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Original Research Article

Evaluation of atrial fibrillation management and cardiovascular risk profile in atrial fibrillation patients: A cross-sectional survey

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ABSTRACT

Objective: The aim of this study to investigate the most frequent risk factors of atrial fibrillation (AF), co-morbidities, complications associated with AF and the use of anticoagulants and other medications in patients who were referred to university hospitals in Lithuania.

Materials and methods: This cross-sectional study enrolled consecutive inpatients and outpatients with AF presenting to cardiologists in the two biggest Lithuanian university hospitals from November 2013 to May 2014. AF diagnosis was confirmed by a 12-lead ECG or 24-h Holter with an episode duration of >30 s.

Results: A total number of 575 patients were recruited, and complete data on clinical subtype were available for 515 patients (mean age of 70.7 years; 48.5% of women). Permanent AF was the most frequent type of AF (46.6%). Common comorbidities were hypertension (85.8%), heart failure (77.9%) and coronary artery disease (51.8%). Amiodarone was the most common antiarrhythmic agent used in 14.6% of the patients, while beta-blockers and digoxin were the most often used rate control drugs (59.6% and 10.7%, respectively). Oral anticoagulants were used by 53.3% of the patients; of them, 95.6% used vitamin K antagonists, while non-vitamin K antagonist were used by only 4.4%. The INR within a therapeutic range (2.0–3.0) was documented in 19.2% of the patients. Other antithrombotic drugs such as aspirin and clopidogrel were used in 13.7% and 2.0% of the patients, respectively; dual antiplatelet treatment was administered in 6.2% of the patients. Of the entire cohort, the mean CHA_2DS_2-VASc score was 3.97 ± 1.6 and the mean HAS-BLED score was 2.25 ± 1.0.

Conclusions: Compliance with the treatment guidelines remains suboptimal and further patient education is needed.

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1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder in clinical practice [1]. Its prevalence increases with age from 0.1% in people younger than 55 years to more than 9% in 80 years old. More than 6 million Europeans suffer from this arrhythmia [2,3]. The recent projections estimate that the number of adults older than 55 years with AF in the European Union will double from 2010 to 2060 [4].

The social and economic burden of AF is steadily increasing in Western countries [5]. Atrial fibrillation is independently associated with increased risk of a variety of adverse outcomes, including 5-fold risk of stroke, 3-fold incidence of congestive heart failure, and 2-fold risk of death [2,6,7]. Only antithrombotic therapy has been shown to reduce AF-related death [8]. AF-related stroke is often more devastating and results in long-term disability comparing to other stroke etiology [2]. The cardiac failure or dysfunction, hypertension, age ≥ 75 [doubled], diabetes, stroke [doubled]-vascular disease, age 65–74, and sex category [female] (CHA_2DS_2VASc) score is a validated tool to estimate the annual risk of stroke or systemic embolism, ranging from <1% to approximately 20% in the absence of oral anticoagulants [9].

Moreover, AF impairs quality of life and results in significant indirect nonmedical costs due to lost work ability and productivity [10]. With these premises, achieving a definite cure for this arrhythmia is highly desirable, and this would have profound social and economic implications. Therefore, it is important to diagnose AF in time, to control risk factors, prevent complications, and provide adequate treatment.

Recent guidelines on the management of AF have been published and updated by the European Society of Cardiology to facilitate the choice of the treatment strategy [2]. Considering the disease relevance and the need of therapy assessment, we investigated the most frequent AF risk factors, comorbidities, AF-associated complications and the use of anticoagulants and other medications of patients who were referred to the two biggest hospitals in Lithuania.

2. Materials and methods

A cross-sectional study was conducted in two tertiary-care university hospitals in Lithuania (Vilnius University Hospital Santariškių Klinikos and Hospital of Lithuanian University of Health Sciences Kauno Klinikos) between November 2013 and May 2014. The study protocol was approved by the Ethics Committee of Vilnius University Hospital Santariškių Klinikos, and all patients provided written informed consent before enrolment. Consecutive inpatients and outpatients were screened for eligibility on arrival to the hospital. Patients with a diagnosis of AF were included, when the AF episode was present in a 12-lead ECG or episode >30 s in duration was recorded on 24-h Holter. The qualifying episode of AF should have occurred within the last year, before enrolment to the registry. No exclusion criteria were defined in order to minimize selection bias.

2.1. Statistical analysis

Univariate analysis was applied to both continuous and categorical variables. Continuous variables are expressed as a mean (standard deviation). Comparison between groups was made by using the non-parametric Kruskal–Wallis test. Categorical variables are reported in percentages. Comparison between categorical groups was made by using the chi-squared or Fischer exact tests if any expected cell count was <5. For all tests, a P value of less than 0.05 was considered to be significant. Statistical analysis was performed using SPSS 20 software.

3. Results

A total of 575 patients were enrolled, although complete data on the clinical subtype of AF were available for 515 patients (mean age, 70.7 years; mean body mass index, 29.4 kg/m^2; 48.5% were female). As displayed in Table 1, 25.4% of the patients had paroxysmal AF; 25.2%, persistent AF; and 46.6%, permanent AF. 2.7% of the patients had first-time documented AF. There were no significant sex differences comparing the AF subtypes, but patients with paroxysmal AF were younger compared with those with permanent AF (mean age 68 vs. 73 years, $P < 0.05$).

3.1. Associated risk factors, comorbidities and prior interventions

Cardiac risk factors and comorbidities were frequent, irrespective of AF. The most common associated comorbidities were hypertension (85.8%), heart failure (77.9%), and coronary artery disease (CAD) (51.8%) (Table 1). Previous stroke was reported in 19.4% of the whole cohort. Chronic liver or kidney disease was reported in 19.1% (Table 2). Patients with permanent AF more often tended to have had previous embolism, hemorrhagic events, and hypercholesterolemia ($P < 0.05$) comparing with other AF type groups. Pacemaker implantation was performed in 22.4% of the whole group.

3.2. Drug therapy

Patients received therapy that was prescribed by a cardiologist, an internal medicine doctor, or general practitioners. Antithrombotic strategies are summarized in Table 3. Oral anticoagulants (OACs) were used by 53.3% of the patients; vitamin K antagonists (VKAs), most often (95.6%). At the time of inclusion to the survey, anticoagulation therapy in the therapeutic range (international normalized ratio value between 2.0 and 3.0) was documented only in 19.2% of the patients. Non-vitamin K antagonists were used in a minority of patients (dabigatran 2.4%, rivaroxaban 2.0%, and apixaban 0%). Dual antiplatelet therapy was administered to 6.2% of the entire cohort. Aspirin was used in 13.7% and the combination of an OAC and antiplatelet (aspirin or clopidogrel) therapy in 5.4% of the patients. None of the patients received triple therapy.

Amiodarone (14.6%) and propafenone (5.8%) were the most often prescribed antiarrhythmic drugs (AADs) (Table 3). Only 0.5% of the patients used dronedarone. Beta-blockers (59.6%)

Table 1 – Clinical characteristics of the study population.

Characteristic	Whole cohort (*n* = 515, 100%)	First detection (*n* = 14, 2.7%)	Paroxysmal AF (*n* = 131, 25.4%)	Persistent AF (*n* = 130, 25.2%)	Permanent AF (*n* = 240, 46.6%)	*P* value
Demographics						
Age, mean (SD), years	70.7 (11)	68.4 (18)	68.0 (12)	69.2 (11)	73.0 (10)	<0.05
Female gender	48.5	50	52.7	46.2	47.5	NS
Concomitant disease						
Hypertension	85.8	71.4	85.4	86.8	86.7	NS
Coronary artery disease	51.8	42.9	50	54.3	51.7	NS
Myocardial infarction	23.9	42.9	20	21.7	25.4	NS
Pacemaker implantation	22.4	14.2	19.2	22.5	24.6	NS
PTCA	18.5	21.4	20	16.3	18.8	NS
CABG	9.2	–	8.5	5.4	12.1	NS
Chronic heart failure	77.9	53.8	74.6	77.3	81.3	NS
Heart failure NYHA III/IV	64.7	85.7	61.9	60.6	67.6	
Valvular disease	33.7	50	35.7	33.3	31.8	NS
Cardiovascular risk factors						
Hypercholesterolemia	40.3	21.4	50.8	39.5	36.1	<0.05
Current smoking or history of smoking	22	28.6	17.8	25.8	21.8	NS
Diabetes mellitus	20	7.1	13	20.8	24.2	<0.05
COPD	8.2	7.1	6.9	6.2	10	NS
Hypothyroidism	7.4	7.1	9.2	6.9	6.7	NS
Hyperthyroidism	6.6	7.1	7.6	5.4	6.7	NS
Co-morbidities						
Hemorrhagic events	13	21.4	5.3	13.1	16.7	<0.05
Malignancy	12.3	14.3	11.5	10	13.8	NS
Physical examination						
BMI, mean (SD), kg/m^2	29.4 (6.3)	28.4 (4.7)	28.3 (6.0)	30.0 (6.0)	29.6 (6.6)	NS
Systolic BP, mean (SD), mmHg	133 (22)	130 (14)	136 (22)	131 (23)	132 (22)	NS
Diastolic BP, mean (SD), mmHg	79 (12)	79 (9)	81 (12)	78 (12)	78 (12)	NS
Heart rate, mean (SD), beats per min	81 (31)	91 (48)	77 (35)	86 (31)	80 (28)	NS

Values are percentage unless otherwise indicated. PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; BMI, body mass index; BP, blood pressure; AF, atrial fibrillation.

Table 2 – Stroke and bleeding risk factors.

Risk factor	Whole cohort (*n* = 515, 100%)	First detection (*n* = 14, 2.7%)	Paroxysmal AF (*n* = 131, 25.4%)	Persistent AF (*n* = 130, 25.2%)	Permanent AF (*n* = 240, 46.6%)	*P* value
Stroke						
Chronic heart failure	77.9	53.8	74.6	77.3	81.3	NS
Hypertension	85.8	71.4	85.4	86.8	86.7	NS
Age >75 years	41.4	42.9	31.3	35.4	50.0	<0.05
Diabetes mellitus	20	7.1	13.0	20.8	24.2	<0.05
Stroke/TIA	19.4	14.3	13.7	19.2	22.9	<0.05
Age 65–74 years	31.8	7.1	35.8	28.5	32.9	NS
Female gender	48.5	50	52.7	60	47.5	<0.05
CHA_2DS_2-VASc, mean (SD), score	3.97 (1.7)	3.43 (2.4)	3.59 (1.6)	3.78 (1.8)	4.33 (1.6)	<0.05
Bleeding						
Hypertension	85.8	71.4	85.4	86.8	86.7	NS
Liver and or/and kidney disease	19.1	14.3	13.0	16.1	24.2	NS
Previous stroke	19.4	14.3	13.7	19.2	22.9	<0.05
Labile INRs	9.3	0	5.3	12.3	10.4	NS
Elderly (age >65 years)	73.4	57.1	66.4	65.4	82.5	<0.05
Alcohol use	9.8	14.3	14.7	5.4	9.2	NS
HAS-BLED, mean (SD), score	2.25 (1.0)	1.71 (0.8)	1.96 (0.9)	2.17 (1.2)	2.5 (1.1)	<0.05

Values are percentage unless otherwise indicated. TIA, transient ischemic attack; INR, international normalized ratio; AF, atrial fibrillation.

Table 3 – Treatment of the study population.

Treatment	Whole cohort (n = 515, 100%)	First detection (n = 14, 2.7%)	Paroxysmal AF (n = 131, 25.4%)	Persistent AF (n = 130, 25.2%)	Permanent AF (n = 240, 46.6%)	P value
Antithrombotic treatment						
VKA	48.9	28.0	26.0	59.0	45.0	<0.05
INR, 2–3	19.2	0	8.6	20.8	22.2	<0.05
INR, <2	67.4	100	80.0	62.3	65.7	0.05
INR, >3	13.4	0	11.4	16.9	12.0	NS
ASA	13.7	21.4	26.9	13.3	5.0	<0.05
Clopidogrel	2.0	0	2.3	1.6	2.1	NS
Dual antiplatelet treatment	6.2	0	10.8	3.9	5.5	NS
Dabigatran	2.4	0	0	11.3	0.8	–
Rivaroxaban	2.0	0	1.0	5.6	1.5	–
Apixaban	0	0	0	0	0	–
Low-molecular weight heparin	8.0	21.4	8.4	6.9	7.5	NS
Unfractionated heparin	1.7	0	3.8	1.5	0.8	NS
Antiarrhythmic treatment						
Antiarrhythmic	20.9	21.4	32.1	28.1	10.8	<0.05
Amiodarone	14.6	21.4	19.8	18.8	9.2	<0.05
Propafenone	5.8	0	11.5	8.6	1.7	<0.05
Dronedarone	0.5	0	0.8	0.8	0	–
Other treatments						
BAB	59.6	42.9	61.8	57.0	60.8	NS
ACE inhibitors	53.0	35.7	58.0	55.4	50.0	NS
Diuretics	49.7	14.3	34.4	49.2	60.4	<0.05
ARBs	23.9	28.6	24.4	16.9	27.1	NS
Statin	18.8	14.3	27.5	19.2	14.2	<0.05
Calcium channel blockers	16.3	14.3	16.8	16.9	15.8	NS
Digoxin	10.7	7.1	3.8	4.6	17.9	<0.05

Values are percentages. VAK, vitamin K antagonist; INR, international normalized ratio; ASA, acetylsalicylic acid; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; AF, atrial fibrillation.

and non-dihydropyridine calcium-channel blockers (16.3%) were used more often as rate control agents than digoxin (10.7%).

3.3. *Stroke and bleeding risk factors*

Table 2 summarizes the most common risk factors for stroke and bleeding as well as the stroke and bleeding risk profile of the study population. The mean CHA_2DS_2-VASc score was 3.97 (SD, 1.6) and the mean HAS-BLED was 2.25 (SD, 1.0), with the highest risk observed in patients with permanent AF. More than 10% of the patients experienced bleeding complications.

The proportions of OAC use by the CHA_2DS_2-VASc score are shown in Fig. 1, which shows VKA use in more than 50%, with each score pointed between CHA_2DS_2-VASc 1 and 8. Only 25% of the patients with a CHA_2DS_2-VASc score of 9 used VKA,

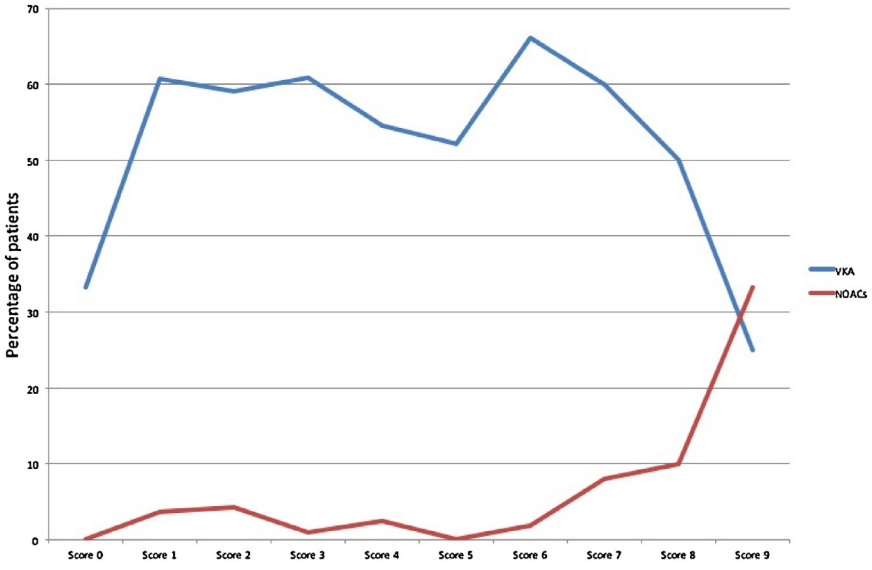

Fig. 1 – Proportions of patients treated with antithrombotic drugs by CHA_2DS_2-VASc score.

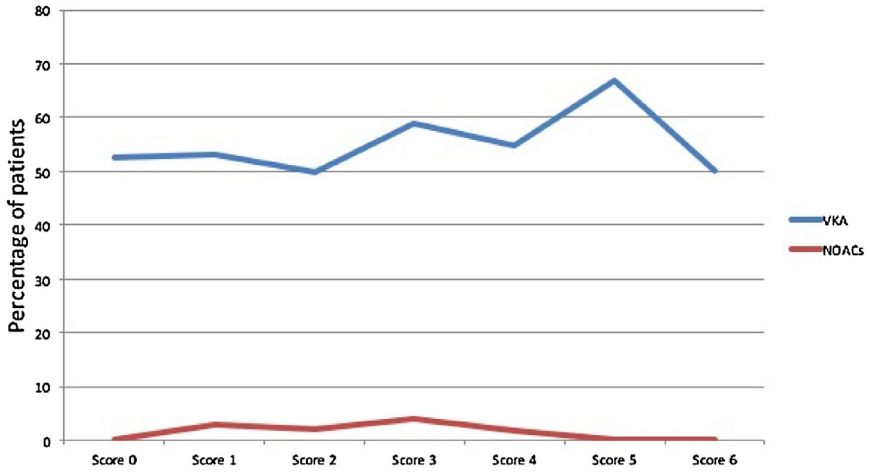

Fig. 2 – Proportions of patients treated with anticoagulant drugs by HAS-BLED score.

whereas the use of a non-vitamin K antagonist was more frequent in those patients.

Fig. 2 displays OAC use according to the HAS-BLED score. There were no particular differences in OAC usage between the groups respective to the bleeding score.

4. Discussion

Our survey provides an important and contemporary view of AF epidemiology and management for the AF population in Lithuania. Data derived from this survey can be used as a baseline for outcome analysis at follow-up, and as a benchmark for future studies.

Patients enrolled in this survey were comparable according to the age of patients in the ATRIUM survey (71.9 ± 9.2 years), Euro Heart Survey (69 ± 10 years), or AFNET study (67 ± 13 years). A large proportion (46.6%) of our patients had permanent AF, which was higher than in the ATRIUM (43%), AFNET (33%), and Euro Heart Survey (29%), and the results were quite different compared to the EORP-AF registry, where the majority (30.3%) of patients suffered from first-time detected AF [9–13].

AF is an arrhythmia that is generally associated with many other cardiac and noncardiac disorders. Based on data from other surveys and registries, hypertension is established as the most common cardiovascular disease [9]. Our data show that hypertension, chronic heart failure (CHF), and coronary heart disease remain common comorbidities in patients with AF. The most frequent cardiovascular risk factors were current or previous smoking, hypercholesterolemia, and diabetes mellitus. The close relationship of AF with concomitant diseases and cardiovascular risk factors is also evident and was noted in the Euro-Heart survey, ATRIUM, AFNET, and EORP-AF registries [10–13].

The data from our survey showed that amiodarone was the most commonly used AAD (14.6%), followed by propafenone (5.8%). Similar data have been found in the AFNET registry [10]. Interestingly, that except from a very small group of patients who were taking dronedarone (0.5%), there was no single patient receiving Class III agent sotalol, probably because this agent is not presented in Lithuania due to marketing reasons despite recommendations and antiarrhythmic effects. The great majority of patients received rate control agents. The type of rate control therapy was similar with the EORP-AF survey, where nearly two-thirds of patients received beta-blockers and as much as 10.0% received digitalis [9].

The ESC Guidelines advocate the initial identification of ''truly low-risk'' patients for stroke and bleeding risk assessment based on (CHA_2DS_2-VASc) and (HAS-BLED) clinical scores. For patients with a CHA_2DS_2-VASc score of 0, who are at low risk, with none of the risk factors, no antithrombotic therapy is recommended, whereas patients with a CHA_2DS_2-VASc score ≥ 2 should be anticoagulated taking into account a HAS-BLED risk score [14]. Most of the guidelines recommend that when oral anticoagulation is indicated, a non-vitamin K antagonist should be considered instead of VKAs, given the greater efficacy, safety, and convenience of a non-vitamin K antagonist compared with VKAs [15]. Our registry showed that anticoagulants were used in 53.3% of the patients and this is much less than in EORP-AF registry where anticoagulants were used in 80%. The low VKA usage is difficult to explain, considering that the mean CHA_2DS_2-VASc risk evaluation score was 3.97 and the mean HAS-BLED risk score of 2.25, whereas the CHA_2DS_2-VASc and HAS-BLED risk scores in EORP-AF registry were 3.24 and 1.37, respectively. It is also worth noting that just a small proportion (19.2%) of the patients had an international normalized ratio (INR) value within the therapeutic range between 2.0 and 3.0.

According to the current AF treatment guidelines, aspirin usage for stroke prevention is weak, with potential for harm [16,17]; therefore, it is not recommended regardless of stroke risk [2]. Meanwhile, results from our study showed that only a minority from our patients were treated with aspirin. A large proportion of patients (one third) received dual antiplatelet treatment. This drug combination has additional efficacy compared with aspirin monotherapy, but also has an additional risk for major bleeding [18]. Anticoagulants signifi-

cantly reduce the risk of stroke compared to placebos. An adjusted dose of VKA was associated with the relative risk reduction of ischemic strokes in 67% of patients. Moreover, the all-cause mortality was significantly reduced (26%) by adjusted-dose VKA vs. control [8].

4.1. *Study limitations*

The current snapshot of AF epidemiology and management might be prone to bias due to the absence of randomization. Due to the survey design, only patients after primary selection and coming to biggest university hospitals where included, and consequently, they could differ from the primary population with AF subjected to the treatment in regional hospitals and outpatient institutions. According to our data, which are only instant picture of patients with AF, it would be difficult to speculate about follow-up, progression of paroxysmal type AF to persistent and permanent AF, continuous usage of anticoagulants or the thromboembolism event rate in inadequately treated patents. Moreover, this observational study did not include data of medical or electrical cardioversion, likewise AF ablations. Also there are no scientific papers about data in Lithuania concerning how many patients with AF are under OACs. A special dedicated registry should be implemented to answer this kind of questions.

5. Conclusions

Our study showed that non-vitamin K antagonists are rarely used drugs. However, when the patient has a high thromboembolic risk score, the incidence of non-vitamin K antagonist usage is going to increase. Probably, while these drugs will not be compensated for by local health institutions, it would be unrealistic to expect higher usage of those drugs.

Also it is worth noting that the HAS-BLED score is still not a popular bleeding risk assessment score among primary and secondary health care specialists. As we can see from the data of our study, in everyday clinical practice, there is no difference in OACs usage in different bleeding risk score groups.

Compliance with the current guidelines remains suboptimal in Lithuania. Therefore, better education is needed for both physicians and patients in order to achieve better treatment results.

Conflict of interest

The authors declare no conflict of interest.

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