

Non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation in secondary stroke and systemic embolism prevention

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Abstract

Background: Oral anticoagulants (OAC) are recommended in all patients with atrial fibrillation (AF) after thromboembolic events without contraindications. It is hypothesized herein, that the majority of patients with AF after thromboembolic events receive OAC and the presence of specific factors, predisposes the use of non-vitamin K antagonist oral anticoagulants (NOACs).

Methods: This is a retrospective study, encompassing patients with AF hospitalized in a reference cardiology center over the years 2014–2017. Thromboembolic events were defined as: ischemic stroke, transient ischemic attack and systemic embolism. Inclusion criteria were the following: diagnosis of non-valvular AF at discharge from hospital, hospitalization not resulting in death.

Results: Among 2834 hospitalized patients with AF, a history of thromboembolic events was identified in 347 (12.2%) patients. In the group studied, of 347 patients with AF after a thromboembolic event, 322 (92.8%) received OAC, including 133 patients on vitamin K antagonist (41.3% of patients on OAC) and 189 patients on NOACs (58.7% of patients on OAC). Among patients treated with NOACs the majority were on dabigatran (116 patients, 61.4%), followed by rivaroxaban (54 patients, 28.6%), and apixaban (19 patients, 10%). Multivariate logistic regression analysis demonstrated that the presence of arterial hypertension reduced the chance for NOACs use (odds ratio [OR] 0.4, 95% confidence interval [CI] 0.2–0.9, $p = 0.04$) and left atrial size ≤ 40 mm was a factor increasing the chance for the use of NOACs (OR 2.5, 95% CI 1.1–5.8, $p = 0.03$).

Conclusions: Nearly all hospitalized patients with AF received OAC in the secondary prevention of thromboembolic complications. NOACs were used for secondary prevention of stroke among patients with AF in patients with fewer comorbidities. (Cardiol J 2021; 28, 6: 896–904)

Key words: atrial fibrillation, oral anticoagulants, secondary prevention, thromboembolic event, stroke

Introduction

Atrial fibrillation (AF) is the most common supraventricular arrhythmia. Thromboembolic events, mainly involving cerebral circulation, constitute its most serious complication [1, 2]. In

developed countries nearly 85% of strokes are of ischemic origin caused by a blockage of blood flow to the brain through narrowed or closed arteries, while 15% of strokes are hemorrhagic [3]. It has been established that AF is associated with a 5-fold increase in the risk of ischemic stroke and is gen-

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erally responsible for 15–20% of all strokes [4, 5]. A history of thromboembolism in a patient with AF is the strongest risk factor for another thromboembolic event [6]. Oral anticoagulants (OAC) should be used for prevention of thromboembolism among patients with AF and the risk factors for such events [7]. Non-vitamin K antagonist oral anticoagulants (NOACs) are used increasingly more often and are characterized by at least a similar or greater effectiveness compared to that of vitamin K antagonists (VKA) [8–11].

The aim of this study was to assess the frequency of use of NOACs among hospitalized patients with AF and a history of thromboembolism, as well as to analyze factors which predispose the choice of NOACs in this group of patients.

Methods

Study group

Patients with AF hospitalized at a reference cardiology center, over the years 2014–2017, were included in this retrospective analysis. The following inclusion criteria of the study were applied: diagnosis of AF at discharge from hospital, hospitalization not resulting in death. Patients with valvular AF (mechanical valve prosthesis, severe mitral stenosis) were excluded from the study. Thromboembolic complications were defined as: ischemic stroke, transient ischemic attack (TIA), and systemic embolism. Anticoagulation treatment was evaluated at discharge from the hospital.

Statistical analysis

Arithmetic means, standard deviations, medians and quartiles were used to describe quantitative data. Distribution of qualitative data was presented as frequency and percentages. Frequencies were compared using the χ^2 test or the exact Fisher test. Normality of distribution was tested with the Shapiro-Wilk test. If the assumption of normality of distribution was fulfilled, the distributions of quantitative variables were compared using the Student t-test, while in the absence of normality of distribution, the U Mann-Whitney test was applied. Uncorrected (crude) and corrected (adjusted) odds ratios (OR) together with 95% confidence intervals (CIs) were determined using a logistic regression model. Multivariate logistic regression analysis included variables with statistically significant OR, confirmed in univariate analysis. All statistical tests conducted were two-sided and zero hypotheses were rejected when $p < 0.05$. The R software v. 3.4.3 (R Core Team (2017). R: A language and

Table 1. Anti-stroke prophylaxis in patients with atrial fibrillation after thromboembolic complications (n = 347).

| Type of prophylaxis | Number and percentage of patients |
|-----------------------------------|-----------------------------------|
| Oral anticoagulants | 322 (92.8%) |
| Vitamin K antagonists | 133 (38.3%) |
| Non-vitamin K oral anticoagulant: | 189 (54.5%) |
| Apixaban | 19 (5.5%) |
| Dabigatran | 116 (33.4%) |
| Rivaroxaban | 54 (15.6%) |
| Antiplatelet medicine / medicines | 9 (2.6%) |
| Low molecular weight heparin | 7 (2%) |
| Without prevention | 9 (2.6%) |

environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>) and STATISTICA v. 12 were used to conduct the analyses.

Results

In a group of 2834 consecutively hospitalized patients with AF, a history of thromboembolic complications was noted in 347 (12.2%) patients. Among the 347 patients with AF after thromboembolic events, 245 (70.6%) patients were diagnosed with stroke, 56 (16.1%) patients with TIA, 37 (10.7%) with systemic embolism, and more than one presentation of thromboembolic complication were noted in 9 (2.6%) patients.

In the group of 347 patients examined with AF after thromboembolic event, 49.6% were male and mean patient age amounted to 75.1 years. Fifty-one (14.7%) patients were under 65 years of age, 104 (30%) patients were aged 65–74, 133 (38.3%) patients were aged 75–84 years, and 59 patients were at least 85 (17%). A 128 (36.9%) patients presented with paroxysmal AF, 48 (13.8%) patients with persistent AF, and 171 (49.3%) with permanent arrhythmia. In the study group of 347 AF patients with a history of thromboembolic events, 322 (92.8%) received an OAC at the time of discharge from the hospital, including 133 on VKA (41.3% of patients treated with OAC) and 189 on NOACs (58.7% of patients with OAC). Table 1 presents pharmacological means of stroke prevention in the study group.

In a group of 189 patients treated with NOACs dabigatran was used most frequently — 116

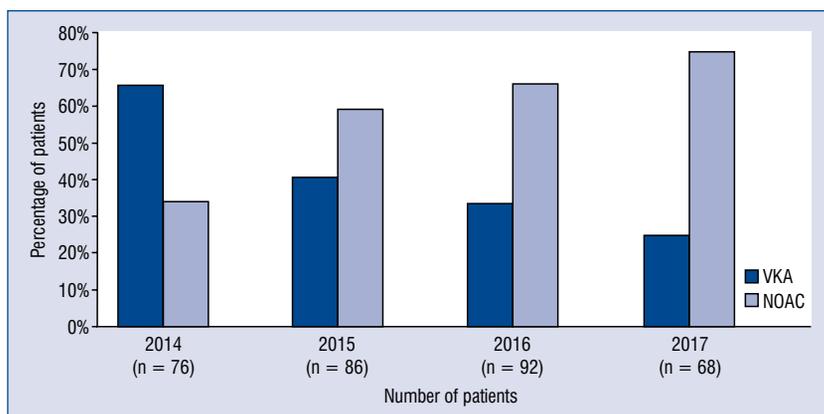


Figure 1. Percentage of patients treated with vitamin K antagonist (VKA) and non-vitamin K antagonist oral anticoagulants (NOAC) with atrial fibrillation after thromboembolic complications hospitalized between 2014 and 2017.

patients (61.4% of subjects were treated with NOACs), followed by rivaroxaban — 54 (28.6% of subjects were treated with NOACs), and apixaban — 19 patients (10% of subjects were treated with NOACs). Standard doses were administered in 76 (40.2%) patients on NOACs, while 113 (59.8%) patients received reduced doses.

The following number of patients with AF and history of thromboembolic events were hospitalized during the years 2014–2017: 76, 86, 92, and 68 patients, respectively. A significant increase in the proportion of patients on NOACs were among all OAC-treated subjects: from 34.2% in 2014 to 75% of subjects in 2017 (Fig. 1).

Patients with AF and a history of thromboembolic events treated with VKA vs. NOACs with regard to age, type of AF, and comorbidities (Table 2) were compared. Patients with AF, who were prescribed a NOACs suffered from arterial hypertension heart failure, or myocardial infarction less often than those receiving VKA. They were also characterized by lower mean CHADS₂ and CHA₂DS₂VASc scores as well as higher left ventricular ejection fraction and smaller left atrial dimension in echocardiographic assessment.

Univariate logistic regression analysis demonstrated that among patients after thromboembolic complications the following characteristics significantly reduced the chance of receiving a prescription for NOACs: arterial hypertension, heart failure, history of myocardial infarction, and CHADS₂ score ≥ 4 points. Among echocardiographic parameters ejection fraction < 50% significantly reduced chance for the use of NOACs in the group studied. However, left atrial size ≤ 40 mm was a factor significantly increasing the likelihood of being prescribed NOACs (Table 3).

Multivariate logistic regression analysis showed that arterial hypertension significantly reduced the chance of NOACs use, while left atrial size ≤ 40 mm significantly increased the likelihood of NOACs administration in patients with AF and a history of thromboembolic events (Table 4).

Discussion

In the present study, encompassing almost 3000 hospitalized patients with AF, thromboembolic events were diagnosed in 12% of subjects. In the PREFER registry thromboembolic complications were noted in 8.4% of patients with AF [12]. A similar proportion of patients with a history of stroke, amounting to 10.5%, was found in the 2nd phase of the GLORIA-AF registry [13]. A higher proportion of patients after stroke/TIA than in the current study was established in the GARFIELD registry — it amounted to 15.2% in cohort I, and 21.4% in cohort II. In the Polish population of patients included in the GARFIELD registry the percentage of patients after stroke/TIA was lower and amounted to 8.3% and 7.9% in cohort I and II, respectively [14]. The population of patients in the present study was higher than in the GARFIELD registry — mean patient age was 75 years, while in the GARFIELD registry it amounted to 67 years in the Polish population; in the European population it amounted to 73 years in cohort II and 72 years in cohort I [14]. Among 2259 British patients with AF remaining under the care of general practitioners, 19% had a history of stroke. Mean age of patients in this study was similar to that in the current study — 76 years [15].

Patients with a history of thromboembolic complications have at least 2 points on the

Table 2. Clinical characteristics of patients with atrial fibrillation vitamin K antagonist (VKA) or non-vitamin K antagonist oral anticoagulant (NOAC)-treated after thromboembolic events.

| Clinical feature | OAC group (n = 322) | VKA group (n = 133) | NOAC group (n = 189) | P |
|---|------------------------|------------------------|-------------------------|-------|
| Age [years] | | | | 0.81 |
| Mean ± SD | 74.9 ± 9.9 | 74.8 ± 9.5 | 74.9 ± 10.9 | |
| Median (Q1–Q3) | 76 (68–83) | 76 (68–83) | 76 (68–83) | |
| Age [years] | | | | 0.61 |
| Age < 50 | 3 (0.9%) | 0 (0.0%) | 3 (1.6%) | |
| Age 50–64 | 45 (14.0%) | 18 (13.5%) | 27 (14.3%) | |
| Age 65–74 | 99 (30.7%) | 43 (32.3%) | 56 (29.6%) | |
| Age > 74 | 175 (54.3%) | 72 (54.1%) | 103 (54.5%) | |
| Female | 165 (51.2%) | 71 (53.4%) | 94 (49.7%) | 0.52 |
| Form of atrial fibrillation | | | | 0.59 |
| Paroxysmal | 161 (50.0%) | 62 (46.6%) | 99 (52.4%) | |
| Persistent | 116 (36.0%) | 51 (38.4%) | 65 (34.4%) | |
| Permanent | 45 (14.0%) | 20 (15.0%) | 25 (13.2%) | |
| Medical history | | | | |
| Hypertension | 258 (80.1%) | 114 (85.7%) | 144 (76.2%) | 0.03 |
| Heart failure | 227 (70.5%) | 106 (79.7%) | 121 (64.0%) | 0.002 |
| Diabetes mellitus | 115 (35.7%) | 47 (35.3%) | 68 (36.0%) | 0.91 |
| Previous stroke | 234 (72.7%) | 99 (74.4%) | 135 (71.4%) | 0.55 |
| Previous TIA | 60 (18.6%) | 26 (19.5%) | 34 (18.0%) | 0.72 |
| Coronary artery disease | 101 (31.4%) | 42 (31.6%) | 59 (31.2%) | 0.95 |
| Myocardial infarction | 91 (28.3%) | 48 (36.1%) | 43 (22.8%) | 0.009 |
| PCI | 53 (16.5%) | 27 (20.3%) | 26 (13.8%) | 0.12 |
| CABG | 31 (9.6%) | 17 (12.8%) | 14 (7.4%) | 0.11 |
| COPD | 29 (9.0%) | 13 (9.8%) | 16 (8.5%) | 0.69 |
| Hyperthyroidism | 21 (6.5%) | 10 (7.5%) | 11 (5.8%) | 0.54 |
| Hypothyroidism | 31 (9.6%) | 10 (7.5%) | 21 (11.1%) | 0.28 |
| CHADS₂ [points] | | | | |
| Mean ± SD | 4.4 ± 1.0 | 4.5 ± 0.9 | 4.3 ± 1.0 | 0.04 |
| Median (Q1–Q3) | 4 (4–5) | 5 (4–5) | 4 (4–5) | |
| CHADS ₂ 2–3 | 58 (18%) | 15 (11.3%) | 43 (22.8%) | 0.008 |
| CHADS ₂ > 3 | 264 (82%) | 118 (88.7%) | 146 (77.2%) | 0.008 |
| CHA₂DS₂VASc [points] | | | | |
| Mean ± SD | 6.5 ± 1.4 | 6.7 ± 1.3 | 6.4 ± 1.5 | 0.08 |
| Median (Q1–Q3) | 7 (6–7) | 7 (6–8) | 6 (5–7) | |
| CHA ₂ DS ₂ VASc 2–3 | 9 (2.8%) | 1 (0.8%) | 8 (4.2%) | 0.09 |
| CHA ₂ DS ₂ VASc > 3 | 313 (97.2%) | 132 (99.2%) | 181 (95.8%) | 0.09 |
| HAS-BLED | | | | |
| Mean ± SD | 2.6 ± 0.8 | 2.7 ± 0.7 | 2.6 ± 0.8 | |
| Median (Q1–Q3) | 3 (2–3) | 3 (2–3) | 3 (2–3) | |
| ECHOCARDIOGRAPHY | | | | |
| EF [%] | [n = 250] | [n = 106] | [n = 144] | 0.04 |
| Mean ± SD | 46.9 ± 12.9 | 44.9 ± 13.7 | 48.4 ± 12.2 | |
| Median (Q1–Q3) | 50 (40–55) | 49.5 (38–55) | 50 (43–55) | |
| EF > 50% | 101 (40.4%) | 34 (32.1%) | 56 (38.9%) | |
| EF 50–30% | 115 (46.0%) | 54 (50.9%) | 61 (42.4%) | |
| EF < 30% | 101 (13.6%) | 34 (32.1%) | 56 (38.9%) | |

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Table 2 (cont.). Clinical characteristics of patients with atrial fibrillation vitamin K antagonist (VKA) or non-vitamin K antagonist oral anticoagulant (NOAC)-treated after thromboembolic events.

| Clinical feature | OAC group (n = 322) | VKA group (n = 133) | NOAC group (n = 189) | P |
|--------------------------|------------------------|------------------------|-------------------------|----------|
| LA [mm] | [n = 248] | [n = 106] | [n = 142] | < 0.0001 |
| Mean ± SD | 47.3 ± 8.2 | 49.6 ± 8.9 | 45.7 ± 7.3 | |
| Median (Q1–Q3) | 46 (42.5–52) | 48.5 (45–54) | 45 (41–50.7) | |
| LA > 40 mm | [n = 246] 205 (83.3%) | [n = 106] 97 (91.5%) | [n = 142] 108 (76.1%) | 0.002 |
| LABORATORY TESTS | | | | |
| Hemoglobin [g/dL] | [n = 321] | [n = 132] | [n = 189] | 0.38 |
| Mean ± SD | 13.2 ± 1.7 | 13.1 ± 1.7 | 13.2 ± 1.6 | |
| Median (Q1–Q3) | 1.2 (12.1–14.3) | 13.2 (12.1–14.2) | 13.2 (12.1–14.5) | |
| GFR [mL/min] | | | | 0.16 |
| Mean ± SD | 55.8 ± 18.6 | 53.7 ± 17.3 | 57.3 ± 19.4 | |
| Median (Q1–Q3) | 54.9 (43.8–66.3) | 53.7 (42.6–65.6) | 56.0 (44.3–67.4) | |
| GFR > 60 | 114 (35.4%) | 43 (32.3%) | 118 (37.6%) | 0.43 |
| GFR 60–46 | 111 (34.5%) | 48 (36.1%) | 63 (33.3%) | |
| GFR 45–30 | 63 (19.6%) | 25 (18.8%) | 38 (20.1%) | |
| GFR 29–15 | 23 (7.1%) | 12 (9.0%) | 11 (5.8%) | |
| GFR < 15 | 1 (0.3%) | 0 (0.0%) | 1 (0.5%) | |

CABG — coronary artery bypass grafting; COPD — chronic obstructive pulmonary disease EF — ejection fraction; GFR — glomerular filtration rate; LA — left atrial; PCI — percutaneous coronary intervention; TIA — transient ischemic attack

Table 3. Factors increasing the chances of using non-vitamin K antagonist oral anticoagulant (NOAC) in patients with atrial fibrillation after thromboembolic complications — univariate logistic regression analysis.

| Factors | VKA group (n = 133) | NOAC group (n = 322) | Crude OR | 95% CI | P |
|----------------------|------------------------|-------------------------|------------|-----------|-------|
| Sex | | | | | |
| Female | 71 (53.4%) | 94 (49.7%) | Ref. level | | |
| Male | 62 (46.6%) | 95 (50.3%) | 1.2 | 0.7–1.8 | 0.52 |
| Age [years] | 74.8 ± 9.5 | 74.9 ± 10.3 | 1.0 | 0.98–1.02 | 0.96 |
| < 65 | 18 (13.5%) | 30 (15.9%) | Ref. level | | |
| 65–74 | 43 (32.3%) | 56 (29.6%) | 0.8 | 0.4–1.6 | 0.49 |
| > 74 | 72 (54.1%) | 103 (54.5%) | 0.9 | 0.4–1.7 | 0.65 |
| Form of AF | | | | | |
| Paroxysmal | 51 (38.3%) | 65 (34.4%) | Ref. level | | |
| Persistent | 20 (15.0%) | 25 (13.2%) | 1.0 | 0.5–2.0 | 0.96 |
| Permanent | 62 (46.6%) | 99 (52.4%) | 1.3 | 0.8–2.0 | 0.36 |
| Form of AF | | | | | |
| Permanent | 62 (46.6%) | 99 (52.4%) | Ref. level | | |
| Persistent | 51 (38.3%) | 65 (34.4%) | 0.8 | 0.5–1.3 | 0.36 |
| Paroxysmal | 20 (15.0%) | 25 (13.2%) | 0.8 | 0.4–1.5 | 0.47 |
| Hypertension | | | | | |
| No | 19 (14.3%) | 45 (23.8%) | Ref. level | | |
| Yes | 114 (85.7%) | 144 (76.2%) | 0.5 | 0.30–0.96 | 0.04 |
| Heart failure | | | | | |
| No | 27 (20.3%) | 68 (36.0%) | Ref. level | 0.3–0.8 | 0.003 |
| Yes | 106 (79.7%) | 121 (64.0%) | 0.5 | | |

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Table 3 (cont.). Factors increasing the chances of using non-vitamin K antagonist oral anticoagulant (NOAC) in patients with atrial fibrillation after thromboembolic complications - univariate logistic regression analysis.

| Factors | VKA group (n = 133) | NOAC group (n = 322) | Crude OR | 95% CI | p |
|--|------------------------|-------------------------|------------|-------------|--------|
| Diabetes mellitus | | | | | |
| No | 86 (64.7%) | 121 (64.0%) | Ref. level | | |
| Yes | 47 (35.3%) | 68 (36.0%) | 1.0 | 0.6–1.6 | 0.91 |
| Previous stroke | | | | | |
| No | 34 (25.6%) | 54 (28.6%) | Ref. level | | |
| Yes | 99 (74.4%) | 135 (71.4%) | 0.9 | 0.5–1.4 | 0.55 |
| Previous transient ischaemic attack | | | | | |
| No | 107 (80.5%) | 155 (82.0%) | Ref. level | | |
| Yes | 26 (19.5%) | 34 (18.0%) | 0.9 | 0.5–1.6 | 0.72 |
| Coronary artery disease | | | | | |
| No | 91 (68.4%) | 130 (68.8%) | Ref. level | | |
| Yes | 42 (31.6%) | 59 (31.2%) | 1.0 | 0.6–1.6 | 0.95 |
| Myocardial infarction | | | | | |
| No | 85 (63.9%) | 146 (77.2%) | Ref. level | | |
| Yes | 48 (36.1%) | 43 (22.8%) | 0.5 | 0.3–0.9 | 0.009 |
| Percutaneous coronary intervention | | | | | |
| No | 106 (79.7%) | 163 (86.2%) | Ref. level | | |
| Yes | 27 (20.3%) | 26 (13.8%) | 0.6 | 0.3–1.1 | 0.12 |
| Coronary artery bypass graft | | | | | |
| No | 116 (87.2%) | 175 (92.6%) | Ref. level | | |
| Yes | 17 (12.8%) | 14 (7.4%) | 0.5 | 0.3–1.2 | 0.11 |
| Chronic obstructive pulmonary disease | | | | | |
| No | 120 (90.2%) | 173 (91.5%) | Ref. level | | |
| Yes | 13 (9.8%) | 16 (8.5%) | 0.9 | 0.4–1.8 | 0.69 |
| CHADS₂ score | 4.5 ± 0.9 | 4.3 ± 1.0 | 0.8 | 0.6–0.97 | 0.029 |
| 2–3 | 15 (11.3%) | 43 (22.8%) | Ref. level | | |
| > 3 | 118 (88.7%) | 146 (77.2%) | 0.4 | 0.2–0.8 | 0.001 |
| CHA₂DS₂VASC score | 6.7 ± 1.3 | 6.4 ± 1.5 | 0.9 | 0.7–1.01 | 0.06 |
| 2–3 | 1 (0.8%) | 8 (4.2%) | Ref. level | | |
| > 3 | 132 (99.2%) | 181 (95.8%) | 0.2 | 0.02–1.4 | 0.10 |
| HASBLED score | 2.7 ± 0.8 | 2.6 ± 0.8 | 0.9 | 0.7–1.2 | 0.56 |
| Ejection fraction [%] | 44.9 ± 13.7 | 48.4 ± 12.2 | 1.02 | 1.001–1.04 | 0.037 |
| Missing value | 27 (20.3%) | 45 (23.8%) | – | | |
| > 50 | 34 (25.6%) | 67 (35.4%) | Ref. level | | |
| 30–50% | 54 (40.6%) | 61 (32.3%) | 0.6 | 0.3–0.995 | 0.048 |
| < 30% | 18 (13.5%) | 16 (8.5%) | 0.5 | 0.2–0.994 | 0.048 |
| Left atrial group [mm] | 49.6 ± 8.9 | 45.7 ± 7.3 | 0.94 | 0.91–0.97 | 0.0004 |
| Missing value | 27 (20.3%) | 47 (24.9%) | – | | |
| > 40 mm | 97 (72.9%) | 108 (57.1%) | Ref. level | | |
| ≤ 40 mm | 9 (6.8%) | 34 (18.0%) | 3.4 | 1.5–7.4 | 0.002 |
| Hemoglobin [g/dL] | 13.1 ± 1.7 | 13.2 ± 1.6 | 1.1 | 0.9–1.2 | 0.38 |
| < 12 g/dL | 31 (23.3%) | 38 (20.1%) | Ref. level | | |
| ≥ 12 g/dL | 101 (75.9%) | 151 (79.9%) | 1.2 | 0.7–2.1 | 0.47 |
| GFR [mL/min] | 53.7 ± 17.3 | 57.3 ± 19.4 | 1.01 | 0.998–1.023 | 0.09 |
| > 60 mL/min | 43 (32.3%) | 71 (37.6%) | Ref. level | | |
| 60–46 mL/min | 50 (37.6%) | 66 (34.9%) | 0.8 | 0.5–1.4 | 0.41 |
| 45–30 mL/min | 26 (19.5%) | 40 (21.2%) | 0.9 | 0.5–1.7 | 0.82 |
| < 30 mL/min | 14 (10.5%) | 12 (6.3%) | 0.5 | 0.2–1.2 | 0.13 |

Data are shown as number (percentage) or mean ± standard deviation. CI — confidence interval; GFR — glomerular filtration rate; OR — odds ratio; VKA — vitamin K antagonist

Table 4. Factors increasing the chances of using non-vitamin K antagonist oral anticoagulant in patients with atrial fibrillation after thromboembolic complications — multivariate logistic regression analysis.

| Factors | Adjusted OR | 95% CI | P |
|--|-------------|---------|------|
| Hypertension | | | |
| No | Ref. level | | |
| Yes | 0.4 | 0.2–0.9 | 0.04 |
| Heart failure | | | |
| No | Ref. level | | |
| Yes | 0.6 | 0.3–1.2 | 0.14 |
| Myocardial infarction | | | |
| No | Ref. level | | |
| Yes | 0.6 | 0.3–1.1 | 0.13 |
| CHA₂DS₂VASc score | | | |
| 2–3 points | Ref. level | | |
| > 3 points | 1.0 | 0.4–2.7 | 0.97 |
| Ejection fraction | | | |
| > 50% | Ref. level | | |
| 50–30% | 0.8 | 0.4–1.4 | 0.39 |
| < 30% | 0.8 | 0.3–1.8 | 0.53 |
| Left atrial | | | |
| > 40 mm | Ref. level | | |
| ≤ 40 mm | 2.5 | 1.1–5.8 | 0.03 |

CI — confidence interval; OR — odds ratio

CHA₂DS₂VASc scale, although usually the score is higher due to age and comorbidities. In the present study the majority of patients were over 75 years and mean CHA₂DS₂VASc of patients treated with OAC amounted to 6.5 points, thus this study group was at the highest risk of thromboembolic events.

Lopatowska et al. [16] analyzed antithrombotic management in AF implemented into practice in a group of 1556 patients. The study showed that the use of OAC increased with increasing CHA₂DS₂VASc score but was less frequent in score ≥ 4 irrespectively of whether it was primary or secondary prevention.

According to the current guidelines of the European Society of Cardiology (ESC) on the treatment of patients with AF, anticoagulation is indicated in men with at least 2 points and women with at least 3 points on the CHA₂DS₂VASc scale. Therefore, each patient who had suffered a thromboembolic complication of AF should receive an OAC [17]. Data from registries demonstrate that clinical practice differs significantly from the guidelines. It is estimated that half of patients with AF

and no risk factors for thromboembolic complications receive an OAC and 1/3 of patients at high risk of thromboembolic events remain without prophylactic anticoagulation [18]. However, only about 10% with AF have absolute contraindications to anticoagulant treatment. Mazurek et al. [19] showed that in a group of 2250 patients with AF contraindications to OAC were present in only 8.3% of subjects. In the same study it was shown that among patients with AF at high risk of thromboembolic events both overtreatment, as well as undertreatment, were associated with significant increases in the risk of stroke, while undertreatment was also associated with increased total mortality [19]. In the present study OAC was administered in 93% of patients, which is in agreement with the reports of other authors, who confirmed that contraindications to OAC are present in approximately one in ten patients with AF. In Darlington Atrial Fibrillation Registry on 2259 patients with AF, a history of stroke was identified in 18.9% of subjects [20]. In this group of patients OAC in monotherapy or combined with an antiplatelet drug was applied in 61.7% of subjects, 1/3 of patients received only an antiplatelet drug, while 6.5% of subjects with AF and history of stroke had no anticoagulation therapy [20]. In the current study OAC was administered in 92.8% of patients with AF and history of stroke, an antiplatelet drug/drugs in 2.6% of subjects, low molecular weight heparin in 2%, and 2.6% of patients were left without prophylactic anticoagulation. In the present study the mean age of patients with AF after a thromboembolic event amounted to 75 years, while in a British study of patients after stroke it was 79.6%. Also, patients in the study herein were characterized by a higher mean CHA₂DS₂VASc score compared to that of the British authors. Significant differences regarding treatment of patients after thromboembolic complications in studies under comparison probably ensue from the fact that in the present study, prophylactic anticoagulation was implemented by a reference cardiac center, while in the British study, by general practitioners.

In the current study the majority of patients on OAC were treated with NOACs. Reduced NOACs doses were used in 60% of patients and dabigatran was the most frequent therapeutic choice. In the SAMURAI-NVAF Study encompassing 1116 patients after stroke/TIA discharged from neurology centers, the majority of patients received VKA compared to NOAC (58.2 vs. 41.8%) [21]. Rivaroxaban, usually a full dose, was the most frequently chosen NOAC in the SAMURAI-NVAF

Study, followed by dabigatran and apixaban, which were most often used in reduced doses [21]. In the Novel Oral Anticoagulants in Stroke Patients (NOACISP)-LONGTERM registry that included 251 patients after stroke, who were treated with an OAC, NOAC was administered in 78% of patients [22]. Over a 1-year observation period full adherence was noted in 77.1% of patients treated with NOAC and 83.3% of patients receiving VKA [23].

The data on anticoagulant therapy in the group of women and men after thromboembolic complications is not consistent. In the present study, no significant differences were noted between the sexes preferring NOACs treatment. However, in the SAMURAI-NVAF study, the group of men after thromboembolism events were treated with NOACs more often than with VKA [21].

In the current study NOACs was prescribed more frequently than VKA in patients with lower thromboembolic risk according to the CHA₂DS₂-VASc and CHADS₂ scales, as well as with non-dilated left atrium, while VKA was used more often than NOACs among patients with arterial hypertension, heart failure, history of myocardial infarction and reduced left ventricular ejection fraction. Multivariate logistic regression analysis demonstrated that diagnosis of arterial hypertension significantly reduced the chance for NOACs administration for secondary prevention of stroke among patients with AF. It may be inferred that NOACs are more likely to be selected in lower-risk patients with fewer comorbidities. In a study that included patients hospitalized over the years 2004–2012 at the documented center, among patients at high risk of thromboembolic complications, the proportion of subjects with a history of thromboembolic events was higher in the group treated with OAC compared to those not treated with OAC [24]. In a Danish study conducted between 2011 and 2013, history of stroke was a factor predisposing the use of NOACs over VKA [25]. In the 2016 ESC guidelines experts recommend a preference of NOAC to VKA or acetylsalicylic acid among patients after stroke [17]. In the present study significant increase was demonstrated in the use of NOACs in patients after thromboembolic events — in 2017, ¾ of patients treated with oral anticoagulation received a NOACs.

Limitations of the study

There are several limitations of the present study. As is the case for all retrospective studies, there exist potential unidentified confounders. Data sources could not ascertain symptom severity of

AF and the date of thromboembolic complication. There was no adjustment for levels of socioeconomic status or education levels of patients in the study group.

Conclusions

Oral anticoagulants were administered for secondary prevention of thromboembolic events in nearly all hospitalized patients with AF. NOACs were used in the majority of patients treated with oral anticoagulation and they were more often used in reduced than standard doses. NOACs were more frequently used for secondary prevention of stroke in AF patients with fewer comorbidities.

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