Does atrial fibrillation pattern affect stroke risk? Data dredging to help the clinician

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This editorial refers to ‘Risk of ischaemic stroke according to pattern of atrial fibrillation: analysis of 6563 aspirin-treated patients in ACTIVE-A and AVERROES’, by T. Vanessche et al., on page 281.

Atrial fibrillation (AF) is the most common arrhythmia worldwide, and has a major impact on morbidity and mortality rates of those affected. In 2010, it was estimated that there were 33.5 million people worldwide with AF and ~5 million new cases each year.¹ AF has been found to double mortality and increase risk of stroke by approximately five-fold.² AF and its pathogenesis and treatment continue to be topics of extensive research.

Vanessche et al. have now evaluated the pattern of AF and its association with stroke risk by examining patients with AF on aspirin alone with a retrospective look at the ACTIVE-A and AVERROES databases.³ A total of 6573 patients were included in their analysis, 24% with paroxysmal, 17% with persistent, and 59% with permanent AF. Non-haemorrhagic stroke was examined as the sole outcome. The study found differing risk of embolic events by AF type, specifically that the incidence increased in permanent and persistent AF as compared with paroxysmal AF. Across the entire study population, a statistically significant hazard ratio of 1.91 (95% confidence interval 1.50–2.43) was seen for permanent/persistent AF vs. paroxysmal AF. This association was also found to be significant regardless of age, gender, history of stroke, or presence of heart failure. This relationship was strongest for patients with CHA2DS2-VASc scores >1, where the analysis has a more robust sample size and corresponding event rates than lower CHA2DS2-VASc scores.

These data should be interpreted in an appropriate contextual framework. The population studied was defined by its unsuitability for anticoagulation, which the authors view as a limitation of the application of these data to the entire population of patients with AF. However, while it is true that this then represents a unique subset of people with AF, it is precisely these patients who pose the greatest challenge in management in clinical practice. The reasons for patients not being on anticoagulation in ACTIVE-A and AVERROES include patient preference, unclear indication for anticoagulation (e.g. CHA2DS2-VASc scores of 0–1), and international normalized ratio (INR) monitoring concerns. These scenarios are frequently encountered among our patients, and therefore data pertaining to these patients may be quite valuable.

A major issue with the classification of AF in clinical practice is that it is quite crude. This was elucidated by Charitos et al., who found a high degree of discordance between clinical assessment of AF and objective device-derived classification of patients with AF with implantable devices (Figure 1).⁵ In their analysis, less than half of patients clinically labelled as having paroxysmal AF, and less than one-third of patients labelled as having persistent AF, had concordant AF classification by device-derived objective data.⁷ The limited accuracy of classifying AF clinically certainly presents a challenge in applying the current data, and suggests the need for more reliable methods, especially if we wish to adopt evidence-based clinical management strategies as a function of AF subtype.

The seemingly dichotomous decision of ‘yes’ or ‘no’ on anticoagulation use for patients with AF can be particularly unsettling, especially as we have learned that ‘low risk interventions’ such as aspirin appear to be minimally if at all effective in modifying stroke risk, especially in lower risk individuals for which the stroke prevention strategy is the most ambiguous. It is precisely these patients in whom the use of additional risk modifiers such as AF type or AF burden could be most useful.

To bring home this message, consider two hypothetical patient scenarios.

Case 1: 45-year-old male with permanent atrial fibrillation and a CHA2DS2-VASc score of 2 who is concerned about initiating anticoagulation because of bleeding risk

The annual risk of stroke of a patient with a CHA2DS2-VASc score of 2 is 1.6%.⁶ However, if you were to consider the current data, the
patients with no additional risk factors for stroke and so the results are not completely applicable. Importantly, however, a few studies with more robust populations of low stroke risk AF patients have corroborated an association between AF burden (as opposed to type) and stroke risk.10

In summary, despite its retrospective nature, the study from Vanessche et al. focuses on AF type as an additional way to stratify stroke risk in AF patients. The largest barrier to applying AF type in management decisions is the ability to classify AF type accurately in clinic practice. For moderate to high stroke risk groups for which there is clear benefit of anticoagulation, these data are unlikely to impact clinical management. However, the current data bring to the forefront an important discussion of whether we can refine stroke risk among low vascular risk patients. It is our belief that it will be possible to do so, especially when combined with other risk-modifying characteristics, such as left atrial functional index, left atrial appendage characteristics, and inflammatory markers. Establishing a more refined risk assessment would have the potential to prevent strokes in relatively young and healthy individuals without exposing truly low risk patients to the hazards of unnecessary anticoagulation.

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References


Figure 1 Atrial fibrillation (AF) burden distribution (by implantable device assessment) separated by clinical classification of AF type (paroxysmal vs. permanent) among patients with documented AF.