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Coronary heart disease in women

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Summary

Cardiovascular disease (CVD) represents the leading cause of death among women as well as men. The number of deaths due to CVD in women are greater than in men. There are significant gender-related differences concerning CVD. It is less known about CHD in women than in men. There is a need to develop a risk score scale for women in Russia, and for further investigations in the field of treatment and prevention of CVD in women.

Keywords

Coronary heart disease, cardiovascular disease, gender differences, women

Introduction

Coronary heart disease (CHD) is the leading cause of death as in men as in women, and absolute numbers of cardiovascular disease (CVD) mortality are greater in women than in men [1, 2]. During lifetime the risk of developing CVD in men is higher than in women [3]. During last years in developed countries the risk of CVD in men is reducing, together with the increase of CVD in women [4].

Common risk factors are the same both for men and women, but some of them like smoking, diabetes mellitus type 2 and arterial hypertension (AH) have bigger importance in women [5]. If young women don't have 5 risk factors: smoking, AH, diabetes mellitus, hypercholesterolemia, body overweight, they rarely develop CHD and CVD. Only 20% of women <40 years fit these low risk criteria, and at the same time 48% have ⩾ 3 metabolic risk factors of CHD [6]. In Russia the occurrence of risk factors, including metabolic ones, in women is a bit higher than in men: high blood pressure (BP) – 48,4% and 46,6%, body overweight – 48,4% and 46,6%, obesity – 32,9% and 18,6%, total cholesterol levels >5mmol/L – 56,4% and 47,8% respectively [7].

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It is well known that increased number and combination of several risk factors has cumulative effect on the risk of CVD development both in men and women [8]. The study, that lasted more than 30 years and involved women of age 18-39 years who didn't have CVD initially, revealed that women without CVD risk had the lowest occurrence of CHD. At the same time women who had one risk factor had 2,4-fold level of morbidity, and women with ≥ 2 risk factors had CHD 5,4 times more often [6]. The SCORE (Systematic Coronary Risk Evaluation) scale is more common in Europe and in Russia, and Framingham Risk Score is more used in the USA. It was demonstrated that according with the Framingham Risk Score, that takes age, AH, smoking, diabetes mellitus and hyperlipidemia into account, the majority of middle age patients are classified as patients of low or moderate risk and > 3/4 of women below 80 years have 10-years Framingham Risk < 10%, and it is not a precise reflection of a real situation [9]. Therefore experts say more and more often that it is necessary to include more women in cardiological studies and it is necessary to take into account specific for female risk factors for prediction of CVD prognosis. In the USA the Reynolds Risk Score was developed especially for CVD risk estimation in women. The most important difference between this score and Framingham Risk score is considering the information about family history of CVD, the levels of high-sensitive C-reactive protein and the levels of glycated hemoglobin in female patients with diabetes mellitus. The Women's Health Study used Reynolds Risk Score and it reclassified 15% of women with the moderate risk into the high risk patients [10].

Gender features of CHD

There are gender differences in complaints and symptoms of unstable CHD, quite often female patients, especially the ones below 55 years, are presented with "atypical" complaints, but due to low awareness of CVD these complaints can be interpreted in a wrong way and acute coronary syndrome (ACS) diagnosis can be not established or established too late [11]. In all age groups women with ACS less frequently have typical chest pain and more often – vasomotor and vegetative symptoms comparing with men [12-14].

It was found that the prognosis for women with recurrent pain and nonocclusive coronary disease is less benignant that it was considered before, and it strongly depends on the number of existing cardiovascular risk factors. 5-years risk of cardiovascular events in women presented with complaints and nonocclusive coronary disease is ~ 50% higher than in women presented with complaints and normal coronary arteries [15].

Women of all age groups have obstructive lesions of coronary arteries more rarely than men [16]. It was described that morphology of atherosclerotic plaques (AP) of male and female is different [17]. AP composition changes during menopause. Women have more inflammatory lesions in coronary arteries than men. Nevertheless, it is supposed that atherosclerosis in middle age women develops slower than in men, atherosclerosis has more diffuse character, and superficial remodeling is common [18]. AP erosion occurs more often in female patients of younger age with ACS, and for male patients and elderly women AP rupture with future thrombus formation [19]. AP erosions can lead to distal embolization with microemboles and dysfunction of microvascular coronary system. Females have ACS without coronary arteries' occlusion more often. Probably, microvascular dysfunction and subendocardial ischemia in case of non-occluded coronary arteries have more importance in women than in men. Women have AP in carotid arteries more rarely and these plaques are more stable than the male ones [20]. At the same time a small prospective study WISE (Women's Ischaemia Syndrome Evaluation) demonstrated that impaired endothelial function is a negative prognostic factor [21]. There is an opinion, that microvascular lesion is the consequence of impaired vasomotor and metabolic regulation of small coronary arterioles and it is one of important CHD risk factors in women and it determines the presence of angina if there is no significant coronary arteries' occlusion [23-25].

CVD progression depends on relation between damage and reparation processes. Endogenous mobilization of endothelial cell precursors playing an important role in reparation processes is associated with improved restoration of endothelium, improved endothelial function and reduced atherosclerotic lesion of vessels. In healthy women of reproductive age stable number of these cells (CD3+KDR+) was bigger than in males, and it didn't differ that much between women in post menopause and men of the same age. These differences reflect gender characteristics of cardiovascular profile, vascular function (endothelial dysfunction) and thickness of intima-media complex of common carotid artery. Endothelial cell progenitors in females are activated according with menstrual cycle and is synchronized with the levels of circulating 17-betaestradiol and it is possible that

they participate actively in protective processes in females before menopause. Experimental works in animal models prove an important role of estrogens in stimulation of vascular inflammation [26].

Vegetative nervous system has an important role in the regulation of cardiovascular system. It is supposed, that activity of sympathetic nervous system is higher in males, and parasympathetic nervous system activity prevails in females. These differences can be explained with the type of fat tissue distribution, hormonal differences, age, presence of obesity, inflammation and psychosocial features. Abnormal vegetative nervous system activity measured by variability of cardiac rhythm is associated with prothrombogenic changes in women with CHD [27].

Coronary angiography is the golden standard for diagnostics of coronary arteries' diseases, but it is not completely appropriate for diagnostic use in women of middle age, because the same symptoms in this category of patients can appear due to abnormal reaction of vessels and vascular reactivity and not because of stenosis. Some studies demonstrated that additional measurement of coronary flow reserve can reveal abnormal vascular reactivity in female patients with angina complaints and nonocclusive coronary artery disease. Intravascular echography allowed to reveal increased thrombotic activity in women with stable and unstable CHD. Therefore to improve CHD diagnostics in female patients it is necessary to use not only coronary angiography but also estimation of coronary flow reserve and intravascular echography, but it is not always possible. Non-invasive techniques like perfusion magnetic resonance imaging, radioscintigraphy, computer tomography-angiography are considered as diagnostic tools for CHD detection in women [28, 29].

Some gender differences in ACS treatment and outcomes are described. In case of myocardial infarction with ST segment elevation percutaneous coronary interventions have equal advantages in men and women. Treatment strategies differ in patients with low risk and myocardial infarction without ST segment elevation. In the FRISCII (The Framingham and Fast Revascularization During Instability in Coronary Artery Disease) and RITA 3 (The Third Randomized Intervention Treatment of Angina trials) studies early invasive intervention in patients with unstable angina and negative biomarkers or in patients with low risk and myocardial infarction without ST elevation led to decrease of mortality in men and not in women [30,31]. In the WISE study increased levels of inflammation markers was associated with unfavorable outcome of CHD in women and they didn't depend on traditional cardiovascular risk factors. Women with ACS usually are older and they have more risk factors. More than that, women have less developed coronary collateral network, less coronary flow reserve, they have more prominent microvascular dysfunction that negatively influences the prognosis. In case of nonocclusive coronary artery disease mortality is higher in women [32, 33]. Hospital mortality of women with ACS is higher than of the same age men [34]. Women develop hemorrhagic complications after coronary interventions especially in case of therapy with glycoprotein IIb/IIIa more often than men [37, 38].

Conclusion

The problem of cardiovascular and metabolic risk in woman of the Russian Federation is very important. Undoubtedly, there are several gender differences in the features of CVD development and clinical course. It is worth to mention, that CHD development and clinical course in women is less studied than in men. It is necessary to develop Russian criteria for the formation of increased risk of CVD group in women and perform further studies aiming to find effective approach of CVD prevention and treatment in women.

Conflict of interest: None declared.

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