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Stroke and bleeding risk evaluation in atrial fibrillation: results of the European Heart Rhythm Association survey

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The aim of this European Heart Rhythm Association (EHRA) survey was to assess clinical practice in relation to stroke and bleeding risk evaluation in atrial fibrillation, particularly regarding the use of risk evaluation schemes, among members of the EHRA electrophysiology (EP) research network. In this EP Wire survey, we have provided some insights into current practice in Europe for the use of these risk assessment schemes. There were some obvious practice differences. However, reassuring information on current practice in Europe was evident, but more focus on renal function is warranted, especially facing the fact that novel oral anticoagulants are used for antithrombotic therapy.

Keywords Atrial fibrillation • Anticoagulation • Stroke • Bleeding • Risk stratification • $CHADS_2$ • CHA_2DS_2-VASc • HAS-BLED • New oral anticoagulants • Warfarin • EHRA survey • EP wire • Guidelines

Introduction

Atrial fibrillation (AF) is the commonest cardiac rhythm disorder, and is associated with an increased risk of mortality and morbidity from stroke and thromboembolism. An essential part of clinical management of AF involves decision making on oral anticoagulant therapy, given that oral anticoagulant therapy significantly reduces stroke (by 64%) and all-cause mortality (by 26%) compared with placebo or control.[1]

Recent guidelines have largely been based on stroke risk stratification schemes derived from the randomized trial data in specific patient populations, and many recognized risk factors have been used to develop stroke risk stratification schemes for AF.[2,3] These factors include congestive heart failure, hypertension, advanced age, diabetes, and previous stroke.[4] Risk stratification schemes, based on these factors, traditionally classified patients into low-, moderate-, and high-risk strata – so that the high-risk patients could be targeted for oral anticoagulant therapy with a vitamin K antagonist (VKA), e.g. warfarin. In 2010, the CHA_2DS_2-VASc risk score was introduced[5] and was recommended for assessment of risk of stroke by the ESC Guidelines.[6] Bleeding risk is traditionally assessed based on various clinical and demographic characteristics; for example, the HAS-BLED score includes information on hypertension, abnormal renal function and abnormal liver function (one or two points), prior stroke, history of bleeding, labile international normalized ratio (INR), elderly (defined as age >65 years), drug therapy, and alcohol intake (one or two points).[7]

The purpose of this European Heart Rhythm Association (EHRA) survey was to explore current clinical practice in relation to stroke and bleeding risk evaluation in AF, particularly regarding the use of risk evaluation schemes, among members of the EHRA electrophysiology (EP) research network.

Methods and results

Participating centres

This survey is based on an electronic questionnaire sent out to the EHRA EP research network participating centres. Responses were received from 47 centres and of these, 74.47% were university

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hospitals, 17.02% private hospitals, and 8.51% 'others'; 16 centres (34.0%) performed ≥400 catheter ablations for all types of arrhythmias within the last calendar year, 9 (19.2%) 200–399, 8 (17.0%) 100–199, 10 (21.3%) 1–99, and 4 centres (8.5%) performed no catheter ablations.

Risk stratification for stroke and bleeding

The majority of participating centres (97.7%) used the CHA_2DS_2-VASc risk score, and all centres used some kind of stroke risk scoring: either $CHADS_2$ (14.3%) or another risk score (2.0%). Details are given in *Table 1* and *Figure 1*.

Asked if they would routinely assess risk of bleeding using any of the existing bleeding risk scores in AF patients who would be candidates for oral anticoagulant therapy or are already taking an oral anticoagulant, 36 (78.3%) replied that they would use the HAS-BLED score, whereas 9 centres (19.6%) would not use any bleeding risk score. One centre would use another bleeding risk score.

Common clinical practice regarding the bleeding risk assessment and management of oral anticoagulant therapy in patients with AF is summarized in *Table 2* and *Figure 2*. Regarding renal function, 34 centres (70.8%) did not think that creatinine clearance values would be prohibitive for initiation of oral anticoagulation (*Figure 1*). None of the centres used any biomarkers for bleeding risk assessment.

Table 1 Current clinical practice regarding stroke risk assessment and management of oral anticoagulant therapy in patients with AF

	N	% of 48
Consider female gender as an independent stroke risk factor		
Yes	5	10.2
Only in female AF patients ≥65 years old	37	75.1
Routinely check for the presence of PAD		
No	27	56.3
Only if patient reports PAD symptoms	18	37.5
No	3	6.2
Routine recommendation of OAC in the presence of single stroke risk factor		
Yes	39	79.6
No	10	20.4
Routine TTR calculation		
Yes	12	25.0
The warfarin clinic/haematology lab provides TTR	18	37.5
No, TTR is not used at all	18	37.5
Consulting a neurologist is considered		
Only in patients with a history of stroke or TIA	9	18.7
Only in patients with overt neurological deficit	10	20.8
In patients with discrete neurological deficit	19	39.6
In all patients at increased risk of stroke	1	2.1
Never	9	18.8

PAD, peripheral artery disease; OAC, oral anticoagulant; TTR, time in therapeutic range; TIA, transient ischaemic attack.

Other risk factors

Various other risk factors for stroke and bleeding were taken into account when considering oral anticoagulation therapy, including echocardiographic variables and type of AF (see *Figure 1* for details).

Discussion

This EP Wire survey provides some insights into clinical practice in relation to stroke and bleeding risk evaluation in AF, particularly into the use of risk evaluation schemes in Europe. In patients with AF, most respondents would routinely estimate stroke risk and a CHA_2DS_2-VASc score of 1 would influence their approach to antithrombotic prophylaxis (39 of 48 centres, 79.6%). As many as 77% (37 of 48) would routinely estimate bleeding risk (e.g. using the HAS-BLED score). However, as reported by 82.61% of the respondents, this would not influence their decision to initiate antithrombotic treatment. Echocardiographic variables were considered in about 50% of the centres (*Figure 1*).

The ESC Guidelines advocate the initial identification of 'truly low-risk' patients based on a simple practical and user-friendly clinical score (CHA_2DS_2-VASc).[6,8] This has to a large extend been adopted by the participating centres in this and previous EHRA survey.[9] The CHA_2DS_2-VASc score has been shown to reliably identify low-risk patients, and had the best predictive value for the absence of thromboembolism during long-term follow-up of a cohort of patients with lone AF.[10] Various proposals to refine stroke risk stratification, with a particular emphasis on identifying 'high-risk' patients with AF using biomarkers have been proposed, which may offer an additional predictive accuracy at the cost of reduced practicality and ease of use.[11] No biomarkers, however, were used by any of the participating centres for bleeding risk assessment, although 10.7% used some biomarkers for stroke risk assessment.

While proteinuria and renal impairment may be risk factors for stroke in AF, a recurrent debate is whether their presence has an independent predictive value in addition to the existing stroke risk scores. In ancillary analysis from the ROCKET-AF (Rivaroxaban Once daily oral direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation) trial and the ATRIA (AnTicoagulation and Risk factors In Atrial fibrillation) cohort, the presence of renal impairment (two points) added to the $CHADS_2$ score (hence, the R_2CHADS_2 score) improved the net reclassification index compared with the $CHADS_2$ and CHA_2DS_2-VASc scores, although there were only minimal differences in c-indices.[12] However, the ROCKET-AF trial was a selected trial-based anticoagulated AF population that excluded patients with severe renal impairment and the broad range of stroke risk was not studied (excluding patients with $CHADS_2$ score 0–1).[13] Furthermore, all patients in ROCKET-AF were on anticoagulation either with warfarin or rivaroxaban. Determinants of renal impairment include heart failure, age, diabetes, vascular disease, and hypertension, which are components of the $CHADS_2$ and/or CHA_2DS_2-VASc scores. In a recent analysis of thrombo-embolic events following catheter ablation of AF, the CHA_2DS_2-VASc score further differentiated thrombo-embolic risk in patients with $CHADS_2$ and R_2CHADS_2 scores of 0–1 and had

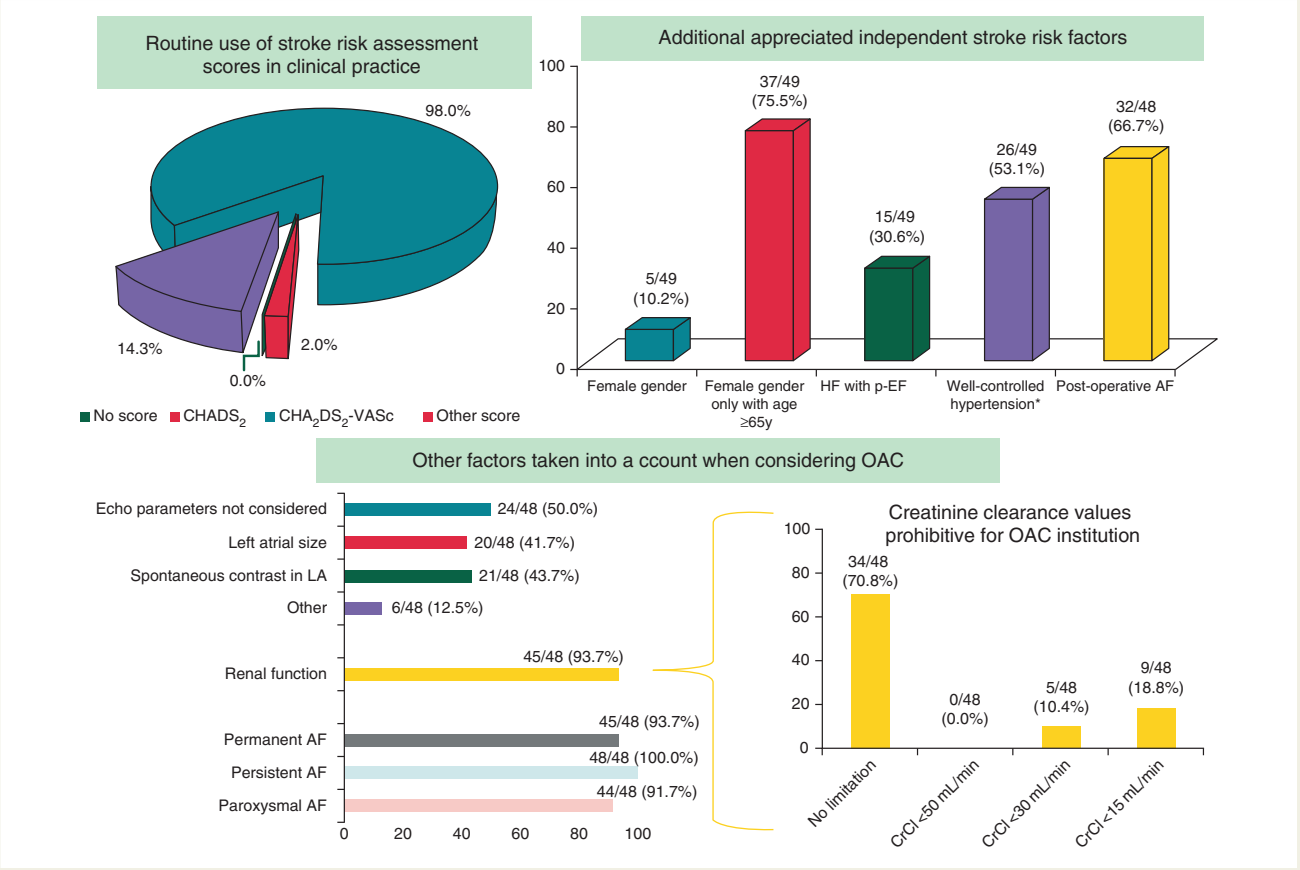

Figure 1 Stroke risk assessment in patients with AF. *Blood pressure not above 140/90 mmHg in a patient diagnosed with arterial hypertension, which is under treatment. $CHADS_2$: Congestive heart failure, hypertension, age 75 years or more, diabetes mellitus, prior stroke or transient ischemic attack. CHA_2DS_2-VASc: Congestive heart failure or left ventricular dysfunction, hypertension, age 75 years or more, diabetes mellitus, prior stroke, transient ischemic attack or other thromboembolic event, vascular disease, age 65–74 years, female gender. HF: heart failure; p-EF: preserved ejection fraction; AF: atrial fibrillation; LA: left atrium; CrCl: creatinine clearance.

Table 2 Common clinical practice regarding bleeding risk assessment and management of oral anticoagulant therapy in patients with AF

	N	% of 48
What HAS-BLED value would be prohibitive for the initiation or continuation of OAT in the AF patient?		
None	5	10.2
Do not use HAS-BLED risk score for this	37	75.1
Regarding hypertension, what is considered a bleeding risk factor		
Only uncontrolled hypertension, with systolic BP values >160 mmHg	31	67.4
Any BP in a patient diagnosed with hypertension, on treatment	4	8.7
Only untreated hypertension	2	4.4
All of the above	8	17.4
None of the above	1	2.2
How often are the AF patients on OAT re-assessed regarding bleeding risk?		
Every 6 months	14	30.3
Once per year	19	41.3
Once in every two or more years	4	8.7
Only at the first visit	9	19.6

HAS-BLED: hypertension, abnormal renal function and abnormal liver function (one or two points), prior stroke, history of bleeding, labile INRs (excluded in this study due to lack of INR data), elderly defined as age >65 years, drug therapy, and alcohol intake (one or two points).
AF, atrial fibrillation; OAT, oral anticoagulant treatment; BP, blood pressure.

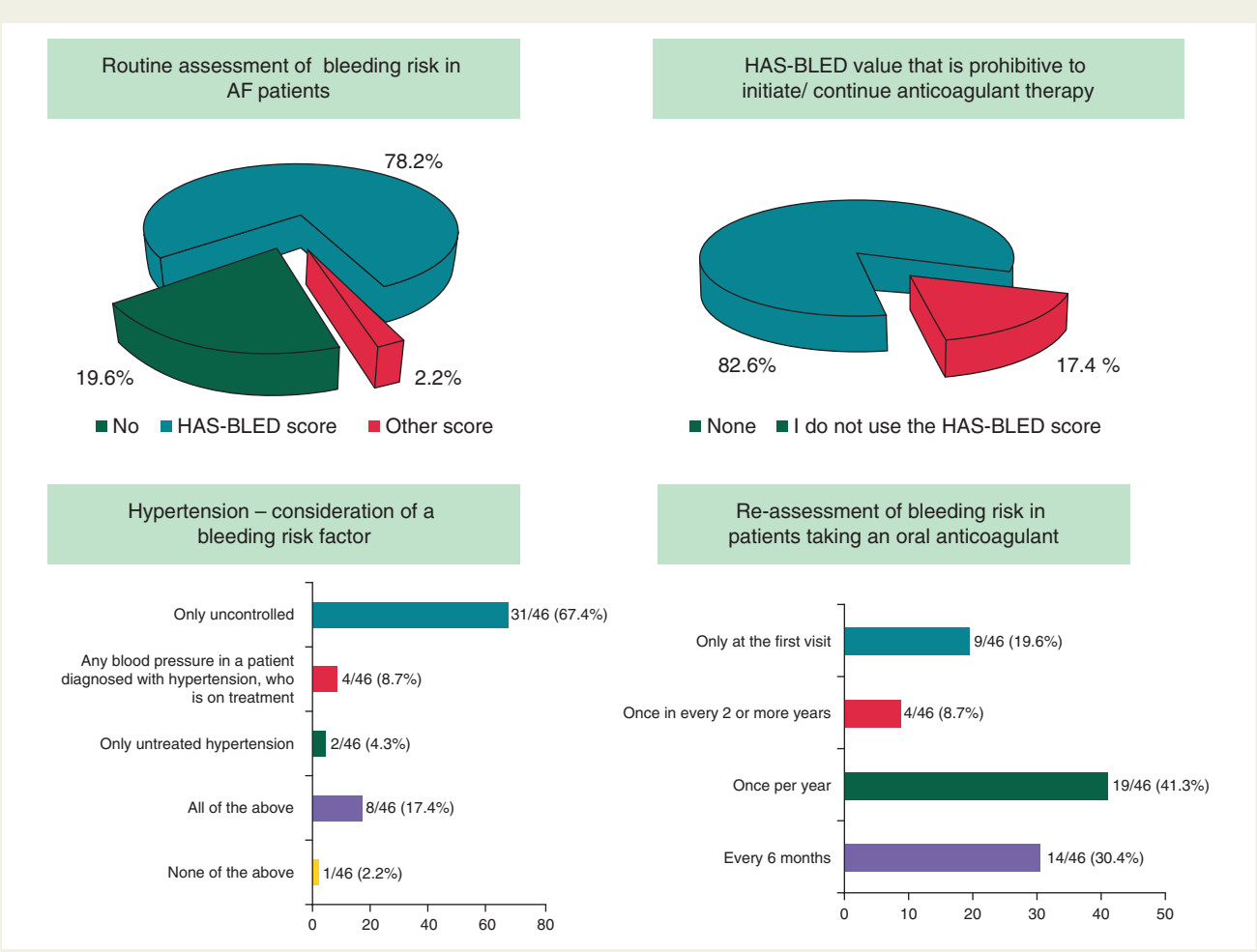

Figure 2 Bleeding risk assessment in patients with AF.

the best predictive value for thromboembolism in patients with AF recurrences.[14]

The ESC Guidelines recommend oral anticoagulation for patients with a CHA_2DS_2-VASc score 2 or more (class I recommendation) and are in favour of this therapy in patients with a CHA_2DS_2-VASc score of 1 (class IIa recommendation).[8] While warfarin remains a viable option, the ESC Guidelines state that new (non-VKA) oral anticoagulants may be preferred over warfarin, given their greater efficacy, safety, and convenience. Non-VKA oral anticoagulants have been increasingly used in Europe, including patients with newly diagnosed AF.[9] However, there are restrictions to the use of non-VKA anticoagulants in patients with a various degree of renal impairment, and each of these agents has been issued with a set of specific rules relating to renal function.[15] In patients with a severe renal impairment and individuals requiring haemodialysis, the new oral anticoagulants are contraindicated, with warfarin remaining the preferred therapy. This further underscores the importance of the assessment of renal function as a risk factor for stroke and bleeding and for the initiation of appropriate antithrombotic prophylaxis.

Conclusions

This EP Wire survey reaffirms some aspects of the ESC Guidelines being considered in centres responding to this survey. Reassuring information on current practice in Europe regarding the use of schemes for both stroke and bleeding risk assessment in AF is evident, although more focus on renal function is warranted, especially facing the fact that novel oral anticoagulants are used for antithrombotic therapy.[15,16]

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