Conclusion

The apparent severity of coronary artery disease in women is related to the later age of onset and the difficulty of diagnosis. Atypicality in the clinical presentation, electrically, contributes to the diagnostic delay. It also appears that unique troponin diagnostic cut-offs may lead to under estimate the pronostic of MI . This is also a reason for delaying the management of MI in women.

An appropriate diagnostic and therapeutic pathway for ACS in women may reduce the inequalities in management between the two sexes.

## References

1. Nichols M, Townsend N, Scarborough P, Rayner M. European cardiovascular disease statistics 4th edition 2012 : Euroheart II. Eur Heart J 2013 ;34:3007
2. De Peretti C, Chin F, Tuppin P, Danchin D, et al. Personnes hospitalisées pour infarctus du myocarde en France : tendances2002—2008. Bull EpidemiolHebd 2012;41:459
3. Madika AL, Mounier-Vehier C. La maladie coronaire de la femme : de vraies spécificités à bien connaitre pour améliorer les prises en charge. Presse Med 2016;45(6 Pt 1):577—87.

4. Gabet A, Danchin N, Juillie`re Y, Olie´ V. Acute coronary syndrome in women: rising hospitalizations in middle-aged French women, 2004–14. *Eur Heart J* 2017; 38:1060–1065.
5. Mehta LS, Beckie TM, DeVon HA, Grines CL, Krumholz HM, Johnson MN, et al. Acute myocardial infarction in women: a scientific statement from the American Heart Association. *Circulation* 2016;133:916–47
6. Puymirat E, Simon T, Steg PG, Schiele F, Guéret P, Blanchard D, et al. Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction. *JAMA* 2012;308:998–1006.
7. Dey S, Flather MD, Devlin G, Brieger D, et al.; Global Registry of Acute Coronary Events investigators. Sex-related differences in the presentation, treatment and outcomes among patients with acute coronary syndromes: the Global Registry of Acute Coronary Events. *Heart*. 2009 Jan;95(1):20-6.
8. Blomkalns AL, Chen AY, Hochman JS, et al; CRUSADE Investigators. Gender disparities in the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: large-scale observations from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) National Quality Improvement Initiative. *J Am Coll Cardiol*. 2005;45(6):832-7.
9. Stangl V, Baumann G, Stangl K. Coronary atherogenic risk factors in women. *Eur Heart J* 2002;23:1738 –52.
10. Casiglia E, Tikhonoffa V, Caffib S, Bascellia A, Schiavon L, Guidotti F et al. Menopause does not affect blood pressure and risk profile, and menopausal women do not become similar to men. *Journal of Hypertension* 2008;26:1983-92.
11. Collins P, Rosano G, Casey C, Daly C, Gambacciani M, Hadji P et al. Management of cardiovascular risk in the perimenopausal woman: a consensus statement of European cardiologists and gynaecologists. *Eur Heart J* 2007;28:2028-40
12. Sabbag et al, Sex Differences in the Management and 5-Year Outcome of Young Patients (<55 Years) with Acute Coronary Syndromes. 2017 Elsevier Inc. All rights reserved. \_ *The American Journal of Medicine* (2017) 130, 1324.e15-1324.e22
13. Dreyer RP, Smolderen KG, Strait KM, Beltrame JF, Lichtman JH, Lorenze NP, D’Onofrio G, Bueno H, Krumholz HM, Spertus JA. Gender differences in pre-event health status of young patients with acute myocardial infarction: a VIRGO study analysis. *Eur Heart J Acute Cardiovasc Care* 2016;5:43–54.
14. American Heart Association. Heart Disease and Stroke Statistics: 2004 Update. Available <http://americanheart.org/downloadable/heart/1072969766940HSSStats2004Update.pdf> Accessed January 15, 2004
15. Canto JG, Goldberg RJ, Hand MM, Bonow RO, Sopko G, Pepine CJ, Long T. Symptom presentation of women with acute coronary syndromes: myth vs reality. *Arch Intern Med* 2007;167:2405–2413.
16. Lichtman JH, Leifheit EC, Safdar B, Bao H, Krumholz HM, Lorenze NP, Daneshvar M, Spertus JA, D’Onofrio G. Sex differences in the presentation and perception of symptoms among young patients with myocardial infarction: evidence from the VIRGO study (Variation in Recovery: role of Gender on Outcomes of Young AMI Patients). *Circulation* 2018;137:781–790.
17. Eastwood JA, Johnson BD, Rutledge T, et al. Anginal symptoms, coronary artery disease, and adverse outcomes in Black and White women: the NHLBI-sponsored Women’s Ischemia Syndrome Evaluation (WISE) study. *J Womens Health (Larchmt)*. 2013;22(9):724–32
18. Gebhard CE, Gebhard C, Maafi F, Bertrand MJ, Stahli BE, Maredziak M, Bengs S, Haider A, Zhang ZW, Smith DC, Ly HQ. Impact of summer season on prehospital time delays in women and men undergoing primary percutaneous coronary intervention. *Sci Total Environ* 2019;656:322–330.
19. Roswell RO, Kunkes J, Chen AY, Chiswell K, Iqbal S, Roe MT, Bangalore S. Impact of sex and contact; Device time on clinical outcomes in acute; Segment elevation myocardial infarction; Findings from the National Cardiovascular Data Registry. *J Am Heart Assoc* 2017;6:e004521.
20. Salton CJ, Chuang ML, O’Donnell CJ, Kupka MJ, Larson MG, Kissinger KV, et al. Gender differences and normal left ventricular anatomy in an adult population free of hypertension. A cardiovascular magnetic resonance study of the Framingham Heart Study Offspring cohort. *VJ Am Coll Cardiol* 2002;39:1055–60.
21. Shah AS, Griffiths M, Lee KK, McAllister DA, Hunter AL, Ferry AV, et al. High sensitivity cardiac troponin and the underdiagnosis of myocardial infarction in women: prospective cohort study. *BMJ (Clin Res ed)*. 2015;350:g7873. doi:10.1136/bmj.g7873.
22. Elsaesser A, Hamm CW. Syndrome coronarien aigu: le risque d’être une femme. *Diffusion* 2004; 109:565-7
23. Apple FS, Ler R, Murakami MM. Détermination de 19 valeurs cardiaques de troponine I et T au 99e centile à partir d’une population commune vraisemblablement en bonne santé. *Clin Chem* 2012; 58:1574-81.
24. Morrow DA, Cannon CP, Jesse RL, Newby LK, Ravkilde J, Storrow AB, et coll. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical characteristics and utilization of biochemical markers in acute coronary syndromes. *Diffusion* 2007; 115:e356-75.