ФАКТОРЫ РИСКА РАЗВИТИЯ ИНФАРКТА МИОКАРДА У ЖЕНЩИН С СОХРАНЕННОЙ МЕНСТРУАЛЬНОЙ ФУНКЦИЕЙ

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Цель. Выявление факторов риска (ФР) инфаркта миокарда (ИМ) у женщин с сохраненной менструальной функцией. *Материал и методы.* Проведено обследование 121 пациентки с диагнозом ИМ в возрасте до 55 лет, находившихся на стационарном лечении в кардиологических отделениях г. Рязани в период 2010-2016 гг. Все пациенты были разделены на 2 группы: 1-ая группа – женщины с регулярным менструальным циклом без менопаузальных симптомов (n=60, средний возраст 48,0±6,1 года); 2-ая группа – женщины в постменопаузе (n=61, средний возраст 49,8±4,3 года). Из когорты обследуемых выделена группа женщин (n=18 в группе 1 и n=15 в группе 2), которые заполнили опросники по питанию и физической активности во время индексной госпитализации (2015-2016) по поводу ИМ. *Результаты.* У женщин 1-ой группы чаще встречались отягощенная наследственность по сердечно-сосудистым заболеваниям (58,3%, p=0,02) и курение (46,7%, p=0,03), чем у женщин из 2 группы. Только в 1-ой группе женщины принимали оральные контрацептивы до наступления ИМ (15%, p=0,005). Наиболее часто встречаемыми ФР были: артериальная гипертензия (>80% пациенток в обеих группах), избыточная масса тела и ожирение (78,3% в 1-ой группе и 83,6% – во 2-ой), сахарный диабет 2 типа (23,3 и 24,6% соответственно). По результатам опросника по пищевым привычкам выявлено недостаточное употребление фруктов и овощей у всех пациенток обеих групп. При анализе результатов опросника International Physical Activity Questionnaire (IPAQ) по физической активности у 72,2% пациенток 1-ой группы зарегистрирована недостаточная физическая активность, у 53,3% пациенток 2-ой группы – выраженная гиподинамия. При биохимическом анализе крови в обеих группах выявлены повышенные средние значения общего холестерина, липопротеидов низкой плотности и триглицеридов, а липопротеиды высокой плотности были в пределах нормы. *Заключение.* Среди ФР возникновения ИМ статистически значимо чаще у женщин с сохраненной менструальной функцией по сравнению с женщинами в постменопаузе встречаются отягощенная наследственность по сердечно-сосудистым заболеваниям, курение и прием оральных контрацептивов, также следует отметить в обеих группах большое распространение артериальной гипертензии, дислипидемии и сахарного диабета, избыточного веса и ожирения, низкой физической активности и недостаточного приема овощей и фруктов.

Ключевые слова: инфаркт миокарда; ишемическая болезнь сердца; менструальная функция; факторы риска; женщины молодого возраста.

RISK FACTORS FOR DEVELOPMENT OF MYOCARDIAL INFARCTION IN WOMEN WITH PRESERVED REPRODUCTIVE FUNCTION

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Aim. Identification of risk factors (RF) for myocardial infarction (MI) among women with preserved menstrual function. ***Material and Methods***. 121 Female patients under 55 years of age, who were hospitalized with MI in the cardiology departments of Ryazan in the period 2010-2016, were studied. All patients were divided into 2 groups. The first group included women with a regular menstrual cycle without menopausal symptoms (n=60, mean age 48.0±6.1 years). The second group consisted of postmenopausal women (n=61, mean age 49.8±4.3 years). Of a cohort of studied women a group of women was isolated (n=18 from group 1 and n=15 from group 2) who, during hospitalization with MI in 2015-2016, filled in questionnaires on nutrition and physical activity. ***Results***. In women of group 1 such risk factors as burdened heredity for cardiovascular diseases (58.3%, p=0.02) and smoking (46.7%, p=0.03) were more common than in women of group 2. Only women of group 1 took oral contraceptives before the onset of MI (15%, p=0.005). The most common RFs were: arterial hypertension (>80% of patients in both groups; overweight and obesity (78.3% of women from group 1 and 83.6% from group 2); type 2 diabetes mellitus (23.3% in group 1 and 24.6% in group 2). According to the results of the questionnaire on food habits, insufficient use of fruit and vegetables was detected among all patients of both groups. In analysis of the results of the International Physical Activity Questionnaire (IPAQ), 72.2% of patients in group 1 experienced insufficient physical activity, and 53.3% of patients in group 2 showed pronounced hypodynamia. Biochemical analysis of blood revealed increased average levels of total cholesterol, low-density lipoproteins and triglycerides, with high-density lipoproteins within the normal range in both groups. ***Conclusion.*** The most common risk factors for myocardial infarction in women with preserved menstrual function in comparison with postmenopausal women were: positive heredity for cardiovascular diseases, smoking and taking oral contraceptives. Besides, a wide spread of arterial hypertension, dyslipidemia and diabetes mellitus, overweight and obesity, low physical activity and lack of fruit and vegetables in the diet of women in both groups should be noted.

Keywords: *myocardial infarction; coronary heart disease; menstrual function; risk factors; young women.*

Mortality from cardiovascular diseases (CVD) is the leading cause of death both in Russia and in the world [1-3]. Here, the leading contributor to death rate is myocardial infarction (MI) which develops in men later than in women [3-5]. The cause of this phenomenon is considered to be a factor of «estrogen protection» of women before menopause [6].

However, despite protective functions of estrogens, recently there has been noted a tendency for development of MI in young women with the preserved menstrual function [7]. Nevertheless, information of peculiarities of risk factors for MI in this category of patients is at the beginning of study and is of undoubted scientific interest.

Thus, the *aim* of this work is identification of risk factors for myocardial infarction in women with preserved menstrual function.

Materials and Methods

The work was conducted at the premises of Ryazan State Medical University in the period 2010-2016. 121 Female patients under 55 years of age diagnosed with MI that were taking treatment in cardiologic units of Ryazan were examined. All patients were divided into 2 groups: the 1st group – women with regular menstrual cycle without menopausal symptoms (n=60 with the average age 48.0±6.1 years) and the 2nd group – women in postmenopausal period (n=61 with the average age 49.8±4.3 years). All the patients were taken history and underwent standard clinical and instrumental examination.

The groups were comparable in age and characteristics of MI. By the depth of damage, the predominating MI was that with Q wave in ECG – 61.7% cases in the 1st group and 65.0% in the 2nd, MI without Q wave was identified in 36.7% and 29.5% of cases, MI in the scar zone was recorded in 1.7% and 4.9%, respectively. The anterior localization of the myocardial lesion was predominating (65.0 and 59.0%), lower localization was recorded in 28.3 and 31.2% of cases, and circular MI - in 6.7 and 6.6%, respectively. Only in the 2nd group posterior (1.6%) and lateral (1.6%) MI were present. Repeated MI developed in 18.3% of women in the 1st group and in 16.4% in the 2nd group.

Besides, from a cohort of studied patients a group was isolated (18 from group 1 and 15 from group 2 who, during hospitalization (2015-2016) for MI, filled in questionnaires concerning nutrition and physical activity. The questionnaires were elaborated according to methods used in the International Integrated Program for Prophylaxis of Infectious Diseases (CINDI) [8]. The questionnaire on nutrition evaluated a regular use of vegetables and fruit per day (the norm is 7 and more portions per day without taking into account bananas and potato); the amount of simple sugars (excessive intake was considered to be 7 and more

spoons of sugar/honey/jam per day [9]; use of salt was considered excessive if to the question «Do you add salt into already cooked food?' a respondent answered 'Yes, without tasting it».

International Physical Activity Questionnaire (IPAQ) (modified by K.G. Gurevich and E.G, Fabrikant) which evaluated optimal physical activity of patients of middle age as 21 points and more, insufficient physical activity as 14-20 points and a pronounced hypodynamia as less than 14 points [10].

Statistical processing of the results was carried out using Statistica 10.0 (StatSoft Inc., США) and MS Excel 2007 programs. In analysis of the results the basic statistical parameters were determined: mean arithmetic (M), standard deviation (δ). For cases of normal distribution and also for equality of sampling variance Student t-test was used. For comparison of standardized parameters χ^2 criterion, and for small samples Yates' correction were used. The differences were assumed to be statistically significant at p<0.05.

Results and Discussion

In literature different RFs for ischemic heart disease (IHD) and MI are described, the most of which act both on men and women. However, there exist gender-specific RFs, such as gestational arterial hyperemia (AH), gestational diabetes mellitus (DM) [9]. Actually, each group of patients is characterized by most specific for them RF. Below the results of study and discussion of RFs are given for women with preserved menstrual function (Table 1).

As it is seen from Table 1, such risk factor as a positive heredity was much more common in the 1st group of patients (58.3%) (if parents of a patient suffered CVD: males under 55 years, women under 65 years). Literature data also confirm the fact of a positive heredity increasing the risk for MI especially in women of young age. Thus, the study of B.A. Hamelin (2003) showed that 66.7% of women with a regular menstrual function with a history of acute coronary syndrome (ACS) before 55 years of age, had a positive heredity for IHD [11].

Table 1

Analysis of Risk Factors and of Related Diseases in Women with MI

Paremeter	1st Group (n=60)	2nd Group (n=61)	p
AH	51 (85.0%)	51 (83.6%)	n.s.
Body mass (by body mass index):			
normal body mass	13 (21.7%)	10 (16.4%)	n.s.
overweight	17 (28.3%)	25 (41.0%)	n.s.
1 degree obesity	15 (25.0%)	16 (26.2%)	n.s.
2 degree obesity	11 (18.3%)	7 (11.5%)	n.s.
3 degree obesity	4 (6.7%)	3 (4.9%)	n.s.
Total number of patients with obesity	30 (50.0%)	26 (42.6%)	n.s.
Total number of patients with overweight	47 (78.3%)	51 (83.6%)	n.s.
Positive heredity	35 (58.3%)	23 (37.7%)	0.02
Smoking	28 (46.7%)	17 (27.9%)	0.03
Type 2 DM	14 (23.3%)	15 (24.6%)	n.s.
Disorder in tolerance to glucose	1 (1.7%)	2 (3.3%)	n.s.
Intake of oral contraceptives	9 (15.0%)	0 (0%)	0.005*
Diffuse-nodular goiter	6 (10.0%)	15 (24.6%)	0.03
Autoimmune thyroiditis	2 (3.3%)	6 (9.8%)	n.s.
Chronic pyelonephritis	9 (15.0%)	14 (23.0%)	n.s.
Urolithiasis	2 (3.3%)	7 (11.5%)	n.s.
Kidney cyst	2 (3.3%)	2 (3.3%)	n.s.
Chronic glomerulonephritis	1 (1.7%)	0 (0%)	n.s.

Note: for comparison of parameters χ^2 criterion was used, *use of χ^2 criterion with Yates' correction; n.s. – difference not statistically significant

The next most significant FR in women with preserved menstrual function is smoking. According to MERIDIAN-RO study, smoking in the Ryazan region is most popular among women of young age [12] which is confirmed by our study: almost half the patients of the 1st group and a third of patients of the 2nd group were smoking at the moment of development of MI in them. Besides, a large Polish study of risk factors for development of ACS in women under 45 years of age identified smoking in 48.7% of patients [13].

A relatively small negative contribution, but with a significant difference between groups, was made by intake of oral contraceptives. At present, risk of development of CVD due to intake of oral contraceptives is low, but, nevertheless, there exist groups of patients where this risk is high:

● patients with familial predisposition;

● patients smoking at the age above 35 years;

● patients with AH, hyperlipidemia, DM and IHD [14].

So, patients of our study taking oral contraceptives fell into one, and sometimes into two groups of risk which created additional probability for development of MI in them.

Besides, a rather common and equally occurring RFs in both groups was AH present in >80% of women. Other studies give ambiguous results about spread of AH among women of young age, for example, in a study of young female patients (under 45 years of age) with ACS, AH was revealed in 48.1% of cases [15]; in another study of women who had ACS before 55 years of age, AH was found in 78% [7]; and in a study of women in whom ACS happened before 50 years of age, AH was identified in 92.6% of patients [16].

Besides AH, other common RFs for MI are overweight and obesity. Overweight was recorded in >75% of patients of both groups

which agrees with the results of another study of women who experienced ACS before 45 years of age and in whom ASC was found in 70% of cases (I.V. Ponomarenko, 2018).

Excessive body mass and obesity are promoted by 2 significant RFs: low physical activity and incorrect diet. Therefore, in the given work analysis of dietary habits and of physical activity of patients was carried out (Table 2).

Table 2

Analysis of Dietary Habits and of Physical Activity of Patients

Parameter	1st Group (n=18)	2nd Group (n=15)	p
Dietary habits			
Insufficient intake of fruit and vegetables	18 (100.0%)	15 (100.0%)	n.s.
Abuse of salt	4 (22.2%)	1 (6.7%)	n.s.
Abuse of simple sugars	7 (38.9%)	7 (46.7%)	n.s.
Disregard of caloric content of dood	14 (77.8%)	11 (73.3%)	n.s.
Physical activity			
Optimal physical activity ($\geq$21 points)	4 (22.2%)	3 (20%)	n.s.
Insufficient physical activity (14-20 points)	13 (72.2%)	4 (26.7%)	0.02*
Evident hypodynamia (<14 points)	1 (5.6%)	8 (53.3%)	0.008*

Note: for comparison of parameters χ^2 criterion was used, *use of χ^2 criterion with Yates' correction; n.s. – difference not statistically significant

Low physical activity was noted in patients of both groups but mostly in the 2nd group. At present a study of physical activity has been conducted in women of young age (under 5 years of age) [18] and in women in menopause (under 60 years of age) [19] some of which surely communicate usefulness of training and reduction of probable CVD in future. According to recommendations on healthy eating [9], it is important to take into account the caloric content of used food products. Nevertheless, the most part of the studied patients of both groups did not count calories in food, besides, about 40% of patients excessively used simple sugars, and absolutely all the patients used insufficient amounts of fruit and vegetables, although, according to Canadian scientists who conducted their study on 35,107 individuals, sufficient use of them alone can prevent 72% (55-87%) of deaths from CVD and cancer [20].

Analysis of biochemical parameters of blood of patients of the 1st and 2nd groups on admission to hospital showed similar disord-ers in the glycemic and lipid profiles and in coagulogram; no significant differences were revealed (Table 3).

Dyslipidemia is a classic RF for development of CVD which may be linked with the above mentioned RFs or be an independent RF. In the given study the incidence of dyslipidemia was comparable among the groups and was present in half the women (hypercholesterolemia – 76.7% in the 1st group and 75.4% in the 2nd group; hypertriglyceridemia – 46.7% and 36.1%; elevated level of LDLP – 58.3% and 57.4%; reduced level of HDLP – 60% and 45.9%, respectively). In many studies, dyslipidemia is given as a RF [7,11,21], but with some discrepancies. For example, women with regular menstrual cycle with a past ACS had hypercholesterolemia in 25.9% [11], and in a study of women who experiences MI under 50, hypercholesterolemia was identified in 70.4% of cases [16]. Another study (O.N. Tkacheva, 2007) with comparison of the lipid profile para-meters of female patients of reproductive age with regular menstrual cycle and of post-

Table 3

Comparative Analysis of Biochemical Parameters of Blood and Coagulogram

Paremeter	1st Group (n=60)	2nd Group (n=61)	p
Total protein, g/l	70.0±7.2	70.0±11.2	n.s.
Total cholesterol, mmol/l	**5.7±2.0**	**5.4±1.6**	n.s.
Creatinine, μmol/l	82.5±23.6	80.3±29.4	n.s.
Urea, mmol/l	5.5±2.2	6.1±3.2	n.s.
TG, mmol/l	**2.2±1.6**	**2.1±1.3**	n.s.
LDLP, mmol/l	**3.5±1.3**	**3.6±1.3**	n.s.
HDLP, mmo/l	**1.1±0.3**	1.2±0.4	n.s.
Glucose, mmol/l	**7.4±3.5**	**8.1±5.3**	n.s.
ALT, UN/l	**32.4±20.0**	**39.1±25.3**	n.s.
AST, UN/l	**41.7±25.2**	**40.2±27.7**	n.s.
Total bilirubin, μmol/l	11.4±4.8	11.9±7.2	n.s.
PTI, %	90.0±1.0	90.0±1.0	n.s.
Fibrinogen, g/l	3.7±1.3	3.5±1.4	n.s.
APTT, sec	**34.3±18.4**	**36.3±24**	n.s.
Thrombin time, sec	**21.0±10.6**	**23.9±14.6**	n.s.

Note: TG – triglycerides, LDLP – low density lipoproteins, HDLP – high density lipoproteins, ALT – alanine aminotransferase; AST – aspartate aminotransferase, PTI – prothrombin index; APTT – activated partial thrombin time. Embolden are values that differ from norm; for comparison Student's t-test was used; n.s. – the difference statistically non-significant

menopausal women, identified a reliably high average values of total cholesterol and LDLP in postmenopause, equally reduced level of HDLP and normal level of triglycerides in both groups [21. The higher average values of lipid profile in postmenopause were probably due to the age of patents in the given study (on average, 10 years older than patients with a preserved menstrual function).

Another important RF for MI is DM and it was rather common in the given study (in a quarter of patients in each group). The incidence of DM was rather high (71.7% in the 1st group and 68.8% in the 2nd). We believe that this phenomenon may be a part of a stressful response to the development of MI. In literature the data are given about patients with hyperglycemia (blood glucose level ≥7.8 mmol/l with no DM in history) being more prone to the following complications during hospitalization: congestive left ventricular failure, cardiogenic shock, disorder in con-

duction; besides, they showed a higher hospital mortality rate. Further on, 69.2% of these patients were diagnosed with prediabetes or DM [20].

Besides mentioned common RFs there also exist less common RFs and the related diseases which could contribute to development of MI, such as stress (3.3 and 4.9%), astheno-depressive syndrome (3.3 and 4.9%), oncological diseases of different localization (3.3 and 4.9%), abuse of alcohol (1.7 and 4.9%), rheumatoid arthritis (3.3 and 1.6%), chronic obstructive pulmonary disease (6.7 and 1.6%). These RFs require further study.

Conclusion

According to the given study, women with preserved menstrual function have a higher statistical incidence of such RFs for MI as positive heredity for cardiovascular diseases, smoking and intake of oral contraceptives in comparison with women in postmenopause.

Besides, in both groups arterial hypertension, dyslipidemia, diabetes mellitus, excessive body mass, low physical activity and insufficient intake of vegetables and fruit were recorded.

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