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Risk Factors for Myocardial Infarction in Women and Men: A Case-Control Study †

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Abstract: A hospital-based case-control study, analyzing risk factors for myocardial infarction, was conducted at the University Clinical Centre in Kragujevac (Serbia). Logistic regression analysis was used to determine odds ratio (OR) with 95% confidence intervals (95% CI). Our study comprised 374 participants: 187 newly diagnosed patients with myocardial infarction and 187 controls. The increase in risk for acute myocardial infarction was associated with obesity (OR = 2.2; 95% CI = 1.1–4.1), stressful life events in personal history (OR = 2.8; 95% CI = 1.5–5.4) and cholesterol level (OR = 7.6; 95% CI = 2.0–28.4) in men, while diabetes mellitus (OR = 5.2; 95% CI = 1.6–16.8), smoking (OR = 3.0; 95% CI = 1.4–6.5) and menopause (OR = 5.6; 95% CI = 1.1–28.7) were associated with increased risk in women.

Keywords: myocardial infarction; risk factors; case-control study

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1. Introduction

Cardiovascular disease has been the leading cause of death in the world, in both sexes, in the last decades [1,2]. Death rates from coronary heart disease are considerably lower in women than in men, but differences decrease with increasing age [3].

Although established risk factors for cardiovascular disease are almost equally prevalent in both genders, numerous studies suggest that the importance of these factors in each gender are not the same [4–6]. Two large meta-analyses that have compared sex disparities in the association between risk factors and coronary heart disease showed that, compared with men, women had a greater ratio of relative risk of coronary heart disease of 44% if they had diabetes [4], and of 25% higher if they were current smokers [5]. In a population-based cohort of UK Biobank [6], systolic blood pressure and hypertension, smoking status and diabetes were associated with higher hazard ratio for myocardial infarction in women compared with men.

The INTERHEART study, a global case-control study, including 27,098 participants from 52 countries, showed that hypertension, diabetes, physical activity, and moderate alcohol use were more strongly associated with myocardial infarction among women than men [7]. The population attributable risk of all nine modifiable risk factors associated with myocardial infarction (hypertension, diabetes, physical activity, alcohol use, abnormal lipids, smoking, obesity, high-risk diet, and psychosocial stress factors) exceeded 94%, and was similar among women and men (96% versus 93%). However, the etiology of myocardial infarction is still not completely elucidated [7–10].

Nevertheless, research on the impact of cardiovascular risk factors in less developed countries is still limited. Only a few studies have been conducted to evaluate the association between the prevalence of cardiovascular risk factors and acute myocardial infarction in

Serbia [11]. The aim of this study was to examine the sex differences in the prevalence of risk factors for myocardial infarction in Serbia.

2. Materials and Methods

A hospital-based case-control study was conducted in 2010 at the University Clinical Centre Kragujevac, Serbia.

At the Clinic for Cardiology, patients were recruited with a newly diagnosed myocardial infarction, which was made by cardiologists in accordance with the National Guidelines for Good Practice, i.e., according to the diagnostic criteria based on the European Society of Cardiology/American College of Cardiology consensus guidelines [12]. The diagnosis of myocardial infarction was no longer than 2 months until the survey was conducted (the mean time interval between diagnosis and interview of cases was 2 weeks). No one refused to participate in the study.

For each case with myocardial infarction, one control was selected, mainly among patients who were at the same time hospitalized at the Clinic of Orthopedic Surgery and Traumatology due to milder conditions (such as gonarthrosis, coxarthrosis, etc.). Controls were without anamnestic or diagnostic data for myocardial infarction. Cases and controls were individually matched by gender, age (±2 years), and place of residence (rural/urban). All selected controls agreed to participate in the survey.

Data from patients and their controls were collected through a direct interview, which lasted 2 h. The survey was always conducted by a medical doctor. The interviews were always conducted in the hospital.

We investigated the following risk factors: occupation, education level, marital status, family history, psychosocial distress, body mass index, blood pressure, cholesterol level, diabetes mellitus, smoking status, alcohol use, coffee consumption, personal medical history, stressful events, and menopause.

Statistical evaluation was performed through logistic regression analysis (univariate and multivariate logistic regression models) to calculate the odds ratio (OR) with 95% confidence interval (95% CI) in order to estimate the association between risk factors and myocardial infarction. Multivariate logistic regression model was made for all variables that were related to myocardial infarction in univariate analyses at a p value of <0.10. Statistical significance was considered when $p < 0.050$. All statistical analyses were performed using SPSS 20.0 (SPSS, Chicago, IL, USA).

3. Results

Our study comprised 374 participants: 187 newly diagnosed patients with myocardial infarction and 187 controls (Table 1). Cases and controls were individually matched by gender, age (±2 years) and place of residence (rural/urban). Just over half of the patients were 65 years old or younger.

Table 1. Characteristics of patients with acute myocardial infarction and their controls.

	Cases (n = 187) No. (%)	**Controls (n = 187) No. (%)**	
Age (≤65 years)	102 (54.5)	96 (51.3)	Matched
Gender (Male)	113 (60.4)	113 (60.4)	Matched
Place of residence (Urban)	136 (72.7)	136 (72.7)	Matched

Among men, a higher proportion of cases than controls had body mass index ≥ 25 kg/m^2 (p = 0.015), stressful events (p = 0.000), family history of myocardial infarction (p = 0.005), diabetes mellitus (p = 0.020), hypertension (p = 0.007), and hypercholesterolemia (p = 0.000) (Table 2). Among women, a higher proportion of cases than controls had diabetes mellitus (p = 0.002), smoking (p = 0.016) and menopause (p = 0.028), as well as some factors at $p < 0.10$, such as urban place of residence (p = 0.055), family history of myocardial infarction

(p = 0.100), coffee consumption (p = 0.092), hypertension (p = 0.094), hypercholesterolemia (p = 0.096), and disorders of thyroid (p = 0.053).

Table 2. Characteristics of patients with acute myocardial infarction and their controls, by gender.

	Gender					
	Male (n = 226)			Female (n = 148)		
	Cases (n = 113) No. (%)	Controls (n = 113) No. (%)	p	Cases (n = 74) No. (%)	Controls (n = 74) No. (%)	p
Age (≤65 years)	69 (61.1)	64 (56.6)	0.499	33 (44.6)	32 (43.2)	0.869
Place of residence (Urban)	75 (66.4)	85 (75.2)	0.143	61 (82.4)	51 (68.9)	0.055
Occupation * (Manual worker)	72 (63.7)	70 (61.0)	0.952	23 (31.1)	26 (35.1)	0.341
Educational level (≤8 years)	24 (21.2)	32 (28.3)	0.218	50 (67.6)	44 (59.5)	0.306
Marital status (with partner)	93 (82.3)	86 (76.1)	0.251	44 (59.5)	47 (63.5)	0.612
Body mass index (≥25 kg/m^2)	86 (76.1)	68 (60.2)	0.015	40 (54.1)	39 (52.7)	0.869
Oral contraceptive use	- (-)	- (-)	-	4 (5.6)	7 (9.5)	0.397
Menopause	- (-)	- (-)	-	72 (97.3)	65 (87.8)	0.028
Stressful events	86 (76.1)	56 (49.6)	0.000	63 (85.1)	60 (81.1)	0.510
Family history of myocardial infarction	66 (58.4)	45 (39.8)	0.005	43 (58.1)	33 (44.6)	0.100
Smoking	85 (75.2)	77 (68.1)	0.238	34 (45.9)	19 (25.7)	0.016
Coffee consumption	101 (89.4)	100 (88.5)	0.832	64 (86.9)	70 (94.6)	0.092
Alcohol use	89 (78.8)	79 (69.9)	0.128	13 (17.6)	15 (20.3)	0.675
Diabetes mellitus	22 (19.5)	9 (8.0)	0.020	17 (23.0)	4 (5.4)	0.002
Hypertension	58 (51.3)	38 (33.6)	0.007	49 (66.2)	39 (52.7)	0.094
Hypercholesterolemia	26 (23.0)	3 (2.7)	0.000	14 (18.9)	7 (9.5)	0.096
Disorders of thyroid	1 (0.9)	0 (0.0)	0.316	12 (16.2)	5 (6.8)	0.053

p, probability value (according to univariate logistic regression analysis). * For retired the occupation before retirement is shown.

Analysis of risk factors for myocardial infarction by gender revealed that the increase in risk for acute myocardial infarction in men was significantly associated with body mass index ≥ 25 kg/m^2 (OR = 2.2, 95% CI = 1.1–4.1, p = 0.025), stressful events (OR = 2.8, 95% CI = 1.5–5.4, p = 0.001) and hypercholesterolemia (OR = 7.6, 95% CI = 2.0–28.4, p = 0.002) (Table 3). Among women, the increase in risk for acute myocardial infarction was significantly associated with menopause (OR = 5.6, 95% CI = 1.1–28.7, p = 0.020), smoking (OR = 3.0, 95% CI = 1.4–6.5, p = 0.005) and diabetes mellitus (OR = 5.2, 95% CI = 1.6–16.8, p = 0.016).

Table 3. Estimated risk —Odds Ratio (95% Confidence Intervals) of acute myocardial infarction in relation to gender.

	Male		Female	
	***OR* (95% CI)**	***p***	***OR* (95% CI)**	***p***
Place of residence (Urban)			2.4 (0.9–5.9)	0.050
Body mass index (≥25 kg/m^2)	2.2 (1.1–4.1)	0.025		
Menopause			5.6 (1.1–28.7)	0.020
Stressful events	2.8 (1.5–5.4)	0.001		
Family history of myocardial infarction	1.6 (0.9–3.0)	0.103	1.6 (0.8–3.5)	0.205
Smoking			3.0 (1.4–6.5)	0.005
Coffee consumption			0.4 (0.1–1.4)	0.139
Diabetes mellitus	2.1 (0.8–5.3)	0.128	5.2 (1.6–16.8)	0.016
Hypertension	1.1 (0.6–2.1)	0.692	1.6 (0.7–3.6)	0.243
Hypercholesterolemia	7.6 (2.0–28.4)	0.002	1.7 (0.5–5.6)	0.382
Disorders of thyroid			3.3 (0.9–12.6)	0.078

Abbreviations: *OR*, Odds Ratio; 95% CI, Confidence Interval; p, Probability value according to multivariate logistic regression analysis.

4. Discussion

Our findings suggest that females who have myocardial infarction are often elderly (in menopause), smoke, or have diabetes. On the other hand, males who have myocardial

infarction are often obese, or have hypercholesterolemia or stressful events. None of the independent associations between risk factors and myocardial infarction were the same in women and men.

Consistent with others [6,7,13], our results showed significant differences in prevalence exposure to traditional risk factors for myocardial infarction among men and women. The INTERHEART study revealed that hypertension, diabetes mellitus, and smoking are more potent risk factors for myocardial infarction in women than in men in less developed countries [14]. Most importantly, the INTERHEART study showed differences between men and women in the impact of risk factors on myocardial infarction: former smoking represented higher risk for men (although current smoking represented a similar risk both in men and women), while hypertension, diabetes mellitus, psychosocial factors, lack of physical activity, and lack of alcohol consumption were more powerful risk factors for acute myocardial infarction in women than in men [7,14].

A recent meta-analysis noted the pooled adjusted female-to-male relative risk ratio of smoking compared with not smoking for coronary heart disease of 1.25 (95% CI 1.12–1.39, $p < 0.0001$) [5]. Some studies suggested that women may be more sensitive than men to some of the harmful effects of smoking [15]. Possible explanations for the significant association between smoking and female sex in our study could be due to hormonal differences regarding interaction with chemicals found in tobacco or due to the proposed antiestrogenic effect of smoking in women, which might, in turn, increase their risk [13].

Diabetes mellitus is a well-established risk factor for cardiovascular disease. Similar to our results, a large meta-analysis, which included over 1.1 million persons from 30 prospective cohort studies, found that the risk for coronary heart disease was 1.52-times higher in women with diabetes than in men with diabetes [16]. The protective female gender effect is lost in diabetic subjects: similar to our study, in a hospital-based case control study conducted in a rural population in India, cases of myocardial infarction were twice as likely to feature a history of diabetes compared to controls [17]. On the contrary, in a large-scale international cohort of patients with diabetes, in patients with type 2 diabetes, rate differences associated with risk factors were greater in men than in women for cholesterol and BMI [18]. The observed sex-related difference in regard to diabetes mellitus could, in part, be explained with different changes in levels of cardiovascular risk factors associated with diabetes in women compared to men, but also with disparities in treatment [4].

Contrary to our results, an analysis of the INTERHEART study found no difference in the risk of first myocardial infarction between men and women who reported experiencing stressful life events, with risk significantly increased in both sexes [19]. These differences could, in part, be due to differences in studied populations and different methods of recording stressful events. In a population-based prospective study from Tromsø, Norway, the association between total cholesterol and risk of MI was stronger for men than women [9]. Many studies have reported that the risk of cardiovascular disease does not differ between sexes in persons with raised cholesterol [20], although the research shows that increased levels of low-density lipoprotein cholesterol have a higher impact on the cardiovascular risk in men than in women [21].

In addition to the well-known shortcomings of case-control studies, a limitation of this study was the relatively small sample size. Further, findings of this and similar studies should be viewed with great caution, as the lack of data on cases of death from myocardial infarction before hospitalization, or immediately at the beginning of hospitalization, might have led to a less accurate assessment of connection between the risk factors and myocardial infarction occurrence. Moreover, there is always a question about potential confounding factors (such as diet and socioeconomic status), that might, at least in part, explain the results of this study.

5. Conclusions

Our study noted sex differences in risk factors for myocardial infarction. Our findings suggest that females who have myocardial infarction are often elderly (in menopause),

smoke, or have diabetes. On the other hand, males who have myocardial infarction are often obese, or have hypercholesterolemia or stressful events. Additional analytic epidemiological studies addressing cardiovascular risk factors are needed.

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Informed Consent Statement: Informed, verbal, voluntary consent was obtained from all subjects involved in the study.

Data Availability Statement: Data are contained within the article.

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