

Red Alert for Women's Hearts

Women and Cardiovascular Research in Europe. ESC/EHN Report November 2009

General Recommendations

Summary

FACTS ABOUT WOMEN AND CARDIOVASCULAR RESEARCH

There are a number of 'red alert' issues related to gender and cardiovascular diseases. Below are the most important findings of the report 'Red Alert for Women's Hearts', of particular relevance for organisations that wish to undertake awareness raising, whether to the general public or the health professionals. ¹

Scientific Research in Women

- Despite an increase in the number and proportion of women enrolled in cardiovascular clinical trials, there is still an under-representation of women, particularly in the field of cholesterol-lowering therapy, ischemic heart disease and heart failure, which may have affected the reliability of subgroup analysis.
- Clinical trials and meta-analyses on cardiovascular diseases did not show a significantly lower efficacy of interventions in women when compared with men, although 50% of the studies did not report an analysis of the results by gender. For some therapies there is even a suggestion for greater efficacy in women than in men, as in the case of cardiac resynchronization therapy in heart failure or thrombolysis after ischemic stroke.

Cardiovascular risk in Women

- Cardiovascular disease is the most common cause of morbidity and mortality for women in most of the world more than osteoporosis and cancer combined. ²
- The identification and control of cardiovascular risk factors represent the basis for the development of a preventive strategy. Unfortunately, women are less likely than men to identify their risk factors and to participate in screening programmes.

¹ More detailed information can be found in the report 'Red Alert for Women's Hearts – Women and cardiovascular research in Europe', Marco Stramba Badiale, November 2009

² More detailed information can be found in "Women's health and Menopause : a comprehensive approach" NIH publication no 02-3284 July 2002

Smoking

- The mortality from cardiovascular diseases is higher in women who smoke than in men who smoke, even after adjustment for other risk factors. It has been shown that women metabolize nicotine faster than men, especially when taking oral contraceptives. Smoking and oral contraceptives exert synergistic effects on the risk of cardiovascular diseases.

Hypertension

- Studies show no significant difference between men and women (except pregnancy, see below)

Diabetes and Metabolic Syndrome

- Women with diabetes, regardless of menopausal status, have a 4- to 6- fold increase in the risk of developing coronary artery disease, whereas men with diabetes have a 2- to 3-fold increase in risk
- Women with diabetes have a poorer prognosis after myocardial infarction and a higher risk of death from cardiovascular diseases than men with diabetes.
- The prevalence of the metabolic syndrome is increasing in both sexes, but has risen particularly in young women where it is mainly driven by obesity.

Cholesterol

- The European Guidelines for cardiovascular disease prevention recommend statins for men and women who had a coronary or a cerebrovascular event, and in primary prevention for men and women with high levels of LDL cholesterol or at high risk for cardiovascular diseases., i.e. diabetes.

Aspirin

- Aspirin in secondary prevention: aspirin induces reductions in coronary events and in total stroke, with a non-significant increase in hemorrhagic stroke. These effects are similar in men and women and all the Guidelines recommend the use of aspirin in patients with ischemic heart disease, cerebrovascular disease or peripheral artery disease.
- For primary prevention of asymptomatic individuals more research is needed.

Ischemic heart disease

- As coronary heart disease develops in women later in life than in men, the symptoms of a heart attack may be masked by other diseases. Furthermore, women have a higher prevalence of silent ischemia and of unrecognised myocardial infarction than men.
- It has been shown that some diagnostic tests and procedures may not be as accurate in women and physicians may avoid using them, leaving some women with undetected coronary heart disease, which may lead to more serious consequences for the delay in the diagnosis.
- Women with clinical findings suggestive of ischemia but without obstructive coronary artery disease on angiography represent a frequent clinical problem and are at elevated risk for cardiovascular events compared with asymptomatic women.
- Women are less likely to undergo non-invasive testing and less likely to be referred for coronary angiography.
- Antiplatelet and statin therapies are used significantly less in women than in men, both at initial assessment and at 1 year, even in those in whom coronary disease is confirmed.
- Women with confirmed coronary disease are less likely to be revascularized than their male counterparts and are twice as likely to suffer death or nonfatal myocardial infarction during the 1-year follow-up period, even after multivariable adjustment for age, abnormal ventricular function, severity of coronary disease and diabetes.

Coronary Revascularization

- The success rate of percutaneous revascularization (PCI) is similar in men and women, as well as the effects of new antithrombotic agents as concomitant therapy and the reduction in restenosis with the wider use of drug-eluting stents.
- Women are undertreated compared with men with prescription of GP IIb/IIIa inhibitors; however several trials have reported more adverse events in women, especially in those at lower risk. Indeed, women experience more bleeding than men whether or not they are treated with GP IIb/IIIa inhibitors. As excessive dosing in women takes place frequently, it may be considered that up to one fourth of this sex-related risk difference in bleeding is avoidable.

Heart Failure

- More men than women suffer from heart failure at younger ages, but after the age of 75 the reverse is true, as more women are affected by heart failure, especially with normal left ventricular ejection. With the increase of life expectancy, which is greater in women than in men, the proportion of older women with heart failure is expected to increase in the future.
- Women with heart failure appear to be less often investigated and treated with evidence-based drugs, even after adjustment for age and important clinical characteristics.

Pregnancy

- Women with previous gestational hypertension are at increased risk for cardiovascular diseases in later life.
- Women with gestational diabetes had an increased risk of developing type 2 diabetes compared with those who had a normoglycaemic pregnancy.
- The 2008 Guidelines for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology provide a recommendation for pregnancy, stating that this condition may lead to deterioration of heart failure due to the rise in blood volume and increase in cardiac output, as well as the substantial increase in extra vascular fluid. Importantly, many medications used in heart failure treatment are contra-indicated during pregnancy.

Atrial Fibrillation

- Atrial fibrillation is associated with an increased long-term risk of stroke, heart failure and all-cause mortality, especially among women. The 2006 European Society of Cardiology Guidelines for the management of patients with atrial fibrillation addresses the gender issues. They define female gender as an additional risk factor for stroke, especially in patients over the age of 75 and recommend antithrombotic therapy with either aspirin or a vitamin K antagonist for prevention of thromboembolism. They also include female gender as a risk factor for frequent recurrence of paroxysmal atrial fibrillation and for drug-induced ventricular arrhythmias.

Stroke

- Approximately 20% of stroke is not explained by the presence of traditional risk factors and it has been hypothesized that genetic factors may play a role. Heritability of ischemic stroke is greater in the female line than in the male line, independent of traditional vascular risk factors.

- Gender differences in the clinical presentation and outcome of stroke have been demonstrated. Women are significantly more disabled in the acute phase, at 3 to 6 months after stroke and 3.5 times more likely to be institutionalized. These results support the existence of gender-differences in stroke incidence, lifetime risk of stroke, age at first stroke, post stroke disability, and institutionalization rates.
- It has been shown that gender differences in clinical management after an acute stroke also exist. A multicenter study conducted in 7 European countries showed that after an acute cerebrovascular event, brain imaging, Doppler examination, echocardiogram, and angiography were significantly less often performed in female than in male patients. Furthermore, there is evidence that women, especially of older age, are less likely to receive lipid lowering drugs and antithrombotic for secondary prevention of stroke.

Thrombolytic therapy for ischemic stroke

- Thrombolytic therapy is the only approved intervention for acute ischemic stroke. A meta-analysis showed that women benefit more than men from this therapy. However, despite the greater efficacy of thrombolytic therapy, the percentage of women who do not receive thrombolytic therapy after acute ischemic stroke is higher compared to men.
- Thrombolytic therapy after stroke should be administered within the first 3-4.5 hours after the onset of symptoms, since after this period the risk of bleedings outweighs the benefit of treatment. The percentage of women who reach the hospital within this time period is lower than that of men and this observation may partially explain the under-treatment of women with thrombolytic therapy.

RECOMMENDATIONS

Awareness and Prevention

- Initiatives which contribute to awareness raising, education and prevention that cardiovascular diseases are the major cause of death in women should be encouraged.
- More opportunities to present on Women and CVD and/or outcome of research on Women and CVD should be created at scientific meetings, conferences, workshops, etc.

Treatment and Rehabilitation

- Initiatives which contribute to improving the knowledge of risk factors, presentation, treatment and rehabilitation of cardiovascular diseases in women should be encouraged.
- Scientific guidelines should systematically address gender differences; when not relevant, the guidelines should still indicate this so that readers are informed that they have been addressed.

Women Specific Research

- Heart Foundations and Cardiac Societies should cooperate with European institutions, national health care authorities and regulatory agencies to promote scientific research on gender differences in cardiovascular medicine and a larger representation of women in clinical trials.

Gender Specific research

- Increased awareness on gender differences supported by multidisciplinary studies is needed.

Control of Risk Factors

- Time trends show a compelling need for more effective lifestyle management in both genders.
- A special effort for preventing smoking initiation and favouring smoking cessation in young women is needed.
- Further understanding is needed about the reciprocal influences of lifestyle, nutrition, exercise and cardiovascular disease development, mainly after menopause.

Diabetes

- Health professionals across specialities should be informed about the specific issues related to women who are diabetic.

Ischaemic Heart Disease, Stroke, Heart Failure, Atrial Fibrillation

- CVD is killer number one among women; the risk of stroke increases drastically after the age of 75. With the increase of life expectancy, which is greater in women than in men, the proportion of older women with heart failure is expected to increase in the future.
- Decision makers and health-care planners need to be aware of these demographic aspects to ensure that adequate provisions are made.

Pregnancy

- Women who experience hypertensive disorders during pregnancy should receive a strict follow-up in order to identify those who may develop hypertension later in life.
- Awareness of the magnitude and timing of the risk of type 2 diabetes after gestational diabetes among patients and clinicians needs to be increased. This could provide an opportunity to test and use dietary, lifestyle, and pharmacological interventions that might prevent or delay the onset of type 2 diabetes in affected women.
- Women with heart failure and other types of CVD should be encouraged to discuss contraceptives and planned pregnancy with a physician in order to take an informed decision based on assessment of potential risks.

Clinical management of CVD

- Research shows unequal access to treatment for women who suffer from CVD. It shows that excessive drug dosing in women takes place frequently and that women more often than men do not reach the hospital in time in order to start appropriate treatment.
- Barriers for achieving equal access to treatment in hospitals after a CVD event must be identified and addressed.
- Steps should be taken to ensure a systematic inclusion of gender-specificity in the training of health-care specialists in general and cardiologists in particular.