

EDITORIAL

Atrial Fibrillation Related Mortality: Another Curve to Bend

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Atrial fibrillation (AF) is the most common arrhythmia encountered in adults and has long been recognized to be associated with age, underlying cardiovascular disease, and increased risk for stroke, heart failure, and dementia.^{1,2} The extent to which AF directly contributes to mortality as opposed to identifying patients with worse underlying cardiovascular disease is not clear. We can expect, however, that with the increase in AF predicted from aging of the population and the increasing prevalence of AF risk factors (including obesity, diabetes mellitus, and hypertension), an increase in mortality associated with AF will be observed. This concern is brought into sharp focus by Tanaka et al in this issue of the *Journal of the American Heart Association (JAHA)*.³ They analyzed primary and contributing causes of death specified by the *International Classification of Diseases, Tenth Revision (ICD-10)* codes in death certificate information reported to the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research database for the period between January 1, 2011 and December 31, 2018. A total of 276 373 cardiovascular deaths had AF as an underlying or primary cause or a contributing cause and were considered deaths related to AF. Strikingly, cardiovascular deaths related to AF increased from 18.0 per 100 000 (95% CI, 17.8–18.2) in 2011 to 22.3 per 100 000 (95% CI, 22.1–22.5) in 2018. The leading primary causes of death related to AF were ischemic heart disease followed by cerebrovascular disease.

See Article by Tanaka et al.

Of concern, the increase in deaths related to AF was not related only to an aging population. The rates of AF-related deaths increased at a faster relative rate in younger adults (35–64 years) compared with older adults (65–84 years). Also of concern, although AF is most prevalent in populations of European descent, in the younger age group death rates were greater for Black men and women than White men and women. This observation is consistent with prior studies and could reflect racial disparities in health care.⁴ Could AF be growing more lethal, in the setting of a decrease in overall cardiovascular health, or more likely, are AF and its associated diseases increasing in the population and starting at an earlier age?

The evidence for an increase in AF-associated mortality is somewhat at odds with the advancements in contemporary therapies for AF management. The pillars of AF management include stroke prevention, rate control when AF is present, and AF prevention or maintenance of sinus rhythm. Over the past decade stroke prevention has improved with availability of direct acting anticoagulants that foster better compliance and were found to be associated with a reduction in all-cause mortality compared with warfarin treatment in a meta-analysis.⁵ Expense is a hindrance to access of these agents for some patients, which could

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contribute to disparities. There is also progress in other aspects of AF management. For years randomized trials failed to show benefit for the “rhythm control strategy” of attempting to maintain sinus rhythm with antiarrhythmic drugs.⁶ Rate control strategies had the advantage of avoiding harmful antiarrhythmic drug toxicities and repeated cardioversions. Antiarrhythmic drug efficacy was often disappointing. In the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study,⁶ rhythm-based treatments in the majority of patients consisted of amiodarone or sotalol with 38% having crossed over to rate control at the 5-year follow-up owing to either side effects or poor efficacy of the drugs. Even in patients with heart failure, which is often aggravated by AF, a routine strategy of rhythm control did not reduce cardiovascular death.⁷ Some systematic reviews of randomized clinical trials even raised the concern that rhythm control strategies may increase stroke and adverse events⁸ and fail to improve outcomes, especially in patients with mild AF symptoms.⁹

With the maturing of catheter ablation for treatment of AF, this therapy has become a better alternative than antiarrhythmic drugs for rhythm control for many patients.^{10,11} Recent randomized trials support better outcomes for maintaining sinus rhythm in patients with recent onset AF, and those who are candidates for catheter ablation, including some patients with heart failure.¹² In the CABANA (Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation) trial,¹³ ablation improved the composite of mortality or hospitalization for cardiovascular causes (hazard ratio [HR], 0.83; 95% CI, 0.74–0.93) and was associated with less AF. In EAST-AFNET 4 (Early Treatment of Atrial Fibrillation for Stroke Prevention Trial), patients with recently diagnosed atrial fibrillation had lower risk of death from cardiovascular causes, stroke, hospitalization for heart failure, or acute coronary syndromes (HR, 0.79; 95% CI, 0.66–0.94; $P=0.005$) with early rhythm control.¹⁴ The patients in this trial were also treated appropriately with anticoagulation and other cardiovascular therapies (renin-angiotensin-aldosterone system inhibitors, beta blockers, and statins) that likely contributed to the outcomes seen. Ablation is more often considered an option for younger patients with relatively recent onset AF, consistent with enrollment in these trials. There is also increasing awareness of AF and availability of consumer health monitoring devices with the potential for early detection of AF.¹⁵ There is great potential for improvements in detection and therapy to have an impact, particularly relevant to the increasing younger population with AF.

The increased AF-related mortality is most likely driven by an increase in AF prevalence. The authors postulate that the growing burden of cardiovascular risk factors is likely contributing to the adverse trend.

The largest impact to reduce AF-related mortality will undoubtedly be through effective measures for prevention of AF.¹⁶ Reversible risk factors for AF include obesity, hypertension, diabetes mellitus, sleep apnea, alcohol consumption, and tobacco use.² There is increasing evidence that lifestyle modifications addressing these factors can meaningfully reduce AF. The recent American Heart Association Scientific Statement on Lifestyle and Risk Factor Modification for Reduction of AF added a fourth pillar of lifestyle modification to the pillars of stroke prevention, rate control, and rhythm control.¹⁶ AF is associated with most forms of heart disease and prevention of coronary artery disease and therapies that improve heart failure can also be expected to reduce AF.

There are important limitations to the study by Tanaka and coworkers.³ Assessing cause of death and presence of AF from death certificates is subject to misclassification. Increased awareness and screening for AF over time may also contribute to the increased classification of death as AF related. The data do not inform us as to whether AF is directly contributing to mortality or is a marker for severity of associated disease. This large database does, however, capture all death certificates in the United States, providing a broad picture without some of the biases imposed by geography or different healthcare systems.

Tanaka and colleagues convincingly found that an increasing number of people who die in the United States are recognized to have AF.³ The findings are consistent with predictions for the aging population but also with the growing burden of cardiovascular risk factors in younger patients. Early diagnosis and intervention for stroke prevention and consideration of maintaining sinus rhythm is important. Prevention through a multidisciplinary approach to address modifiable AF risk factors and optimize treatment of associated comorbidities is needed to bend this mortality curve.

ARTICLE INFORMATION

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Disclosures

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