Increased Stroke Risk in Atrial Fibrillation Patients With Heart Failure
Does Ejection Fraction Matter?

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Stroke is a devastating complication of atrial fibrillation (AF), causing substantially greater neurological deficit than strokes in non-AF patients, as well as longer hospital admission, higher rates of death, and reduced ability to function independently. The risk of stroke in AF is not homogeneous and is closely associated with common patient characteristics, as summarized by the CHA2DS2-V AS score, which incorporates heart failure, hypertension, age, diabetes mellitus, female sex, prior stroke or embolic events, and vascular disease.¹

In patients with AF, heart failure has been strongly associated with increased stroke/thromboembolism and mortality and independently adds to risk prediction of outcomes.² Congestive heart failure is represented by the C criterion in the CHA2DS2-V AS score to represent the higher stroke risk associated with recent decompensated heart failure irrespective of ejection fraction (thus including heart failure with reduced ejection fraction [HFrEF] and heart failure with preserved ejection fraction [HFP EF]), as well as moderate-severe left ventricular systolic impairment on echocardiography.¹ This is in contrast to older risk scores, where heart failure only referred to recent decompensated heart failure, and there was some uncertainty whether HF rEF or HFP EF or asymptomatic systolic impairment should be included.³ Of note, there is a reasonable evidence base linking a clinical diagnosis of heart failure with stroke and systemic embolus (relative risk of 1.6–3.1 across 5 studies).²

In the current issue of Stroke, Sandhu et al⁴ add to a growing body of data examining whether adverse outcomes are similar in patients with HFP EF compared with those with HF rEF. As HFP EF is now the commonest form of heart failure,⁵ unpicking the effect of heart failure on stroke outcomes in AF is vital for accurate risk stratification and appropriate use of anticoagulation for stroke prevention.⁶

Using data from heart failure patients on antiplatelet agents enrolled in the ACTIVE A and W trials, Sandhu et al⁴ identified no difference in the risk of stroke, transient ischemic attack, or systemic embolism between AF patients with HFP EF and HF rEF. This finding is similar to published data from other post hoc assessments of randomized trials⁷–⁹ and observational cohort studies.¹⁰–¹² None have identified a significant difference in incident stroke according to type of heart failure, although a trend toward more strokes in HFP EF was observed overall. In a large retrospective cohort study, McManus et al reported that preexisting AF was associated with ischemic stroke only in patients with HFP EF.¹³

A major limitation in the study by Sandhu et al⁴ is the lack of stratified randomization for type of heart failure, with significant differences in several baseline characteristics independently associated with stroke, including age, sex, heart failure etiology, and prescribed medications. Application to clinical practice is also limited by differing definitions of HFP EF and methodology for determination of HF, which may affect the observed associations with stroke outcomes.¹⁴

Nonetheless, a strength of the current analysis, however, is the long follow-up period, which at a mean of 3.6 years is considerably greater than in other published studies. Whether more severe forms of left-ventricular systolic dysfunction are associated with a greater incidence of stroke remains unclear, particularly as these patients are more likely to die and hence not develop embolic events. In one study, the rate of a composite outcome, including death, was highest in patients with systolic dysfunction, although still considerable in those with HFP EF.⁸

Stroke is an infrequent cause of death in AF,¹⁵ and even in well-treated HF r EF patients, stroke is responsible for only 4% of deaths.¹⁶ A focus on preventing progressive heart failure is therefore of particular importance in this patient group. AF may be related to heart failure as a cause and an effect, and yet the respective roles of heart failure on the progression of AF and of AF on progression of heart failure or change in EF are understudied in epidemiological studies. Future studies of heart failure and AF should consider these aspects to improve our understanding of their complex inter-relationship.³ However, the data from Sandhu et al⁴ and others actually simplifies stroke risk stratification for AF patients and would support the continued inclusion of heart failure in its entirety, regardless of classification into HFP EF or HF rEF. AF patients with ≥1 additional stroke risk factors merit effective stroke prevention, and the latter require oral
anticoagulation, whether given as a Vitamin K Antagonist (eg, warfarin; with a high time in therapeutic range, >70%) or a Non-Vitamin K Antagonist Oral Anticoagulant. Clinicians should not deprive patients of anticoagulants, particularly in heart failure where there seems to be a particularly low uptake of guideline-recommended anticoagulant use.11

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