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Cardioversion differences among first detected episode, paroxysmal, and persistent atrial fibrillation patients in the RHYTHM AF registry in Poland

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Abstract

Background: *The aim of the publication is to show differences among patients with the first detected episode of atrial fibrillation (AF), paroxysmal, and persistent AF patients, for whom cardioversion was planned in the hospital setting in Poland.*

Methods: *We present an analysis of the Polish cohort of the multicenter, multinational RHYTHM-AF registry. Consecutive patients in the hospital setting, aged ≥ 18 years, with documented AF at the time of enrollment, and for whom cardioversion of AF is one of the planned therapeutic options were recruited. Follow-up data was collected 60 days after enrollment.*

Results: *Five-hundred-and-one patients were recruited, 483 with a defined AF type: 88 — first detected, 191 paroxysmal, and 204 persistent AF. CHA_2DS_2VASc scores were not significantly different between the groups, while treatment with vitamin K antagonists (VKA) was significantly lower in paroxysmal AF group than in persistent AF patients. Primary electrical cardioversion was most commonly performed in patients with persistent AF (90.4%), while primary pharmacological cardioversion — in the first detected AF (80.0%) and paroxysmal AF patients (76.7%). During 2 months of follow-up, the rate of rehospitalization and complications was comparable among the groups.*

Conclusions: *Despite their comparable CHA_2DS_2VASc scores, patients with persistent AF were more frequently treated with VKA antagonists than other groups. Recurrence of AF within 2 months after restoring sinus rhythm was present in about 25% of the patients, and the rate of complications was not different among the three groups.* (Cardiol J 2015; 22, 4: 453–458)

Key words: atrial fibrillation, cardioversion, registry

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice. Its prevalence increases with age. It has been estimated that over 6 million people in the European Union have AF [1]. AF significantly increases the risk of stroke and decreases the quality of life [2]. The risk of death from AF-related stroke is doubled and the cost of care is increased 1.5-fold [1]. The risk of

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death is increased two times in AF, independently of other known predictors of mortality [3].

The natural course of AF starts with the first detected episode, then the majority of patients AF is paroxysmal and within a few years AF becomes persistent (intermitted with cardioversion) or permanent (when cardioversion is no longer planned) [1].

The aim of our publication is to show differences among three groups of patients, those with the first detected episode of AF, paroxysmal, and persistent AF, for whom cardioversion is planned in the hospital setting in Poland.

Methods

Study design

RHYTHM-AF is a prospective observational study in 10 countries: Australia, Brazil, France, Germany, Italy, Netherlands, Poland, Spain, Sweden, and the United Kingdom. Patients with recent onset AF considered for cardioversion were enrolled from participating hospitals and acute care centers between May 2010 and June 2011 [4, 5]. General characteristics of the Polish population and major results have been reported [6, 7]. Here we present analysis of the results in Poland by AF type.

Study population

Centers recruiting patients were selected to be representative of those treating AF in participating countries. All patients at least 18 years old with documented AF as confirmed by electrocardiogram and in whom a cardioversion was one of the planned therapeutic options were considered for the study. They included patients in whom actions were undertaken in anticipation of cardioversion (e.g., scheduled cardioversion, anticoagulation, oral loading) and for whom informed consent was obtained. Only patients who were already enrolled in the current trial, enrolled in a separate trial, and those with atrial flutter were excluded.

Primary pharmacological cardioversion (PCV) was considered successful if sinus rhythm (SR) or atrial rhythm was obtained within 24 h after its initiation. Primary electrical cardioversion (ECV) was defined as successful if SR was obtained and maintained for at least 10 min after the last shock. The definitions of first detected episode, paroxysmal and persistent AF were according to current guidelines [1].

All patient data were collected via a remote web-based data collection form using the multilingual software solution EBogen© developed by the IHF Ludwigshafen, Germany (the coordinating center for the study).

Statistical analysis

All data are presented as mean and standard deviation, median and interquartile range or number and percentage of the population, depending on the characteristic of the parameter. All comparisons were made using χ^2 or Mann-Whitney-Wilcoxon tests. Because of multiple comparisons (about 50) Bonferroni correction was applied, we considered a p value < 0.001 statistically significant.

Results

Five-hundred-and-one patients were included in the analysis, 483 of whom had a defined AF type: 88 had the first detected episode of AF, 191 paroxysmal AF, and 204 persistent AF. The characteristics of the study group, stratified by AF type are shown in Table 1. Patients with persistent AF were younger and less frequently female. Concomitant diseases were not different except for history of heart failure (most frequent in patients with persistent AF). CHA_2DS_2VASc scores were slightly different among the three groups, with the lowest scores in persistent AF patients. Treatment with vitamin K antagonists (VKA) was significantly less frequently applied in the paroxysmal AF group than in the persistent AF patients. AF as the primary reason for admission was less frequent in the first detected episode group — in this group acute coronary syndrome as the primary reason for admission was more frequent than in other groups.

An overview of the AF characteristics is shown in Table 2. A lack of AF symptoms was most common in persistent AF (20.1%), on the other extreme, only 6.8% of patients with paroxysmal AF had no symptoms. Palpitations and chest pain were most prevalent in the paroxysmal AF group, while fatigue — in persistent AF. The mean frequency of dizziness was 9.2% in the whole cohort and was not significantly different among groups.

Selected additional parameters are shown in Table 3. Notably potassium level was significantly different among groups, with the highest value in persistent AF patients (still potassium level was within normal range among the three groups of patients).

Cardioversion data are shown in Table 4. Time to first cardioversion was the longest in persistent AF patients. Primary ECV was applied to the highest proportion of patients with persistent AF (90.4%), while primary PCV — to first-detected AF (80.0%) and paroxysmal AF patients (76.7%).

Table 1. Baseline characteristics of the registry group.

	Total (n = 501)	First detected (n = 88)	Paroxysmal (n = 191)	Persistent (n = 204)	P
Age*	64.2 ± 12.1	65.2 ± 13.2	66.8 ± 12.0	61.9 ± 11.4	< 0.0001
Women	193 (38.5)	36 (40.9)	92 (48.2)	59 (28.9)	< 0.001
BMI*	29.1 ± 4.6	29.2 ± 5.1	28.6 ± 4.3	29.6 ± 4.6	0.22
Hypertension	375 (75.0)	65 (73.9)	153 (80.5)	144 (70.6)	0.07
Diabetes	104 (20.8)	22 (25.0)	34 (17.8)	41 (20.1)	0.38
Hyperlipidemia	238 (52.3)	38 (48.7)	91 (54.5)	102 (52.8)	0.70
Previous MI	80 (16.0)	14 (15.9)	36 (18.8)	28 (13.7)	0.38
Heart failure	120 (24)	10 (11.4)	36 (18.8)	64 (31.4)	< 0.001
Valvular heart disease	90 (18.5)	9 (10.6)	28 (15.5)	45 (22.2)	< 0.05
CHADS2 score*	1.5 ± 1.0	1.4 ± 1.1	1.5 ± 1.0	1.4 ± 0.9	0.59
CHA2DS2-VASc score*	2.7 ± 1.7	2.6 ± 1.7	3.0 ± 1.8	2.3 ± 1.5	< 0.01
VKA treatment	294 (58.7)	7 (8.0)	101 (52.9)	175 (85.8)	< 0.0001
Ventricular rate at enrollment**	105 (86–130)	120 (100–140)	120 (100–130)	90 (75–110)	< 0.0001
Primary reason for admission:					
AF	403 (80.4)	55 (62.5)	158 (82.7)	176 (86.3)	< 0.0001
ACS	23 (4.6)	14 (15.9)	7 (3.7)	2 (1.0)	< 0.0001

*Mean ± standard deviation; **Median (interquartile range); data are shown as numbers (%); AF — atrial fibrillation; ACS — acute coronary syndrome; BMI — body mass index; MI — myocardial infarction; VKA — vitamin K antagonists

Table 2. Atrial fibrillation (AF) characteristics of the registry group.

	Total (n = 501)	First detected (n = 88)	Paroxysmal (n = 191)	Persistent (n = 204)	P
Time since first AF episode*	1,201.5 (269.0–3,551.0)	NA	1,423.0 (423.0–3,993.0)	988.0 (237.5–2,748.0)	NA
Duration of current episode*	1.0 (0.0–58.0)	0.0 (0.0–2.0)	0.0 (0.0–1.0)	79.5 (32.5–211.5)	< 0.0001
Symptoms:					
No symptoms of AF	71 (14.2)	13 (14.8)	13 (6.8)	41 (20.1)	< 0.001
Shortness of breath	157 (31.3)	29 (33.0)	55 (28.8)	65 (31.9)	0.72
Fatigue	197 (39.3)	23 (26.1)	61 (31.9)	108 (52.9)	< 0.0001
Palpitations	317 (63.3)	54 (61.4)	150 (78.5)	105 (51.5)	< 0.0001
Chest pain	84 (16.8)	20 (22.7)	46 (24.1)	13 (6.4)	< 0.0001
Dizziness	46 (9.2)	8 (9.1)	21 (11.0)	16 (7.8)	0.56

*Median (interquartile range); data are shown as numbers (%); NA — not applicable

Table 3. Additional tests (echocardiography, laboratory measurements).

	Total (n = 501)	First detected (n = 88)	Paroxysmal (n = 191)	Persistent (n = 204)	P
Potassium	4.3 (4.0–4.6)	4.2 (3.9–4.6)	4.2 (3.9–4.5)	4.4 (4.1–4.6)	< 0.001
TSH	1.4 (0.8–2.1)	1.2 (0.8–1.6)	1.3 (0.7–2.1)	1.4 (1.0–2.3)	< 0.05
LA [mm]	44.0 (40.0–47.0)	43.0 (38.0–46.0)	43.0 (38.0–46.0)	45.0 (41.0–47.0)	< 0.05
LVEF < 45%*	73/358 (20.4)	16/77 (20.8)	12/112 (10.7)	37/154 (24.0)	< 0.05

*Number/number of patients with echocardiography data (%); data are shown as median (interquartile range) or number (%); LA — left atrium, LVEF — left ventricular ejection fraction; TSH — thyroid-stimulating hormone

Table 4. Cardioversion details and reasons for no cardioversion attempt.

	Total (n = 294)	First detected (n = 55)	Paroxysmal (n = 116)	Persistent (n = 115)	P
Patients with any CV	294 (58.7)	55 (62.5)	116 (60.7)	115 (56.4)	0.53
Time to first CV [h]*	9:55 (1:48–30:37)	4:07 (1:17–27:28)	2:29 (0:43–22:20)	24:25 (8:42–40:14)	< 0.0001
Primary ECV	148 (50.3)	11 (20.0)	27 (23.3)	104 (90.4)	< 0.0001
Primary ECV successful	131 (88.5)	11 (100)	24 (88.9)	90 (86.5)	0.42
Primary PCV	146 (49.7)	44 (80.0)	89 (76.7)	11 (9.6)	< 0.0001
Primary PCV successful	110 (75.3)	39 (88.6)	64 (71.9)	6 (54.5)	<0.05
No CV attempt	n = 207	n = 33	n = 75	n = 89	
Reasons**:					
Spontaneous SR	55 (26.6)	12 (36.4)	37 (49.3)	5 (5.6)	< 0.0001
Left atrial thrombus	16/124 (13.7)	1/4 (25.0)	0 (0.0)	14/79 (17.7)	< 0.05
Spontaneous echocontrast	5 (2.4)	0 (0.0)	0 (0.0)	5 (5.6)	< 0.05
Size of LA	8 (3.9)	0 (0.0)	1 (1.3)	4 (4.5)	0.26
Duration of AF uncertain	27 (13.0)	10 (30.3)	3 (4.0)	13 (14.6)	< 0.001
Planned CV after discharge	92 (44.4)	16 (48.5)	24 (32.0)	51 (57.3)	< 0.01
Refused by patient	6 (2.9)	1 (3.0)	1 (1.3)	2 (2.2)	0.83
Procedure expected to be ineffective	13 (6.3)	0 (0.0)	2 (2.7)	7 (7.9)	0.11
Other reason	26 (12.6)	5 (15.2)	9 (12.0)	10 (11.2)	0.89

*Median (interquartile range); **Choosing more than one option was available; data are shown as numbers (%); AF — atrial fibrillation; CV — cardioversion; ECV — electrical cardioversion; LA — left atrium; PCV — pharmacological cardioversion; SR — sinus rhythm

Table 5. Discharge and follow-up data.

	Total (n = 501)	First detected (n = 88)	Paroxysmal (n = 191)	Persistent (n = 204)	P
Duration of hospital stay [h]*	69:00 (27:25–120:20)	75:22 (43:34–157:14)	67:18 (12:12–93:04)	68:17 (48:52–121:20)	< 0.001
VKA treatment at discharge	388 (77.4%)	37 (42.0%)	142 (74.3%)	194 (95.1%)	< 0.0001
Amiodarone at discharge	71 (14.2%)	8 (9.1%)	23 (12.0%)	38 (18.6%)	0.05
Propafenone at discharge	106 (21.2%)	12 (13.6%)	53 (27.7%)	40 (19.6%)	< 0.05
Sotalol at discharge	24 (4.8%)	0 (0.0%)	14 (7.3%)	9 (4.4%)	< 0.05
Rhythm at discharge — SR	348 (69.5%)	65 (73.9%)	161 (84.3%)	114 (55.9%)	< 0.0001
Rhythm at discharge — AF	140 (27.9%)	20 (22.7%)	25 (13.1%)	86 (42.2%)	< 0.0001
Follow-up:					
Current rhythm — SR	352 (71.0%)	67 (77.0%)	162 (85.7%)	114 (56.4%)	< 0.0001
Current rhythm — AF	137 (27.6%)	19 (21.8%)	26 (13.8%)	84 (41.6%)	< 0.0001
Recurrence of AF	127 (25.4%)	12 (13.6%)	67 (35.1%)	47(23.2%)	< 0.001
Rehospitalization	96 (19.2%)	13 (14.8%)	53 (27.7%)	29 (14.3%)	< 0.01
VKA treatment	382 (76.6%)	33 (37.5%)	142 (74.7%)	192 (94.6%)	< 0.0001
Aspirin	149 (29.9%)	53 (60.2%)	53 (27.9%)	39 (19.3%)	< 0.0001
Clopidogrel	41 (8.2%)	19 (21.6%)	11 (5.8%)	11 (5.4%)	< 0.0001
Amiodarone	70 (14.0%)	9 (10.2%)	22 (11.6%)	37 (18.2%)	0.09
Propafenone	102 (20.4%)	11 (12.5%)	53 (27.9%)	37 (18.2%)	< 0.01
Sotalol	24 (4.8%)	0 (0.0%)	13 (6.8%)	10 (4.9%)	< 0.05

*Median (interquartile range); AF — atrial fibrillation; SR — sinus rhythm; VKA — vitamin K antagonists

Spontaneous occurrence of SR was most prevalent in the paroxysmal AF group (almost 50% of the patients that had not undergone cardioversion, 19.1% of the whole group of paroxysmal AF), while it was present in only 2.5% of the whole group of persistent AF.

Discharge and follow-up data are shown in Table 5. Hospital stay was the longest in patients with the first detected episode of AF. SR at discharge was most common in the paroxysmal AF group (84.3%), and the least common in the persistent AF (55.9%). VKA treatment at discharge was most common in the persistent AF group. After 2 months of follow-up the trends in SR maintenance and in VKA treatment were the same. Of note is that treatment with VKA markedly increased in all three groups (first detected, paroxysmal, and persistent AF) comparing baseline vs. discharge and follow-up. Patients with the first detected episode had the highest frequency of aspirin and clopidogrel treatment. Treatment with antiarrhythmic IC and class III drugs was not different among group. The rate of rehospitalization was comparable, with a trend towards a higher frequency in paroxysmal AF (more than 25% of patients within 2 months). Recurrence of AF was most common in patients with paroxysmal AF (35.1%), and the least frequent in patients with the first detected episode of AF (13.6%).

The rate of adverse events during hospitalization was comparable among the three groups, with sporadic events like myocardial infarction, pulmonary embolism, transient ischemic attack, or heart failure (1 or 2 patients in the whole group). During the 2 months of follow-up the overall frequency of adverse events was low, with 3 strokes, 5 bleeding incidents, and 5 incidents of heart failure, with no differences among the groups.

Discussion

The multicenter, prospective RHYTHM AF registry has demonstrated that cardioversion of AF in real-life patients has a high success rate. The characteristics of the whole Polish cohort of RHYTHM AF registry has been published before [5, 6]. Here we looked for possible differences among three subgroups of these patients, the ones with the first detected, paroxysmal, and persistent AF.

The foremost difference was the one in the VKA treatment. The distribution of risk factors was almost uniform among analyzed subtypes of AF, but the patients with persistent AF were younger and the prevalence of men over women was much higher than in the other groups — that explains why despite the same $CHADS_2$ score, there was a trend towards a lower CHA_2DS_2-VASc score in the persistent AF patients. They were also significantly more frequently treated with VKA than the paroxysmal AF patients were. Based on the CHA_2DS_2-VASc score (mean value 2.3 ± 1.5) one can assume that persistent AF patients were treated correctly, but the paroxysmal AF patients were markedly undertreated with VKA. A similar trend was observed in the Polish cohort of the RecordAF registry [8]. The difference between the rhythm control and rate control strategy patients in their $CHADS_2$ score (score 2 or more: 31.1% vs. 47.8% respectively) was much lower than the difference in the VKA treatment frequency (40.3% vs. 80.4%). Such a phenomenon has already been observed in the Euro Heart Survey on Atrial Fibrillation — physicians tend to weigh the perceived AF burden when deciding on antithrombotic treatment [9]. This strategy (i.e., refraining from antithrombotic treatment) is discouraged by the current guidelines but the problem persists. In our cohort, treatment with VKA in all groups is markedly higher comparing baseline vs. discharge and follow-up — this might suggest that physicians in the hospitals are more adherent to the guidelines than cardiologists in the outpatient clinics.

Another important difference among the patients with first detected, paroxysmal, and persistent AF was in the symptoms of AF. About 20% of patients with persistent AF showed no symptoms of AF, as opposed to only 6% of patients with paroxysmal AF. Those results resemble closely the ones reported in RecordAF registry — in the group of rhythm control strategy 92.4% of patients had symptoms, while in the group of rate control strategy — 81.5% [8]. Nevertheless, these data still should be interpreted with caution: symptomatic patients are substantially more likely to be admitted to the hospital to undergo cardioversion.

Palpitations and chest pain were frequent in the patients with the first detected episode and those with paroxysmal AF, while fatigue was reported by about half of the patients with persistent AF. Compared to the present cohort, in a large retrospective analysis of patients with AF consulted in an Emergency Department, the frequency of chest pain was comparable (15%), shortness of breath was slightly less common (20.7% vs. 31.3% in our cohort), while frequency of fatigue was four times less common (9.4% vs. 39.3%) [10].

As could be expected, pharmacological cardioversion was the most common option used in

paroxysmal and first detected AF, while ECV — in persistent AF. This is in agreement with the current guidelines [1] and the results of Euro Heart Survey [11]. Spontaneous SR restoration was reported in about 20% of patients with paroxysmal AF, while only in 2.5% of patients with persistent AF. Since the first detected episode of AF could be paroxysmal or persistent, the frequency of spontaneous SR restoration in that group was somewhere between those for paroxysmal and persistent groups — almost 14%. Those rates were similar to the ones published so far [12, 13].

Patients with the first detected episode of AF had a longer hospital stay and a higher frequency of aspirin and clopidogrel use — acute coronary syndrome as a triggering factor and the primary cause of hospitalization was relatively common in those patients.

At discharge SR was present in about 70% of all patients, but in only 55.9% of patients with persistent AF. During 2 months of follow-up recurrence of AF was observed in about 25% of patients — the rate comparable to previous results [14], and the frequency of rehospitalization was about 19% in the whole group (27.7% in the paroxysmal AF) — in one of the earlier studies 33–35% of patients had recurrent visits on Emergency Department during a 6-months of follow-up [15]. In the Euro Heart Survey on Atrial Fibrillation registry, the rate of rehospitalization within 1 year was between 41% (first detected AF episode) and 54% (paroxysmal AF) [9].

Limitations of the study

Small sample size and crude, unadjusted analyses are the major limitations of our study. Follow-up period was very short (the registry was planned majorly for baseline and hospitalization characteristics of patients with AF for whom cardioversion was planned). The observations should be therefore interpreted with caution.

Conclusions

Patients with persistent AF were younger and the ratio of men to women was significantly higher than in other groups. Despite comparable CHA_2DS_2-VASc scores, patients with persistent AF were at all time-points (admission, discharge, follow-up) more frequently treated with VKA antagonists than the other groups were. Primary ECV was most commonly applied to patients with persistent AF, primary PCV — to first detected AF and paroxysmal AF patients. Recurrence of AF within 2 months after restoring SR was present in about 25% of the patients, and even in the first detected episode group it occurred in more than 10% of patients. The results show that in an unselected group of patients with AF, anticoagulant treatment is still substantially less common than recommended by current guidelines.

Conflict of interest: P. Włodarczyk — Employee of MSD Poland.

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