

## A COMPARISON OF GENDER DIFFERENCES IN CLINICAL AND ANGIOGRAPHIC CHARACTERISTICS IN YOUNG ADULTS WITH MYOCARDIAL INFARCTION

Balaian NM <sup>✉</sup>, Shebzukhova MM, Grachev NS, Muradianc AA, Shostak NA

Acad. A. I. Nesterov Department of Faculty Therapy, Pediatric Faculty,  
Pirogov Russian National Research Medical University, Moscow, Russia

The article presents the analysis of clinical and angiographic characteristics and risk factors of myocardial infarction (MI) in men and women aged <45 years. The study included 35 patients with acute MI (15 females, 20 males) of the 14th Department of Cardiology, N. I. Pirogov City Clinical Hospital No. 1 (Moscow). The average age of female and male patients was 41.2 and 39.6 years, respectively. The majority of patients of both sexes had ST-elevation MI (STEMI) (88.6 %), among which Q-wave MI accounted for 60.0 % of cases and typical MI accounted for 71.4 % of cases. Sixty percent of patients of both sexes had no previous history of CHD. Almost all risk factors (dyslipidemia, hypertension, early family history etc.) were seen more often in women compared to men, except smoking which was found to be a risk factor in 55 % of men vs. 6 % of women ( $p < 0.05$ ). The coronary angiography data showed the prevalence of the right type of coronary circulation (70 % of patients) and single-vessel disease (80 %) with coronary stenosis of more than 75 %. The time to diagnosis was 2.1 times greater in women than in men accounting for an average of 9.2 and 4.3 hours, respectively. The main causes of delayed MI diagnosis before admission were late patient referral or diagnostic errors.

**Keywords:** myocardial infarction, young age, angiographic data, gender-specific characteristics, risk factor

✉ **Correspondence should be addressed:** Nina Balaian  
Leninsky pr-t, d. 8, corp. 10, kab. 217, Moscow, Russia, 119049; nina.balaian@yandex.ru

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## ГЕНДЕРНОЕ СРАВНЕНИЕ КЛИНИКО-АНГИОГРАФИЧЕСКИХ ОСОБЕННОСТЕЙ ИНФАРКТА МИОКАРДА У ПАЦИЕНТОВ МОЛОДОГО ВОЗРАСТА

Н. М. Балаян <sup>✉</sup>, М. М. Шебзухова, Н. С. Грачев, А. А. Мурадянц, Н. А. Шостак

Кафедра факультетской терапии имени академика А. И. Нестерова, педиатрический факультет,  
Российский национальный исследовательский медицинский университет имени Н. И. Пирогова, Москва

В статье представлены результаты исследования по определению клинико-ангиографических особенностей и факторов риска развития инфаркта миокарда (ИМ) у мужчин и женщин моложе 45 лет. В исследование включили 35 больных острым ИМ (15 женщин и 20 мужчин), пациентов 14-го кардиологического отделения Городской клинической больницы № 1 имени Н. И. Пирогова (Москва). Средний возраст женщин составил 41,2 года, мужчин — 39,6 года. В подавляющем большинстве случаев встречался ИМ с подъемом ST (88,6 %), Q-образующий (60,0 %), типичный вариант (71,4 %). У 60 % молодых пациентов обоих полов в анамнезе отсутствовали симптомы ИБС. Практически все изученные факторы риска (дислипидемия, артериальная гипертензия, ранний семейный анамнез и др.) были свойственны женщинам в большей степени, чем мужчинам. Исключение составило курение, которое являлось риском для 55 % мужчин и только для 6 % женщин ( $p < 0,05$ ). Данные коронароангиографии продемонстрировали превалирование правого типа коронарного кровоснабжения (70 % пациентов) и однососудистого поражения (80 %) с сужением коронарных сосудов более чем на 75 %. На верификацию диагноза ИМ у женщин тратили в 2,1 раза больше времени, чем у мужчин: в среднем 9,2 и 4,3 ч соответственно. Основными причинами поздней диагностики ИМ на догоспитальном этапе были несвоевременное обращение пациентов к врачу или неправильный диагноз.

**Ключевые слова:** инфаркт миокарда, молодой возраст, ангиографические данные, гендерные особенности, фактор риска

✉ **Для корреспонденции:** Балаян Нина Мурадовна  
Ленинский пр-т, д. 8, корп. 10, каб. 217, г. Москва, 119049; nina.balaian@yandex.ru

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Coronary heart disease (CHD), the lethal manifestation of which is myocardial infarction (MI), is one of the main causes of death in the developed countries [1]. It has been commonly considered as a disease of men, and the risk of its development in women has often been underestimated [2].

Male gender is a risk factor of CHD, especially in people under 45 years of age [3, 4]. Low incidence of CHD in women of this age is associated with a protective effect of the blood estrogen on the endothelium [5]. Numerous studies have shown that the decrease in estrogen in menopausal women is associated with the development of the endothelial dysfunction

and lipid deposition in the vessel wall, which may eventually lead to atherosclerosis [6, 7]. Furthermore, the mortality rate after the first MI and surgical myocardial revascularization in women is higher than in men [8, 9]. It was found that 26 % of women and 19 % of men over 45 years of age die within a year after the first MI. Five-year mortality rates are 47 % and 36 %, respectively [10]. Complications, such as heart failure and stroke, are more likely to develop in women [10].

The pathogenesis of CHD in women is not fully understood; it is not always possible to timely diagnose and cure the disease [3]. High female mortality from MI may be associated

with the underestimation of the severity of coronary pathology and various risk factors as well as patients' negligence to their health. Numerous studies have shown that many women with acute coronary syndrome do not receive appropriate therapy [11–13], coronary stenting [11–14] or timely reperfusion [12, 13, 15–19].

Researchers are increasingly interested in the gender aspect of cardiovascular diseases in young adults, as their early diagnosis and treatment have a significant social and economic impact. Nevertheless, the data on the characteristics of the CHD pathogenesis in young women are still scarce [3]. The present study is aimed to determine the clinical and angiographic characteristics and risk factors of myocardial infarction in men and women under 45 years of age.

METHODS

The study included 35 patients with acute MI (15 females, 20 males) of the 14<sup>th</sup> Department of Cardiology, N. I. Pirogov City Clinical Hospital No. 1 (Moscow). The average age of female and male patients was 41.2 and 39.6 years, respectively. The inclusion criteria were age <45 years and the presence of myocardial infarction (in accordance with the diagnostic criteria described in [20]). Exclusion criteria were age >45 years, concomitant cardiovascular pathology, and severe pathology of the liver and kidneys. All patients gave informed consent.

We have analyzed the patients' data obtained through questionnaires and the results of a standard clinical check-up that included anthropometric measurements, body mass index (BMI) calculation, history taking, health assessment at the time of our study (reduced tolerance to physical exercise during a treadmill test), assessment of the risk factors (smoking, alcohol consumption, eating habits, family history, hypertension, diabetes, lipid profile and intake of oral contraceptives). The results of the following laboratory and instrumental tests were also used:

- lipid profile (cholesterol, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triacylglycerols and atherogenic index);
- cardioteests (measuring the levels of creatine kinase-MB, troponin and myoglobin);
- blood coagulation profile (international normalised ratio, activated partial thromboplastin time, prothrombin index and fibrinogen);
- chest X-ray;
- electrocardiogram (12 standard leads at rest);
- transthoracic echocardiography using the Aplio MX ultrasound scanner (Toshiba, Japan); to assess left ventricular hypertrophy and systolic and diastolic dysfunctions, the end-

systolic and end-diastolic volumes and left ventricular ejection fraction were measured;

- coronary angiography using the Infinix VC-i (Toshiba) angiography system (the procedure was performed on 12 women and 18 men).

Data were statistically processed using BioStat 2009 5.8.3.0 (AnalystSoft, USA) software. To determine the significance of differences (p <0.05), Student's t-test was applied.

RESULTS

The majority of patients (88.6 %) had ST-elevation MI (STEMI), among which Q-wave MI accounted for 60.0 % of cases and typical MI accounted for 71.4 % of cases (Table 1). Forty percent of patients of both sexes had no previous history of CHD (angina pectoris or previously diagnosed CHD). The average time to MI diagnosis in women was 2.1 times greater than in men (p <0.05) accounting for an average of 9.2 h. The main causes of delayed MI diagnosis before admission were late patient referral or diagnostic errors.

Analysis of key cardiovascular risk factors has shown that all of them, except smoking, are more typical in women (Table 2, Fig. 1). Only 7 % of the patients had no risk factors, whereas 1 out of 3 women had a combination of two factors; over 50 % of women had a combination of three risk factors.

Assessment of the coronary bed characteristics based on the coronary angiography data revealed that 70.0 % of patients had the right type of coronary circulation and single-vessel disease (80.0 %) with >75.0 % coronary stenosis (Table 3, Fig. 2). Interestingly, no patient in the female group had multivessel disease, which confirms the literature data on the rarity of this form of disease in younger adults [20]. Lesions were most commonly found in the anterior interventricular artery (in 4 women and 5 men) and right coronary artery (in 3 women and 7 men). Only one woman and two men had a normal angiogram, in other cases atherosclerotic coronary stenosis of varying degrees was found (Fig. 2).

The diastolic dysfunction was found to be the most frequent MI complication in both groups observed in 55.0 % of men and 60.0 % of women (Fig. 3). The systolic dysfunction was less common: it was found in 45.0 % of men and 20.0 % of women. The left ventricular aneurysm and arrhythmias were found only in the female group.

DISCUSSION

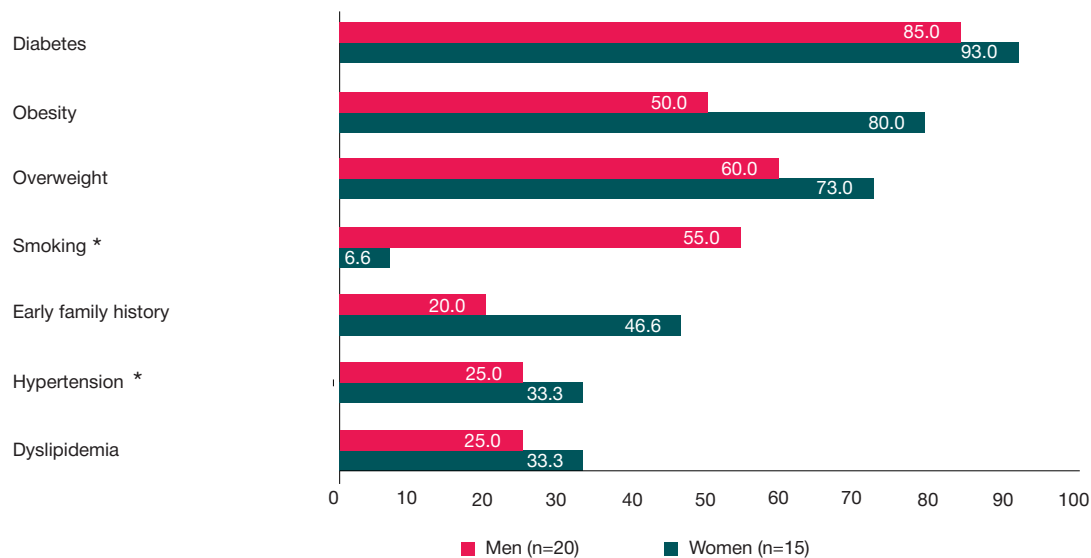
Dyslipidemia was the most common risk factor in our study, both in men and women, which correlates with the data from international studies involving young patients [3]. It was shown that blood cholesterol levels directly correlated with the CHD

Table 1. Characteristics of myocardial infarction (MI) in young adults (<45 years) (\* — p <0.05)

Parameter	Women (n = 15)	Men (n = 20)	Total (n = 35)
Average time to diagnosis. h	9.2 ± 2.4	4.3 ± 2.1*	6.5 ± 4.5
MI without ST-elevation	4 (26.7 %)	0	4 (11.4 %)
MI with ST-elevation	11 (73.3 %)	20 (100.0 %)	31 (88.6 %)
Q (+)	7 (46.7 %)	14 (70.0 %)	21 (60.0 %)
Q (-)	8 (53.3 %)	6 (30.0 %)	14 (40.0 %)
Typical MI	10 (66.7 %)	15 (75.0 %)	25 (71.4 %)
Atypical MI	5 (33.3 %)	5 (25.0 %)	10 (28.6 %)
MI complications	10 (66.7 %)	12 (60.0 %)	22 (62.8 %)
History of CHD	6 (40.0 %)	8 (40.0 %)	14 (40.0 %)

**Table 2.** Quantitative characteristics of some of the risk factors of cardiovascular disease in young adults (<45 years) with myocardial infarction (\* — p <0.05)

Parameter	Women (n = 15)	Men (n = 20)
Systolic blood pressure, mmHg	163.0 ± 29.9	176.0 ± 27.4*
Diastolic blood pressure, mmHg	88.0 ± 13.2	98.0 ± 19.7
Body mass index, kg/m <sup>2</sup>	33.0 ± 6.1	32.0 ± 6.1
Waist circumference, cm	102.0 ± 24.7	111.2 ± 8.9*
Smoking index (pack-years)	2.2 ± 6.1	14.2 ± 15.2*
Cholesterol, mmol/l	5.0 ± 1.1	5.2 ± 1.3
Triacylglycerols, mmol/l	1.6 ± 0.3	1.6 ± 0.4
HDL, mmol/l	1.5 ± 0.4	1.7 ± 1.7
LDL, mmol/l	2.3 ± 0.2	2.4 ± 1.1

**Fig. 1.** The prevalence of key risk factors in young adults (<45 years) with myocardial infarction. The proportion of patients with at least one risk factor is shown, % (\* — p <0.05)

risk. Blood cholesterol level above 6.76 mmol/l indicated a risk of developing CHD and a 4–5 fold risk of MI compared to the individuals with normal cholesterol levels [2].

It is known that arterial hypertension, which is a risk factor for CHD, is more common in women over 65 than in men of the same age [1]. Hypertension was the second most common risk factor in our study, and despite the small study population, we discovered the same tendency in younger adults (<45 years): 80 % of women and 50 % of men were susceptible to high blood pressure (Fig. 1). The risk of death from CHD in women with hypertension was 10 times higher than in young women without hypertension, and 1.5 times higher than in men [1]. The data collected by the American Heart Association (AHA) confirm that hypertension is one of the major risk factors of MI in women, population attributable risk here being 36 %, which indicates a possibility of reducing MI incidence by 36 % on eliminating the risk factor [8].

We have also found that women had a family history of early CHD and MI more often than men (73 % and 60 %, respectively). The international literature emphasises the importance of this factor for younger patients [3, 21], especially males [22].

Almost half of our female patients were overweight, one-third were obese. According to the Framingham Heart Study, the risk of CHD in obese women is 2 times higher than in women with normal body weight [23]. This conclusion was confirmed by the Nurses' Health Study [1, 24].

In the developed countries, smoking is one of the most

common risk factors for CHD among people of both sexes under 45 years of age [1]. Young women are especially sensitive to the effects of nicotine [25] and young adults make up a greater proportion of smokers [22]. According to the studies from China and other countries, 70 to 90 % of young patients with acute myocardial infarction are smokers [3, 26, 27]. Young patients with ST-elevation MI are also more likely to smoke than older patients [3].

It is generally known that diabetes mellitus [DM] significantly increases the risk of CHD and IM [1]. In our study diabetes was found in every third woman and every fourth man. It was shown that the risk of MI associated with the metabolic syndrome is significantly higher in young women than in elderly women [28]. Furthermore, DM is associated with a higher risk of cardiovascular disease in women compared to men [29, 30].

In our study, the equal proportions (60 %) of men and women under 45 years of age had MI as the first clinical manifestation of CHD. The typical form of MI was diagnosed in 75 % of men and 67 % of women, while the incidence of atypical forms was slightly higher in women. This is consistent with the data obtained by other researchers [31–33]. We also found that in younger women coronary stenosis was less frequent and less severe than in young men. The same tendency was observed by Lebedeva et al. [2]. According to the AHA, the gender aspect of clinical manifestations affects the quality of CHD diagnosis and management of patients: women are often misdiagnosed, their myocardial revascularization is delayed,

Table 3. Coronary angiography in young adults with myocardial infarction

Parameter	Women (n = 12)	Men (n = 18)	Total (n = 30)
Left type of coronary circulation	1 (8.3 %)	5 (27.7 %)	6 (30.0 %)
Right type of coronary circulation	8 (66.7 %)	13 (72.3 %)	21 (70.0 %)
Balanced type	3 (25.0 %)	0	3 (10.0 %)
Single-vessel disease	10 (83.3 %)	14 (77.7 %)	24 (80.0 %)
Two-vessel disease	2 (16.7 %)	1 (5.6 %)	3 (10.0 %)
Multivessel disease	0	3 (16.7 %)	3 (10.0 %)
Intact vessels	1 (9.1 %)	2 (10.0 %)	3 (10.0 %)

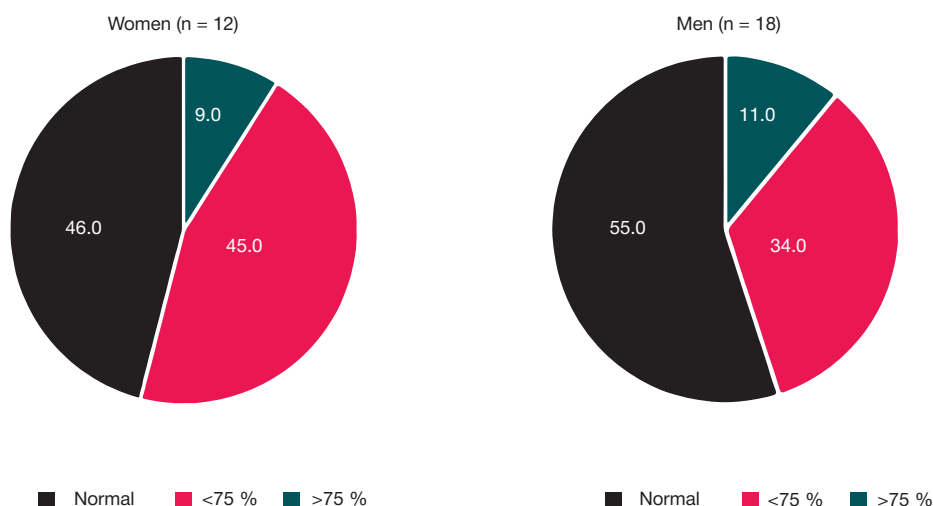


Fig. 2. The distribution of patients within the group by the degree of the coronary artery constriction, %



Fig. 3. The incidence of myocardial infarction complications in young adults (<45 years). The proportion of patients with at least one complication type is shown, %

and mortality caused by MI among them is increasing [2, 8]. A number of studies have shown that women with MI receive therapy later than men [34-37]. Kaur et al. [37] reported that the average time elapsed from the onset of MI symptoms to the moment the patient finally visited the doctor was 53.7 and 15.6 h for women and men, respectively. Our data were different:  $9.2 \pm 2.4$  and  $4.3 \pm 2.1$  h, respectively ( $p < 0.05$ ).

CONCLUSIONS

MI was the first clinical symptom of the coronary heart disease in 60 % of cases in men and women under 45 years of age.

Women started to seek medical advice 2.1 times later than men. This indicates a lack of suspicion among doctors and awareness among female patients concerning the risk of MI, especially in young women. Men and women were typically diagnosed with ST-elevation MI, Q-wave MI and typical MI; however, atypical MI was more often seen in women. The most common risk factors for MI were dyslipidemia, hypertension, family history of CHD and overweight. Our analysis showed that young women were at greater risk of CHD than young men. The causes of early atherogenesis in young women require further research. Raising awareness of MI symptoms among young women is also highly important.

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