

EDITORIAL COMMENT

Is There Still a Sex Difference According to the Coronary Revascularization Strategy?*



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Sex-related differences in the prevalence and clinical outcomes of coronary artery disease (CAD) have been frequently reported in the literature. Several studies have suggested that women undergoing percutaneous coronary intervention (PCI) are at a higher risk of adverse outcomes than men. However, a sex disparity in the clinical outcomes has mainly been derived from the different clinical and anatomic characteristics between the sexes such as an older age, higher prevalence of hypertension and history of a stroke, and smaller vessel diameter in women. That disappeared after an adjustment for the age and comorbidities (1,2). In addition, unmeasured confounders (eg, a different prevalence in microvascular disease or diastolic dysfunction, hormonal differences, and socioeconomic factors) may also contribute to the clinical outcomes in women with CAD (3-5) and may preclude any definitive conclusions (Figure 1). Although there have been several studies about sex differences after PCI in different subsets of diseases (eg, acute coronary syndrome, ST-segment elevation myocardial infarction, and small vessels), there are still limited data on the long-term outcomes in patients with left main coronary artery (LMCA) disease.

In this issue of *JACC: Asia*, Yang et al (6) examined the long-term effects of sex and different related

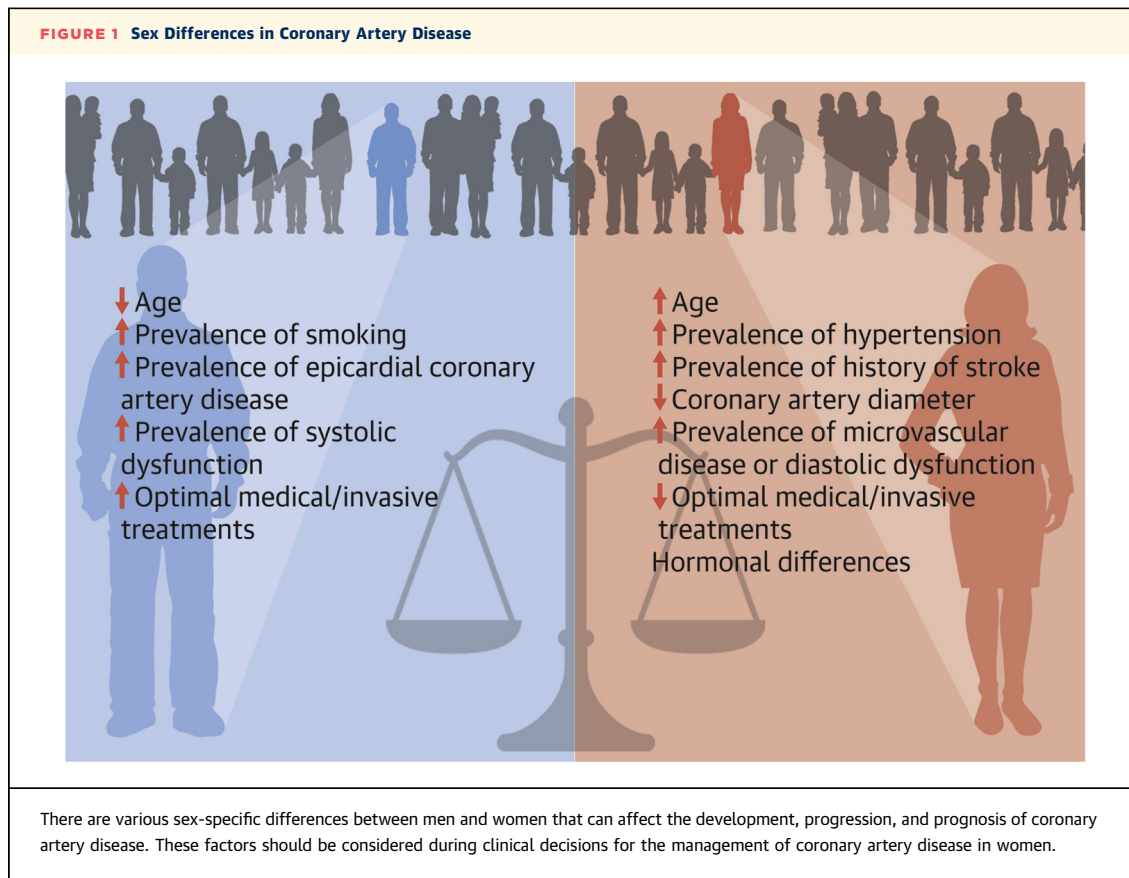
outcomes after PCI or coronary artery bypass grafting (CABG) for LMCA disease from the PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) trial. The PRECOMBAT trial was a prospective, multicenter, open-label, randomized controlled trial of patients with unprotected LMCA disease who were assigned to receive PCI with first-generation sirolimus-eluting stents or CABG at 13 hospitals in the Republic of Korea between April 2004 and August 2009 (7). Eligible patients had to have a significant de novo unprotected LMCA stenosis (>50% by visual estimation) with or without any additional target lesions (>70% by visual estimation) and had to be considered by the physicians and surgeons at each hospital to be suitable candidates for either PCI or CABG. Of the 600 patients, 459 (76.5%) were male. Compared with males, females had a lower proportion of current smokers and a higher EuroSCORE (European System for Cardiac Operative Risk Evaluation). However, sex was not independently associated with an increased risk of major adverse cardiac or cerebrovascular events at 10 years. Further, there were no significant interactions between sex and treatment modality with PCI or CABG in terms of the 10-year major adverse cardiac or cerebrovascular events.

The strength of the present study was the long follow-up duration and higher incidence of a complete revascularization. In the SYNTAXES (SYNTAX Extended Survival) study, an interaction between the sex and treatment with PCI or CABG was observed at 5 years and was no longer present by 10 years. The rate of complete revascularization (CR) in the SYNTAXES study was 59.3% in men and 62.2% in women (8). In the current study, CR was performed in 69.7% of men and 68.1% of women. A meta-analysis of 35 studies showed that CR was associated with a mortality

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benefit irrespective of the revascularization modality (9).

The investigators provided valuable insights on the long-term clinical outcomes of the different types of revascularizations between sexes in patients with LMCA disease. However, the results from this study need to be interpreted with a recognition of the limitations.

First, the revascularization strategies are advancing as time goes by. In this study, PCI was performed with first-generation drug-eluting stents (DES). Because of an improved design, thinner strut, and better polymer of the second-generation DES, they have better clinical outcomes than first-generation DES, especially in complex lesions and procedures (10). Also, new techniques to improve CABG outcomes and graft patency have been adopted. Moreover, the increasing adoption rate of physiology assessments and imaging guidance should be considered. Therefore, the clinical outcomes might differ under contemporary clinical practice. Second, the original study was underpowered as a result of the unexpectedly low event rates. Further, the number of women was only one-third of the entire

population, and that could result in an insufficient statistical power. Third, LMCA disease is not a homogeneous subset, and the clinical outcomes are influenced by the location of the disease, lesion complexity, and stenting techniques. The SYNTAX (SYnergy between PCI with TAXUS and Cardiac Surgery) score and EuroSCORE, which take into account the lesion complexity and patient risks, were lower than those in the SYNTAX study (8). Therefore, this result hardly represents the wide spectrum of LMCA disease in daily practice. Fourth, medical therapies such as potent P2Y₁₂ inhibitors have also evolved as much as the PCI and CABG technology and have been associated with a clinical benefit. Finally, it has been reported that women remain at a higher risk for bleeding and vascular complications than men (11,12). To assess the net clinical benefit, bleeding events, as well as ischemic events, should also be considered.

In summary, the long-term clinical outcomes after revascularization of LMCA disease did not differ between men and women; however, there was a sex difference in the baseline characteristics. We must place adequate effort into understanding the biology, which is sex specific and differs between men and

women. As children are not small adults, women are not small men.

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