Women and men with stable coronary artery disease: different risk factors but similar outcomes!

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Published online: 24 January 2013
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Men and women differ in terms of presentation and management in coronary artery disease (CAD). In recent years many clinical trials have provided evidence that there are substantial gender differences in the pathophysiology, clinical presentation, diagnosis, and treatment of CAD [1–5]. Although women have a higher atherosclerotic burden, they are more symptomatic and have a lower prevalence of obstructive CAD than men [6–10].

Whether these gender differences translate into different clinical outcomes in stable CAD has been unclear. While some reports found gender differences in outcomes for stable angina or acute coronary syndromes, others did not [11–15]. Furthermore, most contemporary studies of CAD patients are limited to a single country or specific geographical region, or a particular manifestation of disease such as angina symptoms or acute myocardial infarction [16–18]. Recently, dr. Gabriel Steg et al. (Paris, France) analysed data from the international prospective CLARIFY registry to compare cardiovascular clinical outcomes in men and women with stable CAD [19]. CLARIFY (*ProspeCtive observational Longitudinal RegIstry oF patients with stable coronary arterY disease*) is an ongoing international prospective observational longitudinal registry in 33,000 patients with stable CAD in 45 countries. One-year outcomes were analysed in 30,977 outpatients with stable CAD of whom 23,975 (77.4 %) were men and 7,002 (22.6 %) were women. Based on risk profiles, women were older than men, were more likely to have hypertension and diabetes, did less exercise and smoked less. Women had more

frequent angina, but were less likely to have undergone diagnostic non-invasive testing or coronary angiography. Women received less optimised treatment for stable CAD. However, 1-year outcomes were similar for men and women: 1) for the composite of cardiovascular death, non-fatal myocardial infarction, or stroke (1.7 vs. 1.8 %, respectively), 2) all-cause death (1.5 vs. 1.6 %), 3) fatal or non-fatal myocardial infarction (1.0 vs. 0.9 %), and 4) cardiovascular death or non-fatal myocardial infarction (1.4 vs. 1.4 %). Fewer women underwent revascularisation (2.6 vs. 2.2 %).

It was concluded by the authors that, although the risk profiles of women and men with stable CAD differed substantially, the 1-year outcomes were similar in terms of mortality and cardiovascular events. These results suggest that there is no discernible excess of cardiovascular events in women with stable CAD compared with men and that, if anything, among younger patients or lower risk patient groups, women actually fare better than men.

The study has been criticised by dr. Eva Swahn (Stockholm, Sweden) in an accompanying Editorial comment [20]. Her main critical comments were the following. *First*, the patients seem to be highly selected, as only 22.6 % were women and, according to epidemiological investigations, the prevalence is usually the same and in fact even slightly higher in women with angina. As the physicians involved were requested to recruit 10–15 stable CAD outpatients, this selection bias could have been avoided by requesting them to recruit 50 % women and 50 % men. This selection might significantly limit the representativeness and generalisability of the results. *Second*, the handling of missing data. At 1-year follow-up, 6.8 % of the patients either withdrew their consent, had no follow-up, or the follow-up was still ongoing. This is a relatively high drop-out rate, whatever the reason. The investigators could have waited for the results of the 1,202 patients who had not completed 1-year follow-up, which would have decreased the drop-out rate considerably. *Third*, as in all observational datasets, the

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adjustment might be influenced by the lack of registration of some possible confounding factors, e.g. non-cardiac comorbidity, contraindications to specific treatment, and reduced kidney function. A glomerular filtration rate <60 ml/min has recently been shown to be far more common in CAD women than men and could have been included in the adjustment.

Despite these shortcomings (also recognised by the authors!), the CLARIFY population is one of the first large international multicentre studies that has analysed data from a gender perspective. The CLARIFY study, being a prospective, observational, longitudinal registry of patients with stable coronary artery disease consisting of >33,000 patients in 45 countries worldwide, has therefore the potential to fill in some of the gaps called for in the Red Alert for Women's Heart. This is a very good attempt to straighten out some nonclarified fields in this cardiovascular area.

In conclusion, the CLARIFY study adds significant value to our CAD gender knowledge as it included a large number of patients from a wide geographical area. Interestingly, similar outcomes for men and women were found despite significant differences in risk factors. Further research remains needed to better understand gender determinants of outcome and devise strategies to minimise bias in the management and treatment of women. Concerted efforts are warranted to modify both physician and patient behaviours by increasing awareness of the prevalence of CAD in women.

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