

## The Challenge of Optimizing Cardiovascular Risk Stratification in Women

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Cardiovascular mortality (CVM) is the leading cause of death in developed countries. The same phenomenon can be observed in developing countries as Argentina, where CVM is well above that of cancer, the second cause of death. However, cardiovascular mortality rates (CVMR) have decreased significantly in both genders over the last 25 years, more prominently in men (-35%) than in women (-27%). (1) During the period 1995-2005, the reduction in mortality rates due to myocardial infarction (MI) and stroke was lower in women compared to men (-11.7% vs. -18.4%, and -33.8% vs. -41.1%, respectively). Although the trend is favorable for both genders, the magnitude of the reduction is smaller in women. Nowadays, one out of every three women still dies due to a cardiovascular disease in our environment, stroke and heart failure being more prevalent than coronary artery disease. (1-3)

In addition, the interpretation of the reasons contributing to this reduction in CVM has been subject to debate: in the United States, approximately 50% of decreased mortality has been attributed to adequate control of the main risk-factors, and the other 50% to changes in medical treatment, particularly in the use of initial treatments for AMI including secondary prevention. An updated version of the IMPACT mortality model, which was previously validated in Europe, New Zealand, and China, was used. (4) The availability of national information would be extremely important for a deeper analysis to plan and ensure continuous monitoring of prevention strategies.

The myth of considering cardiovascular disease (CVD) as men's illness has been overcome in the USA as well as in other societies. Awareness of CVD as the leading cause of death among women has increased from 30% in 1997 to 54% in surveys conducted in 2009. (5) The results of a survey performed in our country including 600 women between 25 and 70 years demonstrated that only 20% of them identified cardiovascular disease as the leading cause of death, yet 53.8%

was sure that cancer in general or breast cancer in particular were the leading causes of death. (6) However, a recent investigation including 601 women between 35 and 65 years revealed that when asked about the representations of coronary artery vulnerability, 41.8% of survey respondents put coronary artery disease in the first place of major risk of death, followed by cervical cancer (33%) and breast cancer (24.5%). This might reflect an evolution in the awareness of coronary artery disease risk. (7)

The dramatic rise in CVM due to all causes of cardiovascular disease in women > 65 years may be probably influenced by the increasing prevalence of the main risk factors, particularly after menopause. In general, as women are older and have more concomitant diseases, when they present cardiovascular disease, the risk of cardiovascular morbidity and mortality has greater impact. The 2005 National Risk Factor Survey (NRFS) demonstrated lower physical activity in women compared to men, and these percentages increased nationwide in the 2009 NRFS (47% vs. 58.5%). (8, 9) The prevalence of obesity (13.9% vs. 17.1%), hypertension (25.3% vs. 35.9%) and high cholesterol levels (27.8% vs. 28.7%), also increased while smoking habits and diabetes decreased (24.9% vs. 22.4% and 11.5% vs. 10.2%, respectively). The adverse trend of conventional risk factors is still a matter of significant concern. Other factors, particularly those prevalent in women as depression or psychosocial factors should be considered due to their impact on cardiovascular disease and on adherence to treatment.

A broad consensus exists about the limitations of the traditional risk scores, as the Framingham Risk Score. These limitations include the narrow focus of considering only the 10-year risk of having a myocardial infarction or coronary death, which underestimates risk, and the fact that subclinical cardiovascular disease may have a relatively high prevalence in women classified as of low risk. (10-12) In women < 75 years, even with diverse risk factors, the 10-year

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risk of coronary artery disease is commonly estimated as less than 10% by the traditional scores. Therefore, few women would qualify for implementing more aggressive strategies for the prevention of cardiovascular disease.

In this setting, the article by Masson et al. published in this issue of the Journal is attractive, as it tries to improve the precision of the two risk scores considered in the analysis: the 10-year Framingham risk score used by the Third Report of the Expert Panel of the National Cholesterol Education Program (NCEP) on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) and the World Health Organization score (WHOS) for Argentina. (13) In this case, the authors defined the presence of subclinical atherosclerosis by the detection of carotid artery plaque (CAP) using ultrasound examination of the carotid arteries in order to determine its power of reclassification in another risk category. The prevalence of CAP was of 29%, consistent with previous publications. (14-16) Interestingly, approximately one third of women considered as having low risk by both scores presented CAP. This finding represents a higher level of atherosclerosis, implying a defined atherosclerotic process with inflammatory and proliferative components. The authors found that the optimal cutoff point of the Framingham risk score  $\geq 3$  could discriminate the presence of CAP with acceptable sensitivity, specificity and negative predictive power and reclassify patients in a different risk category than the one they previously had. In a recent review, Peters describes that the presence of CAP reclassifies patients and increases the intermediate predictive value compared to coronary artery calcium scoring (greater value) and intima-media thickness (lower value). (17)

As the authors mentioned, incorporation of markers of preclinical disease might allow making decisions about the depth and magnitude of the prevention strategy. Recent analyses of clinical trials considering lower cutoff points to define cardiovascular risk suggest that treatment with statins appears to be cost-effective and might save costs. (18)

Further research in asymptomatic female patients is needed to quantify the cost-effectiveness ratio and the impact of imaging for the detection of subclinical atherosclerosis on the management of cardiovascular risk factors and their clinical implications.

The ideal risk maker, either a biomarker or an imaging study, does not exist. This marker should have good discriminatory and reclassification power, as well as being economical and applicable to large populations. Meanwhile, the sensible use of technology could help to discriminate cardiovascular risk in women, in whom cardiovascular disease still represents the leading health problem in developed and developing countries.

#### Conflicts of interest

None declared

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#### **EXPLANATORY NOTE ABOUT THE AUTHORSHIP OF AN ORIGINAL ARTICLE**

In the original article “Correlation Between CHA<sub>2</sub>DS<sub>2</sub>-VASc Score and Atrial Thrombus in Patients with Atrial Fibrillation Undergoing Cardioversion” published in the 2013 April issue of the *Argentine Journal of Cardiology* [Rev Argent Cardiol;81(2):144-50] that received the XXXVIII Argentine Congress of Cardiology Award, the name of one of the authors, Dr. Elio D. Barrera, was omitted.

The order of the list of authors is then as follows: “Norberto G. Allende, Elio D. Barrera, Carlos Rodríguez Pagani, Eduardo Carrasco, Gerardo Marambio, Guillermo López Soutric, Federico Cintora, Fanny Calvo, Ricardo Pérez de la Hoz”