Is AF inevitable as we age?

Unfortunately, yes. Atrial fibrillation (AF) is highly prevalent in our aging society and is an independent predictor of morbidity and mortality. Early observational data from the Framingham Heart Study revealed a five-fold increased risk of stroke among patients with AF.

Data from a more recent review of Framingham shows that lifetime risks for AF increase as risk factor burden worsens with age.

Participants were included at index ages of 55, 65 or 75, and followed up to the age of 95. The study assessed several known risk factors for AF, including blood pressure, smoking, alcohol consumption, body mass index, diabetes and history of heart failure or myocardial infarction.

As risk factor profiles went from optimal to borderline to elevated, AF risks increased (borderline – risk profile, 33 percent; elevated risk profile, 38 percent). The overall lifetime risk for AF was 37 percent for index age 55, but dropped to 23 percent among participants with optimal risk factors. Men had higher lifetime AF risk than women. Obesity was the most significant risk factor for lifetime development of AF.

Is AF ever truly resolved?

Unfortunately, no. AF is a progressive systemic disease. Not much has changed or is new regarding treatment. Nary a new anti-arrhythmic drug has shown promise. The novel oral anticoagulants are no longer new and ablation has yet to show improved outcomes. To examine risks for stroke or transient ischemic attack (TIA) in patients with “resolved AF” U.K. researchers retrospectively compared 11,000 patients whose AF was considered resolved with 15,000 patients with unresolved AF, and 22,000 with no history of AF. Resolved AF is usually secondary to AF ablation or anti-arrhythmic therapy. During a median follow-up of roughly three years, the rate of stroke or TIA among those with resolved AF was 59 percent higher than among those with no AF. Mortality rates followed a similar pattern.

Only 17 percent of patients had a current anticoagulant prescription when they were diagnosed with resolved AF. The authors conclude that these patients (who obviously had a relapse) would benefit from continued anticoagulant prophylaxis, but treatment rates in this group are extremely low.

Take home for the clinician: In our practice, I advocate that patients continue anticoagulation unless their CHA2DS2-VASc score is low (< 2 for women and < 1 for men) or their AF is truly secondary to a reversible cause like hyperthyroidism.
**Does caffeine increase or decrease the risk of new onset AF?**

Surprisingly, caffeine seems to offer beneficial effects and appears to decrease AF risk.

Authors of a recent meta-analysis set out to determine, with greater assurance than historic results provide, whether caffeine is associated with increased risk of new-onset AF. Abdelfattah and colleagues suggest that theirs is the first meta-analysis to standardize caffeine intake across the included studies—thus providing greater reliability.⁴

An average 12-ounce cup of coffee was estimated to contain 140 mg of caffeine. Coffee consumption is linked to a decreased risk for coronary heart disease, stroke, cardiovascular disease, heart failure and type 2 diabetes mellitus.

The analysis found that the risk of new onset AF was lower in those who drank ≥ 4 cups of coffee/day vs. those who drank <2 cups/day. The study found no significant difference in incident AF with coffee intake of <2 cups/day vs. >2 cups/day.

This data supports conclusions from a state-of-the-art comprehensive review of the impact of caffeinated beverages on cardiac rhythm.⁵ Large-scale population-based studies and randomized controlled trials suggest coffee and tea are safe and may reduce the incidence of arrhythmia. Although there is no clearly defined threshold for caffeine harm, a regular intake of up to 300 mg per day appears to be safe and may even be protective against heart rhythm disorders.

**Take home for the clinician:** Many clinicians continue to counsel patients with atrial or ventricular arrhythmias to avoid all caffeinated beverages, particularly coffee, despite an absence of evidence to support this approach. In individual cases where a clear temporal association between arrhythmia episodes and caffeine intake is apparent, then I recommend avoidance. Otherwise, we tell patients that three to four cups of caffeine is perfectly fine, and is probably beneficial.

**Does atrial flutter equal AF in stroke risk scoring?**

It appears that atrial flutter has a lower stroke risk. AF and atrial flutter (AFL) are often regarded as interchangeable when managing stroke risk. We’ve assumed this for years. However, a new study in *JAMA* suggests clinical outcomes are worse for patients with AF, even if they have the same values on the standard CHA2DS2-VASc scoring system.⁶

“The current recommended level of CHA2DS2-VASc score ≥ 2 for women and ≥ 1 for men used to prevent ischemic stroke in patients with AFL should be re-evaluated and prospectively studied,” concluded lead author Yu-Sheng Lin, MD.

Lin and coauthors studied nearly 220,000 individuals from a national database in Taiwan, matching by age and sex those with AF, AFL and neither condition. Patients with AF were older, more often female and had the highest CHA2DS2-VASc scores, which indicate greater stroke risk.

After stratification by CHA2DS2-VASc score, the researchers noted the following event rates per 100 person-years:

- Ischemic stroke: 3.08 for AF patients, 1.45 for AFL and 0.97 for control individuals
- Heart failure hospitalization: 3.39 for AF, 1.57 for AFL and 0.32 for controls
- All-cause mortality: 17.8 for AF, 13.9 for AFL and 4.2 for controls
The incidence of stroke increased in all three groups as CHA2DS2-VASc scores went up, but the researchers found the risk of stroke for AF patients with a score of 1 was similar to that of AFL patients with a score of 2. Likewise, a score of 2 for AF patients signaled a similar risk as a score of 4 for those with AFL.

**Take home for the clinician:** The findings suggest that AFL shouldn’t be treated the same as AF per present guidelines, but this data needs further corroboration. I might use this information in my decision process for adding an oral anticoagulant to an AFL patient with high bleeding risk (I might need a score of 3 for a man and 4 for a woman who has AFL and high-bleed risk before I would anticoagulate.).

**Is the burden of AF associated with the risk of ischemic stroke and other thromboembolism in PAF?**

*Greater AF burden is associated with a higher risk of stroke in paroxysmal atrial fibrillation (PAF) patients not taking anti-coagulation versus lower burden. In the May issue of JAMA Cardiology, Go and colleagues present the results of their analysis of 2,133 patients with PAF who underwent 14-day, continuous ambulatory electrocardiographic monitoring.*

The data provides compelling evidence of a dose-response association between the burden of PAF and stroke risk. After adjusting for CHA2DS2-VASc scores, they identified a more than five-fold increased risk of stroke in patients with the highest tertile of AF burden while not taking anticoagulants. More importantly, the absolute risk of stroke among those with an AF burden of more than 11 percent and no anticoagulation was 2.9 events per 100 person-years, which is roughly comparable with a CHA2DS2-VASc score of 2 to 3 in that score’s original derivation cohort.

**Take home for the clinician:** Greater AF burden is associated with a higher risk of ischemic stroke independent of known risk factors in adults with PAF. Knowing the burden of AF may assist with shared decision making for stroke prevention strategies—especially in those with low CHA2DS2-VASc scores. (I might anticoagulate a patient with chronic AF and lower CHA2DS2-VASc than a patient with PAF.)

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**Are direct oral anticoagulants safe in patients with end-stage renal disease?**

*The answer might be yes, according to a retrospective analysis of dialysis patients with AF prescribed apixaban. Patients with AF and end-stage renal disease (ESRD) who are on dialysis have elevated risks for thromboembolic events and bleeding. Investigators analyzed 2010–2015 data from the U.S. Renal Data System on 25,523 patients with ESRD on dialysis who began oral anticoagulation (apixaban or warfarin). Patients were matched on a prognostic score for each outcome (apixaban, 2,351 patients; warfarin, 7,053 patients).*

Following the FDA's apixaban approval, new prescriptions for ESRD patients with AF increased annually. Overall, the risk of stroke/systemic embolism was 11.9 per 100 person-years. Risks for thromboembolism did not differ between apixaban and warfarin, but apixaban was associated with a lower risk for major bleeding (hazard ratio, 0.72). In a sensitivity analysis, the standard apixaban dose of 5 mg twice daily was associated with lower risks for stroke and systemic embolism than half-dose 2.5 mg apixaban (taken by 56 percent of patients).

**Take home for the clinician:** Despite a lack of clinical safety and efficacy data, direct oral anticoagulants are increasingly used in ESRD patients with AF. Apixaban in these patients is associated with reductions in thromboembolism and major bleeding. Only the standard apixaban dose conferred these benefits, but most patients were prescribed the reduced dose, possibly suggesting inappropriate under-dosing. These results are compelling but insufficient for the routine recommendation.

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References


2. Staerk L, et al. Lifetime risk of atrial fibrillation according to optimal, borderline, or elevated levels of risk factors: Cohort study based on longitudinal data from the Framingham Heart Study. *BMJ* April 26 2018; 361: k1453.


8. Siontis KC et al. Outcomes associated with apixaban use in end stage kidney disease patients with atrial fibrillation in the US. Originally published 24 Jul 2018 *Circulation* 2018; 0:CIRCULATIONAHA.118.035418