Is There a Sex Difference of Cardiovascular Risk Factors in Patients with Acute Myocardial Infarction?

LARISA ANGHEL[1,2], CRISTINA PRISACARIU[1,2]*, CATALINA ARSENESCU GEORGESCU[1,2]

[1] Cardiovascular Diseases Institute Prof. Dr. George I. M. Georgescu, 50 Carol I Blvd, 700508, Iasi, Romania
[2] University of Medicine and Pharmacy, Grigore T. Popa, 16 Universitatii Str, 700115, Iasi, Romania

Conventional cardiovascular risk factors, such as hypertension, diabetes, smoking, and dyslipidemia, increase the risk of developing acute myocardial infarction. Primary prevention studies have shown that early detection and aggressive treatment of risk factors prevent cardiovascular events. In women, coronary artery disease appears up to 10 years later in life than in men. We analyzed the presence of conventional risk factors in patients with acute myocardial infarction and compared findings according to sex. We observed that more than 90% of patients included in the study had at least one of these risk factors, hypertension and diabetes predominated in women and smoking was more frequent in men. Because many of these risk factors are modifiable and amenable to treatment, an early detection and aggressive treatment can prevent cardiovascular events.

Keywords: risk factors, acute coronary syndrome, atherosclerosis, clinical study.

Cardiovascular disease is currently the most common cause of morbidity and mortality worldwide, with the highest rate in Eastern Europe (58%) compared to developed countries, where cardiovascular disease mortality decreased to 38% [1].

Relevant differences have been reported in the genesis, develop-ment and pathophysiology of coronary atherosclerosis between women and men, which have not been fully unraveled [1,2]. In women, coronary artery disease (CAD) appears up to 10 years later in life than in men and prevalent angiographic obstructions are less severe at all ages [3,4]. It is speculated that this age difference is due protection against atherosclerotic plaque development by circulating estrogens, of whose concentration drops dramatically to menopause. Despite this explanation, hormone replacement therapy after menopause did not have the expected protective effect [3].

Numerous evidences suggest that cardiovascular disease worldwide is less

detected in women. Compared to men, women requires health care later on after the onset of symptoms, later coronary reperfusion therapy is applied, rarely take aspirin or beta blockers in the first 24 hours from the presentation and have a higher risk of bleeding complications associated with antithrombotic therapy. Although coronary artery disease is the most common cause of death worldwide, regardless of the gender of the patient, statistically can be observed that the percentage of men who die from coronary heart disease is higher than that of women, whereas in case of cerebrovascular disease, the ratio is reversed [4,5].

Among patients with coronary artery disease, 80%–90% present at least one conventional risk factor, such as hypertension, diabetes, smoking, and dyslipidemia, which increase the risk of developing coronary artery disease [6]. On the other hand, lipid profile modification after a cardiovascu-lar event related to acute coronary syndrome (ACS) has been recognized. Primary prevention studies have shown that the early detection and aggressive treatment of risk factors prevent cardiovascular events [7].

Several hypotheses have been formulated in order to explain the higher in-hospital mortality in women with acute myocardial infarction with ST-segment elevation (STEMI) compared to men: the presence of more comorbidities, the higher ischemic time or the suboptimal use of reperfusion strategies [8]. It has not yet been established whether female sex through biological and sociocultural differences, is itself a risk factor for in-hospital mortality of patients with STEMI.

Experimental part

The aim of our study was to identify the risk factors for the in-hospital mortality of patients with STEMI and to compare these findings according to sex. We also recorded the prevalence of conventional risk factors such as smoking, hypertension, dyslipidemia, and diabetes and we compared the findings according to the sex of the patients.

The presence or absence of a history of conventional risk factors (hypertension, diabetes, dyslipidemia, and pre-vious and/or current smoking) was recorded at the time of admission to the coronary care unit and was based on patient/family self-report or previous medical records. The serum levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were determined within the first 24 h of admission. We defined high serum levels as TC $\geq$ 200 mg/dL, LDL-C $\geq$130 mg/dL, and TG $\geq$ 150 mg/dL; a low serum level of HDL-C was defined as $\leq$ 40 mg/dL. The body mass index (BMI) was also recorded. Patients were classified as normal (BMI $\leq$ 24.9 kg/m²), overweight (BMI 25–29.9 kg/m²), or obese (BMI $\geq$ 30 kg/m²).

Coronary angiography was performed in the laboratory of hemodynamics in our institution and interpreted by interventionist cardiologists. We determined the stenosis percentage of the main epicardial coronary arteries, and the extent of CAD was categorized as one-vessel, two-vessel, or three-vessel disease, according to the number of affected vessels.

Patients were stratified by sex for analysis. Categorical variables were reported by frequency and percentage;

* email: prisacariu88@yahoo.com; Phone:+40.724310081

groups were compared using the chi-square or Fisher's exact test. Continuous variables were reported as medians and percentiles according to their distribution and analyzed with a one-sample Kolmogorov–Smirnov test; comparisons were made with the Mann-Whitney U-test. The results were reported using two-tailed significance. Significance was set at $P \leq 0.05$. All analyses were performed with SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA) statistical software.

Results and discussions

During the study period, from September 2011 to September 2012, at the Cardiology Clinic of the Institute of Cardiovascular Diseases Prof. Dr. George I. Georgescu Iasi were hospitalized 652 patients diagnosed with acute myocardial infarction who met the inclusion criteria and which were divided into two groups, according to the biological sex: 207 (31.7 %) women and 445 (68.3 %) men.

Patients enrolled in the study were aged between 29 and 90 years, with a mean age of 62.65 ± 11.8 years. The mean age of the female population was 68.20 ± 10.8 years (limits: 40-90 years) with a coefficient of variation of 14.9%. The men had a mean age of 60.67 ± 11.6 years (limits: 29-89 years).

Arterial hypertension

More than half of the patients included in the study were hypertensive (52.3%).

Hypertension (summing up both treated and untreated hypertension) was found in 68.6% of women and only in 44.6% of men, the difference being statistically significant: $p < 0.01$. There were no significant differences between personal history of pharmacologically untreated hypertension: 17.9% women, 15.1% men, $p = 0.989$. But a statistically significantly percentage of women were receiving antihypertensive treatment (50.7%) compared to only 29.5% of men, with a p value < 0.01. We then compared, within each batch, the proportion of patients receiving pharmacologic treatment with those who were hypertensive but not treated: women with antihypertensive tratement were significantly ($p < 0.01$) more than those

without medication. In the male group, there was a difference only at the limit of statisticaly significance ($p = 0.045$) in favor of those with treatment (fig. 1).

Diabetes mellitus

Almost a quarter of the patients had diabetes mellitus (24%).

It was present in a number of 77 women, representing 37.2% of them, and only in 18% of the male population, with a statistically significant difference, $p < 0.01$. Most of the diabetic patients had type 2 diabetes mellitus with significant differences between the two groups: 36.7% of women were registered with this type of diabetes compared with only 17.3% of men: $p < 0.01$.

Dyslipidemia

Only 16.3% of patients were diagnosed with abnormal lipid profile.

The percentage was higher for men, 17.1% compared to 14.3% for women, but without a statistically significant difference: $p = 0.97$. In the male group, 6.1% of patients were under normolipemiant treatment, and 11% knew of their affection, but they had no treatment. In the female group, there were 6.8% of patients with normolipemiant treatment and 7.7% of women were diagnosed with lipid disorders but they had no treatment (fig. 2).

Most patients included in the study were overweight, with a BMI ≥ 25 kg/m², and men had a higher frequency than women (77.6% versus 77.2%, respectively; $P=0.84$). Obesity, irrespective of its grade, was found in 35.45% of patients included in the study, in 36.72% of women and 24.01% of men, without a statistically significant difference between the two groups, $p = 0.164$.

Smoking status

Smoking was the most frequently observed risk factor in both groups. More than half (54.1%) of the patients included in the study were or had been smokers. The number of male smokers and former smokers (301, representing 67.8%) was about three times the number of women with this status (51, representing 24.7%), with a significant difference: $p < 0.01$.
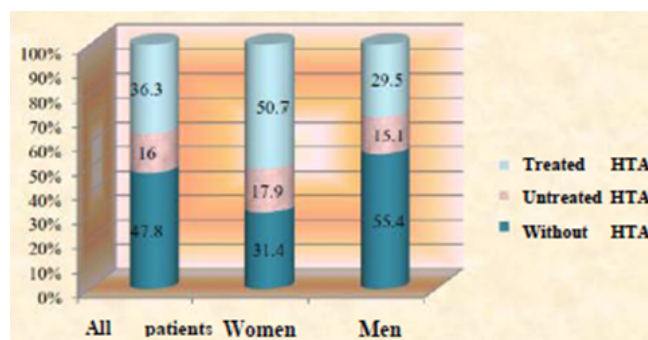

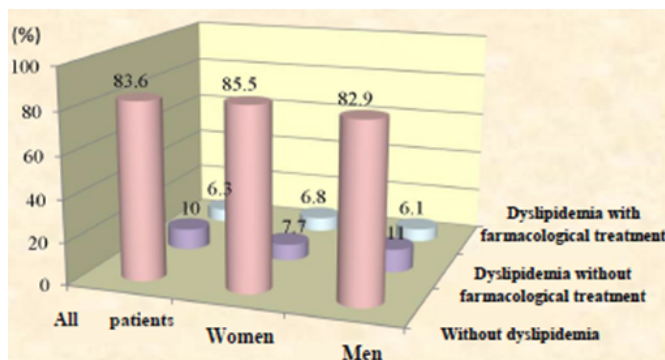Fig. 1. Hypertensive status in patients included in the study

Fig. 2. Presence of dyslipidemia in patients included in the study

Table 1
SYMPTOMS OF PATIENTS AT HOSPITAL ADMISSION

Patients	All patients		Women		Men		Significance
Symptoms	Frequency	Percent %	Frequency	Percent %	Frequency	Percent %	P value
Tipical chest pain	509	77.9	137	66.2	372	83.6	p=0.001; S
Atipical chest pain	143	22.1	70	33.8	73	16.4	p=0.027; S
Total	652	100	207	100	445	100	

Family history of early coronary artery disease

Approximately one fifth (18.5%) of patients had a family history of early coronary artery disease. More men (19.8%) had a family history of early coronary artery disease, and the difference with women with this risk factor (15.8%) was statistically significant (p <0.05).

Chest pain characteristics

We also studied the symptoms at presentation and we discovered that the chest pain was the most frequent symptom at presentation. Analyzing the onset of the symptoms, we observed a maximum onset of the symptoms in the morning, between 6 and 12 o'clock, then between 12 and 24 o'clock, and the lowest frequency was registered between 24 and 06 o'clock. This order was the same in both groups, according to the the sex of the patients.

More than half of the patients (three quarters) had typical chest pain at onset of the acute event. Difference from those who have described atypical or equivalent symptoms of chest pain, was statistically significant: p <0.001 (table 1).

Biological profile

The mean values of glycemia, platelets, fibrinogen and LDL cholesterol were significantly higher in women compared to men. In the same time, men had significantly higher values for cTnI, CKMB, triglycerides and CRP. There were no differences between the two subgroups on the mean values of total cholesterol and HDL-cholesterol. The blood lipid analysis showed that the average levels for LDL-C were 113.55 mg/dL for women and 110.3 for men, P < 0.05. Trigliceride values were higher in men than in women (144.1 mg/dL versus 138.1 mg/dL, respectively; *P*< 0.05. The most frequent lipid alteration (63.6%) was low levels of HDL-C, followed by high triglyceride levels (49.3%), high levels of LDL-C (21.3%), and high levels of total cholesterol (24.1%) (table 2).

In our study, we found that the prevalence of conventional risk factors in patients with acute myocardial infarction was very high, more than 90% of patients presented at least one of the four risk factors (smoking, hypertension, diabetes, and dyslipidemia). The lipid profile analysis demonstrated the presence of some type of dys-lipidemia, with low HDL-C levels having the highest prevalence also in men and women.

There is little information on the prevalence of conventional risk factors in patients with acute coronary syndrome and significant coronary artery disease. One of the most relevant advances in the knowledge of coronary artery disease is the role played by the different risk factors in its development, in which smoking, arterial hypertension, diabe-tes, and dyslipidemia participate as independent factors [9,10].

The role of these factors in the prognosis of acute coronary syndrome patients has become of great interest and it is possible to establish a relationship between the number of conventional risk factors for coronary artery disease and mortal-ity after the first myocardial infarction. In a study published by Canto et al. [10], it was analyzed the relation between a number of five traditional risk factors (hypertension, smoking, dyslipidemia, diabetes, and family history of CAD) and intrahospital mortality in patients with a first myocar-dial infarction. They found that of 542,000 patients analyzed, 81% had one to three risk factors, 4.5% had four or five risk factors and only 14.4% did not have identified risk factors, However, these studies included all of the acute coronary syndrome patients without analyzing patients with angiographically significant CAD. We found a higher prevalence of conventional risk factors than that reported in ACS patients, as 93.7% of our patients had at least one risk factor, and there was no sex-dependent difference (men, 93.6%; women, 94.2%). The differences in the prevalence of conventional risk factors in our study compared with reports in the literature arise because our population included patients with acute myocardial infarction demonstrated angiographically, and this popula-tion has not been reported previously. Saab et al. [11] studied 941 patients with a first acute coronary syndrome, and 98% of them presented at least one risk factor, but they also considered age > 65 years, renal failure, and a family history of coronary artery disease as risk factors, none of which were included in our study.

Women in ACS registries tend to be older than men and are more prone to hypertension and diabetes. In contrast, smoking and dyslipidemia are higher in men [12-14]. These data are similar to those found in our study, in which women were older and more frequently had a history of hypertension and diabetes. Smoking was more frequent in men.

It is known that the presence of risk factors favors the development of recurrent cardiovascular events and that is a relationship between cholesterol level and cardiovascular disease [8]. The results of an observational study show that in patients with ST-segment elevation myocardial infarction, among the strongest predictors of in-hospital death was untreated dyslipidemia [6]. Clinically

Table 2
BIOLOGICAL PROFILE AT HOSPITAL ADMISSION. N – NUMBER OF PATIENTS; X – AVERAGE VALUE;
V% - COEFFICIENT OF VARIABILITY; S – CLINICAL SIGNIFICANT; NS – CLINICAL INSIGNIFICANT

Patients	Women			Men			P-value
Parameter	N	X	V%	N	X	V%	
Glicemia	205	192.8	47.3	436	158.7	44.2	p<0.001; S
Platelets	204	279430	27.2	438	252986	31.4	p<0.001; S
Fibrinogen	201	507.2	31.1	428	466.8	37.4	p<0.001; S
Leukocytes	207	12374.9	36.95	444	12257.6	32.2	p<0.001;S
cTnI	31	0.89	144.6	55	1.88	140.6	p<0.05; S
CK MB	205	100.56	93.5	442	108.8	101.9	p<0.01; S
LDL-C	181	113.55	32.4	423	110.3	31.9	p<0.05; S
Triglycerides	184	138.1	54.8	430	144.1	71.2	p<0.05; S
Total cholesterol	184	190.5	22.7	431	187.9	23.9	p>0.05; NS
HDL-C	182	49.48	27.8	428	50.3	26.7	p>0.05; NS

significant alterations in lipids occur after an ACS. From the time of admission until the next morning, in patients with myocardial infarction, the TC and LDL-C levels can undergo a change of 7% and 10% [15].Therefore, current guidelines recommend mea-surement of serum lipids after admission for patients with an acute coronary event. This is of importance because in-hospital lipid testing was strongly associated with the initiation of statin therapy at discharge in patients with an ACS cardio-vascular event [16-17].

Conclusions

The prevalence of conventional risk factors, such as smoking, hypertension, diabetes and dyslipidemiawas very high in patients with acute myocardial infarction, more than 90% of patients included in the study had at least one of these risk factors. Hypertension and diabetes predominated in women and therefore caused higher comorbidity, which could have prognostic implications. Smoking was more frequent in men. Many of these risk factors are modifiable and amenable to treatment, an early detection and aggressive treatment can prevent cardiovascular events.

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