Cardiovascular and Metabolic Science www.ancam.org.mx

Chapter 15

Vol. 33 Supplement 5
October-December2022

doi: 10.35366/108056

Heart failure in women

Insuficiencia cardiaca en la mujer

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INTRODUCTION

Heart failure (HF) is a global pandemic, affecting 26 million people in 2017.[1] In 2019, about 6.5 million were diagnosed with HF in the United States, 3.6 million (55.4%) were women.[2] Despite advances in treatment, morbidity and mortality remain high.

In Latin America, the incidence of HF is 199/100,000 person-years; it is the leading cause of hospitalization and re-hospitalization after three months.[1,2]

It is a clinical syndrome with cardinal symptoms (dyspnea, fatigue) accompanied by signs (pulmonary crackling rales, systemic edema). It is due to a structural and/or functional abnormality of the heart that causes elevated intracardiac pressures and or inadequate cardiac output at rest and or during exercise.[3-5] It is due to myocardial dysfunction (systolic, diastolic, or both), and the pathology of valves, pericardium, endocardium, alterations of cardiac rhythm, and conduction abnormalities can cause or contribute to its occurrence.[3-5]

Identification of the etiology of the underlying cardiac dysfunction is mandatory in the diagnosis of HF since the specific pathology may determine subsequent treatment.[3-5]

It presents in different phenotypes, depending on the measurement of the left ventricular ejection fraction (LVEF): a) with reduced LVEF (HFrEF) ≤ 40%; b) with mid-range LVEF (HFmEF) 41-49%; c) with preserved LVEF (HFpEF) 40-50%.[3-5]

Due to geographic, economic, and cultural diversity and different health protocols, the causes of HF are heterogeneous between countries. In South America, Chagas disease and rheumatic valve disease are frequent causes.[1,2]

Differences at the cellular level that impact the phenotype in men and women have recently been identified. Women have estrogen-dependent changes in the transcription of messenger RNA, which means that the mitochondria behave differently from men, more resistant to changes in pressure overload and oxidative processes.[6]

HF is more prevalent in men and determines higher mortality in women. Phenotypically, men have more HFrEF, while the incidence of HFpEF is almost three times higher in women. Women may have HFrEF from specific causes such as peripartum cardiomyopathy, cardiotoxicity, or *tako-tsubo*.[7,8]

PATHOPHYSIOLOGY OF HEART FAILURE IN WOMEN

The pathophysiology of HF in women is complex and is related to many intrinsic and extrinsic factors.[7,8]

Women usually have a smaller, stiffer ventricle, and under stress conditions, they develop concentric hypertrophy, and to maintain the filling volume, they need a higher heart rate at rest.[6] Despite this, and thanks to the estrogenic effect, it has less fibrosis, and the myocytes have a lower tendency to apoptosis, so the presentation of symptoms due to HF is later.[6] When women reach menopause, the protective estrogenic effect is lost. Because of the hypertrophy induced by pressure overload and a more significant increase in

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How to cite: Delgado P, Rosales C, Rota A. Heart failure in women. Cardiovasc Metab Sci. 2022; 33 (s5): s471-s473. https://dx.doi.org/10.35366/108056

end-diastolic pressure, they can develop HF symptoms[6] *(Figure 1)*.

When the level of estrogens falls, occur greater activation of the renin-angiotensin-aldosterone system, more arterial stiffness, and added to specific biological factors and risk factors such as high blood pressure (HBP), endothelial dysfunction appears, with less availability of nitric oxide, increased collagen synthesis, microvascular dysfunction, and fibrosis. Therefore, LV diastolic dysfunction and HF symptoms develop. More than 50% of patients have five or more comorbidities. In women, HBP, obesity, and diabetes occupy a relevant role.[6-8]

DIAGNOSIS

HF is diagnosed as a syndrome with symptoms and signs corroborated by elevated concentrations of natriuretic peptide, NTproBNP.[3-5] Laboratory tests and an electrocardiogram should be added. Transthoracic echocardiography (TTE) remains the gold standard for determining structural changes and LVEF. LVEF stratification is necessary due to different prognoses and therapeutic responses.[3-5]

The NYHA classification is used to characterize symptoms and functional capacity along with a 6-minute walk. The Kansas test is necessary for follow-up, evaluating the quality of life, and prognosis. Cardiac MRI, computed tomography, and radionuclide imaging also assesses LVEF.[3-5]

Noninvasive stress imaging (stress echocardiography, single photon emission computed tomography, and positron emission tomography for detecting myocardial ischemia) is used to guide invasive investigation and coronary revascularization.[3-5]

Coronary angiography and hemodynamics, with the measure of filling pressures or end-diastolic pressures of the LV, pulmonary artery pressures, systolic volumes, and cardiac output, can contribute to the etiological diagnosis.[3-5]

TREATMENT

Several recent clinical trials have provided treatments with better results for patients with HF, introducing inhibitors of the sodium-glucose cotransporter 2 (iSGLT2) and angiotensin receptor-neprilysin inhibitors (ARNI).[3-5]

Therapeutics in HFrEF include four classes of drugs: a) iSGLT2; b) ARNI, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor antagonists (AIIRAs); c) beta-blockers (BB) and d) mineralocorticoid receptor antagonists (MRA), all with indication

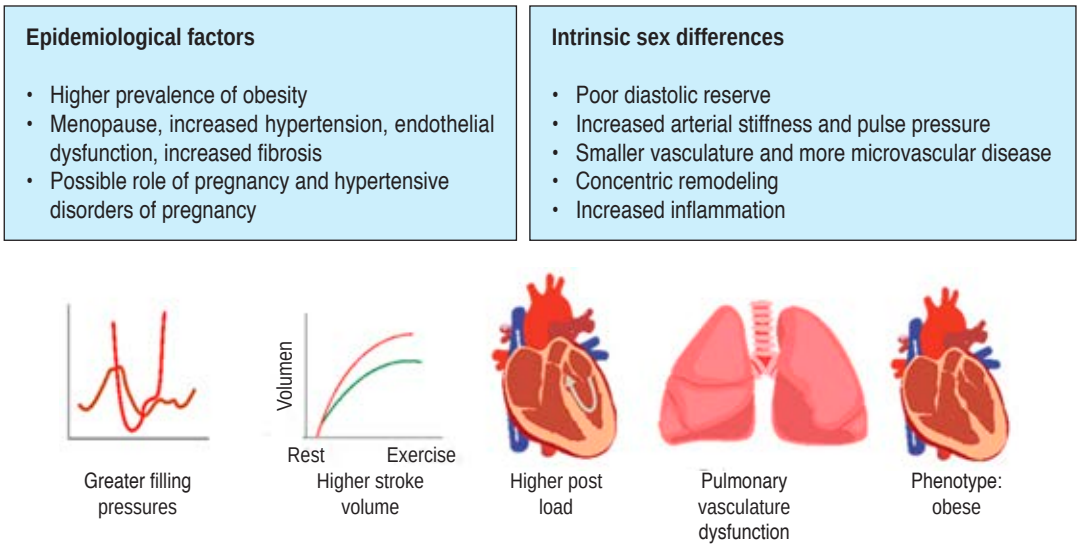

Figure 1: Epidemiological factors and by sex in heart failure.
Adapted: Lam CS et al.[6]

I-A.[3-5] Patients with improved HFrEF should maintain drug treatment.[3-5]

In patients with HFrEF, SGLT2 inhibitors have IIa recommendation, and those used in HFrEF (ACEI-ARB-ARNI; MRA and BB) have IIb indication.[3-5]

In patients with HFpEF, iSGLT2 have IIa indication; MRA and ARNI have IIb indication; BBs are not indicated in these patients.[3-5]

Women have been underrepresented in cardiovascular clinical trials, including those for HF, and there are no specific guidelines on treating HF in women.[3-5,9,10]

Thus, it is necessary to expand the involvement of women in clinical trials on HF so that the treatments with the best results in them become part of the specific guidelines.

CONCLUSION

HF mortality rates are higher in women, and the prevalence is higher in men. In addition, men have more modalities of HFrEF, while women have more HFpEF than the former. HBP is the most common cause of HF in women and ischemic heart disease in men. Therefore, sex-specific studies (risk factors, pathophysiology, treatment) are necessary to allow even better results in patients with HF.

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