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Sex and Race/Ethnicity Differences in Atrial Fibrillation

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Atrial fibrillation (AF), a worldwide epidemic, contributes to frequent hospitalizations, stroke, heart failure, disability, mortality, and health-resource consumption (1). AF affects people differently with regard to sex, race, ethnicity, and socioeconomic status, and reviews of these differences have highlighted related care disparities.

Accordingly, the American College of Cardiology's Cardiovascular Disease in Women Committee sought to compare these findings in patients with AF to identify potential interventions that may help to rectify disparities of care. This writing group reviewed >200 English-language papers about these disparities to summarize them and identify important knowledge gaps. The most pertinent findings are presented here with recommendations to decrease these disparities in the future.

Globally, it is estimated that 23.1 million women and 23.2 million men had AF (atrial fibrillation and atrial flutter) in 2016, with numbers expected to rise (1). The prevalence of AF in the United States was 5 million in 2010 and is projected to be ~12 million by 2030; the cost was ~26 billion U.S. dollars in 2005 (1). Men of European ancestry have a higher incidence and lifetime risk of developing AF.

We found publications of racial/ethnic differences compared Non-Hispanic whites to blacks, as well as considerable differences by sex and socioeconomic status. Differences in sex and race/ethnicity of patients with AF exist in: 1) epidemiology; 2) lifetime stroke risk; 3) mortality; 4) symptoms and quality of life; and 5) treatment. After adjustment for risk factors, compared with their white counterparts, other races/ethnicities had lower incidence rates of

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AF: blacks (hazard ratio [HR]: 0.84; 95% confidence interval [CI]: 0.82 to 0.85), Hispanics (HR: 0.78; 95% CI: 0.77 to 0.79), and Asians (HR: 0.78; 95% CI: 0.77 to 0.79; all $p < 0.001$) (2).

The overall lifetime risk of AF comparing sexes appears similar, yet AF does not affect women and men similarly at any given age. The lifetime risk and age-adjusted incidence rates vary by sex, race/ethnicity, and risk factor burden. The lifetime risk of AF according to risk factor burden, after adjustment for competing risk of death at age 55 years, is higher in men compared with women (optimal risk factor burden: men 29.8%, women 20.5%; borderline risk factor burden: men 39.7%, women 28.0%; elevated risk factor burden: men 43.3%, women 34.6%) (3). Whites have a higher incidence than blacks, and white men have a higher incidence than white women for all levels of risk factor burden, including smoking, alcohol consumption, body mass index, blood pressure, and diabetes (2,4). In patients with the elevated risk factor burden, the incidence rate of AF (mean age 54.2 years) per 1,000 person-years adjusted for age was higher in whites compared with blacks (white men 9.1, black men 6.0, white women 6.0, black women 4.1) (4).

In the ARIC (Atherosclerosis Risk In Communities) cohort, the lifetime AF risk varied by sex in whites but not in blacks among people age 45 to 55 years (5). White men had a 36% lifetime risk of developing AF versus 30% in white women. Black women had a 22% lifetime risk of developing AF versus 21% in black men (5). The Framingham Heart Study (European ancestry) suggested that at age 55 years, the lifetime risk of AF varied by sex, as well as by the presence and burden of AF risk factors, as summarized in **Figure 1** (3). Also, white men and women have a higher lifetime risk of developing AF versus their black counterparts (5).

Women and blacks with AF are both less likely to be prescribed oral anticoagulants. Registry data found women with AF were significantly less likely to receive oral anticoagulants at all stroke risk scores using the CHA_2DS_2-VASc algorithm (1 point for Congestive heart failure, Hypertension, Age >65 years, Diabetes, Female Sex, and Vascular disease, and 2 points for Stroke and Age >75 years) and less likely to receive oral anticoagulants than men (6). A Medicare database study (2010 to 2011) reported that blacks and Hispanics versus whites, as well as women versus men, were less often given oral anticoagulation for stroke prevention, potentially contributing to the excess mortality in these groups (7).

Women compared with men, and blacks compared with whites with AF have higher mortality. In a meta-analysis of 30 studies with over 4.3 million participants, in absolute terms, AF was associated with a higher all-cause mortality in women compared with men: 1.8 (95% CI: 1.1 to 2.6) per 1,000 patient-years (8). The study found that the pooled relative risk of all-cause mortality for those with AF versus those without AF was higher in women compared with men (relative risk [RR]: 1.69 [95% CI: 1.50 to 1.90] vs. 1.47 [95% CI: 1.32 to 1.65]). The ratio of relative risks for women compared with men for mortality was 1.12 (95% CI: 1.07 to 1.17). The excess mortality risk in women compared with men was similar in sensitivity analyses, including mode of ascertainment, region, number of study participants, and year of study (8). Similarly, compared with men, women had a significantly greater ratio of relative risks for several outcomes including stroke (RR: 1.99; 95% CI: 1.46 to 2.71) and heart failure (RR: 1.16; 95% CI: 1.07 to 1.27) (8). In hospitalized patients, blacks with AF have a higher mortality versus whites with AF (odds ratio: 1.90; 95% CI: 1.50 to 2.50) (9).

Women compared with men and blacks compared with whites are more likely to be symptomatic with AF (10). Women and blacks with AF also have more functional impairment, more limitations in daily activities, and lower quality of life versus men. In some studies, women and blacks had lower quality-of-life scores even after adjustment for comorbidities (10).

In a large observational study of Medicare patients with AF from 2010 to 2011, women, blacks, and Hispanics, compared with white men, were all more likely to receive rate control treatment than rhythm control treatment. This was particularly true for catheter ablation versus rate control therapy (7). Another study found similar racial/ethnic treatment differences of AF. Black and Hispanic individuals were more likely to receive rate control strategy (67% in whites, 72% in blacks, and 80% in Hispanics). White men were more likely to be treated with cardioversion, antiarrhythmic drugs, and interventional therapies for AF, including catheter ablation and surgical maze procedure (10).

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation
CI = confidence interval
HR = hazard ratio

KNOWLEDGE GAPS

There is a significant difference in the prevalence of AF by sex, with a 3:2 male to female ratio that has not been fully explained. However, this observation does not consider age-related differences and the predominance of women in our elderly population. Addressing this sex knowledge gap could provide direction for novel approaches

FIGURE 1 Summary of Sex and Racial/Ethnic Differences in AF

Epidemiology of AF in men and women by risk factor burden			
	Risk Factor Burden*		
	Optimal	Borderline	Elevated
Lifetime Risk (%) of AF in men and women according to risk factor burden, after adjustment for competing risk of death at age 55 years[a]			
Men	29.8%	39.7%	43.3%
Women	20.5%	28.0%	34.6%
Incidence rate of AF per 1,000 person-years adjusted for age (mean age, 54.2 years)[b]			
Black women	0	1.7	4.1
White women	2.0	2.7	6.0
Black men	0	2.6	6.0
White men	4.0	5.2	9.1

Epidemiology and risk	
Higher incidence	White Men
Higher age adjusted prevalence	Women
Higher lifetime risk in whites	Men
Higher lifetime risk in blacks	Same in women and men
Higher risk of death from AF	Women and blacks†
Symptoms and quality of life	
Longer duration of symptoms	Women and blacks
More functional impairment and limitation of ADLs	Women and blacks
Worse quality of life scores	Women and blacks
Risk and Prevention of Stroke	
Higher risk for AF-related stroke	Women and blacks
Less likely to receive anticoagulation	Women, blacks and Hispanics
Rate and rhythm control	
More rate control than rhythm control including drugs, cardioversions, and catheter ablations	Women, blacks and Hispanics

*Investigators classified risk factor burden based on presence of smoking history, body mass index category, systolic and diastolic blood pressure categories, hypertension treatment, and/or diabetes category. The Framingham Study included alcohol category, but the ARIC Study did not. †In hospital mortality only for blacks. ADLs = activity of daily living; AF = atrial fibrillation. [a]Data from Framingham Heart Study (European ancestry), at age 55 years, Staerk et al. (3). [b]Data from ARIC (Atherosclerosis Risk In Communities) Study, Huxley et al. (4).

to forestall or even prevent the development of AF in men and women.

There is more published data reporting on and studying sex differences compared with racial/ethnic differences in patients with AF. Nevertheless, in the analysis reported, it appears that there are significant racial/ethnic differences, with whites having higher rates of AF versus blacks. An overview of data on AF in sex and racial/ethnic differences indicates that women and blacks have a lower incidence and prevalence, but a poorer prognosis with AF including an increased risk for stroke, heart failure, and mortality. Reasons for these differences are unclear, but genetic, socioeconomic, and other factors likely play a role. Again, addressing this gap could yield clues to the mechanism(s) of AF.

There are widespread sex and racial/ethnic differences in epidemiology, risk factors, disease manifestations, and clinical outcomes, as summarized in **Figure 1**. Further, people of different sex, ages, races, and ethnicities have different incidences of cardiovascular disease and may react differently to AF therapies.

SUMMARY AND CONCLUSIONS

AF is a complex disease with sex and racial/ethnic differences in epidemiology, risk factors, treatment, and outcomes. Compared with white men, women and certain ethnic groups with AF often experience longer lasting and more frequent symptomatic AF episodes, have worse quality of life, have more drug-related adverse events, have lower rates of anticoagulation, have less aggressive care in terms of rate versus rhythm management, and have a higher adjusted risk of death. It is likely that the lower rates of oral anticoagulation in appropriate patients may be responsible for the higher stroke risk and worse outcomes in women and certain ethnic groups. The use of antiarrhythmic drugs requires closer follow-up than rate controlling drugs, and their proarrhythmic risk may contribute to worse outcomes in patients who are not frequently monitored.

FOR THE FUTURE

We need to continue to increase our understanding of these differences to decrease disparities of care across patient populations to improve outcomes from AF in all patients regardless of sex and race/ethnicity. We suggest that as cardiologists and cardiology organizations, our responsibilities to decrease health care disparities include: 1) disseminating information about health care disparities in AF by cardiology organizations; 2) using shared decision tools for the use of oral anticoagulation in all patients at risk for stroke and thromboembolism; 3) offering equitable treatments to decrease symptoms and improve the quality of life of all patients with HF; and 4) taking measures to decrease risk from antiarrhythmic drugs such as more frequent visits and monitoring for side effects.

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