
Coronary heart disease in women. Past gaps and current understanding

Giuseppe Mercurio, Giuseppe M.C. Rosano*

*Department of Cardiovascular Sciences, University of Cagliari, Cagliari, *Department of Internal Medicine, San Raffaele-Tosinvest Sanità, Rome, Italy*

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Address:

Prof. Giuseppe Mercurio
Dipartimento di Scienze
Cardiovascolari
Università degli Studi
di Cagliari
S.S. 554, bivio di Sestu
09042 Monserrato (CA)
E-mail:
mercurio@pacs.unica.it

Women live longer than men, making up the majority of the population of older individuals, which, in turn, is growing rapidly thanks to the increase of longevity. This is the reason why the elucidation of health issues related to older women is important and pressing.

Cardiovascular disease, primarily the atherosclerotic coronary heart disease (CHD), is the leading cause of death in women and kills more than the next 14 causes of death combined¹. Despite its proportions, there is a well-established assumption that heart disease is a man's disease and most women believe they will die of cancer, especially breast cancer. The substantial underestimation of the problem prompted the paradoxical allegation that "perhaps the most important risk factor for CHD in women is the misperception that CHD is not a woman's disease"².

As for CHD, a large epidemiological disparity exists between the female and male genders. The incidence of the disease is significantly lower in premenopausal women in comparison with men, but it increases dramatically with age, reaching almost the same frequency in the two sexes between 75 and 80 years of age. This difference was incorrectly ascribed in the past to harmful behaviors of the male sex – including smoking and incorrect eating habits –, rather than to physiological sex differences. More recently, as it became clearer that these socially determined unhealthy behaviors are not sufficiently explanatory for the higher risk of CHD in men, this misconception was reviewed, but it still retains serious negative influences on all aspects of management and outcome of CHD.

The origin of the gender gap with regard to CHD represents one of the most interest-

ing epidemiological questions. Women share with men the same risk factors for CHD, that is age, family history, smoking, hypertension, lipoproteins, and diabetes mellitus, even though with a different relative importance; but some factors, for instance the cessation of the reproductive status, are unique for women. Negative effects of menopause include unfavorable changes in metabolic parameters and circulatory control. It has been suggested that these changes result from a reduction in the level of estrogen³.

Over the past years remarkable progress has been made concerning our knowledge of cardiovascular risk factors related to gender: some of these, such as diabetes, high-density lipoprotein and triglyceride levels, seem to have a greater impact on CHD in women compared to men. Moreover, a higher incidence of systemic hypertension, and a positive family history were noticed in women. For optimal assessment and management of CHD we should further improve our consciousness of the differential impact that cardiovascular risk factors might have on men and women. At the moment, most strategies for coronary risk factor prevention are similar for both sexes. Indeed, the magnitude of the effect of some factors differs between men and women; consequently preventive interventions should be unique to women. For instance, diabetes and hypertension are cumulative risk factors and particularly noxious in the female gender in triggering CHD and stroke. Therefore, their early detection is mandatory, as well as a more intensive therapy to prevent the acute vascular consequences.

Frequently, the first presenting symptom of CHD in women is angina pectoris,

whereas in man an acute myocardial infarction (AMI), either symptomatic or silent, is more recurrent. A large number of factors influence the evaluation of this symptom in women, including the physician's perception of the likelihood of the disease. Pain at rest is more frequent in women than men, and it appears during mental stress or sleep. Very often the typical chest pain irradiates to jaw, back, or neck, or rather is flanked or replaced by nausea and palpitation⁴. In women, also nausea and dizziness are common alarming indicators of myocardial ischemia. Other symptoms include breathlessness, perspiration, and fullness in the chest⁵.

The reasons for these differences in symptoms are, at least in part, justified by identifiable, gender-related mechanisms. Women show a higher prevalence of vasospastic and microvascular angina⁶, associated with atypical chest pain. On the other hand, the female patients display differences inherent to gender in regard with plaque composition, endothelial function, and hemostasis, that are liable for specific physiologic responses, and also for the characteristic clinical manifestations⁷. Indeed, women suffering from chronic angina are usually older than men, and have a higher probability of co-morbidities and worse clinical characteristics, such as older age, hypertension, diabetes, and heart failure⁸.

The aforementioned gender differences in clinical appearance emphasize the need of good history taking, and careful cardiovascular risk factor assessment in the evaluation of women with chest pain.

Although women with chest pain are less likely to experience a subsequent AMI, either fatal or not⁹, women and men with exertional chest pain have the same relative risk of coronary death¹⁰. Another evidence that shows how the prognosis of CHD is not more favorable in women includes the early mortality after AMI comparable with that of men, if not worse¹¹. A not very recent study had provided an alarming picture in this respect¹², maintaining that survival chances were reduced in women with AMI, both in hospital and after discharge, as they were deprived of the same opportunities granted to men in terms of disease assessment and therapeutic intervention. From the study, it could be observed that women with AMI: reached the hospital in a longer time, were less easily admitted to the coronary care unit and to the thrombolytic treatment, and showed more severe AMI, with higher Killip classes and a slightly higher mortality during admission. Finally, they received less secondary prophylaxis in terms of beta-blockers or aspirin upon discharge. The situation has not changed much after about a decade, as the established drugs for secondary prevention – lipid-lowering drugs along with those already quoted – are still underused, especially, and this is paradoxical, in female patients at highest risk¹³.

The recent advance of percutaneous transluminal coronary angioplasty (PTCA) and its application to female specific problems is an example of how gender-

related limits can be overruled. A minor success rate of PTCA, a higher in-hospital mortality, and many more adverse events were observed in the past¹⁴. Atherosclerosis in women starts during the menopausal period and grows rapidly, unlike in men, where the process takes several decades to develop; the resulting different composition probably makes the plaques unstable, more prone to rupture and to dissect during PTCA¹⁵. The introduction of new generation stents has improved its immediate outcome, making PTCA a very safe procedure also in women^{16,17}.

Therefore, the association between skillful operators, who are well aware of the particular problems of PTCA in women and technological developments (i.e. stents with low profile and higher tractability and pushability, suitable for the smaller and more tortuous female vessels) minimized the worse baseline higher risk profile (older age, hypertension, more diabetes, higher risk for thrombotic complication), as well as the possible influence of genetic, gender-related risk factors.

In conclusion, the peculiarities of clinical presentation of CHD in women make the evaluation of a new symptom more complex and require a gender-based diagnostic approach, much more accurate and individualized, to women suspected for CHD. In addition, awareness of the higher morbidity and mortality in women dictates the need for early detection and more aggressive therapy of the risk factors. Although advantages from proven effective therapies appear in both short- and longer-term outcomes, there is evidence that subjects with suspected or established cardiovascular disease do not benefit fully from recent advances in the detection and management of CHD. The risk is that, in a time of increased emphasis on coronary preventive strategies, improvement in the prompt evaluation of chest pain syndromes, and increase in the performance of myocardial revascularization, the likelihood of CHD presence in women is underestimated. In this case, it is unlikely that women be persuaded to correct their own lifestyle, as well as, in case of symptoms, to perceive that their own life is at stake. Similarly, the cardiologist is induced to neglect the risk assessment and to pursue an aggressive treatment of CHD, once this is detected.

Cardiovascular disease mortality rates have decreased in men during the past 20 years, but have steadily increased in women. To avoid a further increase, to which the predicted extension of diabetes will contribute, it is mandatory that patients, physicians and public opinion hurry up in the recognition and management of CHD in the female sex. Data regarding women and CHD, however sometimes conflicting, are rapidly evolving.

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