

EDITORIAL COMMENT

Unequal Treatment and Yentl Syndrome

Are We Providing Appropriate Care for Our TAVR Patients?*



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In 2003, the Institute of Medicine's "*Unequal Treatment*" report noted that racial and ethnic disparities in health care do exist and that many sources, including health care systems, providers, hospital administrators, and patients, play a role in such disparities.¹ *Unequal Treatment* offered recommendations for improvements with suggestions for future research initiatives and collection of data. During that same time, Dr Bernadine Healy used this term *Yentl syndrome* to point out the underdiagnosis and inconsistent treatment of women with ischemic heart disease compared with men, thereby leading to poorer outcomes in the former group.² These sex and racial biases and disparities were existent nearly 2 to 3 decades ago, and it is imperative to investigate whether we have learned from previous inconsistencies and whether similar practices still occur now. More specifically, have we recognized that significant sex-based, racial, and ethnic disparities in the diagnosis, management, and outcomes of aortic stenosis (AS) do exist and tried to correct past shortfalls when it comes to managing patients with transcatheter aortic valve replacement (TAVR)?

A historical backdrop reveals that women undergoing surgical aortic valve replacement have traditionally faced higher risks and poorer outcomes.³ However, in this issue of *JACC: Asia*, Kim et al⁴ shed light on the complex narrative surrounding TAVR outcomes and unveil inconsistent findings regarding sex-specific differences. Some studies have reported comparable survival rates between men and women

post TAVR, whereas other studies have suggested a potential survival advantage for women. Therefore, Kim et al⁴ tried to assess whether sex-specific differences in baseline clinical and anatomical characteristics affect clinical outcomes after TAVR and investigated the impact of sex on clinical outcomes among different racial groups, particularly between Asians and non-Asians.

The observational study conducted by Kim et al⁴ looked at 1,412 patients from the TP-TAVR (Trans-Pacific TAVR) Registry with severe AS who underwent TAVR at 2 major centers in the United States and 1 major center in South Korea. Data were retrospectively collected for cases performed before initiation and prospectively thereafter. All 3 databases were standardized, and then baseline demographics, functional status, clinical risk factors or coexisting conditions, surgical risk score, anatomical or hemodynamic parameters, procedural characteristics, and outcomes were collected. The primary outcome was a composite of death from any cause, stroke, or rehospitalization after 1 year.

Overall, the study suggested that there were significant differences between male and female patients regarding demographics, comorbidities, and hemodynamic or anatomical findings. Male patients were younger and had a significantly lower Society of Thoracic Surgeons score, which could reflect a delay in TAVR indication or patient selection. Conversely, male patients had a higher prevalence of diabetes, smoking, hyperlipidemia, a previous history of myocardial infarction, percutaneous coronary intervention, or bypass surgery, atrial fibrillation, and peripheral vascular disease. Such sex-specific differences in baseline characteristics were more noticeable in the non-Asian cohort than in the Asian cohort. Regarding anatomical characteristics, female patients had smaller aortic valve areas and annular sizes and a higher mean left ventricular ejection fraction compared with male patients. These features were consistent in both the Asian and non-Asian patients.

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Procedural characteristics revealed that female patients more frequently underwent implantation of self-expandable valves and smaller TAVR valves. There were no significant sex-specific differences in the rates of in-hospital clinical events except for stroke, which was more prevalent in women than in men. In the non-Asian cohort, the implantation of a new permanent pacemaker was more frequent among male patients, but new onset atrial fibrillation was more frequent among female patients.

Overall, there were no significant sex-specific differences in 30-day rates of the primary composite outcome and its components, except that the 30-day stroke rate was significantly higher in women than in men. This trend was similar for each racial group but statistically significant only in the non-Asian cohort. Importantly, this study showed that the 1-year observed rate of the primary composite of death, stroke, or rehospitalization was similar between male and female patients (27.9% vs 28%, respectively; log-rank $P = 0.752$). There were no sex-specific differences in the adjusted risks of all-cause mortality and rehospitalization in the overall cohort or each racial group. This trend was consistent in both the Asian and non-Asian cohorts. Regarding each component of primary outcome, the unadjusted 1-year rate of all-cause mortality was significantly higher in men than in women in the overall cohort. There was no significant relationship between sex and racial group with respect to each component of all-cause mortality, stroke, or rehospitalization, except for cardiovascular death (P for interaction = 0.028).

The TP-TAVR registry, being a multinational, multicenter study involving major institutions in the United States and South Korea, ensures a diverse patient group, thus accounting for variations in health care systems, demographics, and clinical practices. Such inclusivity enriches the generalizability of the study's findings. However, Kim et al⁴ do recognize that there are limitations to this study, including its observational design, possible intersite variability, lack of long-term results, and limited database. Despite these limitations, there was still an effort made to investigate the presence of different clinical and anatomical characteristics of Asian patients compared with non-Asian patients and the impact of sex on the clinical outcomes of TAVR between these groups of patients. Kim et al⁴ concluded that there were

significant differences in baseline clinical and anatomical characteristics between male and female patients. However, the observed and adjusted rates of the primary composite outcome of death, stroke, or rehospitalization and all-cause mortality after 1 year, contrary to historical trends, were not significantly different between men and women following TAVR. This consistency holds true across both Asian and non-Asian cohorts, and it challenges preconceived notions about sex-specific differences in TAVR outcomes.

An important observation pertains to the higher incidence of stroke in female patients, particularly in the non-Asian cohort. We highlight the need for further investigation into the factors contributing to this disparity, including baseline characteristics, procedural variables (including TAVR valve choice), and potential post-TAVR medication differences.

We commend Kim et al⁴ for initiating the data collection and research. Previous studies revealed that various issues arise in non-White patients when it comes to diagnosis and treatment of AS.⁵⁻⁸ Although this study suggests nonsignificant primary outcomes between male and female patients (and between Asians and non-Asians) at 1 year, future research, including long-term analyses, will be instrumental in solidifying these insights. The possibility that sex and racial minorities may encounter other challenges during diagnosis, management, and final treatment for their AS still requires further investigation. Determinants that adversely affect overall health, other medical comorbidities, time to therapy for AS symptoms, and even implicit biases within the health care field may factor into the challenges faced by women and ethnic minorities. What is most obvious is that further research is needed to achieve a better understanding about whether such sex and racial disparities occur on a long-term basis.

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