

Gender Difference in the Application of Reperfusion Therapy in Patients with Acute Myocardial Infarction

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Gender difference in the application of reperfusion therapy in patients with acute myocardial infarction (AMI) has been an ongoing topic for more than 20 years [1]. Reports have repeatedly shown that women with AMI were less likely to undergo reperfusion treatment than men, and this persists to the current era [2–5]. In early trials, percutaneous coronary intervention (PCI) was also associated with more procedure-related complications and higher mortality in women than in men [6, 7]. Cardiologists worldwide have since been working on closing the gender gap in care. In 2005, the European Society of Cardiology launched the Women At Heart initiative to raise awareness and improve the quality of care for women with cardiovascular disease, and that year, women and cardiovascular disease were hot topics at the European Society of Cardiology and American Heart Association congresses. Numerous sessions and articles have been fuelling this gender difference debate, and in January 2006, *Circulation* devoted an entire section to highlighting women's heart disease. The gender gap has meanwhile narrowed, and in more recent studies, reported differences between the genders were less pronounced. However, gender differences are still existent as illustrated in the article from Halvorsen et al. [8] from the University Hospital in Oslo.

The authors evaluated whether recent reports on the improved outcome for women undergoing PCI affects

the current treatment provided in real-life situations at 1 single center and whether these reports consequently led to better outcomes. They examined the use of invasive evaluation, revascularization rates and both short- and long-term outcomes. Although the age-adjusted mortality rate was similar in women and men, there were still significant disparities in treatment. Women with non-ST-segment elevation myocardial infarction (NSTEMI) were less likely to undergo invasive evaluation and PCI than their male counterparts.

There has been much debate on whether women with acute coronary syndrome (ACS) should be treated the same as men. In ACS, there is no evidence of gender differences regarding the benefit of primary PCI for patients with ST-segment elevation myocardial infarction (STEMI). Halvorsen et al. [8] show that the gender gap, in terms of the likelihood of STEMI patients receiving invasive procedures (coronary angiography and PCI), if adjusted for age, does not exist anymore. However, gender differences in invasive evaluation and treatment were still observed for NSTEMI patients in their Norwegian patient cohort. Several trials of unstable angina and NSTEMI indicate that women do not benefit from a routine, early invasive treatment strategy as much as men [9–12]. In the Fifth Organization to Assess Strategies in Acute Ischemic Syndromes Investigators (OASIS-5) trial, women with NSTEMI did not benefit from a routine in-

vasive strategy [13]. However, another recent publication showed that an invasive strategy in NSTEMI patients has a comparable benefit in men and in high-risk women, but not in low-risk women [14].

Worldwide, women have angina more often than men [15], and early coronary angiography may be useful for risk stratification. However, it is well documented that coronary angiography usually shows less extensive atherosclerosis in women. Women who present with ACS have a higher incidence of nonobstructive coronary artery disease. Most trials showed around 20% or greater excess of normal or nonobstructive arteries in women [10, 11, 16]. Among ACS patients, the risk-adjusted odds ratio of significant coronary artery disease was 0.47 for women compared with men [17]. Halvorsen et al. [8] confirmed this finding in their cohort: a greater percentage of women than men with NSTEMI had no obstructive coronary artery disease at the time of angiography (23.0 vs. 8.3%). This could, in part, explain the lesser use of PCI in these women, but the benefit of an early invasive strategy for women remains unclear.

Women admitted for ACS in the University Hospital in Oslo were still less likely to receive evidence-based medication than men, even after adjustment for age. This can be partly explained through the concomitant use of platelet inhibitors (aspirin, clopidogrel) and warfarin due to atrial fibrillation. The gender gap in treatment should not be disturbing but reassuring when based on reliable gender-specific data. Increased use of antiplatelet drugs has been suggested to play a role for improvements in long-term mortality after AMI [18]. One finding in the study of Halvorsen et al. [8] is of particular interest. No gender differences were observed in treatment delay, especially in the symptom-to-balloon time. Numerous other studies have reported that women with ACS come later to hospital which delays the start of therapy. Are Nor-

wegian women more aware of heart disease or is there another explanation?

The findings of this study advance our basic knowledge on gender-specific treatment and suggest that men and women now have fairly similar adjusted outcomes after PCI. It is important to have such outcome data to help us understand the reasons for gender disparities in the treatment of AMI.

We still do not know if and why the gender gap still exists or whether it is just a question of age, female conditions and biological differences right down to the cellular level. The gender gap in the application of reperfusion therapy in patients with AMI narrowed with advancing age [19]. The contemporary American National Registry shows women are still less likely to receive reperfusion than men. This difference is largest among young patients, and the gender differences in in-hospital mortality are age dependent in both STEMI and NSTEMI patients [20].

Crude in-hospital mortality of STEMI and NSTEMI patients was higher overall for women than for men. However, after adjustment for age and/or comorbidities, reported mortality was approximately the same. The results from Norway raise the question whether long-term survival was lower in women, especially in those with NSTEMI. The higher mortality rate observed in women compared with men after interventional treatment [21] has been explained by differences in body size and clinical risk factors, anatomical differences, basic biological differences [22, 23] and the differing pathophysiology of ACS conditions according to age [24]. However, this article, along with other recent data, suggests that men and women now have a fairly similar adjusted outcome after PCI [19]. This outcome improvement in women could be due to more invasive evaluation, PCI and stenting as well as better procedural management of anticoagulation.

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