

Women with acute coronary syndromes have a worse prognosis — why? The need to reduce ‘treatment-seeking delay’

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Introduction

The risk of cardiovascular disease (CVD) in women has been historically underestimated due to a misperception that females are protected against CVD [1]. Nowadays it is known that CVD is the No 1 killer of women in the United States and worldwide. According to WHO data from 2004, CVD is responsible for 43% of deaths in men and 55% of deaths in women [2]. The US Center for Disease Control and Prevention Report attributes 38% of deaths in women to coronary artery disease, compared with only 22% to cancer [3]. The onset of disease is about ten years later in women than in men, however in women the incidence of the disease increases rapidly after menopause [2].

Women are under-diagnosed, less likely to undergo invasive procedures and they less often receive guidelines in terms of recommended therapy. Women are still under-represented in clinical trials. In clinical studies in acute coronary syndromes (ACS), the percentage of women increased from 20% in 1966–1990 to 25% in 1991–2000 [2].

Gender disparities

Women with ACS are generally older, with more clustering risk factors than men, and are less likely to present with ST elevation. They reach hospital later, which results in less extensive administration of thrombolysis and fewer percutaneous coronary interventions (PCI). There are differences in the pathophysiology of CVD between men

and women. New findings from the Women’s Ischemia Syndrome Evaluation (WISE) NHLBI study support the concept of a multifactorial model where sex hormones interact with traditional and novel risk factors, especially inflammatory process biomarkers (CRP), leading to an increase in the functional expression of atherosclerotic plaque and vascular or metabolic alterations resulting in worsening outcomes for women [4].

Gender differences analysis was performed in the Euro Heart Survey of Acute Coronary Syndromes. Women with ST segment elevation myocardial infarction (STEMI) were less likely to receive reperfusion therapy than men (43% vs 53%), and they more often developed heart failure. One reason why they less often received reperfusion therapy is delayed hospitalization [5].

In women, despite the fact that they are less likely to have significant coronary narrowings and relatively more often have preserved left ventricular function, a greater incidence of ischemic events and greater mortality has been observed, compared to men. This fact was reappraised by Johnson et al. [6] who called it the “gender-paradox”.

The risk of being female

Women have a worse prognosis after an acute myocardial infarction than do men, with a mortality rate about twice as high. This can be explained by worse clinical profile: at presentation, women are older, and have more co-morbidities, diabetes, hypertension, and obesity [7].

A large international registry found women with ACS were generally treated less aggressively, were less likely than men to undergo coronary

angiography, to have revascularization, to receive antiplatelet, including glycoprotein IIb/IIIa inhibitors, statin and angiotensin-converting enzyme inhibitors therapies [8]. The greater risk of bleeding in women treated with IIb/IIIa antagonists is attributable to a lack of dose adjustment to body size and renal function compared to men [8].

Due to small coronary vessels size, stents are less likely to be implanted in women; dissection of coronary arteries is more often observed. After PCI procedures, women more often have anginal pain, which hampers their activity and worsens their quality of life.

Treatment-seeking delay

The period between the onset of symptoms and entry into the healthcare system is termed 'treatment-seeking delay'. It can be divided into three phases: decision time, transport time and therapy time [9]. Failure to recognize the symptoms of ACS, both by a female patient and a first contact physician at the time of admission, contributes to a delay in seeking treatment. Symptoms of CVD in women are 'atypical' compared to those of men. McSweeney et al. [10] showed that up to 50% of women presenting with an acute myocardial infarction had no prior chest pain symptoms; 95% of the women experienced such prodromal symptoms as fatigue, shortness of breath, weakness, sleep disturbances, indigestion and anxiety and did not recognize them as cardiac-related, meaning they did not call the emergency services.

The prompt opening of an infarct-related artery results in the reduction of infarct size, systolic function preservation and mortality decrease. The extent of myocardial salvage decreases significantly when the ischemic time is longer than 90 min. Boersma et al. [11] has reported the relationship of symptoms onset to treatment delay on the absolute benefit of mortality reduction in patients with STEMI. De Luca et al. [12] showed that among patients with STEMI undergoing mechanical reperfusion, symptom-onset-to-balloon time, but not door-to-balloon time, affected one year mortality especially in high risk patients. The authors also showed that every minute of delay in primary angioplasty for STEMI affected one-year mortality [13].

In this issue of *Cardiology Journal*, Sadowski et al. [14] analyzed the gender-related benefit of transport to primary angioplasty based on 10,708 patients from the Polish Registry of Acute Coronary Syndromes (PL-ACS). The authors demonstrated the gender differences on presentation with ACS.

Women with ACS were older, with more clustering of risk factors. The time from symptoms onset to PCI was longer in women.

The authors showed that mortality after hospital discharge at all time points (in hospital, one month, six months and 12 months) was significantly higher in women than in men. The mortality however depended on total ischemic time (time measured from onset to balloon time) regardless of mode of transport (directly to cathlab or transferred from another hospital). This important observation by Sadowski et al. [14] indicates the need for an additional public health effort to reduce time delay to PCI.

Although major advances in transport time and therapy time have been made, little progress has been achieved in reducing patients' delay in seeking treatment i.e. in reducing decision time, which should be an important clinical and research priority.

There is a need for greater awareness of how CVD causes mortality in women. It requires a combination of educational activities among women patients and medical and scientific society in general.

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