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Original research article

Pharmacological stroke prevention in the elderly with atrial fibrillation in Poland – Results of PolSenior study

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ABSTRACT

Introduction: Atrial fibrillation (AF) is the most frequent clinically significant arrhythmia, especially common in the elderly. As it is known, AF is associated with increased risk of stroke. Little is known about pharmacological cardiovascular prevention in the elderly with AF in Poland.

Objectives: The purpose of the study was to evaluate the frequency of pharmacological stroke prevention among the elderly with AF in Poland and its association with clinical characteristics and concomitant cardiovascular risk factors.

Patients and methods: The analysis included elderly (≥65 years) participants of the PolSenior study performed in years 2008–2012.

Results: The study group consisted of 4979 people (mean age: 79.3 ± 8.7 years). Among them, there were 875 patients (18.7%) with documented history of AF. Pharmacological prevention with the use of vitamin K antagonists (VKA) was applied by 117 (13.4%) of the elderly with AF, including 15 (1.7%) on dual therapy. Additionally, 386 (45.3%) subjects with AF were using oral antiplatelet therapy (OAPs), mostly aspirin. Acenocoumarol was much more often used than warfarin. New oral anticoagulant drugs (NOACs) were not used at all. Only personal income was associated with the use of VKA. No significant correlation was found for the age, sex, place of residence and level of education.

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Conclusions: The study was unique to determine the frequency of pharmacological stroke prevention among elderly people with AF in Poland. It occurred that oral anticoagulant drugs were applied too rarely in this group of patients. Educational programs should be developed among general practitioners concerning current recommendations for patients with AF.
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1. Introduction

Atrial fibrillation (AF) is the most common clinically significant arrhythmia and one of the most important cardiovascular risk factors, especially in the elderly [1]. According to the latest studies the prevalence of AF in the general population of most European countries is about 2% [2–4] and – as it was shown in some meta-analyses – it doubled in the last decade [5]. The prevalence of AF increases with aging. In subjects younger than 49 years it is present in 0.12–0.16%, in those aged 60–70 years – in 3.7–4.2%, and in people aged 80 or older in 10–17% [5–8]. As it was described in our previous paper, AF was present in almost 20% of Polish people aged 65 years or older [9].

As it is well known, AF is associated with increased risk of stroke [5,10,11]. It is estimated that AF is responsible for about 20% of strokes (so called cardiogenic strokes) [12]. According to the latest guidelines [13–16] in all subjects with AF oral anticoagulant drugs should be considered using CHA_2DS_2VASc or – or less recommended – $CHADS_2$ score [17].

Little is known about pharmacological cardiovascular prevention in the elderly with atrial fibrillation in Poland. Therefore, the purpose of the study was to evaluate the frequency of use of cardiovascular pharmacological preventive therapy among the elderly with AF in Poland and its association with clinical characteristics and concomitant cardiovascular risk factors.

2. Patients and methods

The study was based on the data collected during the implementation of a multicenter, publicly funded research project commissioned by the Polish Ministry of Science and Higher Education called "Medical, psychological, sociological and economic aspects of aging of people in Poland (PolSenior)" (PBZ-MEiN-9/2/2006). A detailed description of the project has been previously published [9]. The project was carried out from October 2008 to April 2012. It was approved by the Bioethics Commission.

The study group included respondents from the PolSenior project aged 65 years and older with documented history of atrial fibrillation (AF).

The following data from the general PolSenior database were used and analyzed: age, sex, place of residence (rural or urban), level of education, personal income, a history of other cardiovascular risk factors, BMI. The frequency of use of drugs was based on the data collected in the medical part of the questionnaire.

Statistical data analysis was performed using SAS version 9.2 (SAS Institute Inc., Gary, NC). The level of statistical significance was $P < 0.05$. The following tests were used: the chi-square test, Fischer's exact test, the Shapiro–Wilk test, the Student's *t*-test, the Wilcoxon rank sum test, and a model of logistic regression. The $CHADS_2$ score was calculated according to the general rules [17].

3. Results

The PolSenior study group consisted of 4979 people (mean age: 79.4 ± 8.7 years). Among them, there were 875 patients (18.7%) with documented history of AF.

There were 455 women (52.0%) and 420 men (48.0%). The mean age of the examined subjects was 78.7 ± 8.0 years, similar for women and men (78.3 ± 8.0 vs. 79.1 ± 8.0 years, respectively, $P = 0.12$).

Among all the examined subjects with AF, 498 subjects (56.9%) used at least one drug in pharmacological prevention of thromboembolic complications of AF. In turn, OAPs were regularly used by 396 subjects (45.3%), whereas vitamin K antagonists (VKAs) by 117 subjects (13.4%). One OAP was used by 362 AF subjects (41.4%), two different OAPs by 34 (3.9%). On the other hand, one VKA was used by 109 (12.5%) and two VKAs by 8 subjects (0.9%). Additionally, 15 persons (1.7%) simultaneously used OAP and VCA (Table 1). New oral anticoagulants (NOACs) were not used at all.

The $CHADS_2$ score was calculated in 679 people (lack of full required subset of data in 196 cases). Treatment with OAPs or VKAs according to the $CHADS_2$ score is presented in Table 2.

The percentage of women using OAPs and/or VKAs (57.9%; $n = 243$) was similar as the corresponding percentage of men ($n = 255$; 56.0%; $P = 0.59$).

Also the mean age (78.7 ± 7.7 years) of respondents taking VKAs and/or OAPs was similar to the mean age (78.8 ± 8.5 years) of those with AF not treated with these drugs ($P = 0.89$).

Table 1 – Frequency of use OAPs and VKAs in the study group (N = 875).

	International drug name	Number of respondents using the drug *n* (%)
OAPs ($n = 396$)	Acetylsalicylic acid	387 (44.2%)
	Clopidogrel	22 (2.5%)
	Ticlopidine	21 (2.4%)
VKAs ($n = 117$)	Acenocoumarol	112 (12.8)
	Warfarin	13 (1.5%)

OAPs – oral antiplatelet drugs, VKAs – vitamin K antagonists.

Table 2 – Management of AF in people with calculated $CHADS_2$ score (n = 679).

Drugs	$CHADS_2$		
	0 points N = 33	1 point N = 138	≥2 points N = 508
OAPs	7 (21.2%)	47 (34.1%)	254 (50%)
VKAs	–	14 (10.1%)	76 (15%)

OAPs – oral antiplatelet drugs, VKAs – vitamin K antagonists.

Most of examined subjects lived in cities (66.4%; n = 580). No difference was found between urban (n = 327; 56.4%) and rural areas residents (n = 170; 57.8%) (P = 0.68) concerning pharmacological prevention of stroke in AF. Also no significant differences were observed between different regions of Poland (data not shown).

No correlation was found between the frequency of use of OAPs and/or VKAs in subjects with AF and the level of education (Table 3).

Personal income had a significant effect on the frequency of use of VKAs ($P < 0.01$), but not OAPs (Table 3). Only 10.8% of participants with the lowest personal income (less than 1000 Polish zloty per month) used VKAs in comparison with 25.9% of those with the highest income (2001 and more Polish zloty per month) (Table 4).

The frequency of other cardiovascular risk factors in the study group is presented in Table 5. The association between the use of OAPs and/or VKAs in AF subjects and the presence or the absence of other cardiovascular risk factors is presented in Table 6.

The logistic regression analysis was made to find which other risk factor was mostly associated with preventive therapy. Among all of the cardiovascular risk factors, hypertension and dyslipidemia were mostly associated with OAP treatment, and previous stroke was associated with VCA treatment (Table 7).

Table 5 – Frequency of other cardiovascular risk factors in PolSenior study participants with atrial fibrillation (N = 875).

Risk factor	n (%)	ND (n)
Previous stroke	105 (12.6%)	4
Pharmacologically treated hypertension	718 (82.1%)	–
Previus myocardial infarct	197 (23.5%)	35
Coronary heart disease (without myocardial infarct)	293 (35.1%)	41
Congestive heart failure	265 (31.8%)	41
Pharmacologically treated diabetes mellitus	203 (23.3%)	5
Pharmacologically treated dyslipidemia	308 (35.2%)	–
Current smoker	59 (6.8%)	2
Overweight/obesity (BMI ≥ 25 kg/m^2)	627 (76.7%)	57

BMI – body mass index, ND – not documented.

4. Discussion

According to the ESC guidelines 2016 oral anticoagulation therapy to prevent thromboembolism is recommended for all male AF patients with score 2 or more in CHA_2DS_2-VASc (female with score 3 or more) and should be considered in male AF patients with score 1 (female with score 2). Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk [16,17].

All of the examined in these study patients with AF had at least one additional risk factor – age ≥65 years (estimated CHA_2DS_2-VASc was ≥1) so in all male patients and most of female patients oral anticoagulants should be considered. As

Table 3 – Pharmacological cardiovascular prevention and education (n = 843, ND in 32 examined subjects).

Level of education	n	OAP and/or VCA n (%)	OAP n (%)	VCA n (%)
Incomplete elementary	89	54 (60.7%)	42 (47.2%)	12 (13.5%)
Complete elementary	374	213 (57.0%)	180 (48.1%)	38 (10.2%)
Professional	112	62 (55.4%)	48 (42.9%)	16 (14.3%)
High school	194	106 (54.6%)	75 (38.7%)	34 (17.5%)
University	74	46 (62.2%)	36 (48.7%)	15 (20.3%)
P		0.76	0.25	0.06

ND – not documented, OAP – oral antiplatelet drugs, VKA – vitamin K antagonists.

Table 4 – Association between personal income and OAPs and VKAs usage (n = 717, ND in 158).

Personal income zloty/mouth	n	OAP and/or VKA n (%)	OAP n (%)	VKA n (%)
Less than 1000	277	156 (56.3%)	129 (46.6%)	30 (10.8%)
1001–1500	245	137 (55.9%)	101 (41.2%)	40 (16.3%)
1501–2000	114	66 (57.9%)	56 (49.1%)	12 (10.5%)
2001 and more	81	56 (69.1%)	40 (49.4%)	21 (25.9%)
P		0.18	0.39	<0.01

ND – not documented, OAP – oral antiplatelet drugs, VKA – vitamin K antagonists.

Table 6 – Frequency of use of OAP and/or VKA in association with presence (+) or absence (–) of cardiovascular risk factors. Data presented as *n* (%).

Risk factor		OAP and/or VKA *n* (%)	OAP *n* (%)	VKA *n* (%)
Previous stroke	(+)	73 (69.5%)	53 (50.5%)	21 (20.0%)
	(–)	423 (55.2%)	341 (44.5%)	96 (12.5%)
	P	<0.01	0.25	0.04
Pharmacologically treated hypertension	(+)	451 (62.8%)	354 (49.3%)	112 (15.6%)
	(–)	47 (29.9%)	42 (26.8%)	5 (3.2%)
	P	<0.01	<0.01	<0.01
Previous myocardial infarct	(+)	127 (64.5%)	110 (55.8%)	26 (13.2%)
	(–)	351 (54.6%)	273 (42.5%)	83 (12.9%)
	P	0.01	<0.01	0.92
Coronary heart disease (without myocardial infarct)	(+)	196 (66.9%)	159 (54.3%)	48 (16.4%)
	(–)	276 (51.0%)	221 (40.9%)	58 (10.7%)
	P	<0.01	<0.01	0.02
Congestive heart failure	(+)	176 (66.4%)	131 (49.4%)	51 (19.3%)
	(–)	296 (52.0%)	248 (43.6%)	56 (9.8%)
	P	<0.01	0.11	<0.01
Pharmacologically treated diabetes mellitus	(+)	118 (58.1%)	94 (46.3%)	24 (11.8%)
	(–)	380 (57.0%)	302 (45.3%)	93 (13.9%)
	P	0.77	0.80	0.44
Pharmacologically treated dyslipidemia	(+)	237 (77.0%)	186 (60.4%)	63 (20.5%)
	(–)	261 (46.0%)	210 (37.0%)	54 (9.5%)
	P	<0.01	<0.01	0.01
Current smoker	(+)	35 (59.3%)	29 (49.2%)	6 (10.2%)
	(–)	462 (56.8%)	367 (45.1%)	110 (13.5%)
	P	0.70	0.54	0.47
Overweight/obesity (BMI ≥ 25 kg/m^2)	(+)	369 (58.9%)	280 (44.7%)	102 (16.3%)
	(–)	106 (55.5%)	94 (49.2%)	14 (7.3%)
	P	0.41	0.27	<0.01
Sex	F	255 (56.0%)	209 (45.9%)	50 (11.0%)
	M	243 (57.9%)	187 (44.5%)	67 (16.0%)
	P	0.59	0.68	0.03

BMI – body mass index, VKA – vitamin K antagonists, F – female, M – male, OAP – oral antiplatelet drugs, (+) – risk factor present, (–) – risk factor not present.

Table 7 – Association of cardiovascular risk factors with OAP and/or VKA treatment. Data are presented as OR (95%CI) and P-value.

Risk factor	OAP and/or VKA		OAP		VKA	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Previous stroke	2.44 (1.36–4.37)	<0.01	1.18 (0.72–1.95)	0.51	2.34 (1.28–4.28)	0.01
Pharmacologically treated hypertension	3.64 (2.33–5.69)	<0.01	2.65 (1.68–4.18)	<0.01	3.60 (1.4–9.28)	0.01
Previous myocardial infarct	1.07 (0.71–1.60)	0.75	1.45 (1.00–2.10)	0.05	0.77 (0.45–1.31)	0.33
Coronary heart disease (without myocardial infarct)	1.37 (0.96–1.94)	0.08	1.39 (1.00–1.93)	0.05	1.17 (0.73–1.85)	0.52
Congestive heart failure	1.63 (1.14–2.35)	0.01	1.06 (0.76–1.49)	0.73	1.89 (1.20–3.00)	0.01
Pharmacologically treated diabetes mellitus	0.91 (0.62–1.33)	0.61	1.00 (0.69–1.43)	0.98	0.66 (0.38–1.15)	0.14
Pharmacologically treated dyslipidemia	2.88 (2.02–4.11)	<0.01	2.04 (1.47–2.81)	<0.01	1.82 (1.16–2.85)	0.01
Current smoker	1.18 (0.63–2.21)	0.62	1.14 (0.63–2.07)	0.66	0.83 (0.33–2.10)	0.69
Overweight/obesity (BMI ≥ 25 kg/m^2)	0.83 (0.57–1.23)	0.35	0.61 (0.42–0.88)	0.01	2.75 (1.37–5.54)	<0.01
Sex (M/F)	1.14 (0.83–1.58)	0.42	0.90 (0.66–1.23)	0.52	1.77 (1.13–2.78)	0.01

BMI – body mass index, VKA – vitamin K antagonists, F – female, M – male, OAP – oral antiplatelet drugs.

follows from our analysis, only about 13% of the examined elderly with AF had used oral anticoagulants, slightly over 45% – OAPs. The most popular drug used by our respondents was ASA (44.2%). Currently, ASA is not recommended any more. Acenocoumarol was much more popular than warfarin – it was used by 12.8% of elderly in comparison to 1.5% of warfarin users. Such situation was probably associated with low availability and higher price of warfarin in the period when

the study was conducted. NOAC were not used by the elderly examined in PolSenior study because they were not available in the period when the research was done (in Europe dabigatran and rivaroxaban were registered in 2011, and apixaban – in 2012).

It seemed that oral anticoagulants were applied too rarely among older people with AF in Poland, both as primary or secondary pharmacological preventive therapy – only slightly more than 20% of elderly after stroke used VKAs. It is comparable to the data presented by some other Polish authors for that period; Bednarski at al. found that oral anticoagulants were prescribed in only 39% of people with AF at discharge from the hospital (despite high stroke risk calculated by CHA_2DS_2VASc or $CHADS_2$ scale) [18].

In the PREFER in AF registry (Prevention of thromboembolic events – European Registry in Atrial Fibrillation) the authors collected data from patients in seven European countries (Austria, France, Germany, Italy, Spain, Switzerland, and the UK) [19]. In this study 7245 patients were enrolled, in the mean age of 71.5 + 11 years. It was conducted from January 2012 to January 2013, so only slightly later than the PolSenior study. But the results are completely different. Among all the PREFER in AF subjects, 94.2% had at least 1 point in CHA_2DS_2VASc score (in PolSenior study 100% – because of age). But in this European study oral anticoagulants were used by 82.3% of all examined people with AF and by 84% of subjects with at least 1 point in CHA_2DS_2VASc (VCAs – 78%; NOACs – 6.1%). OAPs as monotherapy were only used by 11.3% of people. The most rarely oral anticoagulants were used in Italy (71.%), the most often – in France (90%).

Also other registries from period 2005–2008 in Europe revealed that usage of oral anticoagulants in AF was much higher in other European countries (about 70%) than in Poland [20,21].

Recent studies showed similar trends [22,23]. Stepinska et al. described the baseline data from the GARFIELD-AF registry (an ongoing prospective, multicenter, international registry of patients newly diagnosed with AF) in Europe. The use of VKAs was generally higher in other European countries (41.9–55.5%) than in Poland (36.9–41.7%). The patients in this study were younger (median age 67).

The only factor associated with the frequency of use of oral anticoagulants in subjects with AF in this study was personal income, similarly to our previous paper, concerning general usage of oral pharmacological stroke prevention in the whole PolSenior population [9]. No significant correlation was found for the age, sex, place of residence and level of education.

Summarizing, oral anticoagulants for stroke prevention among elderly patients were used too infrequently and aspirin was overused in Poland in 2008–2012. It is necessary to carry out the current research in similar population of older AF patients.

5. Limitation of the study

Atrial fibrillation, coronary heart disease and congestive heart failure were recognized only when they were documented. Because lack of all data to calculate CHA_2DS_2VASc, less recommended $CHADS_2$ was used. HAS-BLED scale could not be also calculated because of the lack of required data. It is an analysis of data from a remote period 2008–2012.

Conflict of interest

None declared.

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