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Sex-specific Risk Factors for Cardiovascular Disease in Women

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Summary

CVD is the leading cause of death for women worldwide. The symptoms of CVD in women may be less specific than in men, so women are less likely to be properly diagnosed and adequately treated. Women experience a proportional increase in cardiovascular risk on risk factors that are common to both genders. In addition, women have endocrine-related factors that increase their susceptibility to CVD. 1 in 3 women die from CVD, and 45% of women over the age of 20 have some form of CVD. [33] We must exploit gender differences to ensure optimal medical care. Detection of CVD risk factors and preventive measures in this regard are essential for proper cardiovascular care among women.

Key words: CVD, cardiovascular disease, women

INTRODUCTION AND PURPOSE

The purpose of this review is to present female-specific CVD risk factors and to show the proportional increase in risk among the cardiovascular risk factors that are common to both genders.

Cardiovascular disease (CVD) is the leading cause of death for women worldwide. CHD and strokes are in the first place. [4,6] In women, apart from the standard ones, there are additional risk factors. [2] The more risk factors a patient has, the higher the cardiovascular risk category she is in. Among the most important are premature menopause, factors related to pregnancy, premature menstruation, polycystic ovary syndrome (PCOS), use of hormonal contraceptives and breast cancer. [2,4,7] Traditional risk factors are the same as for men and include, among others, hypertension, diabetes, overweight / obesity, hyperlipidemia, cigarette smoking, atrial fibrillation, and low socioeconomic status. [3,9] The rates of death from CHD among women are significantly lower than for men in each age group, but they are getting closer with aging. [4]

An accurate diagnosis is extremely important for timely appropriate treatment and improved survival. The symptoms of a heart attack in women often differ from that in men, which can make an accurate diagnosis difficult. Research from the UK shows that a woman's risk of misdiagnosis is 37% higher with STEMI and 29% higher with NTEMI than men. [10] In women, symptoms are more likely to be anxiety, shortness of breath, pain in the back, shoulder or jaw, and nausea and vomiting. [4,10] Exercise is a frequent cause of cardiovascular events in men, and emotional factors in women. [10] Women have poorer control of BP, lipids, and DM than men. [1]

Statins have been documented to reduce the incidence of cardiovascular events regardless of gender. Women are less likely to receive the statin dose recommended by the guidelines than men. They also more often stop therapy or even refrain from taking it. [11] The female sex is a risk factor for the appearance of musculo-skeletal ailments in the course of statin therapy. [12]

DESCRIPTION OF THE STATE OF KNOWLEDGE

We can divide cardiovascular risk factors into common for both sexes and those that occur only in women. Risk factors that are common to both genders include age, smoking, overweight / obesity, hypertension, hyperlipidaemia, and diabetes. [1] Risk factors for pregnancy-related CVD include gestational hypertension / pre-eclampsia, GDM and PTD. [2]

The first cardiovascular risk factor that is common to both sexes is age. It is an unmodifiable factor. Estrogens are cardioprotective in premenopausal women and delay the onset of CAD for several years. The risk of developing CAD for both genders is equal to around 55 years of age. [1, 13]

The remaining of the above-mentioned factors common to both sexes are modifiable. The first is high blood pressure. The risk of developing hypertension increases more in older women

than in older men of a similar age. Endogenous estrogens have a vasodilating effect and help to maintain proper blood pressure in premenopausal women. [1] Some studies show that postmenopausal women are unlikely to experience a reduction in nocturnal BP <10%. Normally, during sleep, blood pressure should drop by 10-20% in relation to daily values, and after waking up, it should increase. [6.17] Additionally, cardiovascular receptor activity has been shown to increase after the menopause, so salt restriction is recommended at this age. [6.16]

Studies on a group of approximately 2.4 million people have shown a 15% higher risk of CAD in women who smoke compared with men who smoke. [14] Obesity in postmenopausal women also has a greater impact on the incidence of CAD, which is associated with the redistribution of adipose tissue to the abdominal region, which contributes to the metabolic syndrome. [15]

Dyslipidemia is also an important cardiovascular risk factor. Elevated levels of LDL-C and triglycerides, and low levels of HDL-C are associated with an increased risk of CVD in men and women. [1] Women treated with statins have a higher risk of myopathy than men. Ezetimibe is an alternative for women who experience muscle pain or require additional LDL lowering, in addition to using statins at the highest tolerated doses. Ezetimibe monotherapy lowers LDL levels by 18%, and as an add-on therapy by 25%. 6,18 An important piece of information when using statins is that they must be discontinued 1-2 months before a planned pregnancy or immediately if the pregnancy is unplanned. The use of bile acid sequestrants is permissible during pregnancy. [18]

Diabetes contributes to increased cardiovascular risk through atherosclerotic events and increases the incidence of congestive heart failure. [22] Although both genders have the same degree of diabetes mellitus, women with type 1 DM have a 37% higher risk of death from any cause and twice the risk of fatal and non-fatal cardiovascular events compared to men with DM. Type 1 diabetes [21] The incidence of type 2 diabetes is higher in young women, in middle-aged men, and similar in older men. [20] The earlier onset of the disease translates into its longer duration, and thus a greater risk of complications. According to the results of the Swedish Heart Registry research, mortality due to CVD is significantly higher if type 2 diabetes is diagnosed before the age of 40. [21] Women with diabetes appear to be less likely to achieve adequate glycemic control and are more likely to require more aggressive treatment of CVD risk factors than men. [1] Atherosclerosis Risk In Communites research proves that DM is a potent risk factor for CVD, and CVD mortality is higher among African Americans compared to African Americans. Similar results were obtained for Caucasians. [22]

Pregnancy complications may be risk factors for maternal CVD in the future. Hypertension in pregnancy is associated with an increased risk of developing chronic hypertension as early as the first year after delivery, a twofold increased risk of CVD-related hospitalization in the 3 years postpartum, and contributing to the development of other risk factors for CVD, such as dyslipidaemia and diabetes. 6,24 This is probably associated with endothelial dysfunction, oxidative stress, inflammatory response, and increased release of procoagulants. [1] Women with a history of GDM have an 8-fold higher risk of developing type 2 DM in the future. [2,25] Additionally, such women are twice as likely to develop a CVD event in the future as compared

to women without GDM. Preterm labor is also associated with an increased cardiovascular risk. Women with a history of PTD have a higher risk of developing type 2 DM, dyslipidemia, chronic hypertension, and subclinical atherosclerosis in the first 10 years postpartum. [2,26] Women who have experienced a miscarriage or stillbirth have a 2-fold higher risk of myocardial infarction, cerebral infarction, and renal-vascular hypertension. 6,27 A meta-analysis of 10 studies found that miscarriage was associated with a 1.45-fold increase in CVD risk, and more than 1 miscarriage was associated with a 2-fold increase in CVD risk. [2.28]. Breastfeeding is a factor that reduces cardiovascular risk. Lactation contributes to the reversal of adverse changes associated with dyslipidemia and insulin resistance, and reduces the risk of hypertension and metabolic disorders in the future. [2, 29]

Autoimmune diseases are more common in women than in men. Rheumatoid arthritis increases the risk of MI 2-3 times and systemic lupus erythematosus 9-50 times compared to the general population. [1,5] These diseases are associated with accelerated atherosclerosis as well as dysfunction of the coronary vessels. [6]

Premature first menstruation is associated with an increased risk of CHD and CVD. It influences the development of hypertension and components of the metabolic syndrome, including type 2 diabetes and dyslipidemia, which contribute to CVD. [2] Another risk factor for CVD is polycystic ovary syndrome (PCOS), which is associated with an increased incidence of arterial hypertension, central adiposis, insulin resistance, dyslipidemia, and metabolic syndrome. [30] Estrogens have their receptors in vascular endothelial cells and in smooth muscles. Estrogen has a vasodilating effect, improves the response of arterial walls to injury, promotes re-endothelialization, inhibits smooth muscle cell proliferation and matrix deposition after vessel damage. [1, 31] Estrogen protects cardiomyocytes against apoptosis and prevents their hypertrophy. [32] It follows that postmenopausal women have a higher risk of CVD because they lose the cardioprotective properties of estrogens.

Hormonal contraception containing estrogens in its composition increases the level of triglycerides and HDL-C and lowers the level of LDL-C, thus affecting the patient's lipid profile. Preparations containing norgestrel or levonorgestrel, which in turn raise the level of LDL-C and lower the level of HDL-C. Progesterone-based contraceptives have a neutral effect on the lipid profile. [2]

Women with PCOS, with a history of premature menstruation and a history of recurrent miscarriages, have a high-risk cardiometabolic karyotype. It is important to monitor their metabolic parameters on an ongoing basis and implement appropriate lifestyle changes as soon as possible. [2]

CONCLUSIONS

CVD is the leading cause of death for women worldwide. There are differences between the sexes in risk factors and response to treatment. Women have specific CVD risk factors associated with hormonal differences and pregnancy-related compared to men. Increased

participation of women in clinical trials on risk factors, prevention and treatment of CVD will provide a better understanding of the pathophysiological basis of CVD in women.

LIST OF REFERENCES

1. Anum Saeed, June Kampanqkaew, Vijay Nambi Prevention of Cardiovascular Disease in Women 2017; doi: 10.14797/mdcj-13-4-185; 13(4): 185–192

2. Anandita Agarwala, Erin D. Michos, Zainab Samad, Christie M. Ballantyne, Salim S. Virani The Use of Sex-Specific Factors in the Assessment of Women's Cardiovascular Risk 2020; doi: 10.1161/CIRCULATIONAHA.119.043429; 141(7): 592-599

3. Robert A. Wild, Kathleen M. Hovey, Christopher Andrews, Jennifer G. Robinson, Andrew M. Kaunitz, JoAnn E. Manson, Carolyn J. Crandall, Rachel Paragallo, Chrisandra Shufelt, C. Noel Bairey Merz Cardiovascular Disease (CVD) Risk Scores,Age or Years since Menopause to Predict Cardiovascular Disease in The Women's Health Initiative 2021; doi: 10.1097/GME.0000000000001753; 28(6):610-618

4. Mark Woodwark Cardiovascular Disease and the Female Disadventage 2019; doi: 10.3390/ijerph16071165; 16(7): 1165.

5. del Rincón I, Polak JF, O'Leary DH, . et al. Systemic inflammation and cardiovascular risk factors predict rapid progression of atherosclerosis in rheumatoid arthritis. *Ann Rheum Dis*. 2015. June; 74 6: 1118– 23

6. Leslie Cho, Melinda Davis, Islam Elgendy, Kelly Epps, Kathryn J. Lindley, Puja K. Mehta, Erin D. Michos, Margo Minissian, Carl Pepine, Viola Vaccarino, Annabelle Santos Volgman, ACC CVD Womens Committee Members Summary of Updated Recommendations for Primary Prevention of Cardiovascular Disease in Women 2020; doi: 10.1016/j.jacc.2020.03.060; 75(20): 2602-2618.

7. Peters S.A., Woodward M. Women's reproductive factors and incident cardiovascular disease in the UK Biobank. *Heart.* 2018;104:1069–1075

8.Bots SH, Peters SAE, Woodward M. Sex differences in coronary heart disease and stroke mortality: a global assessment of the effect of ageing between 1980 and 2010. *BMJ Glob. Zdrowie*. 2017; 2 :e000298. doi: 10.1136/bmjgh-2017-000298

9. Backholer K., Peters SAE, Bots SH, Peeters A., Huxley RR, Woodward M.Sex differences between socioeconomic status and cardiovascular disease: a systematic revew and meta-analysis. *J. Epidemiol. Zdrowie społeczności.* 2017; 71 :550-557. doi: 10.1136/jech-2016-207890

10. Wu J., Gale CP, Hall M., Dondo TB, Metcalfe E., Oliver G., Batin PD, Hemingway H., Timmis A., West RM Impact of initial hospital diagnosis on mortality for acute myocardial

infarction: A national cohort study. *Eur. Serce J. Acute Cardiovasc. Opieka.* 2018; 7 :139–148. doi: 10.1177/2048872616661693

11. Nanna MG, Wang TY, Xiang Q i in. Różnice płci w stosowaniu statyn w praktyce środowiskowej . *Wyniki Circ Cardiovasc Qual* 2019; 12 : e005562

12. Stroes E, Thompson P, Corsini A i in. Objawy mięśniowe związane ze statynami: wpływ na terapię statynami — Oświadczenie panelu Europejskiego Towarzystwa Miażdżycy dotyczące oceny, etiologii i leczenia . *Eur Serce J* 2015; 36 : 1012–22

13. McSweeney JC, Rosenfeld AG, Abel WM, . i in.; Rada ds. Pielęgniarstwa Sercowo-Naczyniowego i Udaru Amerykańskiego Towarzystwa Kardiologicznego, Rada ds. Kardiologii Klinicznej, Rada ds. Epidemiologii i Zapobiegania, Rada ds. Nadciśnienia, Rada ds. Stylu Życia i Zdrowia Kardiometabolicznego oraz Rada ds. Jakości Opieki i Badań Wyników. Zapobieganie chorobie niedokrwiennej serca i jej doświadczanie jako kobieta: stan wiedzy: oświadczenie naukowe American Heart Association . *Obieg* . 2016. 29 marca; 133 13 : 1302–31

14. Benjamin EJ, Blaha MJ, Chiuve SE, . i in.; Komitet Statystyki Amerykańskiego Towarzystwa Kardiologicznego i Podkomitet Statystyki Chorób Serca i Statystyk Udaru Udaru – 2017: Raport Amerykańskiego Towarzystwa Kardiologicznego . *Obieg* . 2017. 7 marca; 135 10 : e146–e603

15. Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE.. Choroba sercowo-naczyniowa u kobiet: perspektywy kliniczne . *Circ Res* . 2016. 15 kwietnia; 118 8 : 1273–93

16. Sacks FM, Svetkey LP, Vollmer WM i in., dla DASH-Sodium Collaborative Research Group. Wpływ obniżonej zawartości sodu w diecie na ciśnienie krwi i dieta w celu powstrzymania nadciśnienia (DASH) . *N Engl J Med* 2001; 344 :3-10

17. Routledge FS, McFetridge-Durdle JA, Dean CR. Stress, menopausal status and nocturnal blood pressure dipping patterns among hypertensive women. *Can J Cardiol* 2009;25:e157–63

18. Grundy SM, Stone JN, Bailey AL, et al. AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019;73:e285–350

19. Huxley RR, Peters SA, Mishra GD, Woodward M.. Risk of all-cause mortality and vascular events in women versus men with type 1 diabetes: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol*. 2015. March; 3 3: 198– 206

20. Huebschmann AG, Huxley RR, Kohrt WM, et al. Sex differences in the burden of type 2 diabetes and cardiovascular risk across the life course. *Diabetologia* 2019;62:1761–72

21. Sattar N, Rawshani A, Franzen S, et al. Age at diagnosis of type 2 diabetes mellitus and associations with cardiovascular and mortality risk: Findings from the Swedish National Diabetes Registry. *Circ* 2019;139:2228–37

22. George KM, Selvin E, Pankow JS, et al. Sex differences in the associations of diabetes with cardiovascular disease outcomes among African-American and white participants in the Atherosclerosis Risk In Communities Study. *Am J Epidemiol* 2018;187:403–10

23. Wu P, Haththotuwa R, Kwok CS, Babu A, Kotronias RA, Rushton C, Zaman A, Fryer AA, Kadam U, Chew-Graham CA, et al. Preeclampsia and Future Cardiovascular Health: A Systematic Review and Meta-Analysis. *Circ Cardiovasc Qual Outcomes*. 2017;10:e003497. doi: 10.1161/CIRCOUTCOMES.116.003497

24. Black MH, Zhou H, Sacks DA, et al. Hypertensive disorders first identified in pregnancy increase risk for incident prehypertension and hypertension in the year after delivery. *J Hypertens* 2016;34: 728–35

25. Bellamy L, Casas JP, Hingorani AD and Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet (London, England)*. 2009;373:1773–1779

26. Tanz LJ, Stuart JJ, Williams PL, Rimm EB, Missmer SA, Rexrode KM, Mukamal KJ and Rich-Edwards JW. Preterm Delivery and Maternal Cardiovascular Disease in Young and Middle-Aged Adult Women. *Circulation*. 2017;135:578–589

27. Ranthe MF, Andersen EAW, Wohlfahrt J, et al. Pregnancy loss and later risk of atherosclerotic disease. *Circulation* 2013;127:1775–82

28. Oliver-Williams CT, Heydon EE, Smith GCS, et al. Miscarriages and future maternal CVD: a systematic review and meta-analysis. *Heart* 2013; 99:1636–44

29. Stuebe AM and Rich-Edwards JW. The reset hypothesis: lactation and maternal metabolism. *Am J Perinatol*. 2009;26:81–88

30. Guzick DS. Cardiovascular risk in PCOS. *J Clin Endocrinol Metab*. 2004;89:3694–3695

31. Brouchet L, Krust A, Dupont S, Chambon P, Bayard F, Arnal JF.. Estradiol accelerates reendothelialization in mouse carotid artery through estrogen receptor-alpha but not estrogen receptor-beta. *Circulation*. 2001. January 23; 103 3: 423– 8

32. Kim JK, Pedram A, Razandi M, Levin ER.. Estrogen prevents cardiomyocyte apoptosis through inhibition of reactive oxygen species and differential regulation of p38 kinase isoforms. *J Biol Chem*. 2006. March 10; 281 10: 6760– 7

33. Benjamin EJ, Muntner, Alonso A, et al., American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics -2019 update; a report from the American Heart Association. *Circulation* 2019;139: e56–528