Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 49, No. 14, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.01.053

EDITORIAL COMMENT

The Controversy in Clinical Results Among Men and Women After Coronary Bypass Operation*

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In 1974, disturbed by slightly higher operative mortality in women than in men after coronary artery bypass graft (CABG) operation, we set out to review our experience with this subject. The overall results of operative mortality, infarction rate, number of grafts, graft patency, and postoperative alleviation of angina were different between male and female patients (1). At the time, about 11% of CABG patients were female. Variations in physical findings and coronary anatomy were suspected as possible factors without consideration to the pathophysiological response to atherogenesis due to genetic or hormonal influences. Surprisingly, in that study, the preoperative cardiac systolic function was better in women than in men, whereas diastolic stiffness was worse.

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The debate propagated over decades, from the late 1970s onward, with controversial results reported in various studies, pro and con, related to the effects of gender in results of CABG (2–4). Most studies included retrospective data or propensity matched analysis of large number of patients from multiple institutions. The findings generally supported the significance of body mass index and associated comorbidities as factors that affect early and late outcomes (5–7).

To define the role of preoperative factors, Humphries et al. (8) have used a unique population-based analysis of detailed clinical data on all adults undergoing CABG in British Columbia, Canada, during 1991 to 2004. Their report, in this issue of the *Journal*, involves 20,229 men and 4,983 women (19.7%). Their study highlights the association between gender and 30-day all-cause mortality after CABG. The important finding is the decline in operative mortality in men and in women over a 14-year period, with a more marked improvement seen in the results in women. Overall, the early mortality was higher in women than in men (3.6% vs. 2.0%, $p < 0.001$) and persisted after adjustment for comorbid factors such as gender, age, and number of bypass grafts but attenuated after adjustment for body surface area.

The findings in the report by Humphries et al. (8) corroborate those from the Northern New England Group (9) and with a review of results of CABG from 8 Canadian provinces (10). Shortcomings in this study are the paucity of comparable clinical and comorbidity data because of the retrospective analysis of the results. Intraoperative coronary quality and size were not recorded, and angiographic coronary runoff and myocardial viability data and success or failure of bypass grafts was not known. Because in-hospital mortality was attributable to cardiac causes in 74% of patients, the same incidence was thought to have prevailed in out-of-hospital deaths.

The baseline patient characteristics showed a significantly higher incidence in women than in men of emergency operations, acute coronary syndrome, angina class III or IV, stroke, heart failure, diabetes, peripheral vascular disease, and systemic hypertension. A number of these differences were statistically significant. In this study, a smaller number of women received mammary (arterial) grafts than men, especially in urgent situations. The incidence was lowest in young women (<50 years old). The use of arterial grafts has had important effects on long-term graft patency as well as early and late survival, especially in women (11).

The operative procedures and the surgical technique of coronary bypass grafting was considered similar for all patients (97% had CABG on pump). From a surgeon's point of view, the tissue of coronary arteries and the saphenous vein grafts in women are generally thin and friable (6,12). This demands greater care in the handling of these structures at surgery by using strong magnifying glasses and very fine suture material, preferably in a motionless setting. Hemostasis is crucial, and frequent blood flow measurements are needed to verify graft patency. Prevalence of these factors and poor quality of anastomosis may lead to long operative procedures and may result in a smaller number of bypass grafts limited to the larger vessels.

Much more research and many more prospective studies on the effects and consequences of atherosclerosis in women are needed considering the interplay of genetic and hormonal influences in addition to presently known comorbidity factors (13,14). The development and eventual susceptibility of a new intimal plaque to rupture after establishment of high coronary blood flow needs special attention in view of observations showing that a smaller number of grafts remain patent, for a long time, in women than in men. Because a randomized trial is not possible and the gender differences in surgical

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

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JACC Vol. 49, No. 14, 2007
April 10, 2007:1559–60

results to a significant degree persist, it is justifiable to consider that the clinical presentation and the surgical outcome of coronary artery disease in men and women are not quite similar or comparable in all aspects. Over the past 30 years the ratio of women to men presenting with coronary artery disease has almost doubled, and there have been large numbers of patients to study, allowing for independent evaluation and reporting of medical and surgical interventional therapy of this disease in women. Future research should encourage the institutions involved in following the Coronary Artery Surgery Database to tabulate and report the results for each group separately. Clearly, as recent research and over 56,800 articles published on this subject indicate, the coronary endothelial system is affected by gender characteristics and genetic factors that result in clinical presentation of atherosclerosis with differing clinical manifestations in men and in women (15).

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