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Gender differences in the clinical presentation, treatment and outcomes of acute myocardial infarction

Spolne razlike u kliničkoj prezentaciji, liječenju i ishodima akutnog infarkta miokarda

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Abstract. ***Aim:*** To assess the epidemiological and clinical differences between men and women with acute myocardial infarction (AMI). ***Patients and methods:*** This retrospective study included 579 patients (352 men and 221 women) who were hospitalized at the Coronary and postcoronary unit at the General Hospital, Karlovac, Croatia, from 2013 to 2016. We determined the frequency, patient's age, type of symptoms, cardiovascular risk the factors, localization, the time from the onset of symptoms to arrival to the hospital, treatment and complications during the hospitalization. ***Results:*** AMI is more frequent in men than in women ($P < 0.001$) and in men it is significantly more likely to occur at an earlier age than in women ($P < 0.001$). Men often have typical symptoms while women have atypical symptoms ($P = 0.045$). More often women have arterial hypertension ($P = 0.017$) and diabetes ($P = 0.025$), while men are more often smokers ($P = 0.001$). There was no difference between the gender regarding hyperlipidemia ($P = 0,674$). Distribution of localization ($P = 0.608$), the time required for the arrival to the hospital ($P = 0.399$) and all the complications of AMI are equal ($P = 0.365$). Men are more likely to receive PCI treatment, while women get the conservative therapy ($P = 0.007$). ***Conclusion:*** Compared with other studies, our women with AMI have less hyperlipidemia and do not come later to hospital than men. Possible causes are dietary habits and genetics or education and good organization of outpatient emergency medical assistance.

Key words: acute myocardial infarction; cardiovascular risk; Croatia; hospital treatment

Sažetak. ***Cilj:*** Ispitati epidemiološke i kliničke razlike između žena i muškaraca s akutnim infarktom miokarda (AIM). ***Bolesnici i metode:*** Ova retrospektivna studija obuhvatila je 579 pacijenata (352 muškarca i 221 ženu) hospitaliziranih u koronarnoj i postkoronarnoj jedinici Opće bolnice Karlovac, Hrvatska, od 2013. do 2016. godine. Utvrdili smo učestalost, dob pacijenata, tip simptoma, kardiovaskularne rizične čimbenike, lokalizaciju, vrijeme od početka simptoma do dolaska u bolnicu, liječenje i komplikacije tijekom hospitalizacije AIM-a. ***Rezultati:*** AIM je češći kod muškaraca nego kod žena ($P < 0,001$) i kod muškaraca je značajno vjerojatnije da će se pojaviti u ranijoj dobi nego kod žena ($P < 0,001$). Muškarci češće imaju tipične simptome, a žene atipične simptome ($P = 0,045$). Žene imaju češće arterijsku hipertenziju ($P = 0,017$) i dijabetes ($P = 0,025$), dok su muškarci češće pušači ($P = 0,001$). Hiperlipidemija je podjednako zastupljena u oba spola ($P = 0,674$). Distribucija lokalizacije ($P = 0,608$), vrijeme potrebno za dolazak u bolnicu ($P = 0,399$) i sve komplikacije AIM-a podjednako su česti ($P = 0,365$). Muškarci se češće liječe invazivnom, a žene konzervativnom terapijom. ***Zaključak:*** U usporedbi s drugim istraživanjima naše žene s AIM-om imaju manju učestalost hiperlipidemije i ne dolaze kasnije u bolnicu od muškaraca. Mogući razlozi su prehrambene navike i genetika ili obrazovanje i dobra organizacija izvanbolničke hitne medicinske pomoći.

Ključne riječi: akutni infarkt miokarda; bolničko liječenje; Hrvatska; kardiovaskularni rizik

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INTRODUCTION

Cardiovascular diseases are currently the leading cause of death in industrialized countries and are expected to become so in emerging countries by 2020. Among these, coronary artery disease (CAD) is the most prevalent manifestation and is associated with high mortality and morbidity[1] .

Age is the dominant driver of cardiovascular risk, and most individuals are already at very high risk at the age of 65 years. Many preventive treatments are still effective at advanced age in terms of postponing morbidity and mortality[2].

Acute myocardial infarction is different in clinical presentation, diagnosis and treatment. In recent years there have been some differences in both sexes. It is important to see possible age differences, risk factors, time of arrival in the hospital, symptoms and conservative or invasive treatment.

Historically, the description of symptoms associated with acute myocardial infarction (AMI) was based on the presentation characteristics of men. Women's symptoms of AMI are often labeled as "atypical" and different from the "classic" symptoms noted in men[3,4] and include a constellation of associated symptoms, usually without chest pain or discomfort[5-8].

High blood pressure (BP) is a leading risk factor for disease burden globally, accounting for 9.4 million deaths and 7.0% of global disability-adjusted life-years (DALYs) in 2010[9]. Elevated BP is a risk factor for CAD, heart failure (HF), cerebrovascular disease (CVD), periferal arterial disease (PAD), chronic kidney disease (CKD) and atrial fibrillation (AF). The risk of death from either CAD or stroke increases progressively and linearly from BP levels as low as 115 mmHg systolic and 75 mmHg diastolic upwards[10].

People with diabetes mellitus (DM) are on average at double risk of CVD[11]. There is mounting evidence for a very high relative risk in younger individuals with type 2 DM (age < 40 years), and additional guidance on care is needed[12].

Smoking is an established cause of a plethora of diseases and is responsible for 50% of all avoidable deaths in smokers, half of these due to CVD. The 10-year fatal CVD risk is approximately doubled in smokers. The BP in smokers < 50 years of age is five-fold higher than in non-smokers[13].

The crucial role of dyslipidaemia, especially hypercholesterolaemia, in the development of CVD is documented beyond any doubt by genetic, pathology, observational and intervention studies[14].

The impact of AMI localization on complications is also unclear. In general, large studies analyzed the occurrence of complications in the post infarction period by anterior or inferior localization but, the results are contradictory[15].

Accurate recognition of the symptoms of AMI in both men and women is crucial for the inability of health care providers to recognize an evolving AMI which may lead to an incorrect diagnosis and delays in treatment[16].

For patients with the clinical presentation of AMI within 12 h after symptom onset and with persistent ST-segment elevation or new or presumed new left bundle-branch block, early mechanical or pharmacological reperfusion should be performed[17].

Complications of AMI include mechanical, arrhythmic, ischemic, and inflammatory (early pericarditis and post-AMI syndrome) sequelae, as well as left ventricular mural thrombus. The onset of each of these complications usually results in explicit symptoms and physical manifestations. Thus, a basic knowledge of the complications that occur in the postinfarction period and the clinical syndromes associated with each, will allow the physician to evaluate and treat the complication appropriately[18].

Our objective was to investigate the presence of epidemiological and clinical differences between men and women with AMI. It will also examine the incidence, patient's age, the type of symptoms, cardiovascular risk factors, localization, time from symptom onset to arrival at the hospital, treatment and complications during hospitalization of AMI.

PATIENTS

A retrospective study was conducted in the period from 2013 to 2016. The study included 579 patients. The patient's age ranged from 32 to 86

years, and the average age was 62.5 years. There were 352 men (60.8%) and 221 (39.2%) women. All patients were hospitalized in the coronary and postcoronary unit in the General Hospital, Karlovac, Croatia. The patients with AMI were divided into two main groups according to gender. The study examined the incidence, characteristics of symptoms (typical and atypical), the incidence of arterial hypertension (AH), diabetes, smoking and hyperlipidemia, localization (anteroseptal, anterolateral, inferior, posterior, and without ST elevation), the time from onset of symptoms to arrival at the hospital (< 6 hours, 6-12 hours, > 12 hours), treatment (mechanical or conservative therapy) and complications (LVEF < 50%, aneurysm, mural thrombus, pericardial effusion, heart failure, death) of AMI.

METHODS

The criteria for inclusion of patients were that the AMI was primary diagnosis of hospital admission.

Diagnostic criteria for AMI were chest pain, electrocardiogram (ECG) changes and troponin elevation. ECG had to have the appearance of ST segment elevation of at least 1 mm in anteroseptal leads (V1-V4), anterolateral leads (V3-V6), inferior leads (D2, D3, aVF), in posterior leads ST-denivelation in V3-V4 and R-wave enlargement in V1-V3 leads and T wave inversion or ST depression for non-ST elevation myocardial infarction (NSTEMI).

The cardiac enzyme troponin T had to be > 1.00 g/L. Low molecular weight heparin (LMWH), alteplase, beta-blocker, acetylsalicylic acid (ASA), angiotensin converting enzyme inhibitor (ACE-i) and statin were used as conservative therapy and in percutaneus coronary intervention (PCI) additionally clopidogrel or ticagrelor. PCI procedure had to be with stent implantation. Left ventricular ejection fraction (LVEF) was assessed with the heart ultrasound (Simpson biplane technique in the apical projection). Complications of AMI were verified by ultrasound of the heart and by x-ray imaging of the heart and lungs.

STATISTICS

This research is explorative. The goal is to identify all potential interaction of variables and differences between groups. The theoretical frequencies are based on the assumption (null hypothesis) that the differences will not be[19]. Data analysis was performed using Chi-square test. The P-value limit is 0,05. Data is processed in SPSS 20.0.

RESULTS

Chi-square test indicates that men more often have AMI than women ($\chi 2 = 26.986$; $P < 0.001$) (table 1), have AMI at an earlier age than women ($\chi 2 = 21.327$; $P < 0.001$) (table 2) and have typical

Table 1. The incidence of acute myocardial infarction by gender

	Men	Women	Total frequencies
Frequencies	352	227	579
Percentage	60.8	39.2	
The expected frequency	289.5	289.5	
Expected percentage	50	50	

Table 2. Acute myocardial infarction by age and gender

		Years		Total frequencies
		<60	≥60	
Men	Frequencies	101	251	352
	The expected frequency	78.4	273.6	
	Percentage by age	28.7	71.3	
Women	Frequencies	28	199	227
	The expected frequency	50.6	176.4	
	Percentage by age	12.3	87.7	
Total	Frequencies	129	450	579

symptoms in AMI more often than women, while women have atypical symptoms ($\chi2 = 4.028$; $P = 0.045$) (table 3). Women more often have AH ($\chi2 = 5.685$; $P = 0.017$) (table 4) and diabetes ($\chi2 = 5.053$; $P = 0.025$) than men (table 5). Men are more often smokers than women ($\chi2 = 11.791$; $P = 0.001$) (table 6). Chi-square test indicates equal frequency of hyperlipidaemia by gender ($\chi2 = 0.117$; $P = 0.674$) (table 7), equal distribution of AMI localization by gender ($\chi2 = 2.708$; $P = 0.608$) (table 8) and equal distribution of arrival times to the hospital in AMI by gender ($\chi2 = 1.839$; $P = 0.399$) (table 9). Chi-square test also indicates that in AMI men more often receive PCI treatment, while women receive conservative therapy ($\chi2 = 7.395$; $P = 0.007$) (table 10). Test indicates equal distribution of all AMI complications by gender ($\chi2 = 5.440$; $P = 0.365$) (table 11).

Table 3. Typical and atypical symptoms of acute myocardial infarction by gender

		Symptoms		Total frequencies
		Typical	Atypical	
Men	Frequencies	244	108	352
	The expected frequency	232.8	119.2	
	Percentage by age	69.3	30.7	
Women	Frequencies	139	88	227
	The expected frequency	150.2	76.8	
	Percentage by age	61.2	38.8	
Total	Frequencies	383	196	579

Table 4. The incidence of arterial hypertension by gender in acute myocardial infarction

		AH		Total frequencies
		Yes	No	
Men	Frequencies	260	92	352
	The expected frequency	271.8	80.2	
	Percentage by age	73.9	26.1	
Women	Frequencies	187	40	227
	The expected frequency	175.2	51.8	
	Percentage by age	82.4	17.6	
Total	Frequencies	447	132	579

AH – arterial hypertension

Table 5. The incidence of diabetes by gender in acute myocardial infarction

		Diabetes		Total frequencies
		Yes	No	
Men	Frequencies	112	240	352
	The expected frequency	124.6	227.4	
	Percentage by age	31.8	68.2	
Women	Frequencies	93	134	227
	The expected frequency	80.4	146.6	
	Percentage by age	41.0	59.0	
Total	Frequencies	205	374	579

Table 6. The incidence of smoking by gender in acute myocardial infarction

		Smoking		Total frequencies
		Yes	No	
Men	Frequencies	123	229	352
	The expected frequency	104.6	247.4	
	Percentage by age	34.9	65.1	
Women	Frequencies	49	178	227
	The expected frequency	67.4	159.6	
	Percentage by age	21.6	78.4	
Total	Frequencies	172	407	579

Table 7. The incidence of hyperlipidemia by gender in acute myocardial infarction

		Hyperlipidemia		Total frequencies
		Yes	No	
Men	Frequencies	166	186	352
	The expected frequency	163.5	188.5	
	Percentage by age	47.2	52.8	
Women	Frequencies	103	124	227
	The expected frequency	105.5	121.5	
	Percentage by age	45.4	54.6	
Total	Frequencies	269	310	579

Table 8. Distribution of localization of acute myocardial infarction by gender

Localization of AMI		Men	Women	Total frequencies
Anteroseptal	Frequencies	66	45	111
	The expected frequency	67.7	43.3	
	Percentage by age	59.5	40.5	
Anterolateral	Frequencies	19	13	32
	The expected frequency	19.5	12.5	
	Percentage by age	59.4	40.6	
Inferior	Frequencies	65	30	95
	The expected frequency	57.9	37.1	
	Percentage by age	68.4	31.6	
Posterior	Frequencies	79	52	131
	The expected frequency	79.9	51.1	
	Percentage by age	60.3	39.7	
NSTEMI	Frequencies	118	82	200
	The expected frequency	122.0	78.0	
	Percentage by age	59.0	41.0	
Total	Frequencies	347	222	569

AMI – acute myocardial infarction; NSTEMI – non-ST elevation myocardial infarction

Table 9. The time from onset of acute myocardial infarction symptoms to arrival at the hospital by gender

The time to arrival at the hospital		Men	Women	Total frequencies
< 6 hours	Frequencies	99	56	155
	The expected frequency	94.2	60.8	
	Percentage by age	63.9	36.1	
6 to 12 hours	Frequencies	106	80	186
	The expected frequency	113.1	72.9	
	Percentage by age	57.0	43.0	
>12 hours	Frequencies	147	91	238
	The expected frequency	144.7	93.3	
	Percentage by age	61.8	38.2	
Total	Frequencies	352	227	576

Table 10. Treatment of acute myocardial infarction by gender

		Treatment		Total frequencies
		Conservative	PCI	
Men	Frequencies	213	139	352
	The expected frequency	228.1	123.9	
	Percentage by age	60.5	39.5	
Women	Frequencies	157	62	219
	The expected frequency	141.9	77.1	
	Percentage by age	71.7	28.3	
Total	Frequencies	370	201	571

PCI = percutaneous coronary intervention

Table 11. Distribution of acute myocardial infarction complications by gender

Complications		Men	Women	Total frequencies
LVEF<50%	Frequencies	89	56	145
	The expected frequency	89.4	55.6	
	Percentage by age	61.4	38.6	
LV aneurysm	Frequencies	12	10	22
	The expected frequency	13.6	8.4	
	Percentage by age	54.5	45.5	
Mural thrombus	Frequencies	23	9	32
	The expected frequency	19.7	12.3	
	Percentage by age	71.9	28.1	
Pericardial effusion	Frequencies	62	40	102
	The expected frequency	62.9	39.1	
	Percentage by age	60.8	39.2	
Heart failure	Frequencies	123	67	190
	The expected frequency	117.1	72.9	
	Percentage by age	64.7	35.3	
Died	Frequencies	33	31	64
	The expected frequency	39.4	24.6	
	Percentage by age	51.6	48.4	
Total	Frequencies	342	213	555

LVEF = left ventricule ejection fraction; LV = left ventricule

DISCUSSION

In our research, we have established certain differences in epidemiological, clinical and therapeutic characteristics of AMI between the two gender.

In patients with AMI we have verified more men than women (60.8 vs 39.2%, $\chi 2 = 26.986$; $P < 0.001$) (table 1). These data are consistent with other results from recent studies where women also had less hospitalizations for AMI than men, but had a more unstable angina pectoris[20-22].

Our male and female patients are older than 60 years, and both sexes are equally represented. In patients under 60 years, there are more men than women (28.7 vs. 12.3%, $\chi 2 = 21.327$; $P < 0.001$) (table 2). The results of other surveys correlate with our results[7].

Typical symptoms of AMI are more common in men (69.3 vs 61.2%), and atypical symptoms are more common in women (38.8 vs 30.7%, $\chi 2 = 4.028$; $P = 0.045$) (table 3). Our findings are similar to the results of other researchers where women also have atypical symptoms of CAD more often than men. Among these the most common are back pain and lower jaw pain, shortness of breath, nausea, fatigue, cough and palpitations[23-26].

Regarding cardiovascular risk factors our tested women had more often than men AH (82.4 vs 73.9%, $\chi 2 = 5.685$; $P = 0.017$) (table 4) and diabetes (41.0 vs 31.8%, $\chi 2 = 5.053$; $P = 0.025$) (table 5). These results also do not depart from the results of recent studies where women are more likely to have AH and diabetes[27-30].

We have verified smoking in male patients with AMI more often than women (34.9 vs 21.6%, $\chi 2 = 11.791$; $P = 0.001$) (table 6). The same results where women have a lower prevalence of smoking than men were also reported by other authors, Johansson ($P < 0.001$)[31] and Roger (23.1 vs 18.1%)[32].

Our results regarding hyperlipidemia were not completely identical with the results of previous studies because we had an equal share of hyperlipidemia in men and women (47.2 vs. 45.4, $\chi 2 = 0.117$; $P = 0.674$) (table 7). In other studies higher proportion of hyperlipidemia was diagnosed in women. For example, Emily also had a significantly higher hyperlipidemia in women than men (118.9 vs. 111.5 mg/dL; $P < 0.001$)[33].

Localization of AMI in our patients did not differ between males and females ($\chi 2 = 2.708$; $P = 0.608$) (table 8). But, unlike our results, Mieszcanska established a higher incidence of inferior AMI in men (44 vs 35%; P = 0,03) while the other localization of AMI between two gender represented equally[34].

Regarding the time passed from the onset of AMI until arriving at the hospital (< 6 hours, 6-12 and > 12 hours), in our patients there was no significant difference in arrival at the hospital between men and women ($\chi 2 = 1.839$; $P = 0.399$) (table 9). These data are different from other results because women usually arrive later in the hospital after the beginning of symptoms. It is believed that women have more atypical symptoms which are often underestimated[35-37]. Therefore, we can be satisfied with a personal assessment of our female patients, as well as with an assessment of emergency medical assistance in the field because our women still come to the hospital at the optimum time from the onset of symptoms.

Our results have shown more men than women treated with PCI method, while women were exposed to conservative treatment method ($\chi 2 = 7.395$; $P = 0.007$) (table 10). These results are similar to the results of previous studies where women often have atypical symptoms that are more difficult to recognize[38]. Women also have more comorbidities and risk for side effects hence doctors do not decide to do PCI treatment[39].

By comparing the frequency of the most common complications of AMI, we have an equal distribution between both gender ($\chi 2 = 5.440$; $P = 0.365$) (table 11). In the literature, the early mortality and a higher incidence of other compli-

Acute myocardial infarction can be prevented by timely education on risk factors. By recognizing the character of the symptoms, the disease can be easily recognized outside the hospital. This is a condition for early hospital admission and treatment with more effective percutaneous coronary intervention than conservative therapy.

cations of AMI are more common in women[40]. Our women are not late in arriving at the hospital (table 9), and this is one of the conditions for reducing the incidence of post-infarction complications.

As a conclusion, we have verified more men than women in patients with AMI. AMI is more common over age of 60 and in younger patients men have more frequent AMI than women. Typical symptoms of AMI are more common in men, and atypical symptoms in women. Women have more often AH and diabetes and men are more often smokers. Hyperlipidemia is equaly present in both sexes. Localization of AMI in our patients did not differ between males and females. There was no significant difference in arrival at the hospital between men and women.

Men are more likely to receive PCI treatment, while women conservative therapy. The frequency of the complications of AMI are equal between both gender.

All these characteristics in our patients with AMI are similar to other studies. But, our women have less hyperlipidaemia. Are the reasons eating habits or genetics, remains to be tested in future studies. Our women are not late in an arrival at the hospital after the onset of AMI symptoms. Are the reasons in the education and good organization of the outpatient emergency medical assistance may be also the subject of future studies.

Conflicts of interest statement: the authors report no conflicts of interest.

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