We are now transitioning into the era of personalised tailored therapy with the application of risk stratification schemes based on easily measured clinical markers beautifully illustrated in determining the risk:benefit of anticoagulation in AF patients. The evolution of the CHADS score to CHA_2DS_2-VASc has refined therapeutic risk assessment coupled with the HASBLED score to assess bleeding risk. However, despite their apparent simplicity to ensure utility, these scoring systems paper over a number of cracks in our knowledge base as reviewed in the paper *by Professor Lip's group*[1]. Herein, the authors highlight a number of issues that are currently overlooked in the risk scoring schemes including racial differences in bleeding & stroke risk and the importance of overall vascular profile which are not addressed in the current scores.

Indeed, in order to deal with some of these problems, other scores are now being developed to further aid clinical decision making. A more refined approach assessing the lability of INR control and other cardiovascular risk factors to differentiate between the suitability of a NOAC versus warfarin has been developed-the SAMe-TT2R2 [sex female, age <60 years, medical history (>2 comorbidities), treatment (interacting drugs), tobacco use (two points), race non-Caucasian (two points)] score to enable informed decisions on those patients likely to do well on warfarin (SAMe-TT2R2 score 0–2) or those who are likely to have a suboptimal time in therapeutic range (SAMe-TT2R2 score >2)[2].

The need to further simplify and optimise risk stratification has been addressed with an integrated *online* risk tool-GARFIELD-AF which utilised 40,000 patients from the GARFIELD-AF GP registry[3]. This scoring system had superior C-statistic predictive values versus CHA_2DS_2-VASc for both stroke *and* 1 year mortality aswell as HASBLED for bleeding events both overall and in lower risk patients. Therefore, we are seeing further evolution of scoring systems to refine patient risk assessment and prognosis.

However, there are knowledge gaps in terms of additional risk factors including genetics and subclinical atheroma burden. At present we do not have enough information to incorporate family history of CVA in the absence of known

coagulopathies e.g. Factor V Leiden deficiency but a number of loci are being identified that could link AF to familial CVA risk in the future[4]. It is very likely that such loci in combination with those that predict resistance to warfarin or indeed NOACs will have an important influence on risk scoring & refining therapy.

Furthermore, factors determining left atrial appendage stasis & local coagulability could modify risk over and above a simple CHA_2DS_2-VASc score which does not take these factors into account[5,6]. This is particularly pertinent in the perceived low CHA_2DS_2-VASc 0/1 cases where such factors may play a more significant role at this lower end of the risk spectrum. These include increased LA dimensions, spontaneous echo contrast, and LAA thrombus and LAA flow peak velocity <20 cm/s measured on echocardiography, and LAA non-chicken wing morphology on multidetector row CT and CMR which are associated with increased risk of stroke in AF patients[7,8]. LA reservoir function has also been associated with increased risk of stroke[5]. Each 1% reduction in LA reservoir function was associated with 7% increased stroke risk of ($p < 0.001$). LA wall structure may also be important- in an MRI study, patients with history of stroke showed significantly more LA fibrosis as compared with patients without stroke ($24.4 \pm 12.4\%$ vs. $16.2 \pm 9.9\%$, respectively; $p < 0.001$)[8,9]. The addition of LA fibrosis extent to a model including the clinical predictors of stroke (congestive heart failure, age >75 years, diabetes mellitus, and hypertension) improved the predictive statistics (shifting the area under the curve from 0.58 to 0.72). However, it remains to be determined whether the addition of these variables to current risk scoring systems would lead to superior stroke risk stratification or enable more cost-effective clinical care.

Despite our ability to improve risk stratification, the advent of easy utilisation of NOACs & wide application of CHA_2DS_2-VASc, there is emerging evidence of both over and undertreatment. This was highlighted in a combined analysis of 3 large international registries of 73,004 patients in 35 countries (GARFIELD-AF, ORBIT-AF I & II) which demonstrated that although there has been a shift away from ant-platelet therapy to NOACs in AF, there appears to be over treatment of low

CHA_2DS_2-VASc patients (0-1) with up to 57% receiving anticoagulation and undertreatment of CHA2DS2-VASc >2 with a very wide range of 31-93% receiving therapy despite similar bleeding risk profiles[10]. This overtreatment of low risk cases including those with CHA_2DS_2-VASc 0 should be a wake-up call to apply the schemes judiciously and ensure targeting of the higher risk cases.

In developed economies, the evolution of gene based & web based risk profiling tools utilising electronic records to screen populations will make these approaches more easily applicable provided they translate into cost-effective benefits particularly in terms of reducing risk of hemorrhagic stroke or fine tuning targeted treatment in low CHA_2DS_2-VASc cases. However, in the developing world where communications and provision of expert healthcare remains challenging, much simpler schemes utilising health care worker pulse checking for screening and simple clinical risk scores will remain the foundation of care for the forseeable future as the challenge here will remain identifying the population at risk with silent AF in the first place. We are only just getting to grips with this in West and we are still failing to ensure even the higher risk patients are anticoagulated, so despite the economic differences there are still major issues in ensuring stroke prevention that need to be addressed even in better resourced healthcare systems.

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