

# Sex and cardiovascular disease



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For many years, cardiovascular disease was considered a male disease. Consequently, common data of registries, clinical trials and the like, were all reported for the entire patient population and only until recently has it become mandatory to report data on males and females separately. Indeed, the evidence for sex differences between females and males in disease mechanisms, clinical presentation and natural history of cardiovascular diseases, as well as the response to medical [1] and interventional treatment strategies is overwhelming [2]. For instance, women bleed more when using oral anticoagulants than men do [3]. In addition, male and female hearts do differ, not only in size and structure, but also in the disease phenotypes of different forms of cardiac conditions [4]. Furthermore, the prevalence of risk factors and risk modulators differ between sexes, with co-morbidities like rheumatoid arthritis and other autoimmune diseases being more frequent in females [5].

Of note, female patients tend to develop heart failure with preserved ejection fraction, while males are more likely to suffer from ischaemic cardiomyopathies or heart failure with reduced ejection fraction (fig. 1, online appendix) [6–8]. Comorbidities, such as arterial hypertension and diabetes mellitus are very common in elderly females, while in males, smoking and hyperlipidaemia are more common. Besides, while myocardial infarction has been considered primarily a male disease, it is now clear that about a third of patients with acute coronary syndromes (ACS) are female [9]. Importantly, in ACS, females tend to present with atypical chest pain, present later to the emergency units than males do and more often have myocardial infarction with non-obstructive coronary artery disease. Finally, there are distinct acute cardiac conditions, primarily occurring in females, such as Takotsubo Syndrome [10], as well as spontaneous coronary artery dissection (SCAD) [11]. Interestingly, while Takotsubo is primarily a disease of post-menopausal woman, SCAD occurs almost exclusively in woman in the fertile age, particularly during and after pregnancy, suggesting the abundance and lack of female sex

hormones are importantly involved in some cardiac conditions affecting women.

Sex differences have also been reported for arrhythmias. For instance, women have a lower prevalence of atrial fibrillation, are of older age at presentation and differ in triggers and substrate [12], as well as clinical presentation (e.g., women are more likely to be symptomatic) and natural history [13, 14]. Women more often receive medical treatment instead of catheter-based ablation [15] and if they undergo such procedures they experience higher rates of complications [16].

It became clear, that in cardiovascular medicine, sex truly matters and has to be considered by physicians when seeing patients of both sexes, in the acute setting and in the clinic [17]. To emphasise this fact, initiatives to incorporate sex as a biological variable into research, design and publication began in 2001 when the landmark publication by the Institute of Medicine, now the National Academy of Medicine, “Does Sex Matter?” was published [18]. In this seminal paper, the institution stated that “biological sex influences health and disease from womb to tomb”. Of further note, the institute clarified that in the English language sex should refer to the biological and gender to the cultural aspects of humans.

In the current and the following special issue of Cardiovascular Medicine on sex and cardiovascular diseases, experts from different parts of Switzerland addressed sex- and gender-relating issues for several conditions, from hypertension and diabetes to chronic and acute coronary syndromes and from cardio-oncology to heart failure. The editors of Cardiovascular Medicine hope that these two special issues on sex and cardiovascular disease will provide a comprehensive overview on what is known today about the influence of sex on different cardiovascular conditions. The articles will give a deeper insight into sex differences and what it means for the diagnosis and management of female patients presenting in the acute and chronic setting.

The full list of references and figure 1 are included in the online version of the article at <https://cardiovascmed.ch/article/doi/cvm.2022.02284>.