

## A Pioneering Argentinean Study to Better Understand the Gender Differences on Patients with Acute Coronary Syndromes.

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Cardiovascular disease is well recognized as the leading cause of death in women. It is estimated that the lifetime risk for developing coronary artery disease (CAD) in women after 40 years of age is 32% (1). Acute coronary syndromes (ACS), including unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), represent a large portion of the clinical presentation of CAD.

ACS it presents in different aspects, and gender is linked to many aspects of these presentations. The reason for gender differences in ACS presentation is likely multifactorial. These differences include, clinical presentation, delay to diagnosis and treatment, accuracy of diagnostic tests, differences in biomarkers, angiographic features, administration of antiplatelet therapies, drug side effects, and higher procedural complications. Previous studies have shown gender differences at each step along the treatment path for ACS patients, especially, women who had an acute myocardial infarction were less likely than men to be admitted to hospitals with revascularization capability (2). They have also demonstrated that in this high-risk population, women were offered cardiac catheterization and percutaneous coronary intervention (PCI) less frequently than men (3,4).

The results from the Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO) IIb study (5) showed that women present significantly more often than men with UA/NSTEMI and often with atypical features. These differences may be accounted for by differences in anatomy, pathophysiology of CAD, for the underutilization of acute antiplatelet therapy on hospital admission, and clinical characteristics in women vs men. In addition, there are conflicting data from randomized trials about the benefit of early invasive treatment in women (6-8).

The data of 3100 female patients enrolled in the Euro Heart Survey ACS showed that female gender in the "real world" was not independently associated with worse in-hospital mortality, irrespective of the type

of ACS (9). This suggests the need for gender-tailored techniques to minimize post-intervention complications and maximize application of evidence-based antiplatelet therapies. Awareness of these gender differences may contribute toward improving care of women with ACS.

The results presented in this issue of the Journal by Mariani et al. (10), confirm prior studies, which showed that women with ACS often did not receive the same interventional treatment as men, although women had similar or even better outcomes after PCI (11). The Epi-Cardio registry aim was to assess gender differences in ACS management in 54 Argentinean cardiovascular care units. From 2005 to 2012 8997 records from patients with ACS diagnosis were collected. Propensity score adjusted analyses and sensitivity analysis were performed. However, in contrast with the above mentioned results from the Euro Heart Survey, the report showed that women were independently associated with lower in-hospital indication for coronary angiography (OR 0.73, 95% CI 0.65 to 0.82), and less use of IIb/IIIa inhibitors in patients with non-ST elevation ACS (NSTEMI-ACS). These analyses of the Epi-Cardio database, suggest that, in the presence of a similar clinical presentation, women were less likely to receive invasive treatment strategy and statin and beta-blocker prescriptions after presenting with ACS. At discharge, women were significantly less likely than men to receive prescriptions for beta-blockers and statins, and more likely to receive prescriptions for benzodiazepines.

In terms of study limitations, even the Epi-Cardio was an observational study; the findings are consistent with previous studies that evaluated the therapeutic opportunity by adjusting for confounding variables such as such: preference of male/female patients or factors that increase the procedure or drug risks (body mass index, renal function, pulmonary disease, blood pressure and heart rate at discharge). This suggests once again, that a gender difference on treatment of ACS is a multifactorial phenomenon and the results cannot be explained by these unmeasured factors.

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As discussed by the authors, while these observational study results are not definitive, it may be a valuable information at the moment of evaluating and adopting new educational strategy and guidelines development, and see whether it helps to correct bias and improve female outcomes. Since Argentina has no updated data on gender bias in the therapeutic approach for patients with ACS, this study by Mariani et al. (10) represents an innovative landmark and provides solid and unprecedented data not only for the region but also to contribute to the results from other global studies dedicated to study this phenomenon.

#### Conflicts of interest

None declared

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