



## Climateric and menopause

### *Climaterio y menopausia*

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#### MENOPAUSE AND RISK OF CARDIOVASCULAR DISEASE. IMPORTANCE OF EARLY PREVENTION

Natural menopause is defined as the permanent absence of menstrual periods, determined retrospectively. Thus, the transition to menopause or perimenopause (PM) begins, on average, four years before the last menstrual period with irregular cycles and metabolic changes with implications for long-term health.<sup>1</sup>

The SWAN study (3,000 women, 42-52 years old, 15-year follow-up) showed changes in the lipid profile from PM, a slight elevation of 6% on average in low-density lipoproteins, and minimal changes in the levels in high-density lipoproteins and its antiatherogenic function.<sup>2,3</sup>

At the end of 2020, the American Heart Association included PM as a sex-specific condition with cardiometabolic impact in the future; PM is considered a transcendental moment to generate lifestyle changes that impact cardiovascular (CV) prognosis in women.<sup>4</sup>

The protective effect of estrogen helps prevent atherosclerosis, that protection is lost after menopause, and it is associated with body changes, increasing visceral fat and decreasing lean mass. Furthermore, visceral adipose tissue secretes proinflammatory substances, determining a chronic proinflammatory state, favoring atherosclerosis, and increasing the risk of cardiovascular disease (CVD). Therefore, a higher incidence of ischemic heart disease (IHD) is observed compared to

young women, and it can manifest as acute coronary syndromes (ACS) with or without angiographically significant coronary lesions, coronary dysfunction (coronary spasm or microvascular dysfunction) or nonspecific chest pain.<sup>1</sup> Also, at the cardiac level, a more significant diastolic dysfunction of the left ventricle (LV) is observed, as well as an increase in the concentric remodeling of the LV, which could make PM women susceptible to heart failure (HF) with preserved ejection fraction.<sup>5</sup>

#### PSYCHOLOGICAL CHANGES IN CLIMACTERIC AND MENOPAUSE

Psychological changes in the climacteric, such as stress and its complex management, result in a higher risk of depression and anxiety that can worsen according to personality and low self-esteem. This can add irritability, which is the most frequent problem and the one that most affects social activities.<sup>6,7</sup>

Vasomotor symptoms: hot flashes and night sweats constitute the most characteristic clinical manifestations of the climacteric, affecting the quality of life, even decreasing libido, causing irritability, fatigue, an embarrassment in public, anxiety, and depression.

Sleep and memory disorders may appear, such as Alzheimer's or dementia.<sup>8</sup> These occur with different intensities and frequencies, affecting alertness with decreased mental activity and productivity.

In addition to fatigue and irritability, these changes affect family and social relationships.

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### IMPORTANCE OF TREATING CARDIOVASCULAR DISEASE IN WOMEN

CVD is the leading cause of mortality in women; among these, coronary heart disease stands out. Both sexes do not respond equally to different *noxa*, the different prevalence of risk factors (RF) for CVD are associated, and their evolution can differ in acute or chronic entities.

The RF associated with CVD are hypertension (HBP), diabetes, obesity, dyslipidemia, sedentary lifestyle, and smoking, among the most important. These cardiovascular risk factors (CVRF) are common to both sexes, but their impact may differ; hence, recognizing these differences is essential for their correct treatment.<sup>9</sup>

Women are underrepresented in clinical trials, this leads in part to a lack of knowledge of the treatment. However, it is assumed that the treatment of CVRF is similar in both sexes without significant evidence of differences in doses, additional benefits, or side effects. There is evidence of converting enzyme inhibitors (ACEI) and Angiotensin Receptor Antagonists (ARA II) in pregnancy, platelet antiaggregant in primary prevention, and thrombolytic therapy in some cases. Women have more adverse effects to ACE inhibitors (cough), calcium antagonists (edema), and diuretics (cramps).<sup>10</sup> It is time to involve gender from the beginning of research for better medical practice.

### HORMONE TREATMENT IN CLIMACTERIC: RISK OR BENEFIT?

Estrogens regulate blood pressure (BP), endothelial function, and cardiac remodeling. Alterations in estrogen levels affect the immune system, related to vascular function and aging. After menopause, there is a tendency for increased BP, central adiposity, insulin resistance, and dyslipidemia.<sup>1,2</sup>

Cohort or case-control studies have shown that hormone therapy (HT) reduces the incidence of coronary heart disease and CV mortality after menopause by 30-50%, especially if administered to younger women. This is due to multiple protective mechanisms of the estrogens, such as nitric oxide-mediated vasodilation, increased flow, and decreased

vascular resistance. Other factors involved are increased cardiac output, facilitation of angiogenesis and an anti-apoptotic effect on cardiomyocytes, antioxidant and anti-inflammatory actions, beneficial changes in the lipid profile, increased sensitivity to insulin, attenuation of the weight gain typical of menopause, and less abdominal adiposity.<sup>2</sup>

The Women's Health Initiative<sup>3</sup> study (27,000 women, average age 63 years) showed no benefit. In this study, the CV risk of coronary heart disease, stroke, and venous thromboembolism was only increased in the combined arm with oral estrogens and progestins. This study had some methodological flaws to consider: advanced age, associated comorbidities, and inappropriate dose schedule. The latest studies show that in younger women, there is a window of opportunity for the use of HT in the first ten years of menopause since they have a healthier arterial system, and it favors cardioprotection due to the mechanisms described.

### CONCLUSION

Hormone therapy could be associated with increased cardiovascular risk in women who start or continue treatment after ten years of menopause and could be neutral or protective in younger women for a limited period.

### REFERENCES

1. Maas AHEM, Rosano G, Cifkova R, Chieffo A, van Dijken D, Hamoda H et al. Cardiovascular health after menopause transition, pregnancy disorders, and other gynaecologic conditions: a consensus document from European cardiologists, gynaecologists, and endocrinologists. *Eur Heart J*. 2021; 42: 967-984.
2. Urzúa EA. Menopausia y riesgo cardiovascular. *Rev Med Chile*. 2016; 144: 1375-1376.
3. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML et al. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA*. 2002; 288: 321-333.
4. El Khoudary SR, Aggarwal B, Beckie TM, Hodis HN, Johnson AE, Langer RD et al. Menopause transition and cardiovascular disease risk: implications for timing of early prevention: a scientific statement from the American Heart Association. *Circulation*. 2020; 142: e506-e532.

5. Sung K-T, Chandramouli C, Lo C-I, Tsai J-P, Lai Y-H, Hsia C-C et al. Association of female menopause with atrioventricular mechanics and outcomes. *Front Cardiovasc Med.* 2022; 9: 804336.
6. Soares CN, Cohen LS. The perimenopause, depressive disorders, and hormonal variability. Review article. *Sao Paulo Med. J.* 2001; 119: 78-83.
7. Afrid I. Psychological and social aspects of menopause. In: Rodríguez-Landa JF, Cueto-Escobedo J. Editors. *A multidisciplinary look at menopause* [Internet]. London: IntechOpen; 2017, visited August 2022.
8. Ramos, MB. Aspectos psicológicos de la menopausia. *Medicina y Salud.* Universidad Autonoma de Mexico (UNAM). Docencia digital 2010. [Visitado el 22 de agosto de 2022] Disponible en: <https://www.docenciadigital.unam.mx/> Disponible en: [www.medicinaysalud.unam.mx/temas/2010/08\\_ago\\_2k10.pdf](https://www.medicinaysalud.unam.mx/temas/2010/08_ago_2k10.pdf)
9. Rodríguez-Guerrero NI. Terapia farmacológica en la mujer y prevención cardiovascular. *Rev Colomb Cardiol.* 2018; 25 (S1): 106-112.
10. Tadic M, Cuspidi C, Grassi G, Ivanovic B. Gender-specific therapeutic approach in arterial hypertension-challenges ahead. *Pharmacol Res.* 2019; 41: 181-188.

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