Commentary: Nuisance or nemesis? Postoperative atrial fibrillation increases long-term mortality regardless of sex

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Central Message

Women have fewer, shorter episodes of postoperative atrial fibrillation. Postoperative atrial fibrillation in both sexes was associated with worse survival.

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Postoperative atrial fibrillation (POAF) complicates approximately 30% of coronary artery bypass grafting (CABG) procedures.¹ POAF has been associated with perioperative adverse outcomes including stroke, reoperation for bleeding, myocardial infarction, and pacemaker use.^{1,2} Patients with POAF are known to have a significantly increased risk of mortality in short-term, midterm, and long-term follow-up. POAF also lengthens hospital stay by 3 to 5 days and increases hospitalization cost from \$10,000 to \$20,000 per patient.³ Although female sex has been found to be protective against new-onset atrial fibrillation,⁴ in general, studies continue to demonstrate poorer outcomes of women after cardiac surgery.⁵⁻⁸ The effect of sex on POAF represents an interesting area of study.

We congratulate Filardo and colleagues⁹ on their study in this issue of the *Journal* addressing this topic. Filardo and colleagues⁹ report a multicenter propensity score-adjusted study comparing the incidence of POAF, perioperative outcomes, and 9-year survival of men and women undergoing CABG. The study investigated 9203 patients from 4 US centers. POAF, defined as any episode detected by electrocardiogram or telemetry during the index hospitalization, regardless of intervention, occurred in 32% of the study population, which is consistent with literature-reported values. POAF risk in women was 5% less than that in men (33% in men vs 27% in women; $P = .04$) in adjusted analyses. Although in-hospital mortalities was equivalent in men and women without POAF ($<1\%$), there was a trend towards higher risk of in-hospital death among women with POAF than among men with POAF (odds ratio, 2.49; 95% confidence interval, 0.94-6.56; $P = .06$). The proportion of patients discharged home in atrial fibrillation was 2.6%. POAF was associated with increased mortality at 9 years (hazard ratio, 1.56; 95% confidence interval, 1.45-1.67). This was equivalently high among men (hazard

ratio, 1.57; 95% confidence interval, 1.49-1.65) and women (hazard ratio, 1.54; 95% confidence interval 1.14-2.07).

This study must be interpreted in the context of a few limitations. First, the study period (2002-2010) may not reflect contemporary CABG practice and POAF management, particularly with the advent of direct oral anticoagulants. Importantly, studying only predischARGE POAF may underestimate incidence. Remote telemetry monitoring after cardiac surgery is currently being investigated in a randomized, controlled trial (NCT02793895); however there is already evidence that atrial fibrillation is underdetected in patients with a recent cryptogenic ischemic stroke or transient ischemic attack. A randomized clinical trial comparing 30-day loop recorder monitoring versus 24 Holter monitoring showed that an absolute difference of 13% in the detection of atrial fibrillation with 30-day monitoring.¹⁰ Filardo and colleagues⁹ performed propensity score adjustment on the basis of relevant risk factors; however, this did not include duration of cardiopulmonary bypass, number of grafts, or completeness of revascularization. These factors both potentially affect the development of atrial fibrillation and may differ by sex. Indeed, studies have shown that female patients receive fewer arterial and total grafts.^{6,8} We applaud Filardo and colleagues⁹ for diligently performing linkage to a death registry to ascertain survival. Late events such as thromboembolism, bleeding, and stroke, which

were not studied, may be key to explaining the observed excess mortality associated with POAF. Finally, there is a lack of information regarding atrial fibrillation management in this study. Regarding pharmacologic management, a randomized clinical trial comparing rhythm with rate control in 523 patients with POAF showed no difference in freedom from atrial fibrillation at 60 days between the 2 groups, suggesting that either treatment may be effective in managing POAF.¹¹ Despite treatment effectively restoring sinus rhythm in more than 94% and more than 84% at 30 and 60 days,¹¹ respectively, we still find POAF to be associated with excess late mortality, and the long-term effect of potential differential treatment by sex remains unknown.

An interesting paradox was found by Filardo and colleagues.⁹ Although Filardo and colleagues⁹ show that POAF is associated with poorer late survival in women and men, and of similar magnitude, they also showed that the early burden of POAF was less in women than men—women had fewer episodes and shorter duration of atrial fibrillation episodes. These findings appear discrepant. There is evidence that women with atrial fibrillation are less likely to undergo cardioversion than men,¹² which reiterates the potential undertreatment of women with advanced cardiac disease that has been pervasively demonstrated in the literature. Although Filardo and colleagues⁹ do not report treatment outcomes, differential treatment could be a missing link between lower burden of POAF and equally poor survival compared with men.¹³

In summary, this is the first propensity-adjusted study to compare post-CABG atrial fibrillation incidence by sex and examine survival as late as 9 years. This important study affirms that POAF is more nemesis than nuisance; its strong adverse effect on long-term survival regardless of sex,

despite its lower incidence in women, should prompt further investigation into pathophysiologic mechanisms and optimal management.

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