

## Red Alert for Women's Hearts

### *Summary for Research Funding Entities*

#### **FACTS ON WOMEN AND CARDIOVASCULAR RESEARCH**

- Cardiovascular disease (CVD) is the leading cause of death in women, accounting for 54% of deaths in women in Europe
- Women usually suffer from CVD 10 years later in their life than men: the risk increases after menopause, partly because of ovarian hormones deficiency that favours hypertension, diabetes, hyperlipidemia, central obesity and the metabolic syndrome.
- Women are under-represented in cardiovascular research:
  - Overall, the 62 randomized clinical trials published between 2006 and mid 2009 enrolled 380.891 participants, 127.716 of them only were women (33.5%)
  - The percentage of women enrolled in each trial ranges between 15 to 60%;
  - Only 50% of clinical trials report the analysis of the results by gender
- This under-representation is particularly noticeable in the fields of
  - cholesterol-lowering therapy
  - ischaemic heart disease
  - heart failure

#### **Risk assessment**

- Women are less likely than men to identify their risk factors and to participate in screening programmes. In addition, existing risk estimation systems often fail to accurately assess the CVD risk of healthy women aged 45 years and older.

#### **Diabetes**

- Women with diabetes have a higher risk of developing coronary artery disease or stroke, a poorer prognosis after myocardial infarction and a higher risk of death from CVD than men. However, they are also more prone to adverse effects of some hypoglycaemic agents (risk of fractures).

## Ischemic Heart Disease

- Within CVD, there are gender differences in the clinical manifestation of CHD: higher prevalence of silent ischemia and of unrecognized myocardial infarction in women, even if angina prevalence is similar.
- Women with confirmed coronary disease are less likely to be revascularized than their male counterparts, and were twice as likely to suffer death or non-fatal myocardial infarction during the 1-year follow-up period, even after multivariable adjustment for age, abnormal ventricular function, severity of coronary disease, and diabetes.
- Women are less likely to undergo an exercise ECG test and less likely to be referred for coronary angiography.
- Significant differences have been demonstrated in the manifestation of acute coronary syndromes, as well as in patients undergoing coronary revascularization procedures. The risk of adverse events during and after the procedures, including coronary dissection and peripheral local bleeding, is greater in women than in men.
- Women are under-treated compared with men, especially with PCI (24.4% for men vs 22.9% for women), prescription of clopidogrel (49% for men, 39% for women) and prescription of GP IIb/IIIa inhibitors (24.8% for men vs 23.8% for women).

## 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 fraction.
- 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.

## Atrial fibrillation

- Atrial fibrillation is associated with an increased long-term risk of stroke, heart failure and all-cause mortality, especially among women.
- Women have a greater risk of developing adverse reactions to drugs than men.

## Gender differences in stroke

- Gender differences in the clinical presentation and outcome of stroke have been demonstrated, e.g. stroke incidence, lifetime risk of stroke, age of first stroke, post stroke disability and institutionalization rates.
- Women are significantly older at their first stroke and have a higher stroke incidence above the age of 85 and a higher lifetime risk of stroke at all ages.
- Gender differences in clinical management after an acute stroke also exist: after an acute cerebrovascular event, brain imaging, Doppler examination, echocardiogram and angiography are significantly less often performed in female than in male patients.

## ***Recommendations for Research Finding Entities***

### *Raccomandazioni per gli Enti Finanziatori della Ricerca*

Scientific research on gender issues in cardiovascular medicine should be promoted. Some subspecialties need specific attention from research funders and research teams:

#### **Gender specific research**

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

#### **Hormone replacement therapy (HRT)**

- Additional research is needed in the field of hormone replacement therapy (HRT) for the relief of symptoms in postmenopausal women, in order to assess with precision the added risk of CVD and breast cancer based on:
  - age of the population
  - time of beginning the therapy since menopause
  - type and mode of administration
  - duration of therapy
  - CVD effects of new agents
  - the type and source of hormone preparation
  - ethnic differences on use of HRT
  - phyto-oestrogens
  - impact of new hormonal preparations

#### **Screening & risk assessment**

- Promote the development and/or adoption of a risk assessment system which can accurately estimate CVD risk to healthy women over 40 years of age, taking into account such variables like diabetes and features of the metabolic syndrome and consequently to improve the existing risk scores.
- Undertake research to establish cardiovascular biomarkers in proximity of menopause.

#### **Diabetes**

- Explore the reasons for gender differences in the adverse effects of some hypoglycaemic agents.
- Encourage research on the risk of developing type 2 diabetes after glycaemic alterations during pregnancy.

## **Obesity and Metabolic Syndrome**

- Research is needed on gender specific pathophysiology of overweight and obesity development in all ages of life.
- Research is needed to better profile gender specific pathophysiology of metabolic syndrome.

## **Ischemic heart diseases**

- Research is needed to elucidate the reasons for the adverse prognosis observed in women with stable angina and proven coronary disease, i.e. less non invasive testing and coronary angiography, less revascularization, anti platelet and statin therapies. This may have lead to a rate of twice as many death and non-fatal myocardial infarction during the 1-year following stable angina in women than in men.
- Encourage research on women with symptoms and signs suggestive of myocardial ischemia but without obstructive coronary artery disease.
- Encourage research on the long term efficacy and safety of early revascularisation in acute coronary syndromes in women and on antithrombotic therapy in women.

## **Heart failure**

- Encourage research on the efficacy and safety of therapeutic interventions for heart failure patients with preserved left ventricular function (more common in women).

## **Stroke**

- The origin on gender differences in stroke incidence and post stroke disability needs to be examined together with the reasons for the under-treatment of women with thrombolytic therapy despite its greater efficacy when compared to men.

## **Pharmacotherapy in women**

- Studies of gender specific differences of the established pharmaceutical armamentarium for Cardiovascular Disease should better reflect women with heart diseases.
- More information and more studies on adverse drug reactions in women is needed.



- Studies on new hormonal preparations and their relations to cardiovascular disease are urgent.

### **Lifestyle management**

- Further understanding is needed about the reciprocal influences of lifestyle, nutrition, exercise and cardiovascular disease development, mainly after menopause.