Can Patients With Atrial Fibrillation Be Optimally Risk Stratified for Stroke and Thromboembolism?

To the Editor:

Atrial fibrillation (AF) has repeatedly been shown to be associated with a substantial risk of stroke, but this risk is not consistent across all populations. Identifying patients at greatest risk of this (sometimes disastrous) complication is problematic. Therefore, the development of various stroke risk stratification models based on data from large clinical studies has proved useful in targeting anticoagulation to those at moderate-high risk of stroke, whereas those considered at low risk are generally offered aspirin as an alternative, despite the limited evidence for aspirin in this setting.1 These stratification models based on data from large clinical studies have been incorporated into various expert consensus2 and evidence-based3 guidelines on the management of AF. Of note, these available stroke risk stratification schema have been developed—and largely validated—using data from patients not receiving oral anticoagulation (OAC) in clinical trial cohorts.4,5

It is therefore with great interest that we read the recent analysis in Stroke by Baruch et al,6 investigating whether stroke risk stratification models can also be applied to patients with AF who are already receiving optimal anticoagulants. Unsurprisingly, the authors demonstrate a rather poor performance of each of the schema assessed in this setting, but given that their study cohort were receiving warfarin or ximelagatran may influence the thromboembolic event rates. Also, their estimations of stroke risk could also have been anticipated from pre-existing literature, where validation studies (usually in nonanticoagulated populations) have consistently demonstrated that no model is ideal and all frequently underestimate stroke risk.4,5 Indeed, the c statistic (assessing the predictive accuracy of these models) in those patients not receiving OAC ranges from 0.63 to 0.70.4

The inadequacy of existing schema is perhaps most obvious among those patients considered at ‘moderate risk’ of stroke. In the article by Brusch et al, the CHADS2; classified the largest cohort of participants as moderate risk (nearly 60%; versus 35% who were classed as ‘high risk’), compared with most participants being classed at ‘high risk’ by the American College of Chest Physicians (96% to 97%), the van Walraven (99.2%) and AF Investigators (85.1%) schema; the c statistics for the various schema in these subjects—all of whom were receiving warfarin or ximelagatran—ranged from 0.53 to 0.65. Given that most guidelines1–3 recommend either aspirin or OAC for ‘moderate risk’ subjects, having a risk stratification schema that classifies most of a particular patient cohort into the ‘moderate risk’ category may confuse clinicians even more, on what is the best treatment for an individual patient.

The reasons for the poor categorization and predictive capacity of stroke risk schema have been explored in detail. AF commonly associates with numerous risk factors, many of which also directly enhance the risk of stroke. Many risk stratification schema try to incorporate these in their assessment, but coronary, carotid and peripheral vascular disease, which by their virtue are still important risk factors for stroke, are often overlooked in clinical trial cohorts? and have even been cited as a ‘less validated or weaker risk factor’ in some guidelines.2 This may partly explain the underperformance of some risk stratification schema. The NICE schema3 categorizes ‘high risk’ subjects as those AF patients with stroke or thromboembolism, or those aged over 75 years with either vascular disease, diabetes or hypertension, or those with clinical evidence of valve disease, heart failure, or impaired left ventricular function on echocardiography. Of note, Baruch et al6 have not assessed the performance of the NICE schema in their analysis, which would be of interest.

Given the difficulties in the application of these risk stratification models, perhaps thromboprophylaxis in AF should be viewed from an alternative perspective. Indeed, given the strong evidence base for OAC in reducing both morbidity and mortality in AF, maybe a shift toward justifying why not to offer anticoagulation to these patients should be encouraged. This was evident in the recent Birmingham Atrial Fibrillation Treatment of the Aged Study (BAFTA) clinical trial, where OAC (international normalized ratio, 2 to 3) was superior to aspirin 75 mg daily even in an elderly (age ≥75 years) population with AF in the primary care setting, with no difference in bleeding rates between the 2 treatment arms—suggesting that more widespread use of OAC therapy for stroke prevention in AF should be supported, ‘unless there are contraindications or where the benefits are not worth the inconvenience’ of such therapy.8

Disclosures

None.

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