

REVIEW ARTICLE

Cardiovascular Disease in Latin American Women Gaps and opportunities

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GDMT: guideline-direct medical therapy; RVD: rheumatic valve disease; CR: cardiac rehabilitation; ICD: implantable cardioverter defibrillation; CRT: cardiac resynchronization. Source: prepared base on summary references 1 to 20.

Abstract

Cardiovascular disease (CVD) remains the leading cause of death in women. This review will address the known disparities in cardiovascular care concerning diagnosing and treating of heart disease in Latin American (LA) women. Gender-specific differences regarding the incidence, treatment, and outcomes of common cardiovascular pathology are increasingly recognized. Today, we identify that women have cardiovascular risk factors (CRFs), specifying the traditional, emerging,

unique, or sex-specific determinants and the social and biological determinants that play a leading role in the prevention of CVD. The purpose of this article is to review the literature on cardiovascular disease in LA women, focusing on ischemic heart disease (IHD), valve disease (VD), heart failure, and cardiac rehabilitation (CR), where disparities continue to affect outcomes. Understanding the unique cardiovascular risk profile and barriers to optimal treatment outcomes in women is imperative to eliminate the current disparities in CVD.

Keywords

Cardiovascular Diseases; Myocardial Ischemia; Women; Latin America.

Epidemiology

Cardiovascular diseases (CVD) continue to be the leading cause of death in women, representing approximately 35% of all female deaths worldwide,

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with 8.4 million deaths per year. Moreover, it was estimated that 275 million women around the world suffered from CVD, mainly affecting women in low- and middle-income countries in 2019.¹ The estimated global age-standardized prevalence is 6,402 cases x 100,000/inhabitants, with ischemic heart disease (IHD) being the leading cause of death from CVD around the world.^{1,2} According to the Pan American Health Organization (PAHO)², the five leading causes of death and loss of health in the Americas, 2000-2019 (general population) are: IHD (rate of 108.1 deaths per 100,000 inhabitants), cerebrovascular accident (ACV) (rate of 47.5 per 100,000), Alzheimer's and other dementias (rate 38.7 per 100,000), chronic obstructive pulmonary disease (COPD) (rate 37.5 per 100,000) and lower respiratory tract infections (rate 1.4 per 100,000). In the Americas, CVD mortality rates vary substantially in women² from one country to another, from a maximum in Haiti (451.2 deaths per 100,000 inhabitants) to a minimum in Peru (66.5 deaths per 100 000 inhabitants) (Figure 1). The burden of CVD continues to increase for almost all countries in the Region when comparing between 2000 and 2019. Further, IHD and stroke are the leading causes of mortality and have remained unchanged in the last two decades.^{1,2}

CVD being the main cause of death for women in the world,^{1,2} continues to be understudied, underrecognized, poorly diagnosed, inadequately managed, and underrepresented in most cardiovascular clinical trials with evidence of a worse prognosis in IHD, valvular diseases (VD), heart failure (CHF), and few referrals to cardiac rehabilitation (CR)^{1,3}

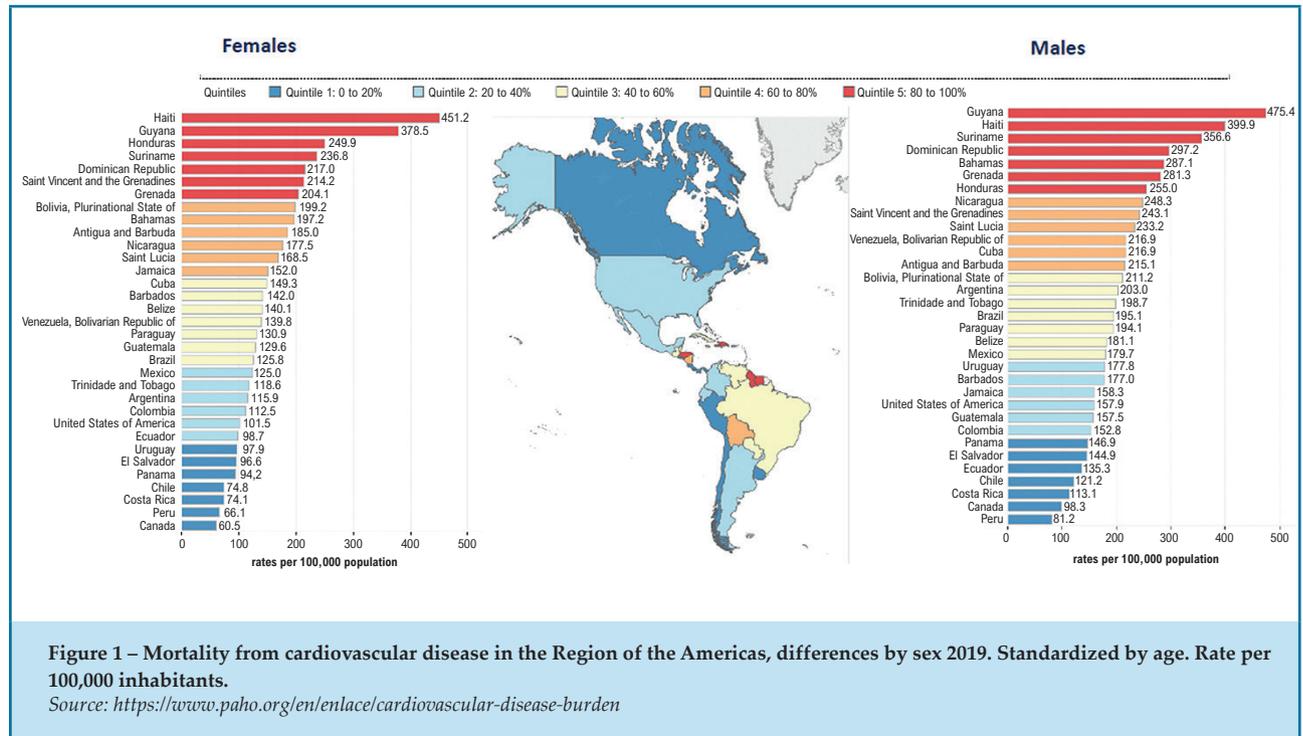
Cardiovascular Risk Factors (CRFs) in American women

Evidence is cumulative with increasing interest to identify differences in CVD in women from an epidemiological perspective, symptom presentation, diagnosis, access to the best treatment, and prognosis.⁵ Understanding the unique cardiovascular risk profile and barriers is imperative for achieving optimal treatment outcomes in women and eliminating current disparities.^{1,4} The recently published Inter-American Society of Cardiology (SIAC) Cardiovascular Prevention Guidelines in Women⁴ recognize the CRFs in women, specifying traditional, emerging, unique or sex-specific and the social and biological determinants that play a leading role in preventing of CVD. Early detection and management of well-established CRFs is essential to improve women's cardiovascular health and reduce early mortality.³⁻⁵

The traditional CRFs are well established and are, in fact, common in the general population. Although men and women share similar risk factors, some are more prevalent or pose a greater risk in women.^{3,4,6} Traditional CRFs include systemic arterial hypertension (HTN), dyslipidemia (DLP), overweight (OW) and obesity (OB), diabetes (DM), smoking, physical inactivity (a sedentary lifestyle), and metabolic syndrome (MS). There are also unconventional or emerging CRFs in which we include those factors that have different behavior in women, such as depression, stress, autoimmune diseases, and oncological treatment. Moreover, there are CRFs unique to women, such as the age of onset of menarche, polycystic ovarian syndrome (PCOS), premature ovarian insufficiency (POI), menopause premature (PNM), hormonal treatments: oral contraceptives (ACOS), hormone replacement therapy (HRT) or menopausal hormone therapy (MHT) and pregnancy complications: hypertensive disorders associated with pregnancy (THAE), gestational diabetes mellitus (GDM), preterm birth (PB) and newborn (NB) low weight.^{4,5} The evaluation of CRFs in women involves a multifactorial universe, sometimes with common characteristics for both sexes and other times with levels of association that are different or specific to the female sex, highlighting the importance of knowledge of these, early warning and measures of change in risk lifestyle or appropriate therapy.

Social and biological determinants such as psychosocial risk factors, intimate partner abuse and violence, socioeconomic deprivation, poor health literacy, environmental risk factors, poverty, malnutrition, migration, uncontrolled fertility, little or no health insurance coverage, health care infrastructure inadequate in remote areas, poor health literacy contribute to cardiovascular risk profiles.

In Latin America, the CARMELA⁵ study (Multiple Evaluation of CRFs in Latin America) documented a prevalence of HTN (18%), DLP(14%), DM (7%), SM (20%), OB (23%) and smoking (30%). The INTERHEART Latin American study found a higher risk of myocardial infarction in women than in men, associated with a higher waist-to-hip ratio, HTN, and DM.^{1,5} The Pure study⁶ recently showed that lipid markers and depression are more strongly associated with CRFs in men, while diet with CRFs in women in LA. In general, the highest proportion of CVD and premature deaths could be prevented by controlling metabolic CRFs and tobacco consumption, which are the main common risk factors for both sexes.^{4,6}



Coronary heart disease and cardiovascular intervention in Latin American women

LA is experiencing a large-scale epidemic of CVDs,^{2,3} related to a high prevalence of CRFs such as DM, HTN, OB, smoking, and DLP. Women have a significant risk of premature death from CVD, with a low perception of the importance of CVD, so they do not get the same coverage as breast cancer campaigns, leading to an underestimation of the magnitude of the problem.^{5,7} Fortunately, increasing attention is being paid to the analysis of differences between men and women in the pathophysiology, diagnosis, and prognosis of CVD.^{1,5}

CRFs are highly prevalent in women in LA,^{4,6,7} added to the identification of sex-specific factors such as PCOS, hypothalamic functional amenorrhea, early menopause, premature birth, preeclampsia, hypertension, and gestational DM. Women also suffer more frequently than men from autoimmune and inflammatory diseases such as lupus or rheumatoid arthritis, which has been shown to double CRFs.^{4,6,7}

The pathophysiology of acute coronary syndrome (ACS) in women is complex and multifaceted. Some presentations are associated with traditional CRFs, some with nontraditional CRFs, and some as the result of sex-specific risk enhancers.

Although progress has been made in early recognition and management strategies for ACS, gender-related differences in mortality continue to exist, and the reasons behind this phenomenon are complex.⁸ Almost half of ACS cases presenting to the emergency department are women, and the most common presentations are non-ST elevation ACS (NSTEMI) and unstable angina.^{8,9} Women develop CVD approximately 10 years later than men, with a mean age of presentation with ACS of 67-70 years and a greater probability of having comorbidities.⁸ Furthermore, female sex independently predicts frailty among elderly patients with ACS, and frail women have a high risk of death despite treatment for ACS. The presentation of ACS in women can manifest with non-specific symptoms such as weakness, respiratory distress or general malaise, leading to a low index of suspicion in the first approaches, which results in a later start of targeted management.^{8,9}

Female patients have a 20% higher risk of short-term mortality after percutaneous coronary intervention (PCI) compared to men, receive guideline-directed medical therapy less frequently, and sometimes receive less frequent intervention strategies based on diagnosis and revascularization.⁹ The risk of undergoing primary PCI recurrence appears to be higher among women over 65 years compared to men.^{8,9} Differences in prognoses after acute myocardial infarction between men and

women cannot be attributed solely to gender-related disparities but may be caused by intrinsic biological differences.^{8,9} For example, men tend to have a higher cardiac autonomic sympathetic activity, while women tend to have more significant parasympathetic activity. Plaque erosion appears to be the most common substrate of ACS in women, while plaque rupture is more likely in men. This could explain the distribution of types of IHD between sexes: women with lower rates of ST-elevation acute myocardial infarction (STEACS) but higher rates of NSTEMI and chronic coronary syndromes. However, in the case of STEACS, women are more likely to develop serious complications such as acute heart failure.^{9,10} Additional relevant considerations include a different impact of traditional CRFs such as smoking and DM, which disproportionately increase the risk of obstructive coronary disease in women.^{6,10} Likewise, HTN, which especially affects coronary microcirculation, has a predominantly impact on postmenopausal women due to the drop in estrogens, which play a protective role.⁹

Symptoms and signs of ischemia without obstructive disease in the epicardial coronary arteries, known as INOCA, are more common in women than men, with a higher prevalence among women aged 45–65 years.^{1,8,9} Although the pathophysiology of angina symptoms in INOCA remains poorly understood, it has been proposed that coronary microvascular dysfunction, or epicardial vessel spasm, or both, have central roles, where the women represent up to 70% of patients with coronary microvascular dysfunction. INOCA is not a benign condition and is associated with an increased risk for major adverse cardiovascular events^{8,9}

Although obstructive coronary artery disease with plaque rupture remains the predominant cause of ACS, an analysis reported an overall prevalence of 6–15% of patients with myocardial infarction with no evidence of obstructive coronary artery disease (MINOCA).^{1,8,9} This represents a condition that is caused by coronary mechanisms (e.g., coronary artery dissection, coronary spasm, and coronary emboli) or is mimicked by myocardial disorders (e.g., myocarditis, takotsubo syndrome, and other cardiomyopathies) or non-cardiac conditions (e.g., pulmonary embolism). MINOCA is more common in women than men (10.5% vs 3.4%; $p < 0.0001$), although outcomes are similar for both sexes. In women presenting with MINOCA, understanding the mechanisms of the underlying disease is essential in providing therapeutic options. There is an absence of data on the prevalence or incidence of LA.^{5,8}

Socioeconomic determinants also play a significant role in the burden and care gaps of CVD between men and women in LA.^{1–5} Acevedo et al,¹⁰ studied 620 women between 35 and 70 years in Chile, where they documented that the prevalence of ideal cardiovascular health was 14.3%, none of the women had a balanced diet, and only 22.6% had a healthy body mass index. A large proportion of women continue to have domestic work and family care roles, and fulfilling them can imply delays in seeking care, with evidence showing that women take an average of an hour longer to reach the hospital emergency room after the onset of symptoms.^{5–10}

Valve disease (VD) in Latin American women

VD has a prevalence of 2.5% in the general population, with an increase in degenerative etiologies in older adults.¹¹ The epidemiology of VD varies substantially throughout the world, with a predominance of functional and degenerative disease in high-income countries and RVD in low- and middle-income countries.

RVD is responsible for the most significant global burden of VD and is more common in women of all age groups. RVD causes 0.7 deaths per 100,000 inhabitants in the Region of the Americas, affecting a large sector of the population, explained by multiple factors, including low-income populations, limited access to health, and pathologies without prevention and treatment programs in the region.^{1,2} Prevalence is especially high among women, for whom the risk of developing RVD is 1.6–2.0 times higher than for men.^{1,2} Research attributes higher risk to socioeconomic and environmental factors (e.g. overcrowding) and sex-specific factors that include pregnancy, exposure to *S pyogenes* through childrearing, inadequate access to health care, and genetics.^{1,8,11,12} The effect of RVD disease on women is of paramount concern, especially among women in their childbearing years, in whom the morbidity and mortality burden is high. Pregnancy represents a critical period for women in the context of RVD. Analysis of data from the Global Rheumatic Heart Disease Registry showed that many women with RVD are young RVD, and 54.8% had mitral stenosis (MS), 49% had CHF, 27% had atrial fibrillation, 26% had pulmonary hypertension.^{1,11,12}

Women and men have the same probability of developing VD. In general, women have more mitral VDs, especially mitral valve prolapse and RVD, and men have more aortic VDs, such as aortic insufficiency (AI) and aortic stenosis (AS).^{11,12}

Mitral VD is more frequent in women.^{1,11} This can be of primary origin: rheumatic, valve prolapse (myxomatous degeneration, thickening of the valves), or secondary: due to alterations in the geometry of the left ventricle, due to IHD, or other dilated cardiomyopathies. Women have more CHF symptoms. Unfortunately, their condition is underestimated, and few patients are referred for intervention.¹² MS is also more common in women; its etiology could be rheumatic or degenerative and is associated with calcification of the mitral annulus in advanced age. A study¹² showed that women are affected significantly less or later by mitral surgery (repair/replacement). In degenerative etiologies, women are less frequently taken for repair (44 vs. 31.9%, $p = 0.001$), with slightly lower long-term survival. Women represented only 36% of patients in the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) study and 25% in MITRA-FR trial; they were younger but had a worse quality of life and functional capacity.^{1,12} TEER produced better clinical outcomes than medical therapy, regardless of gender. The reduction in CHF hospitalizations was less pronounced in women. Female sex is independently selected with a lower adjusted risk of death at two years (HR, 0.64; 95% CI, 0.46-0.90; $p = 0.011$). In MS, the treatment of choice is mitral valvuloplasty with a catheter and balloon, followed by valve surgery.^{11,12}

Men are at higher risk of developing AS. Women with AS have less valvular calcium but a more significant amount of fibrosis, are older at the time of disease presentation, and are in a worse functional class, with hypertrophic ventricles and better left ventricular ejection fraction (LVEF).^{1,11,12} AS is more common in men associated with bicuspid aorta. Women treated with surgical aortic valve replacement (SAVR) are older, have more advanced disease, and have high operative mortality. Female sex was an independent predictor of mortality.^{11,12} Furthermore, the results of transcatheter aortic valve implantation (TAVI) by sex do not show differences in implant success. The female sex is combined with an increase in vascular complications and major bleeding but with a lower incidence of paravalvular leak, pacemaker implantation, and better medium-term survival.^{1,11,12} The Latin American Clinical Guidelines on TAVI vs SAVR in patients with severe AS¹³ were recently published, and the most relevant conclusions of the study were to suggest performing TAVI instead of SAVR in patients over 75 years of age with AS living in LA and

who are candidates for a transfemoral approach. This recommendation is based on a moderate level of evidence and is conditional, meaning that, in some cases, surgery may be a better option.

Women with VD have been underrepresented in studies and tend to be diagnosed and referred for interventions late.^{1,4,12}

Heart Failure in Latin American Women

Data about Heart Failure (CHF) in LA is scarce. Few studies have evaluated the incidence and prevalence of CHF in LA. To date, the reported incidence of heart failure is 199 cases per 100000 person-years with a prevalence of 1%.⁵ Women living in LA are exposed to a mix of traditional CRFs for CHF, neglected diseases and social determinants of health.^{1,5} LA is currently facing a widespread epidemic of CRFs, and compared to other regions, Chagas' heart disease continues to be a burden in LA, and more data is needed about differences in prognosis. The highest incidence of Peripartum cardiomyopathy (PCM) in LA has been reported in Haiti, although more information is needed about this disease.^{1,2,5}

Women's Hearts differ considerably compared to men's hearts.^{1,7,14} These differences are structural and physiological. They have lower left ventricle mass, greater contractility, different apoptosis rates, smaller coronary vessels, higher resting heart rates, different responses to catecholamine, smaller vascular beds, and small bodies.^{7,13,14} Hormonal differences are presumed to alter the endothelial response to injury and different responses to the renin-angiotensin-aldosterone system. In consequence, some measures change; LVEF is higher in women than men with higher stroke volume for a given end-diastolic volume in smaller cavities.^{1,13} Biomarkers also have differences, including, for example, that the levels of the natriuretic peptides are higher in women than men.^{7,14}

Clinical presentations in CHF, talking about the syndrome (signs and symptoms), are mostly the same. However, women present different phenotypes in HF; reduced, mildly reduced, and preserved with a predominance of preserved phenotype (HFpEF).^{1,7,14} The situation with women is that they do not look for attention as men do; they are the caregivers. In fact, this predominance does not have a specific pathophysiological mechanism that explains sex differences in prevalence. However, some hypotheses

include chronic inflammation and microvascular dysfunction in women.¹⁴ Furthermore, traditional risk factors (OB, DM, HTN, and ICD) preferentially contribute to the development of HFpEF in women, and emerging data show that sex-specific risk factors including, early menopause, adverse pregnancy outcomes, and other reproductive factors, are also significant risk factors for HFpEF in women.^{1,3,4} There are other etiologies sex-specific, like CPM and probably cardiotoxicity, because of the predominance of the association with the treatment of breast cancer.^{1,5}

Concerning the medical management of CHF in women, we see that in every trial of CHF, the treatment has a low rate of enrolled women, between 14% and 45%, which has evidently been underrepresented.^{5,14} Reduced phenotype does not have specific differences in the response the guideline-directed medical therapy (GDMT). However, analyzing the preserved ejection fraction in clinical trials such as The Paragon trial, and The TopCat, there was a positive response in the women subgroup. TopCat Trial¹⁵ in post hoc analysis of non-pre-specified subgroup showed no differences in the rates of primary outcome and CHF hospitalization. Significant reduction in all-cause mortality with spironolactone in women (HR 0.66; 95%CI: 0.48–0.9; $p = 0.01$), but not in men, and sex-treatment interaction ($p = 0.024$). In Paragon Trial¹⁶, the hazard rate for the primary outcome was 0.73 (95% CI: 0.59–0.90) in women and 1.03 (95% CI: 0.84–1.25) in men with p interaction = 0.017, predominately related to CHF hospitalization (33% RRR, p interaction = 0.005). SGLT 2 did not show any difference between women and men in the rate of primary outcome and HF hospitalization.^{1,5,16}

In the context of devices, women receive fewer devices such as implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy (CRT) than men. Furthermore, a low rate of counseling from their treating physicians has been documented. CRT is associated with greater benefits in women than men.^{1,5,14} These benefits seem to be greater at a lower QRS duration of 130 milliseconds in women compared with 140 milliseconds in men.^{5,7} In an individual-level meta-analysis of MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy), RAFT (Resynchronization–Defibrillation for Ambulatory Heart Failure Trial), and REVERSE (Resynchronization reVERses Remodeling in Systolic Left Ventricular Dysfunction), there was a 76% reduction in HF or death (HR: 0.24; 95% CI: 0.11–0.53) from CRT-D

for women with no significant benefit in men at a QRS duration between 130 and 149 milliseconds; both women and men benefited from CRT-D with a QRS duration 150 milliseconds.^{5,14}

Other therapies like OHT (Orthotopic Heart Transplant) and temporary mechanical support (LVADs) seem to be scarcely offered to women. Only 25% account for OHT.¹⁷ Women who get into OHT groups are older and in the later stages of the disease, with more comorbidities, including allosensitization, pulmonary hypertension, OB, and malnutrition; possibly making them poor candidates for this therapy. Some papers suggested that there was an increase in mortality, bleeding, and cerebrovascular complications in women undergoing LVAD implantation. However, we must remember women's low enrollment, so these statements are inconclusive.¹⁴

Large registries have shown the benefit of LVADs in women, though with some reported differences. INTERMACS¹⁷ Registry demonstrated no difference by sex in mortality, bleeding, first infection, or dysfunction of the device (pulsatile or continuous); however, women had a shorter time to the first neurological event compared to men (HR 1.44). The REVIVAL Registry showed an additional burden in terms of physical limitation, reduction in a 6-minute walk, and depression in women compared to men without impacting the mortality, duration of mechanical support, and incidence of emergency transplantation.^{14,17}

CR in Latin American women

CR is defined as the set of activities aimed at improving the clinical, physical, and psychological state of patients suffering from CVD, such as ACS, CHF, patients undergoing cardiac surgeries, and patients with electrical devices, pacemakers, ICD or CRT, achieving a successful functional status in their families and adequate reintegration into society.^{18,19} This task involves physical training, control of CRFs, and psychosocial support by a multidisciplinary team. Current data available in the literature confirm that CR structured in secondary prevention programs, exercise training, health education, and counseling can reduce cardiovascular mortality. However, participation rates in CR are not only low for both men and women but also there is evidence of sex differences in access.¹⁹ CR has been shown to reduce cardiovascular mortality by at least 26%, this effect being more marked in women.¹⁸ Differences in the referral of patients for CR could be explained by

the older age of the women, the higher percentage of functional dependence, and the worse clinical outcomes upon admission. However, these erroneous beliefs must be overcome, since CR programs are helpful to improve clinical performance and functional status also in a sicker population of women.^{18,19} The benefits for women who participate in CR are similar to those for men and refer to improving functional capacity and control of CRFs. Prognosis in women with IHD has been strictly related to exercise capacity, and a 1 ml/kg/min improvement in VO₂ is associated with a 10% reduction in cardiac mortality.^{8,19}

Main barriers to CR in Latin American women

Despite high levels of CR recommendation, participation rates are very low, varying from 10 to 34%.¹⁸ Unfortunately, CR utilization is low among women. Demographic, socioeconomic, and social factors specific to women, as well as and barriers related to health systems and socio-environmental factors have been described. The Barriers to Cardiac Rehabilitation in Women study^{1,19} showed results from the first global evaluation of the International Council on Cardiovascular Prevention and Rehabilitation and concluded that limitations in access to CR programs are identified in LA due to restrictions in attending, limitations in transportation, family responsibilities, high cost and low level of referral.

Women with SCA tend to be older, with multiple comorbidities and on many occasions fulfill the role of family caregivers, or mothers as heads of the home, often causing collective needs and responsibilities to be prioritized before their individual health.^{1,19} Barriers related to medical care must also be considered, and solutions proposed by the actors, such as an easy referral to the rehabilitation program after an ACS or cardiac surgery, offering flexible schedules, increasing health coverage, prioritizing entry to CR must be implemented. Recently, After the COVID-19 pandemic, the option of tele-rehabilitation began to be worked on the cardiologists' knowledge of the program's benefits, the presence of a leading rehabilitation physician, and the experience of the rehabilitation center are also relevant for referral.^{18,19}

Gaps and Opportunities

In our region, there are critical disparities between different subgroups of women who are socially disadvantaged for reasons of race, ethnicity, income levels, and educational level. In addition, women are not adequately represented

in clinical studies, nor allowing the evaluation of all CRFs and their impact on cardiovascular health.⁵⁻⁸

Women are underrepresented in most clinical cardiovascular trials, creating a paucity of evidence of GDMT for female patients.²⁰ Women are far less likely than men to undergo advanced therapies, including PCI, coronary artery bypass grafting, valve replacement, or defibrillator implantation, LVAD implantation, or heart transplantation.⁷⁻¹⁹ Women are often referred late for invasive therapies, and they have more comorbidities and worse outcomes.^{1,3} Even though women appear to derive substantial survival benefits from advanced therapies, they are less likely to be referred for such therapies.⁷⁻¹⁹

Cardiac rehabilitation. There is an urgent need to address these widespread gaps in knowledge and care delivery to reduce sex/gender-based disparities and achieve equity.²⁰ To achieve this objective, it is necessary to promote advances in research, optimize the diagnosis, prevention and treatment of CVD in women with innovative solutions through the interdisciplinary participation of highly experienced, integrating related specialties such as gynecology and generating accurate work teams; raise awareness, empower and engage communities, to ensure access to healthcare and quality health for all.^{4,7,20} (Central Illustration).

In LA, we have major challenges to face. Women are particularly at risk of premature death from CVDs.^{1,2} Understanding the unique cardiovascular risk profile and barriers to optimal treatment outcomes in women is imperative to eliminate current disparities in CVDs. Non-traditional CRFs are not comparatively evaluated in the region and generate an unmet need in CVD research in women.²⁰

Approximately 1,125,000 women of reproductive age are infected with *Trypanosoma cruzi*, the parasite that causes Chagas disease. Screening women for Chagas disease during early reproductive age is an opportunity to prevent Chagas disease transmission and to reduce the risk of CVD complications associated during pregnancy.^{1,5}

Prevalence of RVD remains high in LA,^{1,2} and young women of childbearing age are disproportionately affected. Multidisciplinary cooperation combined with appropriate preconception counseling and antenatal care is crucial to reducing complications from rheumatic heart disease in pregnancy. It is essential to raise awareness about it and create political incentives to address RVD and its implications as part of an integrated rheumatic heart disease prevention and control program.^{1,20}

CR programs are well known for reducing mortality and rehospitalization rates and improving quality of life. A broad and complex variety of modifiable and non-modifiable barriers limit CR participation in women. New delivery models for CR, with flexible and personalized programs, including home-based and/or smartphone-based CR, appear to be promising approaches to help improve the delivery of CR to women.^{18,19}

Thus, this gap between men and women is framed in terms of the form of care presented and received in the case of CVD with an arsenal of CRFs and socioeconomic determinants in the process of being better defined and integrated into specific management routes and appropriate.¹⁻²⁰ Awareness campaigns, education of healthcare providers, and further sex-specific research are warranted to solve the real gender disparities that exist and contribute to elevated mortality rates for women with CVD.

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Conception and design of the research, acquisition of data, analysis and interpretation of the data, writing of

the manuscript and critical revision of the manuscript for intellectual content: Dueñas-Criado KA, Peña AH, Rodríguez-González MJ, Fajardo A.

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