

Highlights from the latest articles in interventional cardiology

Gender differences in interventional cardiology

Evaluation of: Stefanini GG, Baber U, Windecker S *et al.* Safety and efficacy of drug-eluting stents in women: a patient-level pooled analysis of randomized trials. *Lancet* 382, 1879–1888 (2013).

In published studies analyzing the safety and efficacy of drug-eluting stents (DES), women have represented only approximately a quarter of the participants. Due to US FDA concerns regarding under-representation of women in medical device studies, a Gender Data Forum was organized by the Women in Innovation Initiative of the Society of Cardiovascular Angiography and Interventions (SCAI) to study outcomes among women treated with DES.

This study performed pooled analysis of 26 trials to evaluate the safety and effectiveness of DES compared with bare-metal stents in 11,557 women. The study was not designed to compare outcomes between men and women; an earlier study by the same group had found similar outcomes among men and women undergoing DES placement [1]. Early-generation DES (sirolimus-eluting Cypher and paclitaxel-eluting Taxus) were also compared with newer generation DES (everolimus-eluting Xience™ and Promus™, zotarolimus-eluting Endeavor™ and Resolute™, biolimus-eluting Biomatrix™ and Nobori®, and sirolimus-eluting Yukon® stents – these last three are not currently available in the USA).

Women treated with bare-metal stents had a higher cumulative incidence of death or myocardial infarction over 3 years of follow-up (12.8%) than those treated with early-generation DES (10.9%) and newer generation DES

(9.2%). Overall, women had similar mortality whether treated by DES or bare-metal stents, but had lower rates of target lesion revascularization if treated by DES, with even further benefit if treated with a newer generation DES. The risk of stent thrombosis was lowest when women were treated with newer generation DES (1.1%); those treated with early-generation DES had more stent thrombosis events (2.1%) than women treated with bare-metal stents (1.3%). These findings are consistent with prior studies of DES that report lower rates of revascularization, but no difference in overall mortality compared with bare-metal stents. Newer generation DES have less risk of stent thrombosis compared with early-generation DES.

This collaborative large-scale analysis of patient-level data demonstrates the feasibility and importance of performing pooled analyses to describe outcomes among minority groups under-represented in clinical trials. The authors conclude that women treated with DES have better outcomes than those treated with bare-metal stents, and that newer-generation DES should be considered the standard of care among women due to the lower risk of stent thrombosis and recurrent myocardial infarction.

Evaluation of: Melberg T, Kindervaag B, Rosland J. Gender-specific ambulance priority and delays to primary percutaneous coronary intervention: a consequence of the patients' presentation or the management at the emergency medical communications center? *Am. Heart J.* 166, 839–845 (2013).

Women with ST-elevation myocardial infarction (STEMI) tend to have longer ischemic times than men. The authors of this study

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analyzed possible factors causing delays to revascularization. Women may describe a different constellation of acute symptoms than men, which could make it challenging for dispatchers to appropriately triage emergency calls. Delays may also result from lower priority designations for ambulance transportation.

This study was a retrospective review of STEMI patients who contacted the emergency medical communication (EMC) service in Norway. Audio logs and medical records of 244 patients (26.6% women) were reviewed. The type and duration of symptoms, ambulance priority designation, and system and nonsystem delays were calculated including overall call-to-balloon times.

Women were older, had more hypertension and less smoking history than men. There were no significant gender differences in symptom presentation. Chest pain occurred equally in both men and women, but women experienced radiation more commonly. More men than women described no chest pain. Rates of out-of-hospital arrest and extent of coronary artery disease by angiography were similar. EMC center dispatchers identified 82% of the STEMI patients as needing urgent ambulance service ('red' alert), with the remaining identified as middle priority for ambulance ('yellow' alert). More women were identified as 'yellow' priority, and multivariable analysis revealed that female gender and having ≥ 2 presenting symptoms were associated with receiving lower ambulance priority. This designation was associated with longer patient delays, dispatch delays, ambulance response time and total ischemic time.

Although women are generally believed to present with more vague cardiac symptoms than men, this study used first-hand accounts of patient calls to EMC and found no significant gender differences in STEMI symptoms. Despite similar symptoms, women were less likely to be given the highest priority for ambulance dispatch. These findings are concerning for gender-related bias among emergency dispatchers. This is a small single-center retrospective study, but highlights the need to eliminate system-related delays in call-to-balloon time for women with STEMI.

Evaluation of: Lin CF, Shen LJ, Hsiao FY, Gau CS, Wu FL. Sex differences in the treatment and outcome of patients with acute coronary syndrome after percutaneous coronary intervention: a population-based study. *J. Womens Health (Larchmt)* doi:10.1089/jwh.2013.4474 (2013) (Epub ahead of print).

Prior studies have reported that female patients with acute coronary syndrome (ACS) are undertreated with evidence-based medications, and are less likely to undergo revascularization. This study assessed whether

women treated with percutaneous coronary intervention (PCI) experienced gender differences in medical therapy and outcomes.

This was a retrospective nationwide cohort study using the Taiwan National Health Insurance Research Database (NHIRD). Patients first hospitalized for ACS who underwent PCI between 1 January 2006 and 31 December 2007 were identified by discharge diagnosis and procedure codes. Of 32,821 patients, 8884 (27%) were women. Use of aspirin, β -blockers, ACEI or ARB, statins, and clopidogrel were evaluated by prescriptions within 1 year of the diagnosis. Propensity score matching was used to match males with similar female covariates including age, ischemic heart disease, cerebrovascular disease, hyperlipidemia, peripheral vascular disease, liver disease, peptic ulcer and gastroesophageal disease, resulting in a matched cohort of 17,768 persons. In the unmatched cohort, women were older and had higher rates of hypertension, diabetes, cerebrovascular disease, renal disease and heart failure.

Women with ACS who underwent PCI were 18% less likely to be treated with aspirin, and 12% less likely to use clopidogrel when compared with the matched cohort of men. Women were 17% more likely to receive β -blockers and 22% more likely to receive statin therapy than men in the matched cohort. Patients who received medical therapy were less likely to be rehospitalized for revascularization, with an adjusted hazard ratio (HR) among women of 0.81 (95% CI: 0.73–0.90) and similar results among men. The adjusted HR for revascularization in women was 0.84 (95% CI: 0.79–0.90) when compared with men in the matched cohort. Rates of rehospitalization for revascularization with stent, PCI or CABG were lower (14, 12 and 37%, respectively) for women than for men in the matched cohort. The authors hypothesize that these findings may be due to women having lower rates of STEMI, less extensive atherosclerosis or simply being less likely to receive interventional therapy. Unfortunately, overall rehospitalization rates for reasons other than revascularization were not captured, as it would be interesting to know whether women were rehospitalized with recurrent angina.

The undertreatment of women with aspirin and clopidogrel has been previously reported and may be related to real or perceived increased risks of bleeding among women; however, this study did not include bleeding history in the analysis. This study increases our awareness of possible differences in therapy based on gender, either due to real gender inequality or to real or perceived bleeding risks. Patients treated with all guideline-based medications had a decreased risk of rehospitalization for revascularization, emphasizing the need to overcome gender-based inequities in order to improve outcomes.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employ-

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Reference

- 1 Stefanini GG, Kalesan B, Pilgrim T *et al.* Impact of sex on clinical and angiographic outcomes among patients undergoing revascularization with drug-eluting stents. *JACC Cardiovasc. Interv.* 5(3), 301–310 (2012).

