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Clinical Outcomes and Imaging Findings in Women Undergoing TAVR

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ABSTRACT

Transcatheter aortic valve replacement (TAVR) has become the standard of care for patients with hemodynamically severe aortic stenosis who are symptomatic but deemed too high risk for surgery. Recent reports suggest that sex differences exist in outcomes following TAVR and in the diagnostic imaging evaluation of patients being considered for TAVR. In this review, the authors explore the differences between men and women in baseline characteristics and outcomes following TAVR, as well as sex differences in the imaging findings of severe aortic stenosis (AS) including the diagnostic challenges in the hemodynamic assessment of severe AS in elderly women, differences in aortic valvular calcification and in the associated myocardial response to severe AS. Additionally, sex differences in imaging findings as they relate to post-TAVR complications including coronary obstruction, annular rupture and prosthesis–patient mismatch are also discussed. (J Am Coll Cardiol Img 2016;9:483–93) © 2016 by the American College of Cardiology Foundation.

With a reported prevalence of 12.4% among elderly patients, aortic stenosis (AS) is considered the most common form of valvular heart disease in ageing Western populations (1). The prognosis of hemodynamically severe and symptomatic AS is poor without valve replacement (2–4). Many elderly patients, however, are considered inoperable due to the prohibitive operative risks associated with multiple comorbidities, which are frequently observed in this population. In this setting, transcatheter aortic valve replacement (TAVR) represents what may be now considered standard care, with randomized trials demonstrating improved clinical outcomes compared with standard therapy in patients considered too high risk for surgery (3), and similar (5) or possibly improved (6) outcomes compared with surgery in high-risk surgical candidates.

Procedural refinement in the last 5 years has led to further improvements in clinical outcomes following TAVR. This has largely arisen through advancement of transcatheter heart valve (THV) technologies and delivery systems; but also as a result of the integration of advanced cardiac imaging into the periprocedural evaluation of TAVR patients. Both multidetector computed tomography (MDCT) and 3-dimensional echocardiography have played critical roles in this regard (7–9). Importantly, however, despite a broad integration of advanced imaging in TAVR, the relative outcomes in men and women remain different as suggested by recent meta-analyses that show a medium-term survival advantage for women following TAVR despite higher rates of short-term complications, particularly major vascular complications (10–12). Moreover, the diagnostic imaging features of patients with severe AS presenting for TAVR; the left ventricular (LV) remodeling in response to severe AS and reverse remodeling following TAVR are different in women compared with men. Accordingly, an imaging-based evaluation of women with severe AS being considered for TAVR should take into consideration these sex-specific differences in presentation and outcomes.

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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVA = aortic valve area

AVC = aortic valve calcium

CMR = cardiac magnetic resonance

LGE = late gadolinium enhancement

LV = left ventricular

LVOT = left ventricular outflow tract

MDCT = multidetector computed tomography

PLFLG = paradoxical low-flow, low-gradient

PPM = patient-prosthesis mismatch

PVR = paravalvular regurgitation

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

ViV = valve in valve

We review herein the comparative differences in: 1) baseline characteristics and outcomes following TAVR in women; 2) imaging findings of severe AS and the associated myocardial response to severe AS in women presenting for TAVR; and 3) imaging findings as they relate to post-TAVR complications that are more common in women.

BASELINE CLINICAL PROFILE AND CLINICAL OUTCOMES FOLLOWING TAVR IN WOMEN

Although most clinical TAVR studies have collectively analyzed data from both sexes, the baseline clinical risk profile and subsequent clinical outcomes following TAVR are clearly different in women compared with men. Although many studies have shown similar pre-procedural risk between women and men (13–20), recent large meta-analyses demonstrate that overall pre-operative risk stratification scores (logistic EuroSCORE) are lower in women presenting for TAVR compared with men (10,11). In the meta-analysis reported by O'Connor et al. (10), which included patient-level data obtained from 11,310 patients (51% female) in 5 registries, including the PARTNER (Placement of Aortic Transcatheter Valve) trial, the Logistic EuroSCORE was 22.2 ± 13.9 in women and 23.9 ± 15.4 in men ($p < 0.001$) despite the fact that sex is a score component by which female sex adds to overall risk. Women presenting for TAVR generally have a lower burden of overall cardiovascular risk factors and atherosclerotic burden, with lower rates of prior myocardial infarction and revascularization, as well as lower rates of previous stroke and peripheral vascular disease, and better LV systolic function at presentation (10). Similar findings have been shown in other sex-based analyses of TAVR patients (11,15–18,20,21). The prevalence of noncardiovascular comorbidities also appears to be different between sexes, with less pulmonary disease, but more renal insufficiency, reported in women compared with men (10,14,15,19).

Several single and multicenter studies, as well as 3 meta-analyses, have specifically evaluated sex differences in medium-term survival following TAVR (**Table 1**) (10–12). Although some single and multicenter studies showed similar survival between the sexes (14,15,20,22,23), large meta-analyses consistently demonstrate improved medium-term survival following TAVR in women (**Figure 1**) (10–12). O'Connor et al. (10) showed that female sex was independently associated with improved survival at a median follow-up of 387 days, despite higher rates of immediate post-procedural complications, including vascular complications, major bleeding, stroke, and cardiac tamponade. Similarly, Conrotto et al. (11). conducted a meta-analysis that included 6,645 patients (50% female) and also demonstrated a lower mortality rate in women compared with men (24% vs. 34%) at a median follow-up of 365 days, again, despite a higher rate of vascular complications and major bleeding. Stangl et al. (12) also showed 30% lower risk of death in women compared with men at medium term follow-up (> 3 months) despite more frequent major vascular complications in a meta-analysis including data from 7,973 patients (53% female). In addition to the aforementioned sex-specific analyses, in a recent risk-adjusted analysis of mortality using data from the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapies) registry, which included more than 12,000 patients (52% female), female sex was associated with improved survival (24). Similarly, in a propensity-matched analysis of TAVR compared with surgery, female sex was the only predictor of improved survival with TAVR on subgroup analysis (25). This survival advantage with TAVR versus surgery was also shown for women considered high-risk surgical candidates in a retrospective analysis of the PARTNER trial, particularly among women considered suitable candidates for transfemoral access (26).

The improved survival among women undergoing TAVR is in keeping with their lower baseline risk profile and longer mean life expectancy. In addition, the incidence of moderate or greater paravalvular regurgitation (PVR), an important determinant of prognosis post-TAVR (27,28), appears to also be less frequent in women (10,11,18). This may offset the negative mortality impact of other complications, particularly major vascular complications and bleeding, which occur more frequently in women. The determinants of survival post-TAVR may also be different between the sexes. For example, LV systolic dysfunction has been shown to be predictive of mortality in both men and women; however, coronary artery disease is only predictive of death in women, but not in men (17).

Frailty is also an important determinant of mortality post-TAVR; however, there are limited data regarding sex differences at baseline, with mixed results previously reported. In some studies, there was no difference in baseline frailty (19,29,30), whereas women were reportedly more frail than men in another study (13). Importantly, frailty has been shown to be predictive of mortality following TAVR,