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EDITORIAL

Risk assessment and therapy decision in patients at low risk for stroke: CHA_2DS_2-VASc vs. $CHADS_2$?

Okan Erdogan*

Department of Cardiology, School of Medicine, Marmara University, Kadikoy, Istanbul, Turkey

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This editorial refers to 'The CHA_2DS_2-VASc score identifies those patients with atrial fibrillation and a $CHADS_2$ score of 1 who are unlikely to benefit from oral anticoagulant therapy'†, by M. Coppens *et al.*, on page 170

The risk of stroke in patients with atrial fibrillation (AF) is a continuum and depends on cumulative assessment of certain clinical risk factors. However, many other unidentified risk factors may still exist, and a low risk patient can become a high risk patient over time. Therefore, trials investigating stroke risk profiles within a certain period of time must be interpreted with caution. Additionally, definitions of some risk factors are inconsistent and may vary from one trial to another. For example, the definition of heart failure is not necessarily the same in all trials and does not mean inclusion of only patients with systolic left ventricular dysfunction. The same is also true for the definition of vascular disease such as myocardial infarction and peripheral artery disease. Some trials included patients according to history only and not according to required objective parameters. Among the available stroke risk stratification schemes, the $CHADS_2$ [Congestive heart failure, Hypertension, Age $\geq$75, Diabetes, Stroke (doubled)] score is most widely used and adopted.[1] However, one of the major limitations of the $CHADS_2$ score is that it does not include many common risk factors for stroke and neglects some others. For example, the presence of vascular disease and female sex, although not included in the $CHADS_2$ score, have already been identified as significant risk factors for stroke in AF. In addition, age 65 to <75 is also disregarded in the $CHADS_2$ score although its value for risk of stroke is unequivocally established by previous trials. Finally, the absence of risk factors for stroke according to $CHADS_2$ score does not directly classify a patient into a 'truly low risk' category because a substantial number of patients still have stroke rates of ~1.5%/year.[1] This might be partially explained by the presence of wide confidence intervals that belong to various categories of the $CHADS_2$ score.[2] Accordingly, the $CHADS_2$ score is deemed to be less strong and discriminative than the CHA_2DS_2-VASc score [Congestive heart failure/left ventricular dysfunction, Hypertension, Age $\geq$75 (doubled), Diabetes, Stroke (doubled)-Vascular disease, Age 65 to <75, and Sex category (female)] while the latter is more inclusive rather than exclusive by incorporating other common risk factors and has better ability to identify the true risk category of patients with AF.[1–4]

Current practice supported by recent guidelines advocates therapy with a vitamin K antagonist (VKA) for a $CHADS_2$ score $\geq$2.[1] However, what is unclear, and remains to be determined, is whether all patients with a $CHADS_2$ score of 1 would be considered as high risk enough and exclusively benefit from VKA therapy or not? An elegant study by Coppens *et al.*[5] might be a partial solution to this complex dilemma. Briefly, the authors tried to determine the ability of the CHA_2DS_2-VASc score to discriminate stroke risk in AF patients with a $CHADS_2$ score of 1 and thereby identify those patients for whom VKA therapy may not be of benefit. After all patients with a $CHADS_2$ score of 1 were reclassified according to the CHA_2DS_2-VASc score, 26% and 74% of them were categorized as having a CHA_2DS_2-VASc score of 1 and $\geq$2, respectively. After 11 414 patient-years of follow-up, the annual incidence of ischaemic or unspecified stroke or systemic embolus (SSE) was 0.9% [95% confidence interval (CI) 0.6–1.3] and 2.1% (95% CI 1.8–2.5) for patients with a CHA_2DS_2-VASc score of 1 and $\geq$2, respectively. Among the new risk factors (vascular disease, female sex, age 65 to <75 years) defined in the CHA_2DS_2-VASc score, only age 65 to <75 years was detected to be the strongest. Finally, the authors concluded that the CHA_2DS_2-VASc score was able to reclassify 26% of patients with a $CHADS_2$ score of 1 to a low annual risk of SSE of 1%, which was low enough to consider withholding VKA therapy.[5] Therefore, they may be treated with acetylsalicylic

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* Corresponding author. Tel: + 90 216 336 0212, Fax: + 90 216 625 45 80, Email: okanerdogan@yahoo.com

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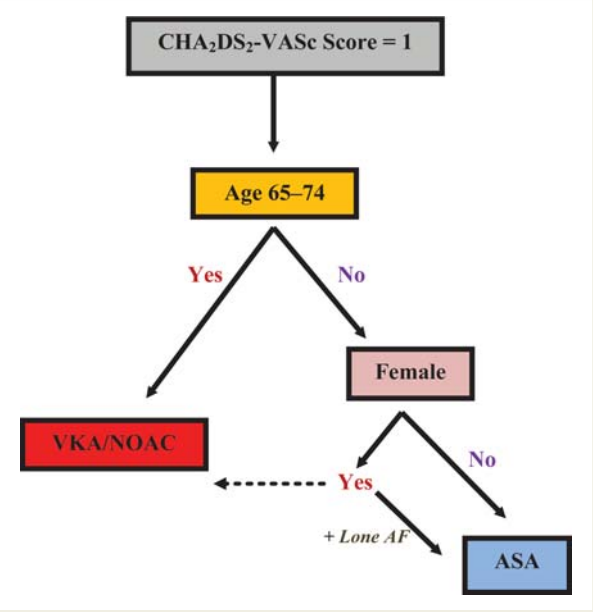

Figure 1 Proposed algorithm regarding how to treat patients with a CHA_2DS_2-VAS_C score = 1 based on the results of the study by Coppens *et al.*[5] and current practice. The dotted line denotes preferred use of a NOAC instead of a VKA based on risk/benefit analysis and cost. NOAC, novel oral anticoagulant; VKA, vitamin K antagonist; ASA, acetylsalicylic acid.

acid (ASA). In contrast, 74% of patients with a $CHADS_2$ score of 1 were reclassified into a higher risk category (CHA_2DS_2-VASc risk score ≥ 2) and they, therefore, may benefit from VKA therapy.

However, a few points need further clarification and merit discussion. First of all, the study population was chosen from previously published randomized trials and may not homogenously reflect some risk factors such as heart failure and vascular disease because of their variable definition as inclusion criteria. In addition, all patients seem to be either on ASA or on ASA plus clopidogrel therapy, which may be responsible for an underestimation of the study results. According to current evidence, the presence of vascular disease is considered as an independent risk factor for stroke. Similarly, heart failure is also regarded as being an important risk factor irrespective of ejection fraction. Although female sex is deemed a risk factor by some studies, only its association with higher age is considered a strong risk factor by the others. Why female sex is a weaker risk factor and a personal history of vascular disease as well as heart failure is not a risk factor in this study might partially be explained by the low numbers of study patients having those risk factors. The very low risk patients with a CHA_2DS_2-VASc score of 1 are men <65 years of age. In clinical practice they are generally treated with ASA despite its uncertain benefits. Similarly, women <65 years of age, especially associated with lone AF, can be identified as 'truly low risk' and treated with ASA only. As expected, age 65 to <75 years in this study is associated with an increased risk of the composite outcome and is the strongest among the other new risk factors. This finding is consistent with other trials that highlight the increased risk of stroke above the age of 65. Thus, age 65 to <75 years that is included in the CHA_2DS_2-VASc score as a risk factor deserves special emphasis and consideration for VKA therapy.

In conclusion, the study published by Coppens *et al.*[5] re-confirms the superiority of the CHA_2DS_2-VASc over the $CHADS_2$ score for discriminating truly low and high risk patients and emphasizes the importance of new risk factors, especially age 65 to <75 years. Based on the results of their study and current practice, I would recommend that patients with a CHA_2DS_2-VASc score of 1 who are 65 to <75 years of age and with no other risk factors be considered high risk enough and would mostly benefit from VKA or novel oral anticoagulant therapy, whereas other low risk patients <65 years of age probably need only ASA therapy (*Figure 1*).

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