Management of patients with newly-diagnosed atrial fibrillation: Insights from the BALKAN-AF survey

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Abstract
Background: BALKAN-AF evaluated patterns of atrial fibrillation (AF) management in real-world clinical practice in the Balkans. The objectives were: to assess the proportion of patients with first-diagnosed AF in the BALKAN-AF cohort and to compare the management of patients with newly-diagnosed AF and those with previously known AF in clinical practice.

Methods: Consecutive patients from 7 Balkan countries were enrolled prospectively to the snapshot BALKAN-AF survey.

Results: Of 2712 enrolled patients, 2677 (98.7%) with complete data were included. 631 (23.6%) patients had newly-diagnosed AF and 2046 (76.4%) patients had known AF. Patients with newly-diagnosed AF were more likely to be hospitalized for AF and to receive single antiplatelet therapy (SAPT) alone and less likely to receive OACs than those with known AF (all p < 0.001). The use of OAC was not significantly associated with the CHA2DS2-VASc (p = 0.624) or HAS-BLED score (p = 0.225) on univariate analysis. Treatment in capital city, hypertension, dilated cardiomyopathy, mitral valve disease, country of residence or rate control strategy were independent predictors of OAC use, whilst non-emergency centre, treatment by cardiologist, paroxysmal AF, palpitations, symptoms attributable to AF (as judged by physician), mean heart rate and AF as the main reason for hospitalization were independent predictors of rhythm control strategy use.

Conclusions: In BALKAN-AF survey, patients with newly-diagnosed AF were more often hospitalized, less often received OAC and were more likely to receive SAPT alone. The use of OAC for stroke prevention has not been driven by the individual patient stroke risk.
1. Introduction

Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia in adults [1]. Owing to its significant association with cardiovascular morbidity and mortality, AF portends significant burden to the patients and healthcare systems worldwide [2,3]. Guideline-adherent management of AF has been associated with improved patients’ outcomes [4–6], but contemporary observational registry-based data showed variable proportion of guideline-adherent management of AF in clinical practice in different world regions [7–12].

Patients with newly-diagnosed AF may have different prevailing risk profiles and outcomes in comparison to those with a history of paroxysmal, persistent, long-term persistent or permanent AF [13,14]. In a large international observational registry-based study, for example, the rates of all-cause mortality, stroke/systemic embolism and major bleeding during a 2-year follow-up were the highest within the first 4 months since new-onset AF was diagnosed [15]. This emphasizes the importance of timely initiation of AF treatment and AF comprehensive care early after the diagnosis of AF has been made. Moreover, physicians should be aware of warning signs of possible early cardiovascular mortality [16].

Contemporary large international AF registries included variable proportion of patients with newly-diagnosed AF, but countries in the Balkan region (encompassing approximately 50 million inhabitants) were largely underrepresented in these registries [17]. A prospective survey conducted in seven Balkan countries showed a fairly good overall use of oral anticoagulant therapy (OAC) for AF-related stroke prevention (73.5%), but the use of OAC was poorly related to the individual stroke risk [18].

The aims of this study were as follows: (i) to assess the proportion of patients with first-diagnosed AF in the BALKAN-AF cohort; and (ii) to compare the management of patients with newly-diagnosed AF and those with previously known AF in routine clinical practice in patients with newly-diagnosed AF in seven Balkan countries.

2. Methods

The design of BALKAN-AF survey has been previously published [17]. The BALKAN-AF registry was designed to prospectively collect real-world data regarding consecutive patients with electrophysiologically documented ‘non-valvular’ AF. Patients were managed by a cardiologist or an internal medicine specialist where cardiologist was not available. Patients were enrolled by university and non-university hospitals and outpatient health centres in Albania, Bosnia & Herzegovina, Bulgaria, Croatia, Montenegro, Romania and Serbia.

This multicentre, observational, snapshot survey was designed and conducted by the Serbian Atrial Fibrillation Association (SAFA). The registry was introduced to the National Cardiology Societies/relevant Working Groups in particular Balkan countries and approved by the National and/or local Institutional Review Board. A signed patient informed consent form was acquired before enrolment. The study protocol corresponds with the ethical guidelines of the 1975 Declaration of Helsinki.

Patients with prosthetic mechanical heart valves, moderate or severe mitral stenosis or any significant valvular disease requiring surgical treatment and those aged <18 years were excluded from the study.

Data were collected using an electronic case report form designed by SAFA. Following information was obtained: patients’ and AF-related characteristics, health care setting, patient’s physical findings and management at enrolling visit, diagnostic procedures related to AF at enrolling visit and/or in previous 12 months and AF treatment at discharge. Stroke risk was assessed according to CHA2DS2-VASC (congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack (TIA), vascular disease, age 65–74 years, sex category) score [19]. Bleeding risk was evaluated according to HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile International Normalised Ratio (INR), elderly >65 years, drugs or alcohol concomitantly) score [19].

Systematic monitoring of centres and follow-up visits were not conducted. National coordinators and participating investigators were responsible for the consecutiveness of enrolled patients and correctness and completeness of entered data.

2.1. Statistical analysis

Categorical variables were presented as absolute frequencies and percentages, and continuous variables as mean and standard deviation (SD). Comparison of categorical variables with normal distribution was performed using Student’s t-test. Continuous variables with skewed distribution were compared with Mann-Whitney test. The descriptive analysis included baseline characteristic of patients with newly-diagnosed AF and those with previously known AF. The association of patient-, AF- and healthcare system-related variables with the management of patients with newly-diagnosed AF was evaluated using univariable logistic regression analyses. The variables with statistically significant association on univariable logistic regression analysis were entered into multivariable logistic regression models to identify multivariable predictors of AF management. Results are expressed as odds ratio (OR) with 95% confidence interval (CI). A two-sided p value of less than 0.05 was interpreted as statistically significant. All analyses were performed using SAS software version 9.4 (SAS Institute, Inc., Cary, NC, USA).

3. Results

Of 2712 patients enrolled in seven participating Balkan countries, complete data required for this analysis were available for 2677 patients (98.7%). Of these, 631 patients (23.6%) had first-diagnosed AF and 2046 (76.4%) had a history of AF (Table 1).

3.1. Demographic and AF-related characteristics

Patients with newly-diagnosed AF were younger, more often had paroxysmal AF and more commonly had symptoms attributable to AF (as judged by the responsible physician/investigator), with higher mean European Heart Rhythm Association (EHRA) symptom score (all p < 0.001) than patients with history of AF (Table 1).

3.2. Physical findings and comorbidity

Patients with newly-diagnosed AF had significantly higher mean heart rate (103.4 ± 33.4 versus 87.4 ± 25.5 beats per minute [bpm], p < 0.001) and less comorbidity (all p < 0.05) than those with a known AF (Table 2).

3.3. Stroke and bleeding risk factors

Mean CHA2DS2-VASc score was lower in newly-diagnosed AF patients than in the previously known AF group (3.0 ± 1.8 vs 3.4 ± 1.9, p < 0.001), and the prevalence of patients with truly low risk of stroke (a CHA2DS2-VASc of 0 in males or 1 in females) was higher in the newly-diagnosed AF group (p = 0.006).

The risk of bleeding (i.e., mean HAS-BLED score) was lower in patients with first-diagnosed AF in comparison to those with a pre-
control as the main treatment strategy was more commonly used in first-diagnosed AF patients (n = 322, 51.0% versus n = 578, 28.3%), whereas rate control (Table 3). Of patients with newly-diagnosed AF and CHA2DS2-VASc score ≥2, 46% received OAC only, whereas 38% received stroke prevention other than OAC or had no antithrombotic therapy (Fig. 2).

3.5. Stroke prevention strategies

Overall, OAC was used in 376 (59.6%) of patients with first-diagnosed AF and 1589 (77.7%) of those with previously diagnosed AF (p < 0.001), Table 3. The use of OAC alone was more prevalent among patients with previously diagnosed AF (n = 1348, 65.9% vs n = 293, 46.4%), who were also more often prescribed a vitamin K antagonist (VKA) in comparison to patients with newly-diagnosed AF (n = 1336, 65.3% vs. n = 291, 46.1%), both p < 0.001. Single antiplatelet therapy alone and triple antithrombotic therapy were used more often in first-diagnosed AF patients than in those with a history of AF (p < 0.001, p = 0.012, respectively), Table 3. Of patients with newly-diagnosed AF and CHA2DS2-VASc score ≥2, 46% received OAC only, whereas 38% received stroke prevention other than OAC or had no antithrombotic therapy [Fig. 2].

Country-specific stroke prevention strategies are presented in Table 4.

3.6. Arrhythmia-directed management strategies

Rhythm control strategy was more often used in first-diagnosed AF patients (n = 322, 51.0% versus n = 578, 28.3%), whereas rate control as the main treatment strategy was more commonly used in those with previously known AF (n = 1357, 66.3% versus n = 265, 42.0%), both p < 0.001. Catheter ablation and atrioventricular node ablation with pacemaker implantation were not performed in first-diagnosed AF patients.

Digoxin was used in 107 (17.0%) of patients with newly-diagnosed AF and in 548 (26.8%) of patients with known AF (p < 0.001). Amiodarone was prescribed in 224 (35.5%) of patients with a new diagnosis of AF and in 438 (21.4%) of patients with previously diagnosed AF (p < 0.001) (Table 3). There were no significant differences in use of other agents for rhythm and rate control (Table 3).

3.7. Other therapies

Loop diuretics were used in 199 (31.5%) of newly-diagnosed AF group and in 921 (45.0%) of group with previously-diagnosed AF (p < 0.001) (Table 3). The use of other drugs is shown in Table 3.

3.8. Determinants of OAC use in patients with newly-diagnosed AF

The use of OAC was not significantly associated with the CHA2DS2-VASc (OR 1.02; 95% CI, 0.93–1.11, p = 0.624) or HAS-BLED score (OR 1.10, 95% CI 0.94–1.28, p = 0.225) on univariate analysis (see the Online supplement).

On multivariable analysis adjusted for country of residence, patients treated in the capital city, those with hypertension, dilated cardiomyopathy (DCM) or mitral valve disease and patients assigned to rate control strategy were more likely to receive OAC, whereas treatment in a non-emergency centre, paroxysmal AF and history of previous bleeding event were associated with decreased likelihood of OAC use (Table 5). Of note, OAC use was positively associated with the residence in Romania.

3.9. Predictors of rhythm control strategy in patients with newly-diagnosed AF

Non-emergency centre, treatment by cardiologist, paroxysmal AF, palpitations, symptoms attributable to AF (as judged by the responsible physician/investigator), mean heart rate and AF as the main reason for hospitalization (all p < 0.05) were independent predictors of the increased use of rhythm control strategy in patients with first-diagnosed AF, whereas fatigue, HF, DCM, mitral

Table 1
Demographic and atrial fibrillation-related characteristics.

| Variable                        | All          | First-diagnosed AF | History of AF | P value |
|---------------------------------|--------------|--------------------|---------------|---------|
| Mean age (years)                | 63.1 ± 10.9  | 67.5 ± 12.1        | 69.6 ± 10.5   | <0.001  |
| Male sex                        | 1485 (55.5%) | 348 (55.2%)        | 1137 (55.6)   | 0.852   |
| Paroxysmal AF                   | 960 (35.9%)  | 403 (63.9%)        | 557 (27.2)    | <0.001  |
| Asymptomatic AF                 | 572 (21.4%)  | 64 (10.1%)         | 508 (24.8)    | <0.001  |
| Symptoms                        |              |                    |               |         |
| Palpitations                    | 1229 (45.9%) | 406 (64.3%)        | 823 (40.2)    | <0.001  |
| Chest pain                      | 644 (24.1%)  | 205 (32.5%)        | 439 (21.5)    | <0.001  |
| Shortness of breath             | 1278 (47.7%) | 297 (47.1%)        | 981 (47.9)    | 0.667   |
| Dizziness                       | 435 (16.2%)  | 103 (16.3%)        | 332 (16.2)    | 0.970   |
| Syncope                         | 120 (4.3%)   | 42 (6.7)           | 78 (3.8)      | 0.003   |
| Fatigue                         | 1074 (40.1%) | 218 (34.5%)        | 856 (41.8)    | 0.001   |
| General non-wellbeing           | 615 (23.0%)  | 158 (25.0)         | 457 (22.3)    | 0.166   |
| Fear/anxiety                    | 267 (10.0)   | 78 (12.4)          | 189 (9.2)     | 0.023   |
| Symptoms attributable to AF*    | 802 (30.0%)  | 311 (49.3)         | 491 (24.0)    | <0.001  |
| EHRA Symptom score (mean)       | 2.2 ± 0.8    | 2.4 ± 0.8          | 2.0 ± 0.8     | <0.001  |
| EHRA I                          | 571 (21.3%)  | 64 (10.1)          | 507 (24.8)    | <0.001  |
| EHRA II                         | 1254 (46.8%) | 294 (46.6)         | 960 (46.9)    | 0.852   |
| EHRA III                        | 712 (26.6%)  | 218 (34.5%)        | 494 (24.1)    | <0.001  |
| EHRA IV                         | 140 (5.2%)   | 56 (8.9)           | 84 (4.1)      | <0.001  |

AF: Atrial fibrillation, EHRA: European Heart Rhythm Association.
* As judged by the responsible physician/investigator.

AF history of AF (1.6 ± 1.0 versus 2.1 ± 1.3, p < 0.001), and the proportion of patients with a HAS-BLED ≥ 3 was higher in the latter subgroup (p < 0.001), Table 2.

Country-specific stroke and bleeding risk distribution is presented in Fig. 1.

3.4. AF management settings and diagnostic assessment

Most participants were seen by a cardiologist in an academic healthcare facility (Table 3). However, patients with newly-diagnosed AF were less commonly enrolled during an outpatient visit (n = 101, 16.0% vs n = 616, 30.1%) and AF was more often the main reason for the hospitalization (n = 369, 58.5% vs n = 968, 47.3%) compared with patients with previously known AF (both p < 0.001). There were no significant differences in the diagnostic assessment at enrolling visit between patients with newly-diagnosed versus previously known AF (Table 3).

3.3. Determinants of OAC use in patients with newly-diagnosed AF

The use of OAC was not significantly associated with the CHA2DS2-VASc score (OR 1.02; 95% CI, 0.93–1.11, p = 0.624) or HAS-BLED score (OR 1.10, 95% CI 0.94–1.28, p = 0.225) on univariate analysis (see the Online supplement).

On multivariable analysis adjusted for country of residence, patients treated in the capital city, those with hypertension, dilated cardiomyopathy (DCM) or mitral valve disease and patients assigned to rate control strategy were more likely to receive OAC, whereas treatment in a non-emergency centre, paroxysmal AF and history of previous bleeding event were associated with decreased likelihood of OAC use (Table 5). Of note, OAC use was positively associated with the residence in Romania.
valve disease and mean CHA2DS2-VASc score value were negatively associated with the use of rhythm control strategy in patients with first-diagnosed AF (Table 5).

### 4. Discussion

In the present prospective, multicentre, observational survey of consecutive in- or outpatients with AF, approximately one out of 4 patients had a first-diagnosed AF. The prevalence of first-diagnosed AF in the BALKAN-AF survey was close to that in one ‘real-world’ European registry [10]. However, the proportion of patients with newly-diagnosed AF ranged from 5.0% to 30.3% in the AF registries [10,20–22]. The present analysis provides novel insights into clinical practice from the largest published prospective AF dataset from the Balkans, a European region that has been under-represented in many prior clinical trials or registries.

The main findings of our study were as follows: (i) different demographic, cardiovascular risk and AF-related profile of patients with first-diagnosed AF in comparison to those with previously known AF (the former were younger, with less comorbidity and

### Table 2

| Variable | All  | First-diagnosed AF | History of AF |
|----------|------|--------------------|---------------|
| | N = 2677 | N = 631 (23.6%) | N = 2046 (76.4%) |
| SBP (mean, mmHg) | 134.6 ± 22.0 | 135.8 ± 23.2 | 134.2 ± 21.6 |
| DBP (mean, mmHg) | 81.0 ± 12.2 | 81.9 ± 12.8 | 80.7 ± 12.1 |
| Heart rate (mean, bpm) | 91.2 ± 28.4 | 103.4 ± 33.4 | 87.4 ± 25.5 |
| NYHA class (mean) | 1.8 ± 1.0 | 1.6 ± 0.9 | 1.8 ± 1.0 |
| NYHA I | 1569 (58.6) | 424 (67.2) | 1145 (56.0) |
| NYHA II | 378 (14.1) | 89 (14.1) | 289 (14.1) |
| NYHA III | 532 (19.9) | 97 (15.4) | 435 (21.3) |
| NYHA IV | 198 (7.4) | 22 (3.5) | 176 (8.6) |

**CHA2DS2-VASc risk factors**

- **HF** 1163 (43.4) 173 (27.4) 990 (48.4) <0.001
- **CHF or LVEF < 40%** 1343 (50.2) 254 (40.3) 1089 (53.2) <0.001
- **Hypertension** 2121 (79.2) 469 (74.3) 1652 (80.7) <0.001
- **Age ≥75 years** 947 (35.4) 211 (33.4) 736 (36.0) 0.356
- **Diabetes mellitus** 668 (25.0) 150 (23.8) 518 (25.3) 0.449
- **Prior stroke/TIA/SE** 386 (14.4) 59 (9.4) 327 (16.0) <0.001
- **Vascular disease** 568 (21.2) 131 (20.8) 437 (21.4) 0.879
- **Age 65–74 years** 882 (32.9) 181 (28.7) 701 (34.3) 0.017
- **Female sex** 1192 (44.5) 283 (44.8) 909 (44.4) 0.852
- **CHA2DS2-VASc (mean) 3.3 ± 1.9 3.0 ± 1.8 3.4 ± 1.9 0.001
- **CHA2DS2-VASc 0 (males) or 1 (females) 162 (6.1) 52 (8.2) 110 (5.4) 0.006
- **CHA2DS2-VASc ≥ 2 2302 (86.0) 512 (81.1) 1790 (87.5) <0.001

**HAS-BLED risk factors**

- **Uncontrolled hypertension** 683 (25.5) 178 (28.2) 505 (24.7) 0.002
- **CKD** 411 (15.4) 78 (12.4) 333 (16.3) 0.024
- **Liver disease** 96 (3.6) 31 (4.9) 65 (3.2) 0.039
- **Prior bleeding** 133 (6.5) 17 (2.7) 116 (5.7) 0.003
- **Aspirin use** 822 (30.7) 195 (30.9) 626 (30.6) 0.877
- **Age ≥65 years** 815 (30.7) 195 (30.9) 620 (30.6) 0.877
- **Female sex** 1192 (44.5) 283 (44.8) 909 (44.4) 0.852
- **HAS-BLED (mean) 1.9 ± 1.2 1.6 ± 1.0 2.1 ± 1.3 <0.001
- **HAS-BLED ≥ 3 823 (30.7) 105 (16.6) 718 (35.1) <0.001

**Other comorbidities**

- **CAD** 821 (30.7) 195 (30.9) 626 (30.6) 0.877
- **Prior MI** 369 (13.8) 88 (13.9) 281 (13.7) 0.967
- **Prior CABG** 100 (3.7) 16 (2.5) 84 (4.1) 0.078
- **Prior PCI/stenting** 225 (8.4) 69 (10.9) 156 (7.6) 0.004
- **PAD** 122 (4.5) 18 (2.9) 104 (5.1) 0.019
- **Carotid artery disease** 56 (2.1) 7 (1.1) 49 (2.4) 0.499
- **Dilated cardiomyopathy** 216 (8.1) 25 (4.0) 191 (9.3) <0.001
- **HCM** 153 (5.9) 20 (3.2) 133 (6.5) 0.003
- **MITRAL valve disease** 845 (31.6) 149 (23.6) 696 (34.0) <0.001
- **Aortic valve disease** 300 (11.2) 56 (8.9) 244 (11.9) 0.044
- **CIED** 159 (5.9) 16 (2.5) 143 (7.0) <0.001
- **COPD** 342 (12.8) 74 (11.7) 268 (13.1) 0.368
- **Obstructive sleep apnoea** 53 (2.0) 10 (1.6) 43 (2.1) 0.441
- **Thyroid dysfunction** 276 (10.3) 54 (8.6) 222 (10.9) 0.102
- **Malignancy** 119 (4.4) 19 (3.0) 100 (4.9) 0.047
- **Dementia** 71 (2.7) 20 (3.2) 51 (2.5) 0.353
- **Dyslipidaemia** 1020 (38.1) 236 (37.4) 784 (38.3) 0.673
- **Anaemia** 373 (13.9) 83 (13.2) 290 (14.2) 0.522

SBP: systolic blood pressure; DBP: diastolic blood pressure; bpm: beats per minute; NYHA: New York Heart Association; CAD: coronary artery disease; CKD, chronic kidney disease; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; PAD: peripheral artery disease; CIED: cardiac implantable electronic device; CHA2DS2-VASc: congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack (TIA), vascular disease, age 65–74 years, sex category, COPD: chronic obstructive pulmonary disease, HF: heart failure, CHF: congestive heart failure; HAS-BLED: hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile International Normalised Ratio, elderly (age >65 years), drugs or alcohol concomitantly, LVEF: left ventricular ejection fraction; TIA: Transient ischemic attack; SE: Systemic embolism; INR: International normalized ratio; HCM, hypertrophic cardiomyopathy. * Vascular disease was defined as prior MI, complex aortic plaque or peripheral artery disease.
lower stroke and bleeding risk, but more symptomatic and more likely to have paroxysmal AF), (ii) differences in the management of AF – patients with first-diagnosed AF were more often hospitalized for AF, less often received OAC but were more likely to receive single antiplatelet therapy alone, and more often were treated with a rhythm control strategy, (iii) the use of OAC for stroke prevention was also significantly different: patients with previously diagnosed AF were more likely to receive OAC alone and less likely to receive NOAC.

### Table 3

**Atrial fibrillation management.**

| Variable | All N = 2677 | First-diagnosed AF N = 631 | Previously diagnosed AF N = 2046 | P value |
|----------|--------------|-----------------------------|---------------------------------|---------|
| **AF management settings** | | | | |
| AF was the main reason for the hospitalization | 1337 (49.9) | 369 (58.5) | 968 (47.3) | <0.001 |
| Outpatient visit | 717 (26.8) | 101 (16.0) | 616 (30.1) | <0.001 |
| Academic healthcare facility | 2161 (80.7) | 467 (74.0) | 1694 (82.8) | <0.001 |
| AF managed by a cardiologist | 2147 (80.2) | 505 (80.0) | 1642 (80.3) | 0.602 |
| **Diagnostic assessment** | | | | |
| Routine biochemistry | 2171 (81.1) | 523 (82.9) | 1648 (80.5) | 0.115 |
| Thyroid hormones measurement | 943 (35.2) | 235 (37.2) | 708 (34.6) | 0.212 |
| Transthoracic echocardiography | 2147 (80.2) | 520 (82.4) | 1627 (79.5) | 0.088 |
| No additional diagnostic assessment | 1479 (55.2) | 367 (58.2) | 1112 (54.3) | 0.086 |
| Holter monitoring (rhythm) | 708 (26.4) | 157 (24.9) | 551 (26.9) | 0.314 |
| **Stroke prevention (at enrolment)** | | | | |
| No antithrombotic therapy | 265 (9.9) | 75 (11.9) | 190 (9.3) | 0.051 |
| Overall OAC | 1965 (73.4) | 376 (59.6) | 1589 (77.7) | <0.001 |
| OAC alone | 1641 (61.3) | 293 (46.4) | 1348 (65.9) | <0.001 |
| VKA | 1627 (60.8) | 291 (46.1) | 1336 (65.3) | <0.001 |
| NOAC | 338 (12.6) | 85 (13.5) | 253 (12.4) | 0.437 |
| Single antiplatelet therapy alone | 321 (12.0) | 120 (19.0) | 201 (9.8) | <0.001 |
| DAPT alone | 120 (4.5) | 56 (8.9) | 64 (3.1) | <0.001 |
| Dual antiplatelet therapy | 241 (9.0) | 54 (8.6) | 187 (9.1) | 0.682 |
| Triple antiplatelet therapy | 83 (3.1) | 29 (4.6) | 54 (2.6) | 0.012 |
| **Symptom management** | | | | |
| Rhythm control | 900 (33.6) | 322 (51.0) | 578 (28.3) | <0.001 |
| Rate control | 1622 (60.6) | 265 (42.0) | 1357 (66.3) | <0.001 |
| **Non-pharmacological AF therapies (at enrolment or in the future)** | | | | |
| AF catheter ablation | 60 (2.2) | 0 (0) | 60 (2.9) | <0.001 |
| AV node ablation with PM implantation | 10 (0.4) | 0 (0) | 10 (0.5) | <0.001 |
| **Pharmacological AF therapies (at enrolment)** | | | | |
| Digoxin | 655 (24.5) | 107 (17.0) | 548 (26.8) | <0.001 |
| Verapamil/Diltiazem | 130 (4.9) | 23 (3.6) | 107 (5.2) | 0.452 |
| Beta blockers | 1961 (73.3) | 449 (71.2) | 1512 (73.9) | 0.242 |
| Propafenone/Flecainide | 250 (9.3) | 62 (9.8) | 188 (9.2) | 0.368 |
| Sotalol | 21 (0.8) | 3 (0.5) | 18 (0.9) | 0.319 |
| Amiodarone | 662 (24.7) | 224 (35.5) | 438 (21.4) | <0.001 |
| **Other therapy (at enrolment)** | | | | |
| ACEI | 1264 (47.2) | 282 (44.7) | 982 (48.0) | 0.179 |
| AT1 receptor blockers | 517 (19.3) | 103 (16.3) | 414 (20.2) | 0.034 |
| Loop diuretics | 1120 (41.8) | 199 (31.5) | 921 (45.0) | <0.001 |
| Statins | 1108 (41.4) | 260 (41.2) | 848 (41.4) | 0.993 |

AF: atrial fibrillation; OAC: oral anticoagulant therapy; NOAC: non-vitamin K antagonist oral anticoagulant; ECV: electrical cardioversion; PM: pacemaker; AV: atrioventricular; ACEI: angiotensin converting enzyme inhibitor; AT1: angiotensin receptor; DAPT: dual antiplatelet therapy.

### Fig. 1

Stroke and bleeding risk in patients with newly-diagnosed AF. AF, atrial fibrillation, B&H, Bosnia & Herzegovina, CHA2DS2-VASc; congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack (TIA), vascular disease, age 65–74 years, sex category, HAS-BLED: hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile International Normalised Ratio, elderly (age >65 years), drugs or alcohol concomitantly.
Fig. 2. The prevalence of stroke prevention strategies by CHA2DS2-VASc and HAS-BLED risk strata. CHA2DS2-VASc; congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack (TIA), vascular disease, age 65–74 years, sex category, DAPT, dual antiplatelet therapy, HAS-BLED: hypertension, abnormal renal/ liver function, stroke, bleeding history or predisposition, labile International Normalised Ratio, elderly (age >65 years), drugs or alcohol concomitantly, OAC, oral anticoagulants, SAPT, single antiplatelet therapy.

Table 4
Country-specific distribution of stroke prevention strategies in patients with first-diagnosed AF.

| Country                  | Albania n = 108 | Bosnia & Herzegovina n = 92 | Bulgaria n = 110 | Croatia n = 23 | Montenegro n = 22 | Romania n = 146 | Serbia n = 131 |
|--------------------------|-----------------|------------------------------|------------------|----------------|------------------|----------------|----------------|
| No antithrombotic therapy (%) | 6 (5.6)         | 13 (14.1)                    | 18 (16.4)        | 3 (13.0)       | 2 (9.1)          | 13 (8.9)       | 20 (15.3)      |
| Overall OAC (%)           | 66 (61.1)       | 31 (33.7)                    | 60 (54.5)        | 15 (65.6)      | 16 (72.7)        | 105 (71.9)     | 83 (64.3)      |
| OAC alone (%)             | 39 (36.1)       | 29 (31.5)                    | 52 (47.3)        | 14 (61.1)      | 9 (40.9)         | 88 (60.3)      | 62 (47.3)      |
| VKAs (%)                  | 57 (52.8)       | 26 (28.3)                    | 27 (24.5)        | 14 (61.1)      | 14 (63.6)        | 91 (62.3)      | 62 (47.3)      |
| NOACs (%)                 | 9 (8.3)         | 5 (5.4)                      | 33 (30.0)        | 1 (4.3)        | 2 (9.1)          | 14 (9.6)       | 21 (16.0)      |
| SAPT (%)                  | 17 (15.7)       | 37 (40.2)                    | 24 (21.8)        | 2 (8.7)        | 3 (13.6)         | 15 (10.3)      | 22 (16.8)      |
| DAPT (%)                  | 18 (16.7)       | 11 (12.0)                    | 7 (6.4)          | 1 (4.3)        | 1 (4.5)          | 13 (9.5)       | 5 (3.8)        |
| Dual therapy (%)          | 17 (15.7)       | 2 (2.2)                      | 5 (4.5)          | 1 (4.3)        | 4 (18.1)         | 10 (6.8)       | 15 (11.4)      |
| Triple therapy (%)        | 10 (9.3)        | 0 (0.0)                      | 3 (2.7)          | 0 (0.0)        | 3 (13.6)         | 7 (4.8)        | 6 (4.6)        |

AF; atrial fibrillation, DAPT, dual antiplatelet therapy, OAC, oral anticoagulants, NOAC, non-vitamin K oral anticoagulants, SAPT, single antiplatelet therapy, VKA, vitamin K antagonists

Table 5
Independent predictors of the use of OAC (alone or in combination) and use of rhythm control strategy in patients with first-diagnosed AF.

| Predictors of use of OAC Multivariate analysis | Predictors of use of rhythm control strategy Multivariate analysis |
|-----------------------------------------------|---------------------------------------------------------------|
| Predictors | OR | 95% CI | p-Value | Predictors | OR | 95% CI | p-Value |
| Capital city | 1.96 | 1.36–2.81 | <0.001 | Non-emergency centre | 2.06 | 1.25–3.37 | 0.004 |
| Non-emergency centre | 0.39 | 0.24–0.69 | <0.001 | AF main reason for hospitalization | 0.39 | 0.14–0.98 | 0.021 |
| Paroxysmal AF | 0.22 | 0.15–0.33 | <0.001 | Treatment by cardiologist | 2.11 | 1.30–3.41 | 0.002 |
| Hypertension | 2.20 | 1.48–3.26 | <0.001 | Paroxysmal AF | 3.52 | 2.35–5.27 | <0.001 |
| DCM | 11.97 | 5.90–2.17 | 0.016 | Palpitations | 1.75 | 1.13–2.71 | 0.011 |
| Mitral valve disease | 1.66 | 1.09–2.53 | 0.017 | Fatigue | 0.52 | 0.39–0.69 | <0.001 |
| Bleeding events | 0.21 | 0.06–0.70 | 0.011 | Symptoms attributable to AF | 2.40 | 1.61–3.58 | <0.001 |
| Rate control | 1.70 | 1.20–2.40 | 0.003 | Mean heart rate | 1.07 | 1.02–1.15 | <0.001 |
| Countries: | | | | HF | 0.59 | 0.41–0.87 | 0.007 |
| Bosnia & Herzegovina | 0.39 | 0.23–0.67 | 0.001 | DCM | 0.32 | 0.11–0.89 | 0.031 |
| Romania | 1.79 | 1.15–2.79 | 0.010 | Mitral valve disease | 0.60 | 0.41–0.89 | 0.013 |

AF; atrial fibrillation, OAC; oral anticoagulants, OR; odds ratio, CI; confidence interval, DCM; dilated cardiomyopathy HF; heart failure, DCM; dilated cardiomyopathy, CHA2DS2-VASc; congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack (TIA), vascular disease, age 65–74 years, sex category.
has not been driven by the individual patient stroke risk (i.e., the CHA₂DS₂-VASc score value), whereas the use of rhythm control strategy has been significantly associated with the presence of AF-related symptoms and (iv) healthcare system-related factors (such as centre type and location) significantly influenced the AF-directed and stroke prevention strategies in patients with newly-diagnosed AF.

4.1. Demographic, cardiovascular risk and AF-related profile of patients with first-diagnosed AF

The mean age of patients with first-diagnosed AF in BALKAN-AF registry and in other AF registries was similar [10,21,23]. The proportion of patients with newly-diagnosed AF and hypertension, diabetes mellitus and prior stroke was higher in the Balkan-AF registry than in the EURObservational Research Programme Atrial Fibrillation Pilot Registry (EORP-AF Pilot) [10], whereas patients with first-diagnosed AF and coronary artery disease (CAD) were less prevalent in the BALKAN-AF cohort. The prevalence of CAD, HF and diabetes mellitus in patients with first-diagnosed AF is consistent with datasets from the Euro Heart Survey on Atrial Fibrillation Pilot Registry [10], whereas prior stroke was less prevalent in the patients from the Euro Heart Survey nearly 15 years ago.

A similar mean CHA₂DS₂-VASc score and mean HAS-BLED score to the patients with first-diagnosed AF from the BALKAN-AF registry was also seen in the EORP-AF Pilot Registry [10] and in the most recent cohort of the FIELD-Atrial Fibrillation (GARFIELD-AF) [24]. The GARFIELD-AF registry recruited patients with newly-diagnosed ‘non-valvular’ AF and at least one risk factor for stroke.

4.2. Management of patients with first-diagnosed AF

In this study, patients with newly-diagnosed AF were more often hospitalized because of AF, than patients with a history of AF. This was also seen in the Central Registry of the German Competence NETwork in Atrial Fibrillation (AFNET) [20]. Patients with first-detected AF received OAC less often but were more likely to receive single antiplatelet therapy alone than patients with previously diagnosed AF in the Balkan region. A similar pattern was found in the AFNET registry [20]. The prevalence of management with antiplatelet therapy was broadly similar among patients with first-detected AF and patients with paroxysmal and persistent AF in the EORP-AF Pilot Registry [10], whereas the management with OAC was more frequent in persistent and permanent AF than in first-diagnosed AF.

In our study, a rhythm control strategy was more often used in patients with newly-diagnosed AF than in those with previously diagnosed AF. According to guidelines, rhythm control strategy is recommended for symptom improvement of AF patients [19]. Given that, the choice of rhythm control strategy should be based on symptoms of AF, not on its duration. In one study [25], a rhythm control strategy was also more often implemented in hospitalized patients. This may be associated with more symptomatic status of patients with first-diagnosed AF than patients with history of AF.

4.3. The use of OAC for stroke prevention in patients with first-diagnosed AF

In our study about 60% of patients with newly-diagnosed AF received OAC. The management with OAC for stroke prevention in BALKAN-AF did not necessarily reflect the individual patient stroke risk (i.e., the CHA₂DS₂-VASc score value) as indicated in guidelines [26]. This is despite stroke prevention being one of the cornerstones of optimal AF management [27]. Overall, the use of VKA was lower, whilst the use of NOAC was slightly higher than in other ‘real-world’ European registry [28]. We also observed significant country-specific differences in the use of antithrombotic therapies that may help in identifying regions where stroke prevention strategies need to be improved.

Despite evident indications for antithrombotic therapy, only 46% of patients with newly-diagnosed AF with CHA₂DS₂-VASc score ≥2 was medicated with OAC. Moreover, 33% of patients with CHA₂DS₂-VASc score of 0 used OAC, and only a minority of these patients were scheduled for ECV or AF catheter ablation.

In the Balkan region, patients with hypertension, DCM were more likely to receive OAC. Due to increased stroke risk of patients with hypertension and DCM with congestive HF, they should be considered for OAC use [19].

In our study, mitral valve disease was an independent predictor of increased OAC use. Mitral stenosis is associated with the increased risk of thrombo-embolism which may be related to the low-flow in the left atrium [29]. The data regarding the risk of stroke in AF patients with mitral regurgitation are controversial [30], thus OAC should be initiated in AF patients with mitral regurgitation based on stroke risk factors using CHA₂DS₂-VASc score [29].

In this study, history of bleeding was related to decreased OAC use in patients with first-diagnosed AF. However, even high bleeding risk score is not an excuse to withhold OACs where recommended because the net clinical benefit (NCB) is even more evident in this group of patients [31]. Bleeding risk which is a highly dynamic process need to be re-assessed regularly [26,31,32]. Modifiable risk factors should be treated optimally where possible, and bleeding risk scores such as the HAS-BLED score used appropriately to flag up high risk patients for early review and follow-up [33].

4.4. The use of rhythm control strategy in patients with newly-diagnosed AF

In the Balkans, symptoms attributable to AF including palpitations were associated with the increased use of rhythm control strategy in patients with newly-diagnosed AF. Management of AF tends to be more symptom directed and patient centred what is similar to other European registry [28]. Moreover, the implementation of rhythm control strategy is based on patient’s symptomatic status [34]. This symptom-oriented approach follows an integrated management of AF according to ABC pathway [35,36]. Interestingly, the use of amiodarone was significantly higher in patients with first-diagnosed AF than in patients with a history of AF despite significantly higher prevalence of congestive heart failure or left ventricle ejection fraction <40% in patients with previously diagnosed AF. Possible reason is that amiodarone might have been overused in the patient with first-diagnosed AF in the Balkan region.

Mitral valve disease was an independent predictor of decreased use of rhythm control strategy. Mitral regurgitation may facilitate the occurrence of AF and make it worse to control with antiarrhythmic agents. However, mitral regurgitation was not correlated with recurrent AF in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) study [37].

In our study, HF and DCM were associated with decreased use of rhythm control strategy in the newly-diagnosed AF patients. According to guidelines, rhythm control strategy should be chosen in patients who develop HF with reduced ejection fraction, as a result of tachycardia-myopathy, to make left ventricle function better after restoration of sinus rhythm [19,38,39].

4.5. Healthcare system-related factors

In our study, patients treated in the capital city were more likely to receive OAC, whilst management in a non-emergency cen-
tre was associated with decreased likelihood of OAC use. Non-emergency centre and management by cardiologist were independent predictors of the increased use of rhythm control strategy in patients with newly-diagnosed AF. Higher likelihood of OAC use in capital cities seems to be associated with their high concentration of tertiary health centres. In one study [25], similar influence of centre location on antithrombotic therapy was showed.

4.6. Knowledge gaps and unmet needs in the BALKAN region

Results of this survey may help to identify knowledge gaps in AF management in daily clinical practice in the Balkans. Our findings show that overall use of OAC is low (approx. 60%) in patients with first-diagnosed AF in the Balkans. The overall use of OAC in patients with newly-diagnosed AF was higher in EORP-AF Pilot Registry [10], whereas was less prevalent in the older registries: Euro Heart Survey and AFNET [20,21]. In our study, the association of OAC use with individual stroke risk is weak. Unfortunately, despite high proportion of patients with newly-diagnosed AF with increased risk of stroke, 11.9% of patients receive no antithrombotic therapy and 19.0% receive single antiplatelet therapy alone. These findings implicate that the management of patients with AF at risk of stroke is not adherent to guidelines [19].

In this study, paroxysmal AF was negatively associated with OAC use. Importantly, ischaemic stroke may occur as commonly in paroxysmal AF as in permanent AF [40]. However, in one study, yearly rates of ischaemic strokes were 2.1% for paroxysmal AF and 4.2% for permanent AF [41]. Indeed, patients with paroxysmal AF and conventional stroke risk factors have indications to OAC [19]. Consequently, the pattern of AF should not affect the management with OAC. The use of antithrombotic therapy was also associated with the health center location and was increased in capital cities. Differences were observed in the management with rhythm control strategy according to physician specialty because cardiologists used rhythm control more often than other specialists. Holistic treatment of patients with first-diagnosed AF should help to solve unmet clinical needs including underuse of OAC, the suboptimal association of OAC with individual stroke risk and limited access to rhythm control strategy. Moreover, integrated AF care requires services accessible for all patients and cooperation between various medical specialists [19].

4.7. Limitations

Our study has a few limitations including the observational study design and lack of follow-up data to assess outcomes. Possible selection bias may occur because of different healthcare setting in participating countries. Moreover, information about patient/prescriber treatment preferences is lacking. Also, data from the survey are limited to the Balkan population, but this is the largest AF dataset from this region. Moreover, physicians were aware that their recommendations on diagnostic assessment and management would be recorded. Registries are likely to attract selected highly motivated patients and their treatment at enrolment may express higher compliance. However, because of enrolment of consecutive patients, the likelihood for a physician to enroll mainly patients with higher compliance is limited.

5. Conclusions

In BALKAN-AF survey, patients with newly-diagnosed AF were more often hospitalized, less often received OAC and were more likely to receive SAPT alone. The use of OAC for stroke prevention has not been driven by the individual patient stroke risk.

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Appendix A. Supplementary material

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References

[1] J. Ball, M.J. Carrington, J.J. McMurray, S. Stewart, Atrial fibrillation: profile and burden of an evolving epidemic in the 21st century, Int. J. Cardiol. 167 (5) (2013) 1807–1824.
[2] M. Zoni-Berisso, F. Lercari, T. Carazza, S. Domenicucci, Epidemiology of atrial fibrillation: European perspective, Clin. Epidemiol. 6 (2014) 213–220.
[3] M.H. Kim, S.S. Johnston, B.C. Chu, M.R. Dalal, K.L. Schulman, Estimation of total incremental health care costs in patients with atrial fibrillation in the United States, Circulat. Cardiovasc. Qual. Outcomes 4 (3) (2011) 313–320.
[4] M. Mazurek, E. Shatzsila, D.A. Lane, A. Wolff, M. Proietti, G.Y.H. Lip, Guideline-adherent antithrombotic treatment improves outcomes in patients with atrial fibrillation: insights from the community-based Darlington atrial fibrillation registry, Mayo Clin. Proc. 92 (8) (2017) 1203–1213.
[5] M. Proietti, A. Nobili, V. Raparelli, L. Napoleone, P.M. Mannucci, G.Y.H. Lip, et al., Adherence to antithrombotic therapy guidelines improves mortality among elderly patients with atrial fibrillation: insights from the REPOSI study, Clin. Res. Cardiol.: Off. J. German Cardiac Soc. 105 (11) (2016) 912–920.
[6] G.Y.H. Lip, C. Laroche, M.J. Popescu, L.H. Rasmussen, L. Vitali-Serdoz, G.-A. Dan, 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, EP Europe 17 (12) (2015) 1777–1786.
[7] J.C. Hsu, M. Ako, M. Abe, K.L. Anderson, A. Avezum, N. Glusenkamp, et al., International Collaborative Partnership for the Study of Atrial Fibrillation (INTERAF): rationale, design, and initial descriptives, J. Am. Heart Assoc. 5 (11) (2016).
[8] B.A. Steinberg, H. Gao, P. Shrader, K. Pieper, L. Thomas, A.J. Cann, et al., International trends in clinical characteristics and oral anticoagulation treatment for patients with atrial fibrillation: Results from the GARFIELD-AF, ORBIT-AF I, and ORBIT-AF II registries, Am. Heart J. 194 (2017) 132–140.
[9] G. Boriani, M. Proietti, C. Laroche, L. Fauchier, F. Marin, M. Nabauer, et al., Contemporary stroke prevention strategies in 11 096 European patients with atrial fibrillation: a report from the EURObservational Research Programme on
Atrial Fibrillation (EORP-AF) Long-Term General Registry, Europace 20 (5) (2018) 747–757.

G.Y. Lip, C. Laroche, G. A. Dan, M. Santini, Z. Kalarus, L. H. Rasmussen, et al., A prospective survey in European Society of Cardiology member countries of atrial fibrillation management: baseline results of EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry, Europace 16 (3) (2014) 308–319.

A.K. Kakkar, I. Mueller, J.P. Bassand, D.A. Fitzmaurice, S.Z. Goldhaber, S. Goto, et al., International longitudinal registry of patients with atrial fibrillation at risk of stroke: Global Anticoagulant Registry in the FIELD (GARFIELD), Am. Heart J. 163 (1) (2012), 13–19.e1.

M.V. Huisman, K.J. Rothman, M. Paquette, C. Teutsch, H.C. Diener, S.J. Dubner, et al., The changing landscape for stroke prevention in AF: findings from the GLORIA-AF registry phase 2, J. Am. Coll. Cardiol. 69 (7) (2017) 777–785.

C. Johannson, E. Dahlqvist, J. Andersson, J.-H. Jansson, L. Johannson, Incidence, type of atrial fibrillation and risk factors for stroke: a population-based cohort study, Clin. Epidemiol. 9 (2017) 53–62.

A.K. Kakkar, I. Mueller, J.P. Bassand, D.A. Fitzmaurice, S.Z. Goldhaber, S. Goto, et al., Risk profiles and antithrombotic treatment of patients newly diagnosed with atrial fibrillation at risk of stroke: perspectives from the international, observational, prospective GARFIELD registry, PLoS ONE 8 (5) (2013) e63479.

J.P. Bassand, G. Accetta, A.J. Camm, F. Cools, D.A. Fitzmaurice, K.A. Fox, et al., Two-year outcomes of patients with newly diagnosed atrial fibrillation: results from GARFIELD-AF, Eur. Heart J. 37 (38) (2016) 2882–2889.

J.P. Bassand, S. Virdone, S.Z. Goldhaber, A.J. Camm, D.A. Fitzmaurice, K.A. Fox, et al., Early risks of death, stroke/systemic embolism, and major bleeding in patients with newly diagnosed atrial fibrillation, Circulation 139 (5) (2019) 787–798.

T.S. Potpara, G.Y. Lip, 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. 36 (30) (2015) 1943–1946.

T.S. Potpara, G.A. Dan, E. Trendaflilova, A. Goda, Z. Kusljuc, S. Manola, et al., Stroke prevention in atrial fibrillation and ‘real world’ adherence to guidelines in the Balkan Region: The BALKAN-AF Survey. Sci. Rep. 6 (2016) 20432.

P. Kirchhof, S. Benussi, D. Kotecha, A. Ahlsson, D. Atar, B. Casadei, et al., 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS, Eur. Heart J. 37 (38) (2016) 2893–2962.

M. Nabauer, A. Gerth, T. Limbourg, S. Schneider, M. Oeff, P. Kirchhof, et al., The Registry of the German Competence NETwork on Atrial Fibrillation: patient characteristics and initial management, Europace: Eur. Pacing Arrhythm. Cardiac Electrophysiol. 18 (9) (2016) 1308–1318.

R. Nieuwlaat, A. Capucci, A.J. Camm, S.B. Olsson, D. Andersen, D.W. Davies, et al., Atrial fibrillation management: a prospective survey in ESC member countries: the Euro Heart Survey on Atrial Fibrillation, Eur. Heart J. 26 (22) (2005) 2422–2434.

E.L. Fosbol, D.N. Holmes, J.P. Piccini, L. Thomas, J.A. Reiffel, R.M. Mills, et al., Provider specialty and atrial fibrillation treatment strategies in United States community practice: findings from the ORBIT-AF registry, J. Am. Heart Assoc. 2 (4) (2013) e000110.

M.V. Huisman, C.S. Ma, H.C. Diener, S.J. Dubner, J.L. Halperin, K.J. Rothman, et al., Antithrombotic therapy use in patients with atrial fibrillation before the era of non-vitamin K antagonist oral anticoagulants: the Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation (GLORIA-AF) Phase I cohort, Europace: Eur. Pacing Arrhythm. Cardiac Electrophysiol. 18 (9) (2016) 1308–1318.

P.N. Apenteng, H. Gao, F.R. Hobbs, D.A. Fitzmaurice, Temporal trends in antithrombotic treatment of real-world UK patients with newly diagnosed atrial fibrillation: findings from the GARFIELD-AF registry, BMJ Open 8 (1) (2018) e019605.

P. Kirchhof, M. Nabauer, A. Gerth, T. Limbourg, T. Lewalter, A. Goette, et al., Impact of the type of centre on management of AF patients: surprising evidence for differences in antithrombotic therapy decisions, Thromb. Haemost. 105 (6) (2011) 1010–1023.