Sex, Symptoms, and Atrial Fibrillation

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You can observe a lot just by watching.
Yogi Berra, When You Come to a Fork in the Road, Take It!, 2001

Registries provide a unique opportunity to observe the contemporary practice of medicine for a defined disease state. Liberated from the strict inclusion/exclusion criteria of clinical trials and the agendas of study sponsors, these real-world cohort studies can provide valuable information about clinical practice, patient outcomes, safety, and comparative effectiveness. In this issue of JAMA Cardiology, the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) was used to examine the differential effect on symptoms, functional capacity, and quality of life that atrial fibrillation (AF) has on men and women and the variability in treatments and outcomes between the sexes. These issues, particularly those not related to stroke and death, are of particular interest when it comes to AF given the growing prevalence of the disease and a treatment approach frequently guided not by the burden of the disease in an individual inasmuch as by the burden of the disease on an individual.

Atrial fibrillation affects men and women differently. The prevalence of AF is lower for women across all age groups. Differential outcomes have been demonstrated, with most studies supporting female sex as an independent risk factor for stroke. Mortality is affected too, as the presence of the arrhythmia appears to negate the overall survival benefit observed in women. Treatment also varies, as women are less likely to undergo pulmonary vein isolation and less likely to receive anticoagulation as 80% of patients with CHADS2 (congestive heart failure, hypertension, age >75 years, diabetes mellitus, and stroke [doubled]) scores greater than 1 were receiving this approach, and anticoagulation was lower in women compared with men.

The ORBIT-AF registry exposes both our progress and stagnation when it comes to AF management. First, it appears that advancement has been made in prescribing anticoagulation as 80% of patients with CHADS2 (congestive heart failure, hypertension, age >75 years, diabetes mellitus, and stroke [doubled]) scores greater than 1 were receiving this therapy, a significant increase compared with older cohort studies. Conversely, digoxin, a drug that neither maintains sinus rhythm nor adequately controls ventricular response, was still being used to treat almost a quarter of patients. The most effective treatment for maintaining sinus rhythm, AF ablation, still appears to be underused, while ablation of the ativoventricular node, the “last-ditch” effort of AF management, was being performed maybe more than is necessary.

While registries provide important contributions to our understanding of how medicine is practiced, they also have significant limitations that cannot be ignored. The ORBIT-AF registry accepted “all comers” and the mean age was significantly higher in women compared with men and higher overall compared with other US and European registries. Accordingly, CHA2DS2-VASc (cardiac failure or dysfunction, hypertension, age...
>75 years (doubled), diabetes mellitus, stroke (doubled)-vascular disease, age 65-74 years, and sex category (female) scores were also greater in women, a factor that may have contributed to the observed differences in quality of life and functional status and may limit the generalizability of the findings to all populations. Furthermore, unlike clinical trials where randomization attempts to ensure that treatment arms are comparable, baseline differences in a registry may allow for residual or unmeasured confounders that cannot be fully accounted for with statistical methods. Indeed, the residual differences between men and women observed in ORBIT-AF cannot be explained by comorbidity burden alone and highlight an important avenue for future research. Data completeness and follow-up may also be problematic as evidenced by the fact that health status data were not available for all patients in ORBIT-AF and less than half the patients who reported health-related quality of life at baseline did so again at the 2-year mark. Overall, patient registries can demonstrate what issues are worthy of future exploration but the findings are usually more hypothesis generating than definitive. The ORBIT-AF registry shows us that “you can observe a lot just by watching,” but in medicine, watching is usually just the beginning.

REFERENCES