



Editorial

Sex differences in cardiovascular medicine: Bilateral internal mammary artery CABG

Stephanie L. Sellers^{a,b}, Kenneth R. Holmes^a, Jonathon A. Leipsic^{a,b,*}^a Department of Radiology, St Paul's Hospital and University of British Columbia, Vancouver, Canada^b Centre for Heart Lung Innovation, St Paul's Hospital and University of British Columbia, Vancouver, Canada

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"It is not the answer that enlightens, but the question."

[Eugene Ionesco]

Sex differences in medicine are well established, particularly with respect to cardiovascular disease. Females develop coronary artery disease later in life, commonly manifest with different symptomatology, and have unique risk factors. There has also been a great deal of focus in the last 30 years on defining the performance of various diagnostic algorithms for coronary disease in men and women [1,2]. Similarly, there is growing evidence of sex interactions in subjects undergoing coronary artery bypass grafting (CABG) with worsened clinical outcomes reported in females compared to males irrespective of the graft used [3–5]. Notably, Swaminathan et al. recently reported that female sex remained an independent predictor of mortality following CABG after multivariate adjustment (odds ratio 1.40, 95% CI 1.36 to 1.43, $p < 0.001$) across all age groups in a large US study [3]. However, reasons for these disparate clinical outcomes between females and male are not well established, but have served as fodder for further investigation.

In this edition of the journal, Saraiva and colleagues performed a 10-year retrospective review of clinical outcomes of patients undergoing CABG at a single center in Portugal [6]. Their focus was primarily on the downstream clinical outcomes following single or bilateral internal mammary artery (SIMA or BIMA) CABG. In their analysis, after adjusting for a number of potential co-variables, BIMA were associated

with a worsened outcome in females. Further, on subgroup analysis of female with the addition of propensity score as a covariate, females undergoing BIMA had a significantly worse survival than those that underwent SIMA ($p = 0.039$).

There are a number of potential explanations for these disparate clinical outcomes. Importantly, CABG is much less commonly performed in females and as a result procedural experience may incur increased risk particularly with the more complicated BIMA procedure [7]. Furthermore, subjects who underwent a RIMA to the RCA were excluded which may again reflect a bias towards more complicated BIMA procedures. Further reasons for disparate clinical outcomes described by the authors are not well established, but do provide the foundation upon which to base future investigations.

These findings are highly interesting but may in fact raise more questions than answers. For example, it is interesting to note that females represented a small component of the cohort (19%) and only a modest number of these females number underwent BIMA (27%). The physiology of how IMA graphs differ in females and males is limited. However, one report documents post-menopausal females undergoing CABG to have impaired endothelial function in the IMA compared with males owing to decreased nitric oxide bioavailability [8]. Female cardiovascular physiology has specific biomarkers and has also been shown to be negatively impacted by a number of unique factors such as stress response, pathophysiology of hypertension, estrogen status, association of smoking with myocardial infarction, and incidence of plaque erosion [9,10]. While it is more clear how these sex-specific factors may drive differ CABG outcomes overall, how does this explain the difference in BIMA *versus* SIMA? In terms of current clinical practice, and future clinical and physiological investigation, how should this be addressed? Should women needing bypass be restricted to a single IMA graft? The results presented certainly cannot provide an answer to this question but do certainly suggest that this should be investigated in a prospective fashion.

Disclosures

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* Corresponding author at: Department of Radiology, St. Paul's Hospital, 1081 Burrard St., Vancouver V6Z 1Y6, British Columbia, Canada.

E-mail address: jleipsic@providencehealth.bc.ca (J.A. Leipsic).

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