Sex and Gender in Cardiovascular Disease

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What is Cardiovascular Disease (CVD)?

The WHO defines cardiovascular diseases as a group of disorders of the heart and blood vessels that includes:

- Coronary heart disease (CHD): disease of the blood vessels supplying the heart muscle;
- Cerebrovascular disease: disease of the blood vessels supplying the brain;
- Peripheral arterial disease: disease of blood vessels supplying the arms and legs;
- Rheumatic heart disease: damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria;
- Congenital heart disease: malformations of heart structure existing at birth; and
- Deep vein thrombosis and pulmonary embolism: blood clots in the leg veins, which can dislodge and move to the heart and lungs.[1]

How Big is the Problem?

Cardiovascular disease (CVD), a major cause of death and serious illness and disability, is costly to healthcare systems and quality of life. In the EU, CVD is the top cause of death in every European country for women and all but six countries for men: death from CVD accounted for 43% in women and 36% in men in the EU.[2,3] Although CVD has declined over the last 40 years, this decline has been smaller for women than for men. Further, over the past decades, there has been a shift in the occurrence of CVD cases towards younger age-groups due to unfavourable life-style changes.[4,5]

Why Gender Matters: Biological Differences

Traditionally regarded as a male disease, cardiovascular disease (CVD) is the number one killer of women worldwide. Only during the last two decades has awareness been rising on how CVD affects women differently from men.[6] The risk of CVD in women is still underestimated in the medical community and in women themselves. The symptoms of heart disease in women can be different from those commonly seen in men, which may be at least partially due to gender differences in communication styles and underlying heart disease.[7,8,9] The persistent misperception that women are "protected" against CVD by their hormones, fuels the ongoing under-recognition of heart disease and leads to a worse treatment of their risk factors even after CVD events.[10] Although the clinical manifestation of heart disease develops 7-10 years later in women compared to men, the burden of adverse CVD risk factors increases more after menopause. This results in a higher number of CVD events and disability at older age.

Smoking and CVD

Smoking increases the risk of CVD in both men and women. Smoking has a particularly harmful effect in young women with a sixty-percent higher risk for heart disease compared to men when controlling for other risk factors.[11] It is, therefore, alarming that an increasing number of young women, especially in the Eastern European countries, have taken up smoking in the past decades.[12] The concomitant use of oral contraceptives further enhances the CVD risk in female smokers.[13]

Diabetes and CVD

Type 2 diabetes poses a greater risk for CVD complications in women than in men. In a analysis of 37 studies, the risk of death from ischemic heart disease was 50% higher in women with diabetes compared to men.[14] Diabetes is an important risk factor for the development of heart failure with preserved ejection fraction (HFpEF), particularly in women.[15] Gestational diabetes is a potent risk factor for diabetes later in life.[16]

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Depression, life stress and CVD

Psychosocial factors are important in the prevention and treatment of CVD.[16] There is growing evidence that the prevalence of depression and various forms of sustained mental stress (anxiety, anger, marital conflicts, work stress etc.) is substantially higher in female patients after acute myocardial infarction (AMI) compared to men, particularly in younger age groups.[17,18] This raises concern as younger age has been identified as a particularly vulnerable phase in which depression significantly acts on premature CVD. There is increasing evidence that patients, who succeed in a substantial reduction of their depression symptoms have a better CVD prognosis than those who did not.

Pregnancy and CVD

Pregnancy is considered as a "stress-test" for heart disease in women. Hypertensive disorders affect approximately 5-10% of all pregnancies and majorly contribute to maternal and neonatal morbidity and mortality worldwide.[19,20] In high-income countries, hypertensive pregnancy disorders (HPD) are the leading cause of maternal mortality, accounting for 16% of maternal deaths. The severe forms of HPD, preeclampsia and the HELLP-syndrome, lead to a two-fold increase in future CVD risk and are now acknowledged as a CVD risk factor.[21,22] Women after HPD develop hypertension more frequently and at younger age than do men.

Although overall risk of death from CVD is low, pregnant women with a pre-existing heart disease have a 100-fold increased risk of death compared to pregnant women without heart disease.[23] Many symptoms of heart disease—such as shortness of breath, fatigue and heartburn—are similar to general pregnancy symptoms, making diagnosis often difficult. Women suffering from a congenital heart disease need to be careful with regard to pregnancy and birth control options as both can increase heart risk.[24]

Men and CVD

Overall, there has been a decline in the mortality and morbidity from CVD in men over the recent decades. However, CVD remains a major health issue for men, especially among the older population as CVD remains their main cause of death. CVD accounts for 36% of deaths for men ranging from 25% of male death in France to 61% in Bulgaria. Premature death from CVD is nearly six times higher in vulnerable regions in Europe in comparison to the rest of the EU, illustrating major inequities across countries. Young men are particularly vulnerable to death from CVD. In 2008, CVD accounted for 160,000 deaths among men and 60,000 deaths among women under the age of sixty-five.[25]

CVD Treatment: Women and Clinical Trials

Women have been underrepresented in CVD clinical trials and when they were included, results were not powered to analyse gender differences. The EuroHeart Project found that in European clinical trials in CVD the proportion of women enrolled varied between 27 and 41%, which did not correctly reflect the percentages of women and men affected by the disease.[26] Clinical studies in pregnancy raise ethical conflicts, but the data are needed. The inclusion of pregnant women in prospective registries is a worthwhile endeavour.

Key Facts: Sex and Gender in CVD

- CVD is the top cause of death of women in all European countries and for men in all but 6 countries, accounting for 40% of deaths in the EU annually.
- Important gender differences exist in symptoms and pathophysiology of heart disease that must be considered in prevention, diagnosis and treatment of CVD.
- After menopause, women have a worse CVD risk factor profile than do men.
- Diabetic women have a greater relative risk of CVD than do diabetic men.
- Smoking presents a greater risk of CVD in younger women than it does in men.
- Psychosocial factors are importantly different between the sexes and should be considered in the prevention and treatment of heart disease.
- More data on CVD in pregnancy are needed.

ABOUT THE EUGENMED PROJECT

Research addressing sex and gender (S&G) in biomedical sciences and health research is emerging as a novel and highly promising field. This interaction between S&G leads to different manifestation of diseases—such as infarction, heart failure, diabetes, rheumatic disease—in women and men. Research in the area will lead to novel, better targeted and, therefore, to more efficient treatment strategies than the previous global approaches, creating additional opportunities for prevention and increased healthy life expectancy.

The EUGenMed Project is coordinated by Charité, Universitaetsmedizin Berlin in partnership with the European Institute of Women's Health and the University Maastricht. The Project is funded by the European Commission under the Seventh Framework Programme and began on October 1st 2013. The Project aims to create a multi-sectorial source of knowledge based on consensus of experts.

The EUGenMed Project will produce an innovative roadmap for implementation of S&G in in biomedicine and health, based on the generation of material and results from four workshops and the final project conference.

For more information, please visit the EUGenMed website: http://eugenmed.eu.

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