EDITORIAL COMMENT

Sex-Related Outcomes After Drug-Eluting Stent

Should We “Never Mind” or “Mind” the Gap?*

Roxana Mehran, MD, Annapoorna S. Kini, MD

New York, New York

Cardiovascular disease (CVD) is the single most common cause of death among women. Although over the past 40 years age-adjusted mortality for CVD in Western countries has decreased, the decline among women is more modest than that of men (1). Moreover, life expectancy has increased, especially in women and, therefore, the prevalence of CVD has increased in this population (2). Age-adjusted inpatient mortality after percutaneous coronary intervention (PCI) in the Nationwide Inpatient Sample database declined between 1995 and 2004, but women continue to have higher mortality rates (3).

Clinical outcome of women after PCI has been challenging. Historically, female sex has been associated with increased complications during and after PCI (4,5). Women undergoing PCI usually present with more comorbid conditions, including hypertension, older age, elevated cholesterol, more complex and diffuse coronary disease, and longer referral time compared with men (5–7). This makes the comparison between men and women nearly impossible. With the significant improvements in angioplasty techniques, the introduction of drug-eluting stents (DES), and the availability of small-size stents, the previously noted sex gap in outcomes seems to have narrowed. Nevertheless, can we claim this with statistical confidence?

In the current issue of JACC: Cardiovascular Interventions, Mikhail et al. (8) try to tackle this question by diving deeply into the databases of all paclitaxel-eluting stent (PES) studies. The authors used patient-based pooled data and statistical analytical methods to compare men and women in the PES studies with long-term follow-up (up to 5 years in randomized and 2 years in registry studies). This is the best that can be done with their available data. But is this enough? Can we really say that PES is effective in the same manner in men versus women? Although close to 10,000 patients were studied in these well-controlled trials, women represented only a small minority of the population. Therefore, the true comparative effectiveness study of PES versus bare-metal stent in women was based on only 1,050 female subjects (655 PES vs. 395 bare-metal stent) and was hardly powered to answer the question of safety and efficacy of PES in women.

Mikhail et al. (8) elegantly analyzed all their PES data and showed that, although the number of female patients in studies has been small (generally under 30%), PES seem to be similarly efficacious in both sexes. In fact, long-term results seem to show favorable results for definite/probable stent thrombosis during the first year in women with PES. Can any of this be definitively proven?

One can never tell, because the numbers continue to be small and not powered to study women.

Inclusion of women in clinical trials for PCI has been a very well-established and important deficiency in the ever-growing clinical trials network in interventional cardiology (3). This challenge is complicated by the well-established comorbid conditions in women compared with men that might exclude women from “Simple-Vanilla” studies. However, even in trials of more complex lesion subsets (the so-called “all comers” studies), we continue to observe a lower enrollment rate of women. This might be secondary to the fact that the prevalence of disease is lower for the same age compared with men (9). However, more complex socioeconomic reasons that might explain why women are more reluctant to enroll in studies have not been evaluated. It is our responsibility to better understand these issues by researching and designing studies for women with data elements that are relevant to women. This is one of the initiatives that are being organized by the U.S. government (Food and Drug Administration, Office of Women’s Health) and professional societies (Society for Cardiovascular Angiography and Interventions/Women in Innovations, American College of Cardiology, European Society of Cardiology, and American Heart Association).

Another important issue not really addressed by Mikhail et al. (8) is that women continue to be at risk for important vascular and bleeding complications after PCI (10–13). With the more potent antithrombotic/antiplatelet agents, the susceptibility of bleeding and complications for women will increase. Furthermore, chronic use of such oral agents after PCI with DES and the need to stop these medications due to bleeding in women more often than men have not been fully evaluated. The use of anticoagulants with improved safety profiles (i.e., less bleeding) in the female population would be prudent but is not yet studied, except

*Editorials published in JACC: Cardiovascular Interventions reflect the views of the authors and do not necessarily represent the views of JACC: Cardiovascular Interventions or the American College of Cardiology.

From the Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai School of Medicine, New York, New York. Dr. Mehran is a consultant for Cardiva, Cordis, The Medicines Company, Regado Biosciences, and she received research grant from Bristol-Myers Squibb/sanofi-aventis. Dr. Kini reports that she has no relationships to disclose.
for sub-group, post hoc, underpowered analyses in women (13,14). A detailed bleeding risk profile assessment in the female population undergoing PCI would be prudent to minimize these complications. Finally, dedicated studies need to be performed for evaluation of the utility of risk score assessment in choosing antithrombotic/antiplatelet agents in the female population.

Reprint requests and correspondence: Dr. Roxana Mehran, Mount Sinai School of Medicine, One Gustave L. Levy Place, Box 1030, New York, New York 10029. E-mail: roxana.mehran@mssm.edu.

REFERENCES


Key Words: PCI ■ gender ■ outcomes.