The personalized antithrombotic management of atrial fibrillation with intermediate thromboembolic risk: a case report

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Background So far there has been little evidence on the antithrombotic treatment of patients presenting with atrial fibrillation (AF) and a CHA2DS2-VASc score of 1 in men (2 in women). However, a recently published position paper suggests a personalized approach in weighing individual risk factors and considering additional patient characteristics and biomarkers for the decision for or against antithrombotic treatment in this intermediate-risk AF population.

Case summary A 63-year-old male patient with a CHA2DS2-VASc score of 1 due to hypertension presents with a first episode of paroxysmal AF. The European Society of Cardiology (ESC) guidelines on the management of AF do not recommend a general antithrombotic therapy in those patients. Therefore, the decision for or against the initiation of oral anticoagulation (OAC) in the presented case is based on recent treatment recommendations of the ESC, that aim to guide clinicians through the question whether to anticoagulate or not.

Discussion Oral anticoagulation in patients presenting with a CHA2DS2-VASc of 1 remains a challenging approach in clinical practice and physicians need to carefully balance the individual benefit of reducing thromboembolic risk with OAC against the potential harm due to an increase in bleeding risk in this patient population. The ESC provided an easily applicable approach for decision-making in patients with AF and a CHA2DS2-VASc score of 1 via consideration of additional risk factors, scoring tools, and established biomarkers. Of note, if an antithrombotic therapy is offered, non-vitamin K antagonist oral anticoagulants should be preferred over vitamin K antagonists based on the beneficial net clinical benefit.

Keywords Case report • Anticoagulation • Atrial fibrillation • CHA2DS2-VASc score • Intermediate risk

Introduction Atrial fibrillation (AF) mirrors the most prominent arrhythmia in clinical practice. It accompanies an increased risk for thromboembolic events and depicts the cause of every 5th diagnosed ischaemic stroke. Clinical practice guidelines recommend the initiation of oral anticoagulation (OAC) for stroke prevention in AF patients with increased thromboembolic risk pictured by a CHA2DS2-VASc score of >2, while OAC should not be considered in individuals with a score of 0. However, there is no clear recommendation provided for individuals with a CHA2DS2-VASc score of 1.
Learning points

- A general recommendation of oral anticoagulation (OAC) therapy in patients with atrial fibrillation (AF) and a CHA₂DS₂-VASc score of 1 might weaken the net clinical benefit due to an increased risk of bleeding events. Oral anticoagulation should not be considered in intermediate thromboembolic risk patients with a HAS-BLED score > 2.
- Additional values for stratification of the individual risk of stroke need to be considered such as: age (> 65 years), Type II diabetes mellitus, type of atrial arrhythmia (AF not atrial flutter), burden of AF (paroxysmal vs. non-paroxysmal), obesity (body mass index ≥ 30), kidney function (proteinuria > 150 mg/24 h or estimated glomerular filtration rate < 45 mL/h), cardiac biomarkers (positive troponin I or T; N-terminal pro-B-type natriuretic peptide > 1400 ng/L), enlarged left atrial volume (> 73 mL) or diameter (> 4.7 cm), and the use of additional scoring tools (ABC stroke risk score). Of most importance, the patients’ individual preference for, or against initiation of OAC must be taken into account.
- Therapeutic decisions should be based on the individual balance between thromboembolic and bleeding risk. Non-vitamin K antagonist oral anticoagulants with a superior net-clinical benefit should be preferred over vitamin K antagonists in AF patients presenting with a CHA₂DS₂-VASc score of 1.

We hereby present the case of a 63-year-old male patient with newly diagnosed AF and evaluate the net-clinical benefit of OAC for stroke prevention in accordance to the recently published current opinion statement of the ESC Working Group on Cardiovascular Pharmacotherapy and the ESC Council on Stroke.¹

Timeline

| Month  | Event Description |
|--------|-------------------|
| May 2019 | Patient felt palpitations for the first time |
| June 2019 | Based on intermittent palpitations a 24-h electrocardiogram (ECG) was performed but did not detect any episode of atrial fibrillation (AF) |
| August 2019 | Patient was admitted to the outpatient department of the local division of cardiology. A 12-lead ECG detected tachycardic AF that lasted for approximately 13 h. |
| August 2019 | Decision against antithrombotic management was made based on a low individual thromboembolic risk and patient’s preference |
| November 2019 | During patient follow-up, no ischaemic event was detected |
| July 2021 | A revaluation of the indication for oral anticoagulation is scheduled for the 65th birthday of the patient when the CHA₂DS₂-Vasc score increases to 2 |

Case presentation

A 63-year-old male patient was admitted to the Division of Cardiology of the Medical University of Vienna due to palpitations. He presented with the medical history of a well-controlled hypertension receiving an antihypertensive therapy of 5 mg of amlopidine per day. Physical examination revealed a blood pressure of 135/83 mmHg, 98% oxygen saturation on room air, and fast irregular pulses. The surface electrocardiogram (ECG) showed tachycardic episode of AF with a heart rate of 148 b.p.m. that converted spontaneously to normo-frequent sinus rhythm during clinical presentation. Based on the first documented episode of AF, the patient’s individual risk for thromboembolic events was assessed. Since no additional comorbidities were present at the time of admission, the patient’s CHA₂DS₂-VASc score was 1 (only one point for hypertension) mirroring an annual stroke rate of 0.6–1.3%.² According to treatment recommendations, initiation of OAC should be considered and was subsequently evaluated via the patient’s individual net-clinical benefit based on the recently published current opinion statement of the ESC Working Group on Cardiovascular Pharmacotherapy and the ESC Council on Stroke.²

The assessment of patients’ individual risk for major bleedings including modifiable risk factors is a key prerequisite for initiation of OAC. To elucidate the individual risk of bleeding during OAC the HAS-BLED score is recommended as a highly validated tool to estimate the risk of bleeding during OAC.² Notably, in patients with a HAS-BLED score of 2 (or greater) an OAC should not be initiated in intermediate thromboembolic risk patients based on an annual bleeding rates of 1.88–3.20% per year, since the risk for bleeding during OAC outweighs the thromboembolic risk.⁶ The clinical characteristics of our patient (independently history of hypertension—which is well-controlled) leads to a total score of 0, that refers to a risk for a major bleeding event of 0.59–1.13% per year. Based on the estimated thromboembolic risk for our patient that refers to 0.6–1.3% per year and an associated bleeding risk of 0.59–1.13% per year, a definite decision for or against the initiation of OAC cannot be undertaken when considering the net-clinical benefit of the therapy. Therefore, refinement of the individual risk of stroke is needed.

The current opinion statement of the European Society of Cardiology (ESC) recommends the additional consideration of easily assessable predictive values.

The authors highlighted that the most prominent values associated with thromboembolic risk refer to age > 65 years, Type II diabetes mellitus, atrial fibrillation (not atrial flutter), and persistence/permanence of atrial fibrillation.² Our patient presented with an episode of self-limiting AF, an age below 65 years and without Type II diabetes mellitus (HbA1c: 5.7%). Additionally, the patient’s clinical presentation (obesity), kidney function, and cardiac biomarkers are recommended in terms of thromboembolic risk stratification.² In the present case, the patient presented without frailty or obesity and in good physical appearance.
Moreover, he reported of no history of nicotine or ethanol abuse. Blood panels and biochemistry showed normal renal function (estimated glomerular filtration rate: 97 mL/min) and non-elevated cardiac biomarkers [N-terminal pro-B-type natriuretic peptide (NT-proBNP): 157 ng/mL; troponin T: negative].

The recent consensus statement mentioned that also imaging values (e.g. left atrial volume or diameter) should be considered in terms of personalized risk stratification.\textsuperscript{2,7} Transthoracic echocardiography in our patient revealed normal systolic function, without signs of valve disease or left ventricular hypertrophy and the left atrial volume was calculated with 69 mL.

As an additional scoring tool, the ABC stroke risk score is recommended by both the guidelines of the management of AF and the recently published consensus statement of the ESC.\textsuperscript{1,2,8} Calculating the ABC stroke risk score for our patient, a thromboembolic risk of below 1% was estimated. Taking the obtained results and patient characteristics into account, the individual thromboembolic risk was considered lower than the associated risk of major bleeding events. Therefore, OAC does not seem to provide a net-clinical benefit in our patient. After a shared decision-making process including the patient’s personal preference, no antithrombotic treatment was started. However, the importance of a well-controlled hypertension and regular follow-ups—including 24-h ECG analysis to elucidate the AF burden—were emphasized. The initiation of OAC [preferably using a non-vitamin K antagonist oral anticoagulant (NOAC)] at the age of 65 years or earlier when developing additional risk factors was agreed. Additionally, in case of progression in the observed frequencies of paroxysmal AF episodes or development of permanent AF, potential opportunities for ablation were discussed with the patient. Within a performed 24-h ECG analysis during a follow-up visit, no arrhythmic episode was detected. Additionally, the patient reported that he was free of any palpitation. The respective decision-making algorithm provided by the ESC Working Group on Cardiovascular Pharmacotherapy and the ESC Council on Stroke is highlighted as Figure 1.

**Discussion**

As compared to ESC guidelines on the management of AF\textsuperscript{1} the recently published current opinion statement of the ESC Working Group on Cardiovascular Pharmacotherapy and the ESC Council on Stroke clearly outlined that therapeutic decisions in patients with a CHA\textsubscript{2}DS\textsubscript{2}-VASc score of 1 should be based on the individual balance between thromboembolic and bleeding risk—and that the therapeutic preference should be on doing no harm rather than avoiding stroke.\textsuperscript{2} In individuals with a CHA\textsubscript{2}DS\textsubscript{2}-VASc score of 1, NOACs with a superior net-clinical benefit and low risk for intracranial bleeding should be preferred over vitamin K antagonists.\textsuperscript{9} There is no evidence in literature that acetylsalicylic acid mirrors an adequate antithrombotic treatment option and should therefore not be considered.\textsuperscript{10}

The present case emphasizes—as highlighted by the ESC Working Group on Cardiovascular Pharmacotherapy and the ESC Council on Stroke—the importance of individually refined risk stratification in patients presenting with AF and a CHA\textsubscript{2}DS\textsubscript{2}-VASc score of 1. A general recommendation of OAC therapy in patients with AF and a

![Decision-making algorithm for personalized antithrombotic management in patients presenting with a CHA\textsubscript{2}DS\textsubscript{2}-VASc score of 1 and atrial fibrillation; adopted from the consensus paper of the ESC Working Group on Cardiovascular Pharmacotherapy and the ESC Council on Stroke.\textsuperscript{2} eGFR, estimated glomerular filtration rate; LA, left atrium; LAA, left atrial appendage; NOAC, non-vitamin K antagonist oral anticoagulant; NT-proBNP, N-terminal pro-B-type natriuretic peptide; OAC, oral anticoagulation; VKA, vitamin K antagonist.](https://academic.oup.com/ehjcr/advance-article/doi/10.1093/ehjcr/ytaa176/5903201)
CHADS2-VASc score of 1 might weaken the net clinical benefit due to an increased risk of bleeding events and there is currently no evidence available from randomized controlled trials in literature that guide physicians through this multi-factorial decision-making. In order to provide a clinical treatment benefit of OAC for patient with a CHADS2-VASc score of 1, refinement of the individual thromboembolic risk assessment is needed. Based on an imbalance in the net clinical benefit, OAC should not be considered in intermediate thromboembolic risk patients with a HAS-BLED score $\geq 2$.\textsuperscript{2,11}

Recent evidence provided a large variety of potential values that proved to be associated with the development of thromboembolic events—many of them are routinely assessed. In this regard, the patient’s age and presence of Type II diabetes mellitus were the most prominent isolated risk factors for stroke.\textsuperscript{11,12} Also the type (atrial flutter vs. AF) and burden of AF (paroxysmal AF vs. non-paroxysmal AF) proved to be major predictors for ischaemic events.\textsuperscript{13}

With regard to imagining markers, left atrial size proved to be a reasonable and easily assessable imaging marker for risk stratification.\textsuperscript{7,14} Routinely available biomarkers for risk stratification such as cardiac troponin (high-sensitivity troponin T or I) and NT-proBNP have already been described previously and were mentioned within the ESC guidelines on the management of AF.\textsuperscript{1} Most importantly, the patients’ individual preference for, or against initiation of OAC must be taken into account.

The patient was satisfied with being involved in the decision-making process. In case of reappearance of AF, further treatment strategies—e.g. cardiac ablation treatment—have been proposed. He acknowledged the need of close-faced clinical follow-up visits and 24-h ECG analysis.

Lead author biography
Andreas Hammer is currently in his 4th year of medical school at the Medical University of Vienna (Austria) and research fellow at the lab of Professor Alexander Niessner. He has sincere interest in cardiology and cardiovascular research. Following his scientific ambitions, he is about to join the PhD programme in the field of vascular biology to further promote his academic career.

Supplementary material
Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

References
1. Kirchhof P, Benussi S, Kotecha D, Ahklsson A, Atar D, Casadei B et al.; ESC Scientific Document Group. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37: 2893–2962.
2. Sulzgruber P, Wassmann S, Semb AG, Doehner W, Widimsky P, Gremmel T et al. Oral anticoagulation in patients with non-valvular atrial fibrillation and a CHADS2-VASc score of 1: a current opinion of the European Society of Cardiology Working Group on Cardiovascular Pharmacotherapy and European Society of Cardiology Council on Stroke. Eur Heart J Cardiovasc Pharmacother 2019;5:171–180.
3. Goto S, Mermil P, Wallentin L, Wojdyla DM, Hanna M, Avezum A et al. Antithrombotic therapy use and clinical outcomes following thromboembolic events in patients with atrial fibrillation: insights from ARISTOTLE. Eur Heart J Cardiovasc Pharmacother 2018;4:75–81.
4. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijs HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 2010;137:263–272.
5. Roldan V, Marin F, Fernandez H, Manzano-Fernandez S, Gallego P, Valdes M et al. Predictive value of the HAS-BLED and ATRIA bleeding scores for the risk of serious bleeding in a “real-world” population with atrial fibrillation receiving anticoagulant therapy. Chest 2013;143:579–184.
6. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijs HJ. Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest 2010;138:1093–1100.
7. Anassie J, Monlezun D, Seelochan A, Siegler JL, Chavez-Keatts M, Tiu J et al. Left atrial enlargement on transthoracic echocardiography predicts left atrial thrombus on transesophageal echocardiography in ischemic stroke patients. Brain Res Int 2016;217:17674676.
8. Hijazi Z, Oldgren J, Lindback J, Alexander JH, Connolly SJ, Eikelboom JW et al. Aristotle and RE-LY Investigators. The novel biomarker-based ABC (age, biomarkers, clinical history)-bleeding risk score for patients with atrial fibrillation: a derivation and validation study. Lancet 2016;387:2302–2311.
9. Coleman CI, Turpie AGG, Bunz TJ, Eriksson D, Sood NA, Baker WL. Effectiveness and safety of rivaroxaban vs. warfarin in non-valvular atrial fibrillation patients with a non-sex-related CHADS2-VASc score of 1. Eur Heart J Cardiovasc Pharmacother 2019;5:64–69.
10. Lip GY, Skjøth F, Rasmussen LH, Larsen TB. Oral anticoagulation, aspirin, or no therapy in patients with nonvalvular AF with 0 or 1 stroke risk factor based on the CHADS2-VASc score. J Am Coll Cardiol 2015;65:1385–1394.
11. Friberg L, Rosenqvist M, Lip G. Net clinical benefit of warfarin in patients with atrial fibrillation: a report from the Swedish atrial fibrillation cohort study. Circulation 2012;125:2298–2307.
12. Chao T-F, Liu C-J, Wang K-L, Lin Y-J, Chang S-L, Lo L-W et al. Should atrial fibrillation patients with 1 additional risk factor of the CHA2DS2-VASc score (beyond sex) receive oral anticoagulation? J Am Coll Cardiol 2015;65:635–642.
13. Savaleva I, Carmin AJ. Clinical relevance of silent atrial fibrillation: prevalence, prognosis, quality of life, and management. Int J Card Electrophysiol 2004;4:369–382.
14. Gupta DK, Shah AM, Giugliano RP, Ruff CT, Antman EM, Griendt LT et al. Effective aNicoradGulation with factor xa next Generation in AF-Thrombolysis In Myocardial Infarction 48 Echocardiographic Study Investigators. Left atrial structure and function in atrial fibrillation: ENGAGE AF-TIMI 48. Eur Heart J 2014;35:1457–1465.