Letters to the Editor

Worse early outcomes in women after coronary artery bypass grafting: Is it simply a matter of size?

To the Editor:

Gender differences in the outcome of coronary artery bypass grafting (CABG) are currently a topic of much-deserved attention and debate. We read with interest the recent article in the *Journal* by Guru and colleagues¹ in which they compared early and late outcomes in men versus women for the 1991-2000 Ontario, Canada CABG experience (n = 54,425). The authors' conclusions were as follows: (1) early CABG mortality is higher in women, even after adjustment for covariate predictors; (2) the risk of mortality in women becomes equivalent or better than that in men by 1 year after CABG; and (3) future research should focus on ways to reduce early mortality in women. We wish to comment, with a focus on early CABG outcomes.

We believe that, as written, the above conclusions might be inadvertently misleading because they suggest to the reader that female gender is itself a culprit in worse early CABG outcomes either directly or indirectly through some yet undetermined gender-related variable or variables. This is surprising because it ignores the authors' own data.¹ Specifically, in the 13,921 patients in whom body surface area (BSA) was available, they found no gender differences in early mortality (hazard ratio, 1.04; $P = .72$) after adjusting for BSA in addition to the other predictors. We therefore contend that Guru and colleagues¹ should have perhaps more accurately concluded that worse early mortality in women is present but is explained by their greater propensity for small body size. A recent article in this *Journal* supports this contention. Koch and associates² convincingly demonstrated that female gender per se is not a cause of worse operative mortality. Their analysis of The Cleveland Clinic CABG experience revealed that early CABG mortality is essentially identical in male versus female patients (2.3% vs 2.1%; n = 945 each; $P = .76$) when patients are

rigorously matched for demographics, including body habitus, risk factors, medications, coronary disease, and cardiopulmonary bypass (CPB).

In discussing their data, Guru and colleagues¹ stated the following: "Women tended to have a lower body size, although their distribution of BSA values did overlap with that of men. In view of this fact, the neutralization of early mortality by adjustment with BSA might have occurred partially because BSA served as a surrogate marker for sex." Equally plausible, one can say that female gender is simply a surrogate marker of small size. Also, although it is true that the BSA distributions in men and women overlap, one cannot ignore that they are significantly different. Indeed, among patients undergoing CABG, women are disproportionately represented at both extremes of body size (small and obese), with important implications on outcome.³ Until matched comparisons, including for body size, demonstrate different outcomes for men versus women, we should not ignore the most compelling objective data, which thus far exculpate female gender.^{1,2}

We also suggest that adopting a "small size—worse early outcomes" as opposed to the authors' "women—worse early outcome" perspective to the issue at hand is advantageous because (1) it is more precise and does not ignore the true potential for worse outcomes in small-sized men as well,⁴ and (2) it is helpful because it perhaps appropriately directs future research efforts toward gaining a better understanding of how and why size alters outcomes in this era of CABG. For example, at least when CPB is used, there is gathering evidence that on-pump hemodilutional anemia is particularly prevalent in smaller patients and might be a major cause of morbidity and mortality.^{4,5} Importantly, this role for hemodilution severity during CPB in CABG outcomes is a gender-shared, readily testable hypothesis, and investigating it will simultaneously address (1) the issues of optimizing CPB circuit design

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and practices and (2) the outcome concerns in women and small patients.

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Reply to the Editor:

We thank Dr Habib and colleagues for their interest in this topic. The issue of whether gender, size, or gender in combination with size can explain the worse early mortality after coronary artery bypass graft (CABG) surgery has been an ongoing debate. There still is no comprehensive evidence of what aspects of gender contribute to this increased early mortality risk; however, a strong association to body size has been previously described.¹ It also has been shown that the gender effect of worse early outcome rates of death and low output syn-

drome remain despite adjustment for body size, even when more detailed clinical data are available.¹ Size is important, but it is not the only factor that distinguishes men from women, and this certainly deserves more research. A recent article by Koch and coworkers² used propensity analysis to match women and men using 68 covariates. As seen in this study, only 26% of women from their entire cohort were matched, which certainly limited the generalizability of the study findings for the entire population of women undergoing CABG surgery. Regardless, likely there are factors other than size for women that lead to worse early outcomes after CABG surgery. There is some evidence to show that off-pump coronary artery bypass surgery might reduce adverse outcomes for women.³ Unfortunately, off-pump coronary artery bypass trials will always have a minority of women and thus not be powered to understand the gender effect fully. Perhaps studies understanding the differential gender response to cardiopulmonary bypass and myocardial ischemia are required to more fully understand why there is a gender difference. Retrospective studies, even with detailed clinical data, will never be sufficient to conclusively identify the cause behind this observation, and size only explains part of the gender story. We can all agree that it is time for the research community to look beyond simple gender differences and work in a concerted manner to try and identify the biologic factors that contribute to gender differences in CABG surgery outcomes.

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Something to expect, diagnose, and treat early

To the Editor:

We read with interest the article entitled "Evolutional aspects of children and adolescents with surgically corrected aortic coarctation: clinical, echocardiographic, and magnetic resonance image analysis of 113 patients."¹ We learned that transverse aortic arch hypoplasia should be corrected concomitantly with coarctation.

Nothing about the chest radiograph or cardiothoracic ratio was mentioned. In the authors' echocardiographic analysis, they did not comment about the dimensions or functions of the cardiac chamber, although left ventricular hyperkinesia and increased ventricular mass are found even in normotensive patients long after successful coarctation repair: increased ventricular mass can provoke rhythm disturbances and might cause an imbalance between muscle and coronary vessel growth, with decreased oxygen reserve. Their series is a select group, and not all patients undergoing operations during this 26-year period were included. Therefore, the study is subject to biases and is weak. The definition of recoarctation is to be broadened to include the systolic gradient between the right arm and leg: measured with a sphygmomanometer, Doppler echocardiography, magnetic resonance angiography, and/or angiography of the aortic isthmus and descending aorta, systolic gradients and diameters equal to or greater than 20 mm Hg at rest or a combination of a right arm-leg pressure gradient of more than 50 mm Hg after the bicycle test and more than 40% reduction in cross-sectional diameter of the aorta at the anastomotic site compared with the aorta at the level of the diaphragm.²

The recoarctation percentage after end-to-end anastomosis (14%) is not correct: it should be 12.53% rather than 14%. The patch aortoplasty figure should be 7.69% rather than 7%. However, this did not affect the order of frequency. We do not understand why the aortic ratio median behaved independently of age at coarctation correction or why there was no significant