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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Anticoagulant and antiplatelet therapy for stroke prevention in atrial fibrillation patients in the clinical practice of a single district hospital in Poland

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Abstract

Background and aim: Retrospective evaluation of stroke risk in all patients with atrial fibrillation (AF) admitted to cardiology, internal medicine, and neurology wards in a single Polish district hospital in 2006 and 2010 using two risk stratification schemes, $CHADS_2$ vs. CHA_2DS_2VASc risk scores and identification of independent predictors of guideline-compliant oral anticoagulant (OAC) treatment.

Methods: We analysed case records of 613 patients with AF (including 300 patients in 2006 and 313 patients in 2010) treated in a district hospital — the John Paul II Western Hospital (Szpital Zachodni) in Grodzisk Mazowiecki, to evaluate their stroke risk and therapy prescribed at discharge.

Results: The mean patient age in the overall study population (49% of men) was 74.3 years (74.8, 77.5, and 71.9 years, respectively, in patients with paroxysmal, permanent and persistent AF). Patients > 75 years old comprised 58.6% of the study group, and those < 65 years old comprised 16.6% of the study group. The most common concomitant diseases were hypertension (65.9%), chronic heart failure (61.7%), coronary artery disease (43.1%), at least moderate mitral and/or tricuspid regurgitation (36.4%), and peripheral arterial disease (36%). Indications for OAC treatment were present in 85% (using the $CHADS_2$ score) or 95% (using the CHA_2DS_2VASc score) patients but this therapy was prescribed at discharge in only 39% of the study group (240 patients). Compared to patients who were not prescribed OAC, those prescribed OAC treatment were younger, more often male, with permanent AF, valvular heart disease, and hypertension. In patients without OAC treatment at discharge, the following conditions were found more frequently than in patients prescribed OAC treatment: paroxysmal AF (49.8% vs. 33.3% in OAC patients), established coronary artery disease (46.1% vs. 38.3%), previous myocardial infarction (27% vs. 18.7%), prior coronary revascularisation (11.2% vs. 6.6%), alcohol abuse (4.2% vs. 0.8%), renal failure (31.6% vs. 21.6%), and stroke or transient ischaemic attack (TIA; 19.3% vs. 12%). In multivariate logistic regression analysis, we identified 5 independent predictive factors associated with prescribing OAC at discharge, including persistent AF vs. paroxysmal AF (odds ratio [OR] = 5.27), permanent AF vs. paroxysmal AF (OR = 1.86), hypertension (OR = 1.50), previous stroke and/or TIA (OR = 0.59), and age > 75 years vs. < 65 years (OR = 0.53).

Conclusions: Despite a high stroke risk as determined by both scores, only 39% of patients received OAC. In the studied population, independent predictors for prescribing OAC at discharge included arterial hypertension (in accordance with the guidelines) and younger patient age, no history of stroke/TIA, and AF other than paroxysmal. The practice of OAC and/or antiplatelet therapy use in AF patients discharged from a Polish district hospital was not compliant with the current ESC guidelines either in 2006 or in 2010.

Key words: atrial fibrillation, stroke prevention, anticoagulation, antiplatelet therapy

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INTRODUCTION

Atrial fibrillation (AF) is the most commonly encountered arrhythmia in the clinical practice. Most severe complications of AF are thromboembolic events, primarily ischaemic stroke.

The risk of stroke increases from 1.5% among subjects aged 50–59 years to 23.5% among those aged 80–89 years [1].

Based on several large population studies, in particular the Atrial Fibrillation Investigators (AFI) and Stroke Prevention in Atrial Fibrillation (SPAF) studies [2], 5 major risk factors of thromboembolic events were identified which were the basis for the $CHADS_2$ risk score popularised in the 2006 European Society of Cardiology (ESC) guidelines and more recently expanded with additional risk factors into a more precise, currently used CHA_2DS_2-VASc risk score. Scores of 1 or more are a class IA indication for antithrombotic treatment.

The aims of the present study included: 1) retrospective evaluation of stroke risk in all AF patients admitted to cardiology, internal medicine, and neurology wards in a single Polish district hospital in 2006 and 2010 using two risk stratification schemes, $CHADS_2$ vs. CHA_2DS_2VASc risk scores; and 2) assessment of therapy prescribed at discharge and identification of independent predictors of guideline-compliant oral anticoagulant (OAC) treatment.

METHODS

Based on hospital records and discharge summaries, we selected 613 patients (including 300 in 2006 and 313 in 2010) with the diagnosis of nonvalvular AF and complete data regarding stroke risk factors ($CHADS_2$ and CHA_2DS_2VASc risk scores) and treatment on discharge. We excluded AF patients with concomitant conditions that required antithrombotic therapy (prosthetic valve, pulmonary embolism, systemic embolism, cancer). We used a questionnaire that included patient characteristics and therapy prescribed at discharge. We included only those patients for whom complete data were available and allowed calculation of risk scores.

Statistical analysis

Associations of selected parameters with OAC prescribed at discharge were evaluated using a multivariate logit regression model. We identified independent predictors of a therapeutic success defined as guideline-compliant treatment. For the final analysis, the following variables were selected using backward elimination: age, gender, AF type, heart failure with left ventricular ejection fraction < 35%, previous stroke or transient ischaemic attack (TIA), hypertension, peripheral arterial disease, anticoagulant and antiplatelet treatment in 2006 vs. 2010, and the specialty of a physician prescribing therapy at discharge.

RESULTS

The mean patients in the overall study population was 74.3 years, including 74.8 years in patients with paroxysmal AF, 77.5 years in patients with permanent AF, and 71.9 years in patients with persistent AF. Patients > 75 years old comprised 58.6% of the study group, patients aged 65–74 years comprised 24.8% of the study group, and those < 65 years old comprised 16.6% of the study group; 49% of patients were men.

The most common type of the arrhythmia was permanent AF, found in 45% of patients, followed by paroxysmal AF in 43% of patients, and persistent AF in 12% of patients.

In the overall study group, as many as 85% of patients had 2 or more stroke risk factors by the $CHADS_2$ score. A single risk factor was present in 13% patients, and no risk factors were identified in only 2% of patients. Two or more stroke risk factors by the CHA_2DS_2VASc score were identified in 95% of patients, 4% of patients scored 1, and only 1% patients scored 0 in the CHA_2DS_2VASc scale. A class IA indication for antithrombotic therapy, defined as score of 1 or more in the CHA_2DS_2VASc scale, was present in 99% of patients (n = 604).

The most common concomitant conditions in the study group are summarised in Table 1.

Oral anticoagulation with a vitamin K antagonist was prescribed in only 39.2% of patients with AF. Patients with the most solid evidence of benefits from OAC (scores > 2 in the CHA_2DS_2-VASc and $CHADS_2$ scales), i.e. patients at the highest thromboembolic risk such as patients with a previous stroke or TIA and patients aged > 75 years received this therapy less frequently than patients without such risk factors (Fig. 1). The type of antithrombotic therapy depending on the CHA_2DS_2-VASc score is shown in Figure 2.

Table 1. Concomitant conditions in the study group

Condition	No. (%)
Hypertension	404 (65.9%)
Diabetes	156 (25.4%)
Heart failure	378 (61.7%)
Previous stroke/TIA	101 (16.5%)
CAD	264 (43.1%)
Previous MI	146 (23.8%)
CABG	20 (3.3%)
PCI	58 (9.5%)
Haemodynamically insignificant MR/TR	223 (36.4%)
Thyroid disease	74 (12.1%)
Alcohol abuse	18 (2.9%)
Renal failure	170 (27.7%)
Pacemaker or ICD	51 (8.3%)
Chronic lung disease	106 (17.3%)
Peripheral arterial disease	221 (36.1%)

CABG — coronary artery bypass grafting; CAD — coronary artery disease; MI — myocardial infarction; PCI — percutaneous coronary intervention; ICD — implantable cardioverter-defibrillator; MR — mitral regurgitation; TR — tricuspid regurgitation; TIA — transient ischaemic attack

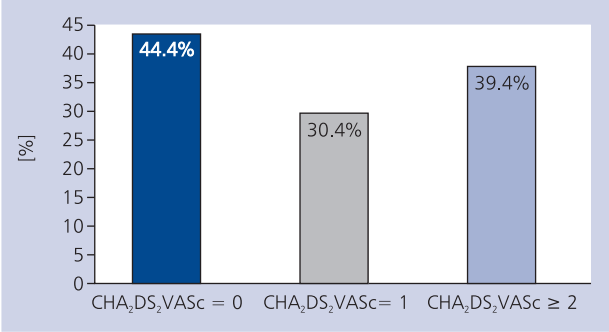

Figure 1. Proportion of patients receiving oral anticoagulant depending on the CHA_2DS_2-VASc score

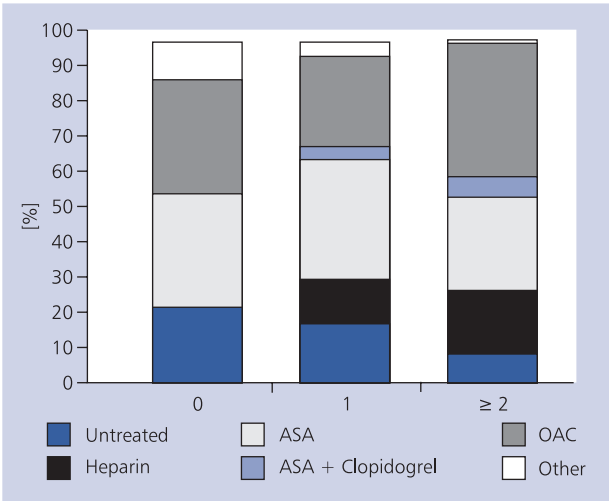

Figure 2. Antithrombotic therapy prescribed depending on the CHA_2DS_2-VASc score (% of patients); ASA — acetylsalicylic acid

Compared to patients who were not prescribed OAC, those prescribed OAC treatment were younger, more often male, more frequently with permanent AF, haemodynamically insignificant valvular heart disease, and hypertension, and were more frequently treated with angiotensin-converting enzyme inhibitors.

In patients without OAC treatment at discharge, the following conditions were found more frequently than in patients prescribed OAC treatment: paroxysmal AF (49.8% vs. 33.3% in OAC patients), established coronary artery disease (46.1% vs. 38.3%), previous myocardial infarction (27% vs. 18.7%), prior coronary revascularisation (11.2% vs. 6.6%), alcohol abuse (4.2% vs. 0.8%), renal failure (31.6% vs. 21.6%), and stroke or TIA (19.3% vs. 12%).

In multivariate logistic regression analysis, we identified 5 independent predictive factors associated with prescribing OAC at discharge (all $p \leq 0.05$), with odds ratios (OR) ranging from 0.52 to 5.27 (Table 2).

Table 2. Factors associated with prescription of oral anticoagulation

	OR	P	95% CI
Age 65–74 years vs. < 65 years	1.20	0.531	0.68–2.13
Age > 75 years vs. < 65 years	**0.53**	**0.019**	0.31–0.90
Female vs. male gender	0.97	0.871	0.66–1.42
Persistent vs. paroxysmal AF	5.27	**0.000**	2.86–9.73
Permanent vs. paroxysmal AF	**1.86**	**0.003**	1.24–2.80
LVEF < 35%	0.80	0.563	0.39–1.68
Previous stroke or TIA	**0.59**	**0.049**	0.34–0.99
Hypertension	**1.50**	**0.050**	1.00–2.23
Patients treated in 2006 vs. 2010	0.97	0.87	0.67–1.41
Cardiologist vs. no specialty	1.35	0.32	0.75–2.42
Specialty other than cardiology vs. no specialty	1.12	0.62	0.73–1.71

Area under ROC curve = 0.6722. Goodness-of-fit test p = 0.2643 (indicating a good-fitting model). Significant predictors were given in bold. OR — odds ratio; CI — confidence interval; AF — atrial fibrillation; LVEF — left ventricular ejection fraction; TIA — transient ischaemic attack

This multivariate analysis indicated that:

- patients aged > 75 years were twice less likely to receive OAC than patients aged < 65 years
- patients with persistent AF were more than 5-fold less likely to receive OAC than patients with paroxysmal AF
- patients with permanent AF were nearly twice less likely to receive OAC than patients with paroxysmal AF
- patients with a previous stroke or TIA were 40% less likely to receive a vitamin K antagonist than patients without a previous stroke or TIA
- patients with hypertension were 50% more likely to receive OAC than patients without hypertension
- antithrombotic therapy in 2006, when the $CHADS_2$ risk score was popularised in the ESC guidelines, did not differ significantly from that in 2010, when the newer CHA_2DS_2VASc risk score was introduced.

Antiplatelet drugs which are poorly effective in the prevention of thromboembolic complications in patients with AF, were used in about 50% of the study population. Acetylsalicyslic acid (ASA) was prescribed at discharge in nearly 48% of patients, including as monotherapy in 35% of patients, clopidogrel monotherapy was prescribed in about 1.5% of patients, and combined clopidogrel and ASA therapy in 7.3% of patients.

The most commonly used low-molecular weight heparin (in more than 95% of cases) was enoxaparin, prescribed in 19.5% of the study population. This drug was used in prophylactic or therapeutic doses particularly in the elderly, non-compliant, or dependent patients, and also those with a high bleeding risk as estimated using the HAS-BLED score,

despite the fact that such therapy is not recommended in the current guidelines.

DISCUSSION

The major value of the present study is a reliable description of antithrombotic treatment for stroke prevention in a sample of 613 patients with AF discharged from a district hospital in the first decade of the 21st century. Until now, such registries comparing the old ($CHADS_2$) and new (CHA_2DS_2VASc) stroke risk scores were not available in the literature. The CHA_2DS_2VASc and HAS-BLED scoring systems were introduced to the current guidelines in 2010, and the current study demonstrates that the use of these scores should result in prescription of OAC therapy in nearly all (98%) patients in the study group.

Our multivariate analysis using a logit regression model revealed predictors of OAC use in AF patients that indicate non-compliance with the current guidelines, and even use of this treatment in ways that are completely against the guidelines.

Clinical studies showed high efficacy of vitamin K antagonists in both primary and secondary prevention of ischaemic stroke in patients with nonvalvular AF [3, 4].

The purpose of this retrospective study was to evaluate the real practice of OAC prescription in AF patients hospitalised in a model, well-equipped district hospital in Poland. A limitation of the study is the fact that we analysed data from years when novel anticoagulants (dabigatran, rivaroxaban, apixaban) were not available in the market yet, although they continue to be infrequently used, mainly due to reimbursement issues.

Similar data were presented by other authors. In the AnTicoagulation and Risk Factors In Atrial Fibrillation (ATRIA) study in 1996–2003, warfarin was used in 55% of 11,082 patients. As recently reported, warfarin treatment in compliance with the guidelines is used in only 42.1% of patients [5].

The most common reasons for OAC non-prescription are perceived high risk of trauma and falls, inadequate patient cooperation, a history of bleeding, and patient preference [5]. As shown in the Euro Heart Survey (EHS) registry, risk stratification is underused by clinicians who do not tailor antithrombotic treatment to individual stroke risk. Also in our study, we did not find a relationship between the rate of OAC prescription and the predicted stroke risk, regardless of whether the newer or older version of the stroke risk score was used [6, 7].

Similarly to the EHS registry, our multivariate analysis showed a paradoxical lack of association between a history of stroke or TIA and age > 75 years and the use of antithrombotic therapy.

In the study population, patients with hypertension were more likely to receive antithrombotic therapy than patients without hypertension. This is at variance with the EHS registry findings demonstrating that the presence of hypertension had no effect on the decision to start OAC therapy. However, both our study and the EHS registry findings indicate an effect of AF type on the use of antithrombotic therapy. Persistent and permanent AF was associated with more frequent OAC use compared to paroxysmal AF. Obviously, this practice is discordant with the current guidelines, as the stroke risk is comparable for all AF types.

A surprising finding in the EHS registry was OAC use in 40–50% of patients with low stroke risk ($CHADS_2$ score 0–1). In our study, OAC therapy was used in about 30–44% of low risk patients, again indicating that interventions are often not based on risk stratification.

The authors of the ATRIA study noted that although OAC use in AF is increasing, still about 50% of these patients do not receive this treatment despite clear indications.

In our study population, as many as 60% of patients were not prescribed OAC at discharge. If low-molecular weight heparin use (as prescribed at discharge) is considered a form of antithrombotic therapy, as was done in the German AFNET study [8], 58% and not 39% of our patients were treated but still 42% were discharged without antithrombotic therapy.

Antiplatelet drugs as the only form of antithrombotic therapy were used in 16.9% of patients in the German registry, compared to 51% of patients in our study (48% on ASA, 3% on clopidogrel). If only OAC and antiplatelet drugs are considered appropriate antithrombotic therapy, 17% of patients in our study did not receive it, but when low-molecular weight heparins are considered an alternative for OAC, as it was done in the German registry, then only 9.8% of Polish patients with AF received no antithrombotic therapy compared to 11.2% of patients in the AFNET study. In this context, treatment used in our study population seems significantly suboptimal but comparable to other reports.

Similar results were also obtained in the previously cited analysis by Zimetbaum et al. [5] from Harvard Medical School that included a very large group of 171,393 patients treated in 2003–2007. In this registry, 20% of patients were low risk ($CHADS_2 = 0$), 61.6% of patients were moderate risk ($CHADS_2 = 1–2$), and 18.4% of patients were high risk ($CHADS_2 = 3–6$). OAC was prescribed in only 42.1% of high risk patients, but warfarin was also used in a similar proportion of moderate and low risk patients (43.5% and 40%, respectively). These date indicate that the actual practice is discordant with the guidelines. Of note, as many as 40% of patients with the $CHADS_2$ score of 0 were prescribed OAC therapy, similarly to our findings. Thus, suboptimal antithrombotic therapy in AF patients in Poland is paradoxically similar to that in a much wealthier country — the USA.

In conclusion, AF treatment remains suboptimal. Keeping in mind, AF is more and more common due to longer life expectancy, it constitutes a major health issue. It often accompanies other diseases, also ones with major health issues [9].

CONCLUSIONS

1. Despite a high stroke risk and the need for OAC as determined by both risk scores, only 39% of patients received OAC at discharge for a district hospital in Poland. As many as 17% of patients were not prescribed either anticoagulant or antiplatelet therapy.
2. In the studied population, independent predictors for prescribing OAC at discharge included arterial hypertension (in accordance with the guidelines) and younger patient age, no history of stroke/TIA, and AF other than paroxysmal (discordant with the current medical knowledge and guidelines).
3. The practice of OAC and/or antiplatelet therapy use in AF patients discharged from a Polish district hospital was not compliant with the current ESC guidelines either in 2006 or in 2010.

Conflict of interest: *none declared*

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Terapia przeciwzakrzepowa w prewencji udaru mózgu u chorych z migotaniem przedsionków w praktyce szpitala powiatowego w Polsce

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Streszczenie

Wstęp i cel: Celem pracy była retrospektywna ocena ryzyka udaru mózgu u pacjentów z migotaniem przedsionków (AF) przyjętych na wybrane oddziały zachowawcze w polskim szpitalu powiatowym w 2006 i 2010 r., na podstawie skal stratyfikacji ryzyka: $CHADS_2$ *vs*. CHA_2DS_2VASc, a także identyfikacja niezależnych czynników predykcyjnych odpowiedzialnych za sukces terapeutyczny (zastosowanie leczenia zgodnego z obowiązującymi wytycznymi).

Metody: Przeanalizowano 613 (300 w 2006 r.) kart wypisowych i historii chorób pacjentów z AF leczonych w powiatowym Szpitalu Zachodnim w Grodzisku Mazowieckim pod kątem oceny ryzyka udaru mózgu i leczenia zaleconego przy wypisie.

Wyniki: Średni wiek analizowanej populacji (49% mężczyzn) wynosił 74,3 roku, w tym 74,8 *vs*. 77,5 *vs*. 71,9 roku, odpowiednio dla: napadowego, utrwalonego i przetrwałego AF. Pacjenci w wieku > 75 lat stanowili 58,6% badanej populacji, a 16,6% stanowiły osoby < 65 rż. Najczęstszymi chorobami towarzyszącymi AF były: nadciśnienie tętnicze (65,9%), przewlekła niewydolność serca (61,7%), choroba wieńcowa (43,1%) oraz co najmniej umiarkowana wada zastawki mitralnej i/lub trójdzielnej (36,4%), miażdżyca tętnic kończyn dolnych lub cechy miażdżycy (36,1%). Spośród analizowanej grupy 85% (wg skali $CHADS_2$) lub 95% osób (wg skali CHA_2DS_2VASc) wymagało stosowania doustnej terapii przeciwkrzepliwej (OAC) przy wypisie, a otrzymało ją 39% (240 osób). Pacjenci, którym przepisano OAC *vs*. osoby niepoddane temu leczeniu byli młodsi, częściej płci męskiej, z utrwalonym AF, wadą zastawkową i nadciśnieniem tętniczym. U chorych bez OAC częściej stwierdzano napadowe AF (49,8% *vs*. 33,3% u chorych z OAC), chorobę wieńcową (46,1% *vs*. 38,3%), przebyty zawał serca (27% *vs*. 18,7%), wywiad rewaskularyzacji wieńcowej (11,2% vs 6,6%), uzależnienie od alkoholu (4,2% *vs*. 0,8%) i niewydolność nerek (31,6% *vs*. 21,6%), a także w tej grupie w wywiadzie występował przebyty udar mózgu lub epizod przejściowego niedokrwienia ośrodkowego układu nerwowego (TIA; 19,3% *vs*. 12%). W wieloczynnikowej analizie regresji logitowej zidentyfikowano 5 niezależnych predykatorów przepisywania OAC: AF przetrwałe *vs*. napadowe (iloraz szans [OR] = 5,27), AF utrwalone *vs*. napadowe (OR = 1,86), nadciśnienie tętnicze (OR = 1,50), przebyty udar mózgu i/lub TIA (OR = 0,59), wiek > 75 lat *vs*. < 65 lat (OR = 0,53).

Wnioski: Mimo wysokiego ryzyka udaru mózgu wyznaczonego na podstawie obu stosowanych skal, jedynie 39% pacjentów otrzymało OAC przy wypisie. W analizowanym materiale niezależnymi czynnikami predykcyjnymi dla przepisania OAC przy wypisie były: nadciśnienie tętnicze (zgodnie z zaleceniami) oraz: młodszy wiek pacjentów, brak przebytego udaru mózgu/TIA i inna niż napadowa forma AF. Zasady stosowania terapii przeciwkrzepliwej i/lub przeciwpłytkowej u chorych z AF wypisywanych z polskiego szpitala powiatowego nie odpowiadały wytycznym ESC ani w 2006, ani w 2010 r.

Słowa kluczowe: migotanie przedsionków, prewencja udaru mózgu, leczenie przeciwkrzepliwe, terapia przeciwpłytkowa

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