Cardiovascular and Metabolic Science www.ancam.org.mx

Chapter 22

Vol. 33 Supplement 5
October-December2022

doi: 10.35366/108063

Current impact of traditional risk factors in women

Impacto actual de los factores de riesgo tradicionales en la mujer

Edith Ruiz-Gastélum,* Alejandra Inés Christen,‡ María Alejandra Ibañez,§ María Romera,¶ Rosa Lidia Castedo-Verdura,‖ Heidi Ivette Alurralde-Saavedra**

INTRODUCTION

Traditional cardiovascular risk factors (CVRFs) play a crucial role in developing cardiovascular disease (CVD), the leading cause of death in women. Among these, arterial hypertension (HBP) stands out as the primary contributor to cardiovascular mortality (CV mort) standardized by age in women worldwide, followed by high LDL cholesterol and diabetes mellitus (DM), factors analyzed in this review *(Figure 1 and Table 1)*.[1,2]

HBP in childbearing age

Endogenous estrogens maintain vasodilation, contributing to blood pressure (BP) control; therefore, hypertension appears a decade later than in men. However, hypertension in women is less controlled. The risk of long-term hypertension increases four times in patients with hypertensive disorders of pregnancy.[3-5]

Mediterranean-style diet or DASH (low in salt, saturated fat, and alcohol; rich in potassium, whole grains, vegetables, and fruits), moderate physical activity, weight control within a healthy range, control of BP values since childhood, and absence of active or passive smoking, are essential in the prevention and initial treatment of hypertension.[3-5]

Pharmacological treatment is started with objective BP (blood pressure) values > 140/90 mmHg. It is necessary to discard secondary hypertension, mainly in adolescence and young adulthood. Antihypertensive drugs allowed during pregnancy are preferred, given the possibility of an unplanned one: alpha methyldopa, labetalol, and long acting nifedipine. Angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin II receptor blockers (ARB) are not recommended.[3-5]

Hypertension in menopause

The incidence of HBP is higher in menopausal women than in men, reaching a prevalence of up to 80% in older adults. Aging and estrogen decline production may trigger a decrease in endothelial nitric oxide and activation of the renin-angiotensin-aldosterone system (RAAS), endothelin, and the sympathetic autonomic nervous system, as vasoconstrictor mechanisms that generate endothelial dysfunction.[3-5]

Hypertensive women develop more isolated systolic hypertension, white coat hypertension, left ventricular hypertrophy (LVH), diastolic dysfunction, heart failure (HF) with preserved ejection fraction, increased arterial stiffness, and chronic kidney disease.[3-5]

The diagnosis, management, and proposed goals in postmenopausal hypertensive women are similar between the genders. For treatment, ACE inhibitors and ARBs are an acceptable option, given the excessive activity of the RAAS in menopause. It must be consider the pharmacodynamic and pharmacokinetic differences that cause more cough with ACE inhibitors, more cramps with thiazide diuretics, and more edema in the lower limbs with calcium blockers.[3-5]

* Hypertension and Cardiovascular Risk Clinic, ISSSTESON. Hermosillo, Sonora, Mexico.
‡ Hospital Presidente Perón de Avellaneda. University Hospital Favaloro Foundation Belgrano Adventist Clinic. Buenos Aires, Argentina.
§ Centro Médico Ambulatorio Cañavera Ibañez Cardiólogos. Montería, Colombia.
¶ Chief of Cardiology Service, Hospital Montes de Oca. Lujan, Buenos Aires, Argentina.
‖ University Hospital San Juan de Dios Santa Cruz, Bolivia.
** Caja de Salud de la Banca Privada. Sucre, Bolivia.

How to cite: Ruiz-Gastélum E, Christen AI, Ibañez MA, Romera M, Castedo-Verdura RL, Alurralde-Saavedra HI. Current impact of traditional risk factors in women. Cardiovasc Metab Sci. 2022; 33 (s5): s492-s496. https://dx.doi.org/10.35366/108063

Dyslipidemias

Various studies demonstrate the correlation between alterations in lipid levels and cardiovascular risk (CVR) in women. Despite this, many women are not aware of their lipid values. This risk factor must be recognized, particularly in postmenopausal women, since it modifies the lipid profile, raising the low-density lipoprotein (LDL-C) concentration by 10-15%. Total cholesterol (TC), triglycerides, and lipoprotein (a) also increase, with a significant decrease in high-density lipoproteins (HDL-C) being observed. The increased atherogenic lipid fractions increment the risk of CVD. Screening for hypothyroidism, a frequent cause of secondary dyslipidemia, is advisable.[6-8]

In pre-menopause, women are protected by endogenous estrogens through their vasodilator action, but the protective effect only delays the onset of CVD for a decade. Even more alarming is that a smaller proportion reaches the established goals of the main current guidelines since they are treated less vigorously than men and have less pharmacological adherence.[6-8] The reduction of CVD in primary and secondary prevention, with statins, has been demonstrated; although the impact is less

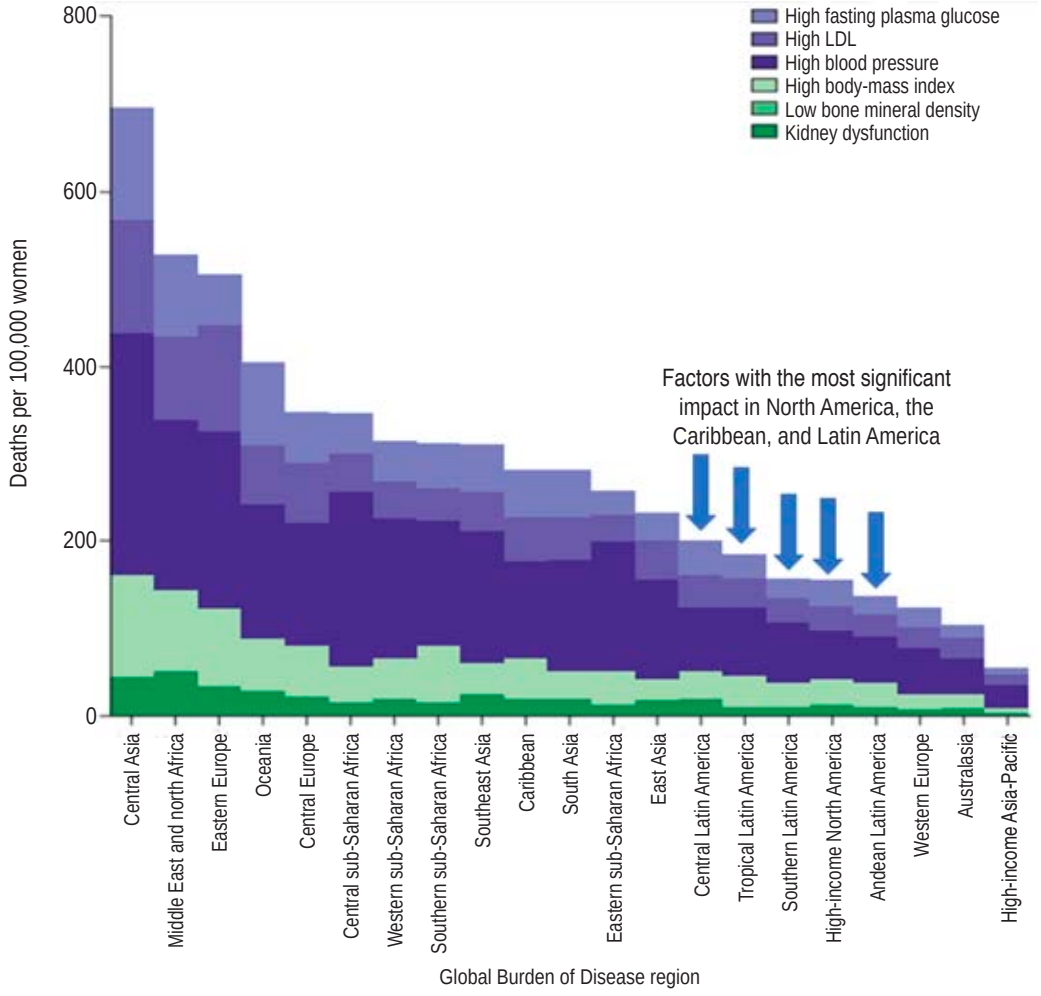

Figure 1: Metabolic risk factors contributing to age-standardized deaths from cardiovascular disease per 100,000 women across all global burden of disease regions in 2019.
Adapted from: Institute for Health Metrics and Evaluation. GBD 2019. Deaths per 100,000-females, age-standardized, 2019. http://ihmeuw.org/5g2x (accessed April 1, 2021).

Table 1: Desirable target goals for cardiovascular risk factors in women.

CVRF	Goal	Considerations in women
Hypertension	Optimal: < 120/80 mmHg Normal: 120-129/80-84 mmHg High normal: 130-139/85-89 mmHg Grade 1 hypertension: 140-159/90-99 mmHg	Rule out secondaries in young people of childbearing age: renal parenchymal disease renovascular (muscular fibrodysplasia), hyperaldosteronism, hypothyroidism, oral contraceptives, illicit drugs, herbal products, pheochromocytoma, coarctation of the aorta, Turner syndrome, Takayasu's arteritis, systemic lupus erythematosus, rheumatic diseases, preeclampsia predisposes to the development of hypertension in the long term. Higher prevalence in postmenopausal women More isolated systolic hypertension More white coat hypertension More left ventricular hypertrophy More adverse effects with some antihypertensives Different drug bioavailability
Dyslipidemia	Primary objective LDL- Very high risk < 55 mg/dL High risk < 70 mg/dL Moderate risk < 100 mg/dL Low risk < 115 mg/dL Secondary objective is non-HDL-C+ Very high risk < 85 mg/dL High risk < 100 mg/dL Moderate risk < 130 mg/dL Low risk not established + non-HDL cholesterol, can be the primary target when the triglyceride level is > 400 mg/dL Serum triglycerides are not a control target	Determination of the lipid profile, particularly in menopause, due to the increased cardiovascular risk Integrate the determination of the thyroid profile (the most frequent cause of secondary dyslipidemia) The scope of goals is lower in women, and also the prescription of lipid-lowering therapies Female gender is a possible risk factor for more side effects Hypolipidemic therapy is not recommended during pregnancy and lactation
Diabetes mellitus	ADA HgA1c < 7% ASA DM who are at increased risk of CVD CAC/AHA HgA1c < 7% ASA There are no specific recommendations for DM CES HgA1c < 7% and < 6.5%, if it can be achieved without hypoglycemia (less stringent in elderly patients) ASA only in very high risk/high risk	Increased CVD risk in women and increased risk of CVD mortality Screening for CV risk 3 months after delivery. Vigilance: in weight changes every 6 to 12 months. Girls have higher rates of DM In youth: increased insulin resistance early childhood to puberty; increases incidence of congestive heart failure and mortality

in women, in primary prevention (16% versus 22% in men), the benefit is significant. However, one problem is the underrepresentation of women in controlled trials, leading to poor statistical power in the results.[6-8]

The guidelines establish that women should receive statins at the maximum tolerated dose; if the goal set by the risk category is not reached, considering the combination with ezetimibe and, in specific scenarios, monoclonal antibodies.[6-8]

It is essential to adopt healthy habits, especially in menopause, dietary-nutritional management, avoiding saturated fats, and having moderate physical activity.[6-8]

The female sex is described as a condition that favors myopathies, but this should not limit exercise prescription.[6-8]

Diabetes mellitus (DM)

DM is one of the causes of the highest morbidity and mortality in the world. The International Diabetes Federation estimates that 1 in 11 adults have diabetes, while 1 in three have glucose intolerance, with type 2 DM (DM2) being the most common. There are differences throughout the life of women, with high rates in youth; men have it more in middle age, and it is similar for both sexes in older ages. There is an increased risk of CV mort in women with DM compared to men. In addition to atherosclerotic events, there is an increased incidence of congestive HF. Early onset of DM in young women translates into a longer duration of the disease throughout their lives and significantly increased mortality in women under 40 years of age.[7-9]

The basis of the treatment is an intervention towards a healthy lifestyle focused on weight loss, physical activity, and pharmacological treatment. Meta-analysis (2019) shows diabetic women with higher CV mort due to coronary heart disease and stroke due to insulin resistance, which begins after birth.[7-9]

Some sex-specific effects in pharmacotherapy for DM: GLP1, similar to glucagon, have lower glycemic control in women but more significant weight loss; thiazolidinediones have a better glycemic reduction in obese women.[7-9]

The EMPA-REG study showed a reduction in CV mort in patients with DM treated with empagliflozin. All patients with DM require aggressive RF reduction. There are no specific recommendations in the guidelines for preventing or treating DM related to sex; they recommend aggressive control of lipids and anti-aggregators only in patients with high CVR.[7-9]

CONCLUSIONS

The recognition, control, and treatment of CVRFs in women are still poor, and they are not treated aggressively enough. Therefore, an individualized approach to these CVRFs is necessary to reduce the excessive burden of CVD in women.[10]

REFERENCES

1. Vogel B, Acevedo M, Appelman Y, Bairey Merz CN, Chieffo A, Figtree GA et al The Lancet women and cardiovascular disease commission: reducing the global burden by 2030. Lancet. 2021; 397: 2385-2438.
2. García M, Mulvagh SL, Merz CNB, Buring JE, Manson JAE. Cardiovascular disease in women. Clinical perspectives. Circ Res. 2016; 118: 1273-1293.
3. Wenger NK, Arnold A, Merz CNB, Cooper-DeHoff RM, Ferdinand KC, Fleg JL et al. Hypertension across a woman's life cycle. J Am Coll Cardiol. 2018; 71: 1797-1813.
4. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M et al. Guía ESC/ESH 2018 sobre el diagnóstico y tratamiento de la hipertensión arterial. Grupo de Trabajo de la Sociedad Europea de Cardiología (ESC) y la European Society of Hypertension (ESH) sobre el diagnóstico y tratamiento de la hipertensión arterial. Rev Esp Cardiol. 2019; 72: 160e-178e.
5. Volberg VI, Rubilar BA, Aquieri A, Giorgini JC, Seijo M, Álvarez JM et al. Consenso de enfermedad cardiovascular en la mujer. Sociedad Argentina de Cardiología. Rev Argent Cardiol. 2021; 89 (Supl 5): 1-191.
6. Cholesterol Treatment Trialists' (CTT) Collaboration, Fulcher J, O'Connell R, Voysey M, Emberson J, Blackwell L et al. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. Lancet. 2015; 385 (9976): 1397-1405.
7. Del-Sueldo MA, Mendonca-Rivera MA, Sánchez-Zambrano MB, Zilberman J, Múnera-Echeverri AG, Paniagua M et al. Guía de práctica clínica de la Sociedad Interamericana de Cardiología sobre prevención primaria de enfermedad cardiovascular en la mujer. Arch Cardiol Mex. 2022; 92: 1-68.
8. Cho L, Davis M, Elgendy I, Epps K, Lindley KJ, Mehta PK et al. Summary of updated recommendations

for primary prevention of cardiovascular disease in women. J Am Coll Cardiol. 2020; 75 (20): 2602-2618.
9. Huebschmann AG, Huxley RR, Kohrt WM, Zeitler P, Regensteiner JG, Reusch JEB et al. Sex differences in the burden of type 2 diabetes and cardiovascular risk across the life course. Diabetologia. 2019; 62: 1761-1772.
10. Regensteiner JG, Reusch JEB. Sex differences in cardiovascular consequences of hypertension, obesity, and diabetes: JACC Focus Seminar 4/7. J Am Coll Cardiol. 2022; 79 (15): 1492-1505.

Correspondence:
Edith Ruiz-Gastélum
E-mail: edithdruizg@hotmail.com