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Simplifying stroke risk stratification in atrial fibrillation patients: implications of the CHA_2DS_2–VASc risk stratification scores

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Atrial fibrillation (AF) is a major risk factor for stroke and thromboembolism but this risk is not homogeneous among patients with AF, being dependent upon associated risk factors such as advancing age, hypertension, congestive heart failure, prior stroke, diabetes mellitus and structural heart disease [1]. Current guidelines [2–4] recommend warfarin for those at high risk, aspirin for low risk and 'either aspirin or warfarin' for those at intermediate risk. Based on stroke risk factors, many risk stratification schemas have been developed in order to categorise a patient's risk of stroke and aid decisions regarding the most appropriate thromboprophylaxis.

Many of the stroke risk stratification schemes employ stroke risk factors that have been derived from non-warfarin arms of clinical trial cohorts. The Stroke Risk in AF Working Group compared 12 stroke risk stratification schemas [5], five of which were based on expert consensus and seven on event-rate analyses. The number of risk factors included in each schema varies between 4 and 8, with all schema including previous stroke/transient ischemic attack (TIA), and almost all included patient age, hypertension and diabetes mellitus [5]. Perhaps the most widely used of the published stroke risk stratification schemes is the $CHADS_2$ score (Congestive heart failure, Hypertension, Age >75, Diabetes mellitus and prior Stroke or transient ischaemic attack) [6], derived from the Atrial Fibrillation Investigators and SPAF risk schema and initially validated in a hospitalised AF cohort [1, 6, 7]. However, the problem with current stroke risk stratification schemas is that, when applied to the same cohort of patients, the absolute stroke rates by risk group and the percentage of patients categorised as low, intermediate or high risk would vary considerably depending upon which stroke risk scheme is employed [5, 8–10].

The majority of stroke risk schema have derived risk factors from non-anticoagulated patients in clinical trials, and as such, these risk factors may not be equally applicable to non-trial cohorts or anticoagulated patients. Indeed, a comparison of five stroke risk schema [1, 6, 7, 11, 12] in non-anticoagu-

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Table 1. Stroke risk stratification with the $CHADS_2$ and CHA_2DS_2–VASc schemas

$CHADS_2$ [6]	Score	CHA_2DS_2–VASc [20]	Score
Congestive heart failure	1	**C**ongestive heart failure/LV dysfunction	1
Hypertension	1	**H**ypertension	1
Aged ≥75 years	1	**A**ged ≥75 years	2
Diabetes mellitus	1	**D**iabetes mellitus	1
Stroke/TIA/TE	2	**S**troke/TIA/TE	2
		Vascular disease (prior MI, PAD or aortic plaque)	1
		Aged 65–74 years	1
		Sex **c**ategory (i.e. female gender)	1
Maximum score	6	Maximum score	10

lated patients from the ATRIA cohort demonstrated that although all five schemas had similar predictive ability, with c-statistics ranging from 0.56 (AFI, ACCP-7) to 0.62 (Framingham), the proportions of patients classified as low, intermediate and high risk varied markedly by risk schema [8]. The percentage of patients categorised as low risk ranged from 11.7 (ACCP-7) to 37.1% (Framingham), intermediate risk from 7.9 (ACCP-7) to 61.2% ($CHADS_2$) and high-risk from 16.4 (Framingham) to 80.4% (ACCP-7) [8].

Given the decline in stroke rates over the last 20 years [13] and the advent of novel oral anticoagulants, there has been a paradigm shift in emphasis on stroke risk stratification to identify the 'truly low risk' patients and to minimise the number of patients classified as intermediate risk [14] given the current ambiguity over the most appropriate thromboprophylaxis ('aspirin or warfarin' being recommended in current guidelines) for this group. As alluded to earlier, stroke risk factors commonly employed in stroke risk stratification schemas were mainly derived from non-anticoagulated trial cohort patients, with the exception of the Framingham schema [11]. Other stroke risk factors, such as female gender [15] and vascular disease (including myocardial infarction, peripheral vascular disease and complex aortic plaque) [16, 17], have been shown to increase stroke risk among AF patients. Furthermore, advancing age, particularly age >65 years, rather than the arbitrary cut-off of ≥75 years, has been shown to increase stroke risk in AF [18]. In one analysis of a large cohort of AF patients with $CHADS_2$ score = 1, those with 'age ≥75' as a single risk factor had the highest stroke risk, being nearly 3-fold greater than those with hypertension alone as a single risk factor [19].

Therefore, in order to optimise stroke risk stratification, a refined form of the 2006 ACC/AHA/ESC guidelines schema [2], the Birmingham 2009 stroke risk schema has been proposed [20]. In the 2006 ACC/AHA/ESC guidelines, female gender, coronary artery disease and age 65–74 were stated as 'less validated' moderate risk factors, as was the evidence base in 2006. Clearly, things have moved on, with new information on these risk factors as discussed above. This new schema is called the 'CHA_2DS_2–VASc' and incorporates female gender [15], vascular disease [16, 17] and age 65–74 years, in conjunction with established stroke risk factors (previous stroke/TIA, hypertension, heart failure/moderate to severe cardiac dysfunction and diabetes mellitus) into an acronym [20]. In short, the CHA_2DS_2–VASc score (Birmingham 2009 scheme) proposes an 'extended' $CHADS_2$ score, as was implied (by text) in the 2006 ACC/AHA/ESC guidelines [21], the latter being in common clinical application (Table 1).

The 'CHA_2DS_2–VASc' schema places greater emphasis on what it terms 'major risk factors', that is, age ≥75 years and previous stroke/TIA, by allocating two points to each, with one point for the presence of each of the other 'clinically relevant non-major' risk factors, with total scores ranging from 0 to 9 [20]. Patients can also be classified as low, intermediate and high risk, with a CHA_2DS_2–VASc score of 0, 1 and ≥2, respectively—although such an artificial categorisation is discouraged, in preference of a risk factor-based approach.

The 'CHA_2DS_2–VASc' scheme has been validated in 1,084 [mean (SD) age 66 (14) years; 59.2% male] non-anticoagulated non-valvular AF patients enrolled in the Euro Heart Survey on AF cohort [20, 21]. The predictive ability of the CHA_2DS_2–VASc scheme was compared to seven other stroke risk schemas: AFI (1994), SPAF (1999), $CHADS_2$ (2001) (classical: 0, 1–2 and ≥3; and revised: 0, 1 and ≥2), Framingham [11], NICE (2006) and ACCP-8 (2008). As with previous comparisons of stroke risk schemas in trial [5, 10] and observational [8, 9] cohorts, the proportion of patients classified into low-, intermediate- and high-risk categories varied markedly by risk schema. Ongoing validations of the CHA_2DS_2–VASc schema in other AF populations will confirm its true value, and initial data on one cohort of nearly 80,000 AF patients have already been presented at the AHA meeting in November 2009 [22].

Patients categorised as 'low risk' by CHA_2DS_2–VASc (9.2%) were truly low risk with no reported thromboembolic events. In addition, CHA_2DS_2–VASc only classified a small percentage (15.1%) of patients to the intermediate-risk group, compared with 61.9% with the $CHADS_2$ (classical) scheme [20]. Furthermore, CHA_2DS_2–VASc demonstrated modest improvement in predictive ability with a c-statistic of 0.606, which was an improvement on NICE 2006 and $CHADS_2$ classical and revised, although the more complex Framingham scheme had the highest c-statistic (0.638) when (artificially) categorising patients into three risk strata, but this scheme requires a risk calculation and produces a large proportion into the intermediate-risk group, which is not practical for everyday clinical use.

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The CHA_2DS_2–VASc scheme could potentially allow simplification of our approach to thromboprophylaxis. Those with a CHA_2DS_2–VASc score of >1 are high risk and should be managed with oral anticoagulation, whether with warfarin (as we have now) or novel oral anticoagulants that overcome the limitations or disadvantages of warfarin. For those with a CHA_2DS_2–VASc score of 1, either oral anticoagulants or aspirin can still be recommended, but with a preference for oral anticoagulants, given the available evidence [23]. The identification of those AF patients at truly low risk (i.e. CHA_2DS_2–VASc score of 0) would allow the recommendation of aspirin or no antithrombotic therapy, although no antithrombotic therapy is suggested given the lack of benefit on thromboembolism and potential for harm with bleeding [24].

Conflict of interest

None declared.

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