



Acute Coronary Syndrome in Women

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Abstract

Cardiovascular disease is the leading cause of mortality for women. Anginal symptoms differ from the classical picture in men, making diagnosis more difficult and delaying effective therapy.

Introduction: This phenomenon is of great relevance for healthcare in women and therefore has been investigated in numerous studies.

Methods: This one year retrospective observational study included 533 patients, of that number 193 were women. The data were collected from medical history, markers of myocardial necrosis, electrocardiography, echocardiography, coronary angiography. We analyse main differences in risk factors- age, obesity, smoking, hypertension, diabetes, symptomatology, treatment, intrahospital complications and mortality. Statistical analyses were done electronically by X2 test, Mann-Whitney test, Kolmogorov-Smirnov test.

Results: In our study women were older than man, that was statistically significant. There was no differences in symptom presentation, but women have mostly atypical symptoms. Women are thicker than man, but man smoke more. There are no distinction by gender in diabetes and hypertension. Treatment was the same for both groups of patients. Frequency of intrahospital complications and mortality was higher in women.

Conclusion: Our study suggest differences in symptom presentation and obesity. Obesity represents world health problem and primary prevention is the key. There are sex differences in in-hospital complications and mortality, so we need improvement in diagnosis procedures and hospital treatment in women.

Keywords: Acute Coronary Syndrome; Women

Introduction

Cardiovascular disease is the leading cause of mortality for women [1]. Ischaemic heart disease develops on average 7 - 10 years later in women compared with men. Acute coronary syndrome (ACS) occurs three to four times more often in men than in women below age of 60 years, but after the age of 75 women represent the majority of patients. Women tend to present more often with atypical symptoms up to 30% in some registries, and tend to present later than men [2]. Although obstructive atherosclerotic disease of the epicardial coronary arteries remains the basic cause of acute myocardial infarction in both sexes, plaque characteristics differ for women, and recent data have suggested a greater role of microvascular disease in the pathophysiology of coronary events among women [3]. Despite being older and having a greater risk factor burden and a greater symptom burden of angina and consequent morbidity and mortality, women paradoxically have less severe obstructive disease of their epicardial coronary arter-

ies at elective angiography than men [4]. Vulnerable plaque rupture predict the occurrence of ACS [5,7]. According to pathological studies TCFA (Thin Cap Fibro Atheroma) is main type of vulnerable plaque susceptible to rupture [6]. Actual frequency of plaque rupture is low and doesn't exhibit clinically, therefore additional factors including increased blood vulnerability has been hypothesized to contribute to clinical manifestation of ACS besides vulnerable plaque rupture [8]. Compared with men, women more commonly present with non-ST-segment-elevation MI (NSTEMI) [9,10], and nonobstructive coronary artery disease (CAD) [9,11,12]. They are more likely than men to experience delays between onset of symptoms and arrival at the hospital; there are also gender differences in the delays between onset of symptoms and initiation of guideline-based treatment and use of various surgical and pharmacologic treatments. Women, on average, have worse outcomes than men following myocardial infarction, with more complications, higher mortality rates, and poorer recovery [13].

Methods

This was a descriptive, observation retrospective study carried out at Cardiology department in University Clinical Centre of Republic Srpska, from January, 2016 to January 2017 a period of twelve months. A total of 533 patients were included in the study population using data from medical history in hospital information system. All those patients who were included are admitted or discharged with diagnosis of acute coronary syndrome. Diagnosis was confirmed by bio humoral markers of myocardial necrosis, electrocardiography, echocardiography and coronary angiography. We compared differences between two groups of patients that were divided by sex- 340 man and 193 women. In these groups we analyses risk factors for acute coronary syndrome, levels of high sensitive troponin, electrocardiography, ejection fraction by echocardiography and differences in coronary angiography. We did research of intra-hospital complications and mortality.

Data analysis

Data was analyzed by SPSS 21. A Pearson C² test was used to compare differences in the frequency of observed characteristics by groups. Mean ± Standard Deviation was determined for quantitative variables. Qualitative variables were expressed as frequencies and percentages. The normality of distribution in the observed features was tested by Kolmogorov-Smirnov test. A nonparametric Mann-Whitney test was used to compare mean values by gender of subjects. P-value of less than 0.05 was considered as significant.

Results

This survey included 533 patients of which 340 or 63.79% were male and 193 or 36.21% were female. Patients covered by this survey averaged 64.8 years (30 to 91 years). The median age of the males were 62 (IQ: 54 - 70), while the median age of the females was 67 (IQ: 61 - 78). This difference is statistically significant, meaning that the female patients are statistically significantly older than the males (Table 1 and Chart 1).

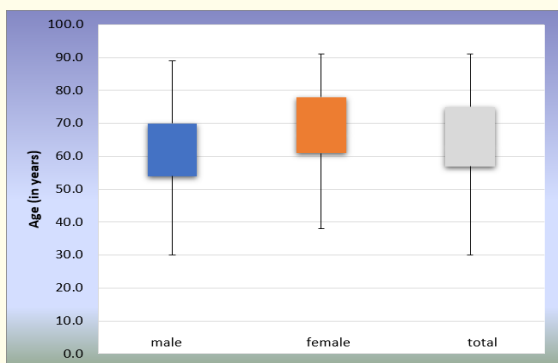


Chart 1: Box-plot diagram for age (in years) by gender.

Gender	Arithmetic mean ± standard deviation	Median (interquartile interval)	Minimum - Maximum
Males	62.75 ± 12.39	62.0 (54.0, 70.0)	30.0 - 89.0
Females	68.40 ± 11.53	67.0 (61.0, 78.0)	38.0 - 91.0
Total	64.80 ± 12.38	63.0 (57.0, 75.0)	30.0 - 91.0
Mann-Whitney U test for independent samples			p < 0.001

Table 1: Basic indicators of descriptive statistics for age (in years) by gender.

Of all patients followed by this survey, 37.34% were obese. 31.47% of the males are obese, while the percentage of obesity is higher among the females and amounts to 47.67% of all subjects tested (Table 2). The difference between male and female by obesity is statistically significant.

Obesity	Gender				Total	
	Male		Female		N	%
	N	%	N	%		
No	233	68.53	101	52.33	334	62.66
Yes	107	31.47	92	47.67	199	37.34
Total	340	100.00	193	100.00	533	100.00
Pearson χ ² test				p < 0.001		

Table 2: Frequency and percentage of patients by obesity and gender.

Of all patients followed by this survey, 25.14% were smokers. Smokers are 32.65% among males, while among female respondents, the percentage of smokers is smaller and amounts to 11.92% of respondents (Table 3). The aforementioned difference between male and female subjects by smoking is statistically significant.

Smoking	Gender				Total	
	Male		Female		N	%
	N	%	N	%		
No	229	67.35	170	88.08	399	74.86
Yes	111	32.65	23	11.92	134	25.14
Total	340	100.00	193	100.00	533	100.00
Pearson χ ² test				p < 0.001		

Table 3: Frequency and percentage of patients by smoking and gender.

Of all subjects followed by this study, 82.74% had elevated blood pressure. 80.59% of male and 86.53% of female subjects had

elevated blood pressure. However, no statistically significant difference was observed between male and female subjects according to elevated blood pressure.

In this study, 26.83% of patients had diabetes, 26.47% of the male and 27.46% of the female. However, no statistically significant difference was observed between male and female subjects for diabetes.

Analysed by type of infarction, STEMI infarction had 68.11% of follow-up subjects, NSTEMI infarction had 29.64% of subjects, and APNS infarction had 2.25% of follow-up subjects (Table 4). No statistically significant difference was observed between male and female subjects by infarction type.

n	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
STEMI	236	69.41	127	65.80	363	68.11
NSTEMI	97	28.53	61	31.61	158	29.64
APNS	7	2.06	5	2.59	12	2.25
UKUPNO	340	100.00	193	100.00	533	100.00
Pearson χ^2 test				p = 0.676		

Table 4: Frequency and percentage of patients by infarction type and gender.

Subjects with STEMI infarction included in this study reported to the physician on average 7.85 hours from the onset of symptoms (1 to 72 hours). No statistically significant difference was observed in the mean values of time from onset of symptoms to the appearance of a physician between male and female subjects.

Of the total number of patients, 30 had atypical symptoms, 93.3 percent of them were women (Table 5).

Symptoms	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
Typical	0	0.00	2	8.33	2	6.67
Atypical	6	100.00	22	91.67	28	93.33
Total	6	100.00	24	100.00	30	100.00
Pearson χ^2 test				p = 0.464		

Table 5: Frequency and percentage of patients according to symptoms and gender.

The arithmetic mean of the input troponin in the subjects followed by this study was 2897.36 (6 to 121567). No statistically significant difference in input troponin values was observed between male and female subjects.

Of all patients followed by this study, 9.94% (11.76% of male and 6.74% of female) had ECG characteristic changes. However, no

statistically significant difference was observed between male and female subjects according to ECG characteristic changes.

Viewed by ejection fraction, 60.04% of respondents had an ejection fraction above 40%, 30.21% of respondents had an ejection fraction of 30% to 40%, and 9.76% of respondents had an ejection fraction below 30%. No statistically significant difference was observed in the ejection fraction between male and female subjects.

Observed by coronagraphy, 46.12% of the subjects had a single-vessel disease, 22.41% had a two-trial, 24.14% three-trial, 5.17% had a four-vessel disease, 0.43% had a left main, 0.65% had no changes, and 1.08% of the subjects the coronagraphy was neat. No statistically significant difference in coronagraphy was observed between male and female subjects.

13.51% of the patients followed by this study had complications in the hospital. Male patients had hospital complications in 10.88% of cases, while in females this percentage was statistically significantly higher and amounted to 18.13% (Table 6).

s	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
No	303	89.12	158	81.87	461	86.49
Yes	37	10.88	35	18.13	72	13.51
Total	340	100.00	193	100.00	533	100.00
Pearson χ^2 test				p = 0.019		

Table 6: Frequency and percentage of patients according to the occurrence of complications in hospital and gender.

Intra-hospital mortality was 8.82% of all patients, 12.44% of females and 6.76% of males. The mentioned difference between males and females is statistically significant (Table 7).

y	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
No	317	93.24	169	87.56	486	91.18
Yes	23	6.76	24	12.44	47	8.82
Total	340	100.00	193	100.00	533	100.00
Pearson χ^2 test				p = 0.026		

Table 7: Frequency and percentage of intra-hospital mortality by gender.

Within one month, mortality was 2.99% of all patients, and no statistically significant difference was observed between male and female patients in this regard.

Discussion

Women are often older when they present with their first acute myocardial infarction, at an average age of 71.8 years compared with 65 years for men [14]. The older age of onset of coronary heart disease in women compared with men is thought to be due to the protective role of circulating estrogens on the vascular endothelium [15]. Direct effects of estrogen on the vascular system include increased release of nitric oxide leading to vasodilation [16,17], regulation of prostaglandin production [18], and inhibition of smooth muscle proliferation [19]. Population studies have shown that estrogen depletion at menopause increases endothelial dysfunction and lipid deposition in the vasculature, which can precipitate the development of atherosclerosis over time [20,21]. However, despite the cardioprotective effects of endogenous estrogen, studies evaluating exogenous estrogen hormone therapy for the primary prevention of coronary heart disease in postmenopausal women have been convincingly negative. In our trial the incidence of cardiovascular events was lower in women than in men, as results of several studies that have recently highlighted the necessity to focus closely on women for several reasons. Compared with men, women more commonly present with non-ST-segment-elevation MI (NSTEMI). In our study we confirm these results. In the study that was done by Judith S, at all, Sex, Clinical Presentation, and Outcome in Patients with Acute Coronary Syndromes” [22] a smaller percentage of women than men had infarction with ST elevation (27.2 percent vs. 37.0 percent, $P < 0.001$), and of the patients who presented with no ST elevation (those with myocardial infarction or unstable angina), fewer women than men had myocardial infarction (36.6 percent vs. 47.6 percent, $P < 0.001$). In this study, it was confirmed that women with acute ischemic syndromes tend to be older than men with such syndromes, and they have higher rates of associated diabetes and hypertension. We also had the similar results. In the INTERHEART study, a history of smoking had a stronger association with myocardial infarction in men compared with women; however, current smoking history did not have significant variation by sex. In our study, more smokers were male and this difference was statistically significant. Obesity is a major risk factor for acute myocardial infarction in women and increases their risk almost 3-fold [23]. In our study that was confirmed, obesity was significantly more prevalent in women (47,6% female, $P < 0,001$). We researched in our sample, that women did not have a higher incidence of arterial hypertension and diabetes mellitus, unlike the results of most other studies [2]. The results of our study have confirmed that acute coronary artery syndrome is presented with atypical symptoms more often in women than in men. Many studies have confirmed this fact. In study, Angina in Women”, Nanette K, at all have confirmed that the most patients with AMI present with typical chest pain or chest discomfort. Women often present with atypical chest pain and angina-equivalent symptoms such as dyspnea, weakness, fatigue, and indigestion [24,25]. A consequence of these atypical symp-

toms is often an underestimation of the severity and a longer delay between symptoms and the first call to an emergency unit in women compared with men [23]. Sex differences in clinical presentation have consequences for timely identification of ischemic symptoms, appropriate triage, and judicious diagnostic testing and management. The detrimental consequences for women are misdiagnosis, delayed revascularization, and higher AMI mortality rates. 13.51% of the patients followed by this study had complications in the hospital. Male respondents had 10.88% of cases in the hospital, while this percentage was significantly higher for female respondents, 18.13% [24]. Women with acute myocardial infarction have a higher hospital mortality rate than men. This difference has been ascribed to their older age, more frequent comorbidities, and less frequent use of revascularization. Women were less likely than men to receive care within the benchmark time for reperfusion therapy (time to treatment from symptom onset < 12 hours 76.0% vs 80.4%, $p < 0.001$) [27]. In study, Gender Differences in Hospital Mortality and Use of Percutaneous Coronary Intervention in Acute Myocardial Infarction”; women were older (75 versus 63 years of age; $P < 0.001$) and had a higher rate of hospital mortality (14.8% versus 6.1%; $P < 0.0001$) than men [26]. In our study intra-hospital mortality was also higher in females 12.44% compared of 6.76% of males.

Conclusions

Our study suggest differences in symptoms presentation and obesity. Obesity represents world health problem and primary prevention is the key. There are sex differences in in-hospital complications and mortality, so we need improvement in diagnosis procedures and hospital treatment for women.

Bibliography

1. Gholizadeh L and Davidson P. “More similarities than differences: an international comparison of CVD mortality and risk factors in women”. *Health Care for Women International* 29 (2008): 3-22.
2. EUGenMed Cardiovascular Clinical Study Group., *et al.* “Gender in cardiovascular diseases: impact on clinical manifestations, management, and outcome”. *European Heart Journal* 37.1 (2016): 24-34.
3. Brieger D., *et al.* “Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events”. *Chest* 126.2 (2004): 461-469.
4. Bairey Merz CN., *et al.* “Insights from the NHLBI-sponsored Women’s Ischemia Syndrome Evaluation (WISE) Study, part II: gender differences in presentation, diagnosis, and outcome with regard to gender-based pathophysiology of atherosclerosis and macrovascular and microvascular coronary disease”. *Journal of the American College of Cardiology* 47 (2006): S21-S29.

5. Merz CN. "The Yentl syndrome is alive and well". *European Heart Journal* 32 (2011): 1313-1315.
6. Schaar JA, et al. "Terminology for high-risk and vulnerable coronary artery plaques: Report of a meeting on the vulnerable plaque June 17 and 18 2003, Santorini, Greece". *European Heart Journal* 25 (2004): 1077-1082.
7. Burke AP, et al. "Coronary risk factors and plaque morphology in men with coronary disease who died suddenly". *The New England Journal of Medicine* 336 (1997): 1276-1282.
8. Ueda Y, et al. "Acute Coronary Syndrome: Insight from Angioscopy". *Circulation Journal* 74 (2010): 411-417.
9. Hochman JS, et al. "Sex, clinical presentation, and outcome in patients with acute coronary syndromes: Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators". *The New England Journal of Medicine* 341 (1999): 226-232.
10. Hochman JS, et al. "Outcome and profile of women and men presenting with acute coronary syndromes: a report from TIMI IIIB: TIMI Investigators: Thrombolysis in Myocardial Infarction". *Journal of the American College of Cardiology* 30 (1997): 141-148.
11. Hasdai D, et al. "Effect of gender on outcomes of acute coronary syndromes". *American Journal of Cardiology* 91 (2003): 1466-1469, A6.
12. Bellasi A, et al. "New insights into ischemic heart disease in women". *Cleveland Clinic Journal of Medicine* 74 (2007): 585-594.
13. Graham G. "Acute coronary syndromes in women: recent treatment trends and outcomes". *Clinical Medicine Insights: Cardiology* 10 (2016): 1-10.
14. Mozaffarian D, et al. "Heart disease and stroke statistics—2015 update: a report from the American Heart Association". *Circulation* 131 (2015): e29-e322.
15. Chakrabarti S, et al. "Mechanisms of estrogen effects on the endothelium: an overview". *Canadian Journal of Cardiology* 30 (2014): 705-712.
16. Khalil RA. "Sex hormones as potential modulators of vascular function in hypertension". *Hypertension* 46 (2005): 249-254.
17. Mendelsohn ME and Karas RH. "The protective effects of estrogen on the cardiovascular system". *The New England Journal of Medicine* 340 (1999): 1801-1811.
18. Hermenegildo C, et al. "Cyclooxygenases regulation by estradiol on endothelium". *Current Pharmaceutical Design* 12 (2006): 205-215.
19. Mercurio G, et al. "Impaired forearm blood flow and vasodilator reserve in healthy postmenopausal women". *American Heart Journal* 137 (1999): 692-697.
20. Rosano GM, et al. "Menopause and cardiovascular disease: the evidence". *Climacteric* 10 (2007): 19-24.
21. Taddei S, et al. "Menopause is associated with endothelial dysfunction in women". *Hypertension* 28 (1996): 576-582.
22. Judith S, et al. "Sex, Clinical Presentation, and Outcome in Patients with Acute Coronary Syndromes". *The New England Journal of Medicine* 341 (1999): 226-232.
23. Benamer H, et al. "Longer pre-hospital delays and higher mortality in women with STEMI: the e-MUST Registry". *Euro Intervention: Journal of EuroPCR in Collaboration With the Working Group on Interventional Cardiology of the European Society of Cardiology* 12.5 (2016): e542-549.
24. Nanette K Wenger. "Angina in Women". *Current Cardiology Reports* 12.4 (2010): 307-314.
25. Goldberg RJ, et al. "Sex differences in symptom presentation associated with acute myocardial infarction: a population-based perspective". *American Heart Journal* 136.2 (1998): 189-195.
26. Carine Milcent, et al. "Gender Differences in Hospital Mortality and Use of Percutaneous Coronary Intervention in Acute Myocardial Infarction". *Circulation* 115 (2007): 833-839.
27. Raffaele Bugiardini, et al. "Sex-related differences in acute coronary care among patients with myocardial infarction: the role of pre-hospital delay". *Journal of the American College of Cardiology*. 65.10 (2015).

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