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RISK FACTORS FOR MYOCARDIAL INFARCTION IN WOMEN AND CAUSES OF DELAYED SEEKING MEDICAL CARE

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Abstract

Myocardial infarction in women represents a significant challenge in modern medicine, as it is characterized by both a high risk of development and specific clinical features. This article examines the main risk factors for myocardial infarction in women, including hormonal changes, hereditary predisposition, lifestyle factors, and the presence of comorbid conditions. Particular attention is paid to the impact of arterial hypertension, diabetes mellitus, obesity, smoking, and psychoemotional stress on the development of the disease. Analysis of these factors highlights the importance of early prevention and timely identification of myocardial infarction risk in women.

Keywords: Myocardial infarction, women, risk factors, postmenopause, hormonal changes, polycystic ovary syndrome, biomarkers, arterial hypertension, diabetes mellitus, obesity, smoking.

Introduction

Subclinical depression, which often remains clinically unrecognized, may increase the risk of cardiovascular diseases in women. In an observational study conducted within the framework of the Women's Health Initiative, data from 93,676 generally healthy postmenopausal women were analyzed over a mean

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follow-up period of 4.1 years. Depressive symptoms were assessed at baseline using the short form of the Center for Epidemiologic Studies Depression Scale. Depressive symptoms above the established threshold were identified in 15.8% of participants.

The presence of depression was associated with a higher prevalence of cardiovascular risk factors and comorbid conditions, with odds ratios ranging from 1.12 for hypertension to 1.60 for a history of stroke or angina pectoris. Among women without pre-existing cardiovascular disease, depression was an independent predictor of cardiovascular mortality (relative risk 1.50) and all-cause mortality (relative risk 1.32) after adjustment for age, race, socioeconomic indicators, diabetes mellitus, hypertension, smoking, hypercholesterolemia, body mass index, and physical activity level. Antidepressant use did not modify the observed associations. These findings indicate the important role of depressive symptoms as an independent risk factor for cardiovascular events in postmenopausal women [15].

Hormonal changes characteristic of the postmenopausal period are considered one of the factors influencing cardiovascular risk and prognosis in women. In an epidemiological analysis including 2,848 women with dysglycemia and high cardiovascular risk, baseline levels of total testosterone and sex hormone–binding globulin (SHBG) were measured, and free testosterone was calculated using the Vermeulen formula. Over a median follow-up period of 6.1 years, during which 73% of participants were postmenopausal, 377 cardiovascular events and 389 deaths were recorded. In Cox proportional hazards regression models, neither total nor free testosterone was associated with the composite cardiovascular outcome, whereas elevated SHBG levels were significantly associated with increased all-cause mortality both in age-adjusted analysis (HR = 1.15; 95% CI 1.06–1.24; $p < 0.01$) and in the fully adjusted model (HR = 1.14; 95% CI 1.05–1.24; $p < 0.01$). These findings highlight the importance of hormonal and

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metabolic factors in shaping an unfavorable cardiovascular prognosis in postmenopausal women [14].

In a study including 73,047 postmenopausal women from the observational arm of the Women's Health Initiative (median follow-up 6.9 years), the association between constipation and the risk of cardiovascular events was examined, including death from coronary heart disease, myocardial infarction, stroke, and coronary revascularization. Constipation was associated with older age, smoking, diabetes mellitus, hypertension, obesity, reduced physical activity, a low-fiber diet, and depression. The incidence rates of cardiovascular events among women with moderate and severe constipation were 14.2 and 19.1 per 1,000 person-years, respectively, compared with 9.6 per 1,000 person-years among women without constipation. After adjustment for demographic, clinical, and psychological factors, the increased risk persisted only in the group with severe constipation (+23%). The authors concluded that constipation in postmenopausal women is a marker of increased cardiovascular risk and may serve as a simple tool for identifying women at higher risk [12].

Early age at natural menopause is considered a potential risk factor for long-term mortality, including cardiovascular disease–related mortality. A meta-analysis included 16 studies comprising 321,233 women. Menopause was classified as premature (<40 years), early (40–44 years), and relatively early (45–49 years). The primary outcomes included hazard ratios (HRs) and relative risks (RRs) with 95% confidence intervals (CIs).The analysis demonstrated a significant association between earlier age at menopause and all-cause mortality (adjusted HR = 1.08; 95% CI 1.03–1.14; p = 0.002; adjusted RR = 1.05; 95% CI 1.01–1.08; p = 0.005), whereas the overall association with cardiovascular mortality was less pronounced. In dose–response analyses, premature menopause was associated with increased all-cause mortality (adjusted HR = 1.10; 95% CI 1.01–1.21; p = 0.034; adjusted RR = 1.34; 95% CI 1.08–1.66; p = 0.007). With regard to cardiovascular mortality, premature menopause demonstrated borderline

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statistical significance (HR = 1.09; 95% CI 1.00–1.19; p = 0.045). Subgroup analyses indicated that differences by sex, country, and follow-up duration may explain data heterogeneity, while the likelihood of publication bias was low. The authors concluded that premature menopause is an independent risk factor for all-cause mortality and potentially for cardiovascular mortality, underscoring the need for early risk assessment and preventive strategies in women with early onset of menopause [6].

In postmenopausal women with inflammatory bowel disease (IBD), the impact of IBD on the risk of cardiovascular disease (CVD) remains unclear, particularly among those without traditional risk factors. In an analysis of 134,022 participants from the Women's Health Initiative, 1,367 women (1.0%) had IBD at baseline, with a mean age of 63.4 years. Cox proportional hazards models were used with adjustment for age, comorbidities, sociodemographic factors, and lifestyle variables. The results showed that after adjustment there were no differences between groups in the risk of coronary heart disease (CHD) (HR 0.96; 95% CI 0.73–1.24), venous thromboembolism (VTE) (HR 1.11; 95% CI 0.81–1.52), or peripheral arterial disease (PAD) (HR 0.64; 95% CI 0.28–1.42). The risk of ischemic stroke was higher among women with IBD (HR 1.41; 95% CI 1.06–1.88), but this association lost statistical significance after additional adjustment (HR 1.31; 95% CI 0.98–1.76). The authors concluded that postmenopausal women with IBD may have an increased risk of ischemic stroke, warranting further investigation and careful consideration in the assessment of cardiovascular health [4].

The role of endogenous sex hormones, particularly estradiol, in shaping cardiovascular risk in postmenopausal women remains a subject of debate. A systematic review analyzed studies published up to October 2022 that assessed the association between total serum estradiol levels and cardiovascular events in postmenopausal women. The review included original studies of various designs evaluating outcomes such as cardiovascular mortality, coronary heart disease,

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myocardial infarction, stroke, venous thromboembolism, heart failure, and cardiovascular-related hospitalizations. Due to substantial heterogeneity of the available data, a narrative synthesis without meta-analysis was performed. Of 9,026 identified publications, eight studies involving a total of 5,635 women were included in the final analysis. Among postmenopausal women not receiving hormone therapy, three studies reported inconsistent findings regarding the association between estradiol levels and the risk of coronary heart disease, while one study demonstrated an association between higher estradiol levels and an increased risk of myocardial infarction. No significant associations were identified between estradiol levels and other cardiovascular outcomes, including cardiovascular mortality, heart failure, and stroke. The authors concluded that the current evidence does not allow a definitive determination of the role of estradiol levels in cardiovascular risk among postmenopausal women, highlighting the need for further studies that carefully consider hormonal status and clinical outcomes [5].

Polycystic ovary syndrome (PCOS) and its individual components are considered potential cardiovascular risk factors in women; however, the contribution of each component to the development of cardiovascular disease remains insufficiently defined. A systematic review and meta-analysis of observational studies evaluated the risk of cardiovascular disease in women with individual PCOS components, including hyperandrogenism, oligomenorrhea/menstrual irregularities, or polycystic ovaries. A literature search of PubMed, Scopus, and Web of Science was conducted up to July 2022 without restrictions. Twenty-three studies involving a total of 346,486 women were included in the analysis. Oligo-amenorrhea and menstrual irregularities were associated with an increased risk of overall cardiovascular disease (RR 1.29; 95% CI 1.09–1.53), coronary heart disease (RR 1.22; 95% CI 1.06–1.41), and myocardial infarction (RR 1.37; 95% CI 1.01–1.88), with no association observed for cerebrovascular disease. These associations persisted after additional adjustment for obesity. Evidence regarding

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the role of hyperandrogenism in cardiovascular risk was inconsistent, and the impact of polycystic ovaries as an independent risk factor was not assessed in the included studies. The authors concluded that menstrual disorders within the spectrum of PCOS are associated with an increased risk of cardiovascular disease and myocardial infarction, highlighting the need for further research on reproductive and hormonal risk factors in women [10].

In healthy postmenopausal women, subclinical atherosclerosis may manifest through various structural and tissue-related changes of the vascular wall, necessitating the use of multiple diagnostic markers. In a cross-sectional study, data from 643 postmenopausal women without clinically manifest cardiovascular disease were analyzed, with a mean age of 61 ± 7 years. The objective was to compare associations between cardiovascular risk factors and two subclinical atherosclerosis measures: carotid intima–media thickness (CIMT) and intima–media echogenicity (IM-GSM). Assessments were performed using high-resolution ultrasound, and risk factors included age, race, body mass index, smoking, physical activity, systolic and diastolic blood pressure, lipid profile, glucose levels, and inflammatory markers. In multivariable analyses, age, Black race, body mass index, and systolic and diastolic blood pressure were significantly associated with CIMT (all $p < 0.05$), whereas age, Hispanic race, body mass index, systolic blood pressure, physical activity, LDL cholesterol levels, and leptin were correlated with IM-GSM (all $p < 0.05$). After adjustment for basic demographic factors, systolic blood pressure contributed more strongly to CIMT, whereas lipids, glucose, inflammatory markers, and adipokines were more strongly associated with IM-GSM. The authors concluded that CIMT and IM-GSM reflect different aspects of subclinical atherosclerosis, and their combined use may improve the assessment of vascular changes in asymptomatic postmenopausal women [8].

The systematic use of hormonal contraceptives in women requires consideration of their potential impact on cardiovascular risk, including the development and

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progression of cardiovascular disease. A systematic review analyzed 14 high-quality studies published between 1998 and 2018, including meta-analyses, cohort studies, case–control studies, and systematic reviews evaluating the association between hormonal contraceptives and venous thromboembolism, ischemic stroke, and myocardial infarction. Synthesis of the available evidence demonstrated that combined oral contraceptives are associated with an increased risk of cardiovascular events, with the magnitude of risk varying according to estrogen dose, type of progestogen, and individual cardiovascular risk factors. The authors emphasized that these findings indicate the need for a personalized assessment of cardiovascular risk during counseling and prescription of hormonal contraceptives, as well as consideration of comorbid factors when selecting contraceptive therapy, which is essential for the prevention of adverse cardiovascular outcomes in women [2].

Sex hormone–binding globulin (SHBG) is considered a potential biomarker of cardiovascular risk; however, its role in predicting coronary heart disease remains insufficiently defined. In a prospective analysis of UK Biobank data, the association between SHBG levels and the risk of coronary heart disease was examined in 128,322 men and 135,103 women without coronary heart disease at baseline. Over a median follow-up of 11.7 years, coronary heart disease was documented in 10,405 men and 4,512 women and included nonfatal and fatal myocardial infarction as well as coronary revascularization. Serum SHBG levels were monotonically associated with a lower risk of coronary heart disease in both men (adjusted HR per log-nmol/L 0.88; 95% CI 0.83–0.94) and women (HR 0.89; 95% CI 0.83–0.96). Mendelian randomization confirmed a causal and dose-dependent association between SHBG and coronary heart disease risk. A cumulative meta-analysis of 11 prospective studies including 216,417 men and 138,282 women showed that higher SHBG levels were associated with a lower risk of coronary heart disease in both men (pooled RR 0.81; 95% CI 0.74–0.89) and women (pooled RR 0.86; 95% CI 0.78–0.94). The authors concluded that

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higher circulating SHBG levels independently predict a lower risk of coronary heart disease in both sexes, while the potential clinical utility of SHBG for cardiovascular risk stratification requires further investigation [9].

With increasing life expectancy among women with hormone-dependent breast cancer, the assessment of cardiovascular safety of anticancer therapy is becoming increasingly important. A meta-analysis of observational studies evaluated the association between the use of aromatase inhibitors and the risk of myocardial infarction in women with estrogen receptor–positive breast cancer. Data from 134,476 patients across eight cohort studies were included. In the overall population, no significant differences in myocardial infarction incidence were observed between users of aromatase inhibitors and patients not receiving this therapy (HR 0.98; 95% CI 0.83–1.17). In a subgroup analysis of women without prior cardiovascular disease, a statistically significant reduction in myocardial infarction risk was noted with aromatase inhibitor use (HR 0.86; 95% CI 0.77–0.96). No significant differences between groups were identified for the risk of ischemic stroke (HR 0.93; 95% CI 0.82–1.07) or heart failure (HR 1.24; 95% CI 0.92–1.66). The authors concluded that, based on real-world clinical data, aromatase inhibitors are not associated with an increased risk of myocardial infarction and may be considered a relatively safe therapy for women with breast cancer, including those with concomitant cardiovascular disease, while emphasizing the need for further studies to clarify long-term effects [1].

In recent years, chronic inflammatory diseases have been regarded as potential contributors to increased cardiovascular risk. A systematic review and meta-analysis of cohort studies examined the association between bronchial asthma and the risk of cardiovascular disease and cardiovascular mortality. The analysis included 29 observational studies with a total of 11,380,027 participants. Among patients with asthma, the overall risk of cardiovascular disease was increased by 30% compared with individuals without asthma (RR 1.30; 95% CI 1.20–1.42). Elevated risks were observed for coronary heart disease (RR 1.35; 95% CI 1.27–

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1.42), angina pectoris (RR 1.48; 95% CI 1.16–1.89), myocardial infarction (RR 1.33; 95% CI 1.25–1.41), and heart failure (RR 1.53; 95% CI 1.04–2.23). In addition, asthma was associated with an increased risk of cardiovascular mortality (RR 1.26; 95% CI 1.05–1.51). The authors concluded that asthma is associated with increased cardiovascular morbidity and mortality, underscoring the role of systemic inflammation and comorbidity in the development of cardiovascular risk [7].

Sex differences in the presentation, risk factors, management, and outcomes of acute myocardial infarction (MI) are well documented; however, because these differences are highly sensitive to cultural and social changes, continuous reassessment of the evidence is required. A contemporary systematic review evaluated the baseline characteristics of men and women presenting with acute MI to secondary, tertiary, and quaternary care centers. The review included more than 1.4 million participants from 18 studies, encompassing primary prospective, cross-sectional, and retrospective observational studies, as well as secondary analyses of registry data. The findings indicated that women were more likely than men to have prior diagnoses of diabetes mellitus, hypertension, cerebrovascular disease, and heart failure, while they were less likely to present with a history of ischemic heart disease or angina, dyslipidemia, or smoking. Further research is needed to elucidate the causes of these differences and the role of sex-specific risk factors in this context, as well as to determine how sex-related differences influence clinical management and outcomes [3].

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women and is associated with an increased risk of cardiovascular disease. In a systematic review and meta-analysis including 20 studies with a total of 1.06 million women, PCOS was associated with a higher risk of composite cardiovascular disease (OR 1.68; 95% CI 1.26–2.23), coronary heart disease (OR 1.48; 95% CI 1.07–2.05), stroke (OR 1.71; 95% CI 1.20–2.44), and particularly myocardial infarction (OR 2.50; 95% CI 1.43–4.38), while the association with

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cardiovascular mortality was less clearly defined. These findings highlight PCOS as a significant and specific risk factor for myocardial infarction in women that remains underestimated in clinical practice and may contribute to insufficient prevention and delayed detection of cardiovascular disease [13].

Endometriosis, a chronic estrogen-dependent inflammatory disease, is associated with an increased risk of cardiovascular disease in women. A systematic review and meta-analysis of six cohort studies involving 254,929 women demonstrated that the presence of endometriosis was associated with a 50% increase in the risk of coronary heart disease (HR 1.50; 95% CI 1.37–1.65) and a 17% increase in the risk of cerebrovascular disease (HR 1.17; 95% CI 1.07–1.29), with no evidence of statistical heterogeneity. These findings support the role of chronic inflammation and hormonal dysregulation as significant contributors to cardiovascular risk in women and underscore the need for earlier identification and risk stratification in patients with endometriosis [11].

Conclusion:

Myocardial infarction in women represents a multifactorial clinical and public health challenge characterized by distinct biological, hormonal, psychosocial, and comorbid risk profiles that differ substantially from those observed in men. The evidence summarized in this review demonstrates that, in addition to traditional cardiovascular risk factors, female-specific and sex-related conditions—including early and premature menopause, polycystic ovary syndrome, endometriosis, hormonal contraceptive use, hormone-dependent malignancies and their treatments, chronic inflammatory diseases, depressive symptoms, and alterations in sex hormone metabolism—play a significant role in the development and prognosis of cardiovascular disease and myocardial infarction in women. Postmenopausal status is associated with complex hormonal and metabolic changes that influence vascular structure, inflammation, and atherosclerotic progression, while psychosocial factors and comorbid chronic

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conditions further modify cardiovascular risk and contribute to delayed diagnosis and suboptimal outcomes. The heterogeneity of findings across studies highlights the need for sex-specific risk assessment strategies, improved awareness of nontraditional and reproductive risk factors, and personalized preventive approaches. Future research should focus on longitudinal, well-designed studies integrating hormonal status, biomarkers, inflammatory pathways, and social determinants of health to refine cardiovascular risk stratification and optimize prevention, early detection, and management of myocardial infarction in women.

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