Adherence to the 4S-AF Scheme in the Balkan region: Insights from the BALKAN-AF survey

Monika Kozieł-Siołkowska[1, 2], Miroslav Mihajlovic[3], Milan Nedeljkovic[3, 4], Nikola Pavlovic[5], Vilma Paparisto[6], Ljilja Music[7], Elina Trendafilova[8], Anca Rodica Dan[9], Zumreta Kusljugic[10], Gheorghe-Andrei Dan[11], Gregory YH Lip[1, 2, 4, 12*], Tatjana S Potpara[3, 4*], on behalf of the BALKAN-AF Investigators

[1]Liverpool Center for Cardiovascular Science, University of Liverpool and Liverpool Heart and Chest Hospital, Liverpool, United Kingdom
[2]1st Department of Cardiology and Angiology, Silesian Center for Heart Diseases, Zabrze, Poland
[3]Cardiology Clinic, Clinical Center of Serbia, Belgrade, Serbia
[4]School of Medicine, Belgrade University, Belgrade, Serbia
[5]Clinical Center Sestre Milosrdnice, Zagreb, Croatia
[6]Clinic of Cardiology, University Hospital Center Mother Theresa, Tirana, Albania
[7]Cardiology Clinic, University Clinical Center of Montenegro, University of Podgorica, Medical Faculty, Podgorica, Montenegro
[8]National Heart Hospital, Coronary Care Unit, Sofia, Bulgaria
[9]Colentina University Hospital, Cardiology Department, Bucharest, Romania
[10]Clinic of Internal Medicine, Cardiology Department, University Clinical Center Tuzla, Medical Faculty, Tuzla, Bosnia and Herzegovina
[11]Medicine University "Carol Davila", Colentina University Hospital, Bucharest, Romania
[12]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark
*Both authors equally contributed to the study

Correspondence to:
Tatjana Potpara, MD, PhD, FESC, Cardiology Clinic, Clinical Center of Serbia, Visegradska 26, 11000 Belgrade, Serbia,
phone: +381 11 3616319,
e-mail: tanjapotpara@gmail.com

DOI: 10.33963/KP.a2022.0053

Received:
October 30, 2021

Accepted:
February 17, 2022

Early publication date:
February 17, 2022

ABSTRACT

Background: The 4S-AF scheme includes stroke risk, symptoms, severity of burden, and substrate severity domain.

Aim: We aimed to assess the adherence to the 4S-AF scheme in patients classified according to stroke risk in *post hoc* analysis of the BALKAN-AF dataset.

Methods: A 14-week prospective enrolment of consecutive patients with electrocardiographically documented atrial fibrillation (AF) was performed in seven Balkan countries from 2014 to 2015.

Results: Low stroke risk (CHA_2DS_2-VASc score, 0 in males or 1 in females) was present in 162 (6.0%) patients. 2 099 (77.4%) patients had CHA_2DS_2-VASc score ≥3 in females or ≥2 in males (high stroke risk), and 613 (22.6%) had CHA_2DS_2-VASc score <3 in females or <2 in males. Seventy-five (46.3%) patients with low stroke risk and 1555 (74.1%) patients with high stroke risk were prescribed oral anticoagulants (OAC). Two thousand six hundred and seventy-seven (98.6%) had data on European Heart Rhythm Association (EHRA) class. Among 2099 patients with high stroke risk, 703 (33.4%) had EHRA class ≥3. Two hundred and seven (29.4%) patients with EHRA class ≥3 and high stroke risk were offered rhythm control; 620 (55.2%) of individuals with first-diagnosed or paroxysmal AF with high stroke risk were offered rhythm control. Two or more comorbidities occurred in 1927 (91.8%) patients with high stroke risk.

Conclusions: OAC overuse was observed in patients with low stroke risk, whilst OAC underuse was evident in those with high risk of stroke. The percentage of highly symptomatic patients with high risk of stroke who were offered a rhythm control strategy was low.

Key words: atrial fibrillation, oral anticoagulants, rhythm control, risk of stroke

WHAT'S NEW?

Data on the use of the 4S-AF scheme in clinical practice are scarce. This study, therefore, provides a novel insight into the adherence to the 4S-AF scheme in real-world atrial fibrillation (AF) patients. Unfortunately, treatment decision-making was not based on the 4S-AF structured scheme in the BALKAN-AF cohort. Using the 4S-AF scheme may facilitate treatment decision-making associated with the management of patients with AF in clinical practice.

INTRODUCTION

Atrial fibrillation (AF) is a substantial source of morbidity and mortality, with a major economic burden for countries worldwide [1]. Moreover, AF is often asymptomatic (but still confers a poor prognosis) [2], and the complexity of AF needs a holistic approach with multidisciplinary, integrated management with active involvement of AF patients [3–5]. This integrated approach to patient evaluation and management is associated with improved outcomes in AF [6] and is also increasingly advocated in various other clinical settings with chronic long-term conditions [7–8].

Currently, the AF guidelines propose a structured characterization of AF including domains with management and prognostic implications to facilitate the evaluation of AF patients by healthcare professionals [9]. The 4S-AF structured scheme includes four domains: Stroke risk, Symptoms, Severity of AF burden, and Substrate severity [9].

The Stroke risk domain with stroke risk assessment is based on the CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack [TIA], vascular disease, age 65-74 years, sex category [female]). The indications for oral anticoagulants (OAC) use are based on the European Society of Cardiology guidelines or other international documents [3, 10].

The Symptom severity domain is associated with the EHRA symptom score and facilitates patient-centered, symptom-directed AF management [4]. The Severity of the AF burden domain describes the density of AF episodes in time and the proportion of time of AF. The Substrate for the AF domain relates to the complexity of AF pathophysiology including characteristics such as age, cardiovascular risk factors, and underlying comorbid conditions, as well as parameters of the left atrium (enlargement, function, and fibrosis of its myocardium) [11].

This *post hoc* analysis aimed to evaluate the adherence to the 4S-AF scheme in the BALKAN-AF cohort in patients classified according to their stroke risk.

METHODS

The design of the BALKAN-AF study has been described previously [12]. This 14-week prospective, multicenter "snapshot" registry of consecutive patients with electrocardiographically documented AF was designed and conducted by the Serbian Atrial Fibrillation Association (SAFA). Consecutive AF patients were enrolled in the survey from December 2014 to February 2015 in cooperation with individual National Cardiology Societies and Associations or Working Groups in Albania, Bosnia & Herzegovina, Bulgaria, Croatia, Montenegro, Romania, and Serbia. Universities, non-university hospitals, and outpatient health centers (a total of 49 centers) were sites involved in the BALKAN-AF study. The respective National Coordinator selected the sites. The registry was approved by the local/national institutional review board in participating countries. The study received ethical approval. A signed patient informed consent form was obligatory in the enrolment process. The study protocol was concordant with the Declaration of Helsinki.

Exclusion criteria included those aged <18 years or patients with prosthetic mechanical heart valves or significant valvular disease with indications for surgical repair.

Data on patient presentation, patient characteristics, healthcare setting, and diagnostic procedures within the last 12 months and at enrolment and AF management at enrolment and discharge were collected and stored using the electronic case report forms (eCRFs). Stroke risk was evaluated using the CHA_2DS_2-VASc score [10]. Truly low risk of stroke was defined as a CHA_2DS_2-VASc score of 0 in males, and 1 in females, whilst the intermediate risk of stroke included male patients with a CHA_2DS_2-VASc score of 1 or females with a CHA_2DS_2-VASc score of 2. High risk of stroke was defined as CHA_2DS_2-VASc score ≥3 in females or ≥2 in males.

Bleeding risk was assessed according to the HAS-BLED score (hypertension, abnormal renal /liver function, stroke, bleeding history or predisposition, labile International Normalized Ratio [INR], elderly [>65 years], drugs or alcohol concomitantly) [13]. The included cardiovascular risk factors, risk scores, and diseases were defined using the individual European Society of Cardiology guidelines, other international guidelines, scientific statements, and textbooks as described previously [14].

Regular monitoring of centers and follow-up visits were not performed due to the relatively short period of the survey. National coordinators and investigators were responsible for validation of the consecutiveness of enrolled patients and correctness and completeness of entered data.

Available domains of the 4S-AF scheme were identified and assessed using data from the baseline visit.

Statistical analysis

Categorical variables were presented as absolute frequencies and percentages. Numerical variables were presented

as mean (standard deviation [SD]) or median with interquartile range (IQR) and compared between groups by Student's t-test or Mann-Whitney's test where appropriate. Comparative analysis between groups was performed using Chi^2 for dichotomous parameters. The descriptive analysis involved stroke prevention, quality of life, management strategies, severity of AF burden, and the Substrate for AF domain in the BALKAN-AF cohort. A two-sided *P*-value of less than 0.05 was considered statistically significant. All analyses were performed using SAS software version 9.4 (SAS Institute, Inc., Cary, NC, US).

RESULTS

The Stroke risk domain

Patients with high risk of stroke were older, more likely to be female, and more likely to have concomitant diseases than those with low or intermediate risk of stroke (all P <0.05), Table 1. Congestive heart failure, hypertension, and coronary artery disease were the most frequent concomitant diseases in individuals with high, low, and intermediate stroke risk. The baseline characteristics of patients are summarized in Table 1.

Of 2712 enrolled patients, 2712 (100.0%) had data on CHA_2DS_2-VASc score. One hundred and sixty-two (6.0%) individuals had a truly low risk; 2550 (94.0%) patients had CHA_2DS_2-VASc score ≥1 in males or ≥2 in females; 2099 (77.4%) patients had high risk of stroke, and 613 (22.6%) individuals had low or intermediate risk of stroke, Table 1.

Patients with high risk of stroke had a higher mean HAS-BLED score than those with intermediate or low risk of stroke (P <0.001), Table 1.

Patients with high risk of stroke were less likely to receive no antithrombotic therapy, warfarin, and dabigatran than those with low or intermediate risk of stroke (all P <0.05), Table 1. Among patients with truly low risk of stroke, 75 (46.3%) patients were medicated with OAC, Table 1.

The Symptom severity domain

Of 2712 patients, 2 677 (98.6%) had data on the European Heart Rhythm Association (EHRA) symptom score: (1) 571 (21.0%) patients had EHRA symptom score of 1; (2) 1254 (46.2%) of individuals had EHRA symptom score of 2; (3) 712 (26.2%) patients had EHRA symptom score of 3; and (4) 140 (5.2%) patients had EHRA symptom score of 4. Among 2 099 patients with CHA_2DS_2-VASc score ≥3 in females or ≥2 in males, 703 (33.4%) individuals had EHRA symptom score of 3 or 4.

Patients with high risk of stroke were more likely to have shortness of breath, chest pain, dizziness, and fatigue than those with low or intermediate risk of stroke (all P <0.001), Table 2.

A rhythm control strategy was implemented in 207 (29.4%) patients with high risk of stroke and EHRA symptom score of 3 or 4. Notably, 620 (55.2%) of patients with high risk of stroke and paroxysmal AF or first diagnosed AF were assigned to rhythm control strategy, while 646 (57.5%) individuals with high risk of stroke and paroxysmal AF or first diagnosed AF were medicated with amiodarone, Table 3. Amiodarone was the most commonly prescribed drug in individuals with high risk of stroke, and EHRA symptom score of 3 or 4.

The Severity of AF burden domain

Patients with low or intermediate risk of stroke were more likely to have first diagnosed AF, paroxysmal AF, or persistent AF than those with high risk of stroke (all P <0.05), Table 4.

The Substrate for AF domain

Patients with high risk of stroke were more likely to have a higher median number of comorbid diseases than those with low or intermediate risk of stroke (P <0.05).

The mean diameter of the left atrium (LA) was higher in individuals with high risk of stroke than in those with low or intermediate risk of stroke (P <0.001), Table 5.

DISCUSSION

The main findings of this study were as follows: (1) OAC overuse was seen in patients with truly low stroke risk, whilst OAC underuse was evident in patients with high risk of stroke; (2) the proportion of highly symptomatic patients (EHRA 3 or 4) with high risk of stroke who were offered rhythm control strategy was low; (3) the proportion of patients with first diagnosed AF or paroxysmal AF with high risk of stroke who received rhythm control was small; and (4) the majority of AF patients with high risk of stroke had ≥2 comorbidities.

Data on the use of the 4S-AF scheme in everyday clinical practice are scarce. This study, therefore, provides a novel insight into the adherence to the 4S-AF scheme in real-world AF patients. The 4S-AF scheme facilitates our evaluation and characterization of the AF patient during the clinical consultation. Moreover, this structured characterization of AF patients provides prognostic information, and this study validates the 4S-AF scheme in the Balkan region. We found that OAC overuse in patients with low risk of stroke and OAC underuse in those with high risk of stroke was common, and seen also in recent European reports [15–17]. Efforts to improve the prescription of OACs in AF patients are, therefore, needed [18], and the availability of NOACs has improved such efforts [19, 20].

The use of NOACs has increased over time in Europe. This finding has been shown in other studies [19–24]. The risk of stroke is closely linked with bleeding risk, and thromboembolic factors such as older age, hypertension, or history of stroke have also been bleeding risk factors [25]. Thus, patients with high risk of stroke have higher bleeding risk than those with low or intermediate risk of stroke.

The EHRA symptom score expresses how physicians weigh the symptoms of AF patients, but in the BALKAN-AF

Table 1. Stroke prevention in patients according to stroke risk

Variable	CHA_2DS_2-VASc score of 0 in males or 1 in females n = 162 (6.0%)	CHA_2DS_2-VASc score ≥1 in males or ≥2 in females n = 2550 (94.0%)	*P*-value	CHA_2DS_2-VASc score ≥3 in females or ≥2 in males n = 2099 (77.4%)	CHA_2DS_2-VASc score <3 in females or <2 in males n = 613 (22.6%)	*P*-value
Age, years, mean (SD)	49.9 (11.4)	70.1 (9.9)	<0.001	72.5 (8.6)	56.7 (9.2)	<0.001
Female gender, n (%)	41 (25.3)	1151 (45.1)	<0.001	953 (45.4)	239 (39.0)	<0.001
BMI, kg/m^2, mean (SD)	26.4 (3.3)	27.8 (4.4)	<0.001	27.8 (4.5)	27.7 (4.0)	0.848
Alcohol abuse, ≥8 units/week, n (%)	7 (4.3)	103 (4.0)	0.860	81 (3.9)	29 (4.7)	0.336
First diagnosed AF, n (%)	52 (32.1)	580 (22.7)	<0.001	455 (21.7)	177 (28.9)	<0.001
Paroxysmal AF, n (%)	79 (48.8)	881 (34.5)	<0.001	668 (31.8)	292 (47.6)	<0.001
Permanent AF, n (%)	17 (10.5)	1071 (42.0)	<0.001	973 (46.4)	115 (18.8)	<0.001
Concomitant diseases, n (%)						
Congestive HF	0 (0.0)	1336 (52.4)	n/a	1240 (59.1)	103 (16.8)	<0.001
Hypertension	0 (0.0)	2121 (83.2)	n/a	1800 (85.8)	321 (52.4)	<0.001
CAD	0 (0.0)	819 (32.1)	n/a	764 (36.4)	57 (9.3)	<0.001
Prior MI	0 (0.0)	369 (14.5)	n/a	359 (17.1)	10 (1.6)	<0.001
PAD	0 (0.0)	122 (4.8)	n/a	120 (5.7)	2 (0.3)	<0.001
Diabetes	0 (0.0)	668 (26.2)	n/a	636 (30.3)	32 (5.2)	<0.001
Prior stroke	0 (0.0)	281 (11.0)	n/a	280 (13.3)	1 (0.2)	<0.001
Prior TIA	0 (0.0)	83 (3.3)	n/a	83 (4.0)	0 (0.0)	n/a
Anemia	7 (4.3)	366 (14.4)	<0.001	337 (16.1)	36 (5.9)	<0.001
Chronic kidney disease	1 (0.6)	410 (16.1)	<0.001	391 (18.6)	20 (3.3)	<0.001
Previous bleeding event	1 (0.6)	132 (5.2)	<0.001	121 (5.8)	12 (2.0)	<0.001
COPD	3 (1.9)	339 (13.3)	<0.001	305 (14.5)	37 (6.0)	<0.001
Cancer	2 (1.2)	117 (4.6)	0.096	106 (5.1)	13 (2.1)	0.004
HAS-BLED score, mean (SD)	0.31 (0.6)	2.1 (1.2)	<0.001	2.3 (1.1)	0.8 (0.8)	<0.001
No antithrombotic therapy, n (%)	44 (27.2)	221 (8.7)	<0.001	174 (8.3)	91 (14.8)	<0.001
Overall OAC, n (%)	75 (46.3)	1890 (74.1)	<0.001	1555 (74.1)	410 (66.9)	0.105
OAC alone, n (%)	70 (43.2)	1571 (61.6)	<0.001	1265 (60.3)	376 (61.3)	0.633
VKA, n (%)	62 (38.3)	1565 (61.4)	<0.001	1301 (62.0)	326 (53.2)	0.012
Warfarin, n (%)	35 (21.6)	520 (20.4)	0.128	408 (19.4)	147 (24.0)	0.002
Acenocoumarol, n (%)	27 (16.7)	1044 (40.9)	<0.001	892 (42.5)	179 (29.2)	<0.001
NOAC, n (%)	13 (8.0)	325 (12.7)	0.320	254 (12.1)	84 (13.7)	0.125
Dabigatran, n (%)	9 (5.6)	166 (6.5)	0.917	125 (6.0)	50 (8.2)	0.022
Rivaroxaban, n (%)	4 (2.5)	111 (4.4)	0.459	89 (4.2)	26 (4.2)	0.797
Apixaban, n (%)	1 (0.6)	48 (1.9)	0.344	40 (1.9)	9 (1.5)	0.575
Single antiplatelet therapy alone, n (%)	12 (7.4)	309 (12.1)	0.289	257 (12.2)	64 (10.4)	0.430
DAPT alone, n (%)	1 (0.6)	119 (4.7)	0.034	107 (5.1)	13 (2.1)	0.003
Dual antithrombotic therapy, n (%)	5 (3.1)	236 (9.3)	0.031	210 (10.0)	31 (5.1)	0.001
Triple antithrombotic therapy, n (%)	0 (0.0)	83 (3.3)	0.035	80 (3.8)	3 (0.5)	<0.001

Abbreviations: AF, atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack (TIA), vascular disease, age 65-74 years, sex category (female); DAPT, dual antiplatelet therapy; HF, heart failure; MI, myocardial infarction; NOAC, non-vitamin K oral antagonist; OAC, oral anticoagulants; PAD, peripheral artery disease; SD, standard deviation; TIA, transient ischemic attack; VKA, vitamin K antagonists

Single antiplatelet therapy alone was defined as aspirin

Table 2. Quality of life in patients according to stroke risk

Variable	CHA_2DS_2-VASc score ≥3 in females or ≥2 in males n = 2099 (77.4%)	CHA_2DS_2-VASc score <3 in females or <2 in males n = 613 (22.6%)	*P*-value
Palpitations, n (%)	904 (43.1)	325 (53.0)	<0.001
Syncope, n (%)	99 (4.7)	21 (3.4)	0.253
Shortness of breath, n (%)	1089 (51.9)	189 (30.8)	<0.001
Chest pain, n (%)	452 (25.8)	102 (16.6)	<0.001
Dizziness, n (%)	376 (17.9)	59 (9.6)	<0.001
Fatigue, n (%)	905 (43.1)	169 (27.6)	<0.001
General not-well-being, n (%)	499 (23.8)	116 (18.9)	0.051
Fear, anxiety, n (%)	209 (10.0)	58 (9.5)	0.994

Abbreviations: see Table 1

Table 3. Management strategies in patients according to the EHRA symptom score

Variable	Patients with CHA_2DS_2-VASc score ≥3 in females or ≥2 in males with EHRA 3 or 4 n = 703	Patients with CHA_2DS_2-VASc score ≥3 in females or ≥2 in males with first diagnosed or paroxysmal AF n = 1123
Rhythm control, n (%)	207 (29.4)	620 (55.2)
Amiodarone, n (%)	199 (28.3)	646 (57.5)
Propafenone, n (%)	40 (5.7)	121 (10.8)
Flecainide, n (%)	1 (0.1)	1 (0.00
ECV, n (%)	14 (2.0)	7 (0.0)
AF ablation, n (%)	8 (1.1)	15 (0.0)

Abbreviations: ECV, electric cardioversion, EHRA, European Heart Rhythm Association; see Table 1

Table 4. Severity of AF burden domain

AF pattern	CHA_2DS_2-VASc score ≥3 in females or ≥2 in males n = 2099 (77.4%)	CHA_2DS_2-VASc score <3 in females or <2 in males n = 613 (22.6%)	*P*-value
First diagnosed, n (%)	455 (21.7)	177 (28.9)	<0.001
Paroxysmal, n (%)	668 (31.8)	292 (47.6)	<0.001
Persistent, n (%)	219 (10.4)	100 (16.3)	<0.001
Long-standing persistent, n (%)	49 (2.3)	15 (2.4)	0.872
Permanent, n (%)	973 (46.4)	115 (18.8)	<0.001

Abbreviations: see Table 1

Table 5. The substrate for AF domain in the BALKAN-AF cohort

Variable	CHA_2DS_2-VASc score ≥3 in females or ≥2 in males n = 2099 (77.4%)	CHA_2DS_2-VASc score <3 in females or <2 in males n = 613 (22.6%)	*P*-value	CHA_2DS_2-VASc score of 0 in males or 1 in females n = 162 (6.0%)	CHA_2DS_2-VASc score ≥1 in males or ≥2 in females n = 2550 (94.0%)	*P*-value
Number of comorbid diseases, median (IQR)	4.7 (3.0–6.0)	2.1 (1.0–3.0)	<0.001	0.9 (0.0–1.0)	4.3 (2.0–6.0)	<0.001
Age ≥75 years	946 (45.1)	112 (18.3)	<0.001	0 (0.0)	947 (37.1)	NA
Obesity	511 (24.3)	160 (26.1)	0.256	38 (23.5)	633 (24.8)	0.536
Active smoker	228 (10.9)	112 (18.3)	<0.001	32 (19.8)	308 (12.1)	<0.001
Alcohol abuse	81 (3.9)	29 (4.7)	0.336	7 (4.3)	103 (4.0)	0.860
LA diameter, mm, mean (SD)	46.5 (7.8)	43.3 (7.4)	<0.001	40.4 (7.5)	46.0 (7.8)	<0.001

Abbreviations: LA, left atrium, IQR, interquartile range, SD, standard deviation; other — see Table 1

cohort, only one-third of patients with EHRA symptom score of 3 or 4 and high risk of stroke received a rhythm control strategy. Half of the patients with first diagnosed AF or paroxysmal AF were offered the strategy. Underuse of the rhythm control strategy in highly symptomatic patients was also been reported previously [26]. However, the EHRA symptom score may not adequately differentiate between AF-related and concomitant chronic conditions-related symptoms. Thus, the assessment of quality of life could be useful in the assessment of the symptom severity domain [9].

Our study used the temporal-pattern based classification of AF based on guideline recommendations. Notably, the above-mentioned classification may be imprecise in distinguishing between paroxysmal and persistent AF. Nonetheless, the utility of the 4S-AF scheme in selecting the AF patients who would be managed by rhythm or rate control strategy has been proposed [27].

Multimorbidity is common in AF, and the majority of the patients from the BALKAN-AF registry with high risk of stroke had ≥2 comorbidities. Approximately half of the individuals with high risk of stroke were ≥75 years old. Cardiovascular risk factors, patient age, and concomitant chronic conditions all play a role in the development and progression of AF [11]. In the Substrate for AF domain, identification and management of cardiovascular risk factors and multimorbidity should be emphasized in the AF-related treatment decisions process, as part of the holistic approach to AF care (based on the Atrial fibrillation Better Care [ABC] pathway) given that this has been associated with improved clinical outcomes [28]. Unfortunately, treatment decision-making in the BALKAN-AF cohort was not based on the 4S-AF scheme, and the introduction of the 4S-AF scheme may help facilitate AF management.

From a Polish perspective, AF management strategies in Poland may differ from those applied in other European countries [29]. The rhythm control strategy in individuals with AF with the use of ablation in cardiology wards seems more frequent in Poland than in other European countries. The limited use of AF ablation in the Balkans may be

associated with limited access to this management option in this region [30]. Similar to patients from the BALKAN-AF registry, undertreatment was observed in a significant proportion of Polish patients at high risk of stroke, while many low-risk patients are overtreated [29–31]. The BALKAN-AF study indicates a high prevalence of co-morbidities among patients with AF, which was also reflected in another Polish registry (RecordAF) [32].

Limitations

Our study has a limitation that should be noted. Since no follow-up was planned, there was no assessment of patient outcomes. Some descriptors, risk stratification scores, and imaging tools were not available in the BALKAN-AF cohort. The 4S-AF system does not include data about bleeding risk, repeated cardioversions or AF ablations, prior and current antiarrhythmic drug therapy, etc. so the above-mentioned data were not incorporated. Data on duration of AF, density of episodes, LA dysfunction/enlargement, LA fibrosis, and data on spontaneous termination of AF were not available.

CONCLUSION

Overall, decision-making was not based on the 4S-AF scheme. OAC overuse was seen in patients with truly low stroke risk, whist OAC underuse was evident in those with high risk of stroke. The proportion of highly symptomatic patients with high risk of stroke who were offered the rhythm control strategy was low. A more widespread introduction of the 4S-AF scheme may help facilitate AF management.

Article information

Acknowledgments: We thank all BALKAN-AF investigators for their hard work.

Conflicts of interest: Milan Nedeljkovic has been a speaker for Bayer Serbia. Gregory YH Lip has been a consultant and speaker for BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo (no personal fees). Tatjana S Potpara has been a consultant for Bayer/Jansen and BMS/Pfizer (no fees). Other authors declare no conflict of interest.

REFERENCES

1. Burdett P, Lip GYH. Atrial fibrillation in the United Kingdom: predicting costs of an emerging epidemic recognising and forecasting the cost drivers of atrial fibrillation-related costs. Eur Heart J Qual Care Clin Outcomes. 2020 [Epub ahead of print], doi: 10.1093/ehjqcco/qcaa093, indexed in Pubmed: 33346822.
2. Wallenhorst C, Martinez C, Freedman B. Risk of ischemic stroke in asymptomatic atrial fibrillation incidentally detected in primary care compared with other clinical presentations. Thromb Haemost. 2022; 122(2): 277–285, doi: 10.1055/a-1541-3885, indexed in Pubmed: 34192776.
3. Corrigendum to: 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2021; 42(5): 546–547, doi: 10.1093/eurheartj/ehaa945, indexed in Pubmed: 33242070.
4. Lip GYH. The ABC pathway: an integrated approach to improve AF management. Nat Rev Cardiol. 2017; 14(11): 627–628, doi: 10.1038/nrcardio.2017.153, indexed in Pubmed: 28960189.
5. Chao TF, Joung B, Takahashi Y, et al. 2021 Focused Update Consensus Guidelines of the Asia Pacific Heart Rhythm Society on Stroke Prevention in Atrial Fibrillation: Executive Summary. Thromb Haemost. 2022; 122(1): 20–47, doi: 10.1055/s-0041-1739411, indexed in Pubmed: 34773920.
6. Romiti GF, Pastori D, Rivera-Caravaca JM, et al. Adherence to the 'Atrial Fibrillation Better Care' Pathway in Patients with Atrial Fibrillation: Impact on Clinical Outcomes-A Systematic Review and Meta-Analysis of 285,000 Patients. Thromb Haemost. 2021 [Epub ahead of print], doi: 10.1055/a-1515-9630, indexed in Pubmed: 34020488.
7. Lip GYH, Ntaios G. "Novel Clinical Concepts in Thrombosis": Integrated Care for Stroke Management-Easy as ABC. Thromb Haemost. 2021 [Epub ahead of print], doi: 10.1055/a-1632-1777, indexed in Pubmed: 34474499.
8. Field M, Kuduvalli M, Torella F, et al. Integrated care systems and the aortovascular hub. Thromb Haemost. 2022; 122(2): 177–180, doi: 10.1055/a-1591-8033, indexed in Pubmed: 34407555.
9. Potpara TS, Lip GYH, Blomstrom-Lundqvist C, et al. The 4S-AF Scheme (Stroke Risk; Symptoms; Severity of Burden; Substrate): A Novel Approach to In-Depth Characterization (Rather than Classification) of Atrial Fibrillation. Thromb Haemost. 2021; 121(3): 270–278, doi: 10.1055/s-0040-1716408, indexed in Pubmed: 32838473.
10. Lip GYH, Nieuwlaat R, Pisters R, et al. 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(2): 263–272, doi: 10.1378/chest.09-1584, indexed in Pubmed: 19762550.
11. Staerk L, Sherer JA, Ko D, et al. Atrial fibrillation: epidemiology, pathophysiology, and clinical outcomes. Circ Res. 2017; 120(9): 1501–1517, doi: 10.1161/CIRCRESAHA.117.309732, indexed in Pubmed: 28450367.
12. Potpara TS, Lip GYH. Balkan-AF Investigators. Patterns in atrial fibrillation management and 'real-world' adherence to guidelines in the Balkan Region: an overview of the Balkan–atrial fibrillation survey. Eur Heart J. 2015; 36(30): 1943–1944, indexed in Pubmed: 26478929.
13. Pisters R, Lane DA, Nieuwlaat R, et al. 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(5): 1093–1100, doi: 10.1378/chest.10-0134, indexed in Pubmed: 20299623.
14. Potpara TS, Dan GA, Trendafilova E, et al. Stroke prevention in atrial fibrillation and 'real world' adherence to guidelines in the Balkan Region: The BALKAN-AF Survey. Sci Rep. 2016; 6: 20432, doi: 10.1038/srep20432, indexed in Pubmed: 26869284.
15. Lip GYH, Laroche C, Ioachim PM, et al. Prognosis and treatment of atrial fibrillation patients by European cardiologists: one year follow-up of the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot registry). Eur Heart J. 2014; 35(47): 3365–3376, doi: 10.1093/eurheartj/ehu374, indexed in Pubmed: 25176940.
16. Lip GYH, Laroche C, Popescu MI, et al. Improved outcomes with European Society of Cardiology guideline-adherent antithrombotic treatment in high-risk patients with atrial fibrillation: a report from the EORP-AF General Pilot Registry. Europace. 2015; 17(12): 1777–1786, doi: 10.1093/europace/euv269, indexed in Pubmed: 26321406.
17. Kirchhof P, Ammentorp B, Darius H, et al. Management of atrial fibrillation in seven European countries after the publication of the 2010 ESC Guidelines on atrial fibrillation: primary results of the PREvention oF thromboemolic events--European Registry in Atrial Fibrillation (PREFER in AF). Europace. 2014; 16(1): 6–14, doi: 10.1093/europace/eut263, indexed in Pubmed: 24084680.
18. Pritchett RV, Bem D, Turner GM, et al. Improving the Prescription of Oral Anticoagulants in Atrial Fibrillation: A Systematic Review. Thromb Haemost. 2019; 119(2): 294–307, doi: 10.1055/s-0038-1676835, indexed in Pubmed: 30669165.
19. Hohnloser SH, Basic E, Nabauer M. Changes in Oral Anticoagulation Therapy over One Year in 51,000 Atrial Fibrillation Patients at Risk for Stroke: A Practice-Derived Study. Thromb Haemost. 2019; 119(6): 882–893, doi: 10.1055/s-0039-1683428, indexed in Pubmed: 30900220.

20. Hohmann C, Hohnloser SH, Jacob J, et al. Non-Vitamin K Oral Anticoagulants in Comparison to Phenprocoumon in Geriatric and Non-Geriatric Patients with Non-Valvular Atrial Fibrillation. Thromb Haemost. 2019; 119(6): 971–980, doi: 10.1055/s-0039-1683422, indexed in Pubmed: 30900223.
21. Kozieł M, Teutsch C, Bayer V, et al. GLORIA-AF Investigators. Changes in anticoagulant prescription patterns over time for patients with atrial fibrillation around the world. J Arrhythm. 2021; 37(4): 990–1006, doi: 10.1002/joa3.12588, indexed in Pubmed: 34386125.
22. Proietti M, Laroche C, Opolski G, et al. AF Gen Pilot Investigators. 'Real-world' atrial fibrillation management in Europe: observations from the 2-year follow-up of the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase. Europace. 2017; 19(5): 722–733, doi: 10.1093/europace/euw112, indexed in Pubmed: 27194538.
23. Ten Cate V, Ten Cate H, Verheugt FWA. The Global Anticoagulant Registry in the FIELD-Atrial Fibrillation (GARFIELD-AF) : Exploring the changes in anticoagulant practice in patients with non-valvular atrial fibrillation in the Netherlands. Neth Heart J. 2016; 24(10): 574–580, doi: 10.1007/s12471-016-0874-y, indexed in Pubmed: 27561277.
24. Apenteng PN, Gao H, Hobbs FdR, et al. UK GARFIELD-AF Investigators and GARFIELD-AF Steering Committee. Temporal trends in antithrombotic treatment of real-world UK patients with newly diagnosed atrial fibrillation: findings from the GARFIELD-AF registry. BMJ Open. 2018; 8(1): e018905, doi: 10.1136/bmjopen-2017-018905, indexed in Pubmed: 29331969.
25. Roldán V, Marín F, Manzano-Fernández S, et al. The HAS-BLED score has better prediction accuracy for major bleeding than CHADS2 or CHA2DS2-VASc scores in anticoagulated patients with atrial fibrillation. J Am Coll Cardiol. 2013; 62(23): 2199–2204, doi: 10.1016/j.jacc.2013.08.1623, indexed in Pubmed: 24055744.
26. Purmah Y, Proietti M, Laroche C, et al. Rate vs. rhythm control and adverse outcomes among European patients with atrial fibrillation. Europace. 2018; 20(2): 243–252, doi: 10.1093/europace/euw421, indexed in Pubmed: 28160483.
27. Rivera-Caravaca JM, Piot O, Roldán-Rabadán I, et al. Characterization of atrial fibrillation in real-world patients: testing the 4S-AF scheme in the Spanish and French cohorts of the EORP-AF Long-Term General Registry. Europace. 2022; 24(2): 202–210, doi: 10.1093/europace/euab202, indexed in Pubmed: 34374759.
28. Yoon M, Yang PS, Jang E, et al. Improved Population-Based Clinical Outcomes of Patients with Atrial Fibrillation by Compliance with the Simple ABC (Atrial Fibrillation Better Care) Pathway for Integrated Care Management: A Nationwide Cohort Study. Thromb Haemost. 2019; 119(10): 1695–1703, doi: 10.1055/s-0039-1693516, indexed in Pubmed: 31266082.
29. Lenarczyk R, Mitręga K, Mazurek M, et al. Polish and European management strategies in patients with atrial fibrillation. Data from the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot). Pol Arch Med Wewn. 2016; 126(3): 138–148, doi: 10.20452/pamw.3322, indexed in Pubmed: 27000745.
30. Kozieł M, Mihajlovic M, Nedeljkovic M, et al. BALKAN-AF Investigators. Symptom management strategies: Rhythm vs rate control in patients with atrial fibrillation in the Balkan region: Data from the BALKAN-AF survey. Int J Clin Pract. 2021; 75(6): e14080, doi: 10.1111/ijcp.14080, indexed in Pubmed: 33548075.
31. Stępińska J, Kremis E, Konopka A, et al. Stroke prevention in atrial fibrillation patients in Poland and other European countries: insights from the GARFIELD-AF registry. Kardiol Pol. 2016; 74(4): 362–371, doi: 10.5603/KP.a2015.0173, indexed in Pubmed: 26365937.
32. Opolski G, Kosior DA, Kurzelewski M, et al. Polish RecordAF. Baseline characteristics of patients from Poland enrolled in the global registry of patients with recently diagnosed atrial fibrillation (RecordAF). Kardiol Pol. 2010; 68(5): 546–554, indexed in Pubmed: 20491018.