ORIGINAL ARTICLE

Epidemiology and management of coexisting heart failure and atrial fibrillation in an outpatient setting

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KEY WORDS

atrial fibrillation, epidemiology, heart failure, treatment

ABSTRACT

INTRODUCTION Atrial fibrillation (AF) is the most common arrhythmia complicating heart failure (HF). The coexistence of these diseases may be partially explained by the presence of common risk factors. Although the effect of AF on the prognosis in HF is still debatable, it is associated with specific complications and affects therapy.

OBJECTIVES The aim of this analysis was to evaluate epidemiology and management of coexisting HF and AF among Polish outpatients.

PATIENTS AND METHODS The present study was performed within the framework of the Polish National Cardiovascular Disease Prevention and Treatment Program, POLKARD 2003–2005, and included patients with HF treated in a representative number of 400 outpatient clinics. Data was collected using questionnaires and included demographic characteristics as well as information about coexisting diseases and treatment, provided by patients and physicians on the basis of the available medical records.

RESULTS The study involved 3682 patients with HF (mean age 67.1 ±11.7 years; 58% of patients were men). AF was present in 38% of the patients. The prevalence of arrhythmia increased with the New York Heart Association class. We observed significant differences between the subgroups of patients with AF and those with sinus rhythm in terms of demographic parameters, risk factors, concomitant diseases, and therapy. Although the use of angiotensin-converting enzyme inhibitors and β-blockers was significantly lower in the subgroup with AF, a multivariable analysis showed that it was associated with specific demographic characteristics and comorbidities rather than with arrythmia itself. Specialty patient care was associated with increased use of therapy aimed to improve the prognosis of HF patients.

CONCLUSIONS Patients with AF constitute a particular subgroup within the population of patients with HF. A specific distribution of risk factors with a significant effect of noncardiac diseases may confound HF therapy in this patient group. Specialty care may be able to optimize treatment in patients with coexisting HF and AF.

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Received: September 22, 2011.
Revision accepted: November 11, 2011.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2011; 121 (11): 392-399

INTRODUCTION Atrial fibrillation (AF) is the most common arrhythmia complicating the course of heart failure (HF). In the developed countries, HF became the most important risk factor of AF, increasing its prevalence about 5-fold both in the case of systolic and diastolic left ventricular dysfunction.[1,2] The coexistence of HF and AF may be partially explained by the presence of common risk factors such as age, hypertension, diabetes, obesity, valvular dysfunction, and coronary artery disease with concomitant electrophysiological and neurohormonal abnormalities.[3-6]

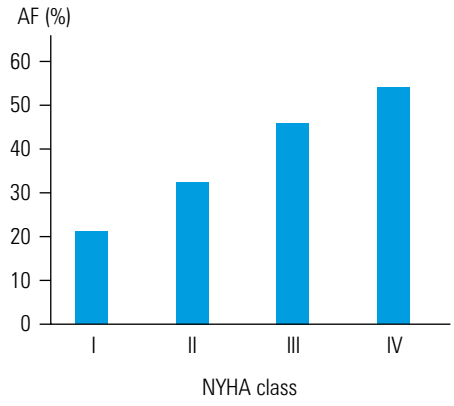

FIGURE The prevalence of atrial fibrillation (AF) in the studied population depending on New York Heart Association (NYHA) functional status

The prevalence of AF increases with the New York Heart Association (NYHA) class and ranges from 5% in asymptomatic patients to more than 50% in patients in NYHA class IV.[7,8] The onset of AF may aggravate the signs and symptoms of HF and requires changes in short- and long-term therapy. The effect of AF on the prognosis in HF is still debatable: increasing evidence demonstrates unfavorable impact of AF; on the other hand, there have been reports showing that AF is not an independent risk factor of HF.[9-12]

The above controversy may be partly explained by complex epidemiology of HF and AF coexistence that involves bilateral self-perpetuating pathomechanisms, the presence of concomitant diseases, specific complications, and differences in therapy. Of note, subgroups of patients with AF, especially older patients, were inadequately represented or simply excluded from clinical prospective randomized trials.[13]

The objective of this analysis was to evaluate the prevalence and management of coexisting HF and AF among Polish outpatients.

PATIENTS AND METHODS The present study was performed within the framework of the National Cardiovascular Disease Prevention and Treatment Program, POLKARD 2003–2005, as part of the evaluation of HF diagnosis and therapy in Poland. The methodology of this evaluation is described in detail elsewhere.[14] The present analysis was based on the data from outpatient clinics and included patients treated by general practitioners (GPs) or specialists.

The selection of participating centers was designed to obtain a representative sample. Randomization among outpatient clinics was based on the governmental registration list, and a representative number of 400 clinics was drawn. The last 5 patients from each unit with diagnosis of HF entered the study. The choice of 400 specialists working in outpatient departments was not random – they were indicated by the GPs included in the study as their consultants.

The survey method was based on questionnaires to be completed by doctors and patients, and included demographic data as well as information about coexisting diseases and treatment. The data concerning several concomitant diseases, cardiovascular risk factors, and patients' treatment were provided by physicians based on medical records.

Statitical analysis Univariate analyses and multivariable logistic regression were used to identify important factors associated with AF presence and the therapy used. In a univariate analysis, the *t* test was used for continuous variables and the χ^2 test for qualitative variables. The logistic regression models were used to identify factors associated with the use of angiotensin-converting enzyme inhibitors (ACEIs) and β-blockers. All analyses were performed using the SAS software version 9.1 (SAS Institute Inc., Cary, North Carolina, United States).

RESULTS Of 3980 patients included in the registry, we used the data of 3682 patients with known status of heart rhythm. Mean age of the patients was 67.1 ±11.7 years; 58% were men. AF was observed in 38% of the patients, and its prevalence increased with the NYHA class: 21% for NYHA I, 32% – NYHA II, 46% – NYHA III, and 54% – NYHA IV (FIGURE 1).

The univariate analysis showed that patients with HF and AF differed significantly from those with sinus rhythm in terms of demographic characteristics, the prevalence of common risk factors, and concomitant diseases. Patients with AF were older and included mostly women. They had lower rate of hypercholesterolemia, coronary artery disease, history of myocardial infarction (MI), or coronary revascularization. On the other hand, AF patients more often suffered from valvular heart disease and noncardiac diseases, such as chronic pulmonary diseases, anemia, renal insufficiency, thyroid diseases, and stroke (TABLE 1).

We observed significant differences between patients with AF and those with sinus rhythm in terms of the access to specialty care and in the prevalence of major drugs used in HF therapy. Patients with AF were more often treated with diuretics (including spironolactone), digoxin, amiodarone, acenocoumarol, and angiotensin receptor blockers (ARBs). They less frequently used specialty care and were less frequently treated with ACEIs, β-blockers, and statins (TABLE 1).

To explain the phenomenon of ACEI and β-blocker underuse in the subgroup of patients with AF, we prepared 2 models of multivariate logistic regression including age, sex, AF, other concomitant diseases, concomitant drugs, and access to specialty care. We found that the presence of AF was not an independent predictor affecting the use of ACEIs and β-blockers (TABLES 2, 3). Lower use of ACEIs and β-blockers – essential in HF treatment – in patients with AF was explained by specific demographic characteristics and the type of concomitant disease and therapy. Another important predictor of ACEI and β-blocker underuse was lack of specialty care.

TABLE 1 Demographic characteristics, comorbidity, risk factors, and treatment in the population of outpatients with heart failure with or without atrial fibrillation

		AF [–] n = 2279	AF [+] n = 1403	*P*
age, mean ±SD		65.4 ±11.9	69.8 ±10.9	< 0.0001
men, n (%)		1400 (61.4)	748 (53.3)	<0.0001
CHD, n (%)		1891 (84.3)	1020 (75.0)	<0.0001
history of MI, n (%)		1071 (47.9)	403 (30.3)	<0.0001
history of revascularization, n (%)		657 (28.8)	178 (12.7)	<0.0001
valvular heart disease, n (%)		360 (16.2)	452 (33.7)	<0.0001
thyroid diseases, n (%)		191 (8.5)	206 (15.3)	<0.0001
history of stroke or TIA, n (%)		257 (11.4)	267 (19.8)	<0.0001
COPD or asthma bronchiale, n (%)		371 (16.4)	302 (22.3)	<0.0001
anemia, n (%)		125 (5.6)	104 (7.7)	<0,05
renal failure, n (%)		186 (8.3)	153 (11.4)	<0.05
peripheral arterial disease, n (%)		528 (23.8)	373 (28.0)	<005
hypercholesterolemia, n (%)		528 (23.8)	373 (28.0)	<0.05
hypertension, n (%)		1783 (78.7)	1066 (77.0)	NS
diabetes, n (%)		623 (27.6)	405 (29.7)	NS
obesity, n (%)		901 (39.9)	520 (37.8)	NS
NYHA class, n (%)	I	122 (5.4)	33 (2.4)	<0.0001
	II	1275 (56.0)	599 (42.7)	
	III	794 (34.8)	673 (48.0)	
	IV	74 (3.2)	88 (6.3)	
ACEIs, n (%)		1930 (84.7)	1143 (81.5)	0.005
β-blockers, n (%)		1775 (77.9)	1046 (74.6)	0.011
diuretics (without spironolactone), n (%)		1523 (66.8)	1129 (80.5)	<0.001
spironolactone, n (%)		984 (43.2)	807 (57.6)	<0.001
digoxin, n (%)		346 (15.2)	692 (49.4)	<0.001
acenocoumarol, n (%)		164 (7.2)	638 (45.5)	<0.001
ARB, n (%)		32 (1.4)	38 (2.7)	<0.005
specialty care, n (%)		1149 (50.6)	657 (46.9)	<0.05

Abbreviations: ACEIs – angiotensin-converting enzyme inhibitors, AF – atrial fibrillation, ARB – angiotensin receptor blocker, COPD – chronic obstructive pulmonary disease, MI – myocardial infarction, CHD – coronary heart disease, NS – nonsignificant, NYHA – New York Heart Association, SD – standard deviation, TIA – transient ischemic attack

DISCUSSION The aim of our study was to evaluate the prevalence and management of AF in a large, representative group of Polish outpatients with HF. We observed that AF is common in this population and is associated with a specific profile of risk factors, concomitant diseases, and therapy. Moreover, treatment with drugs that improve prognosis in HF is suboptimal in the subgroup with AF, which results from demographic characteristics and comorbidities rather than from arrhythmia itself.

The prevalence of AF in patients with HF is generally high both in clinical studies and in the outpatient setting. It increases with severity of HF ranging from 4.2% (Studies of Left Ventricular Dysfunction Prevention Trial; 2/3 of the patients in NYHA class I)[7] to 49.8% (Cooperative North Scandinavian Enalapril Survival Study; all patients in NYHA class IV),[8] with intermediate values in studies including patients in NYHA classes II and III. In large European surveys of hospitalized patients with HF, the prevalence of AF was 42% in the population of the EuroHeart Failure Survey (EHFS),[15] 38.7% in acute HF patients from the EuroHeart Failure Survey II,[16] and 35% at admission to hospital in the EuroObservational Research Programme.[17] There are significant differences in the prevalence of AF between particular countries participating in the EHFS: from 33% in Denmark to 66% in Belgium.[15] The prevalence of AF between outpatients with HF is generally lower: 30.8% in the American IMPROVE HF,[18] 25% in the European IMPROVEMENT-HF.,[19] 22.7% in the Italian IN-CHF,[20] and 37% in the Japanese JCARE-GENERAL.[21]

TABLE 2 Multivariate analysis of factors affecting the use of β-blockers. The model of multivariate logistic regression included age, sex, presence of specialty care, NYHA class, presence of coronary disease, hypertension, valvular heart disease, atrial fibrillation, diabetes, anemia, COPD, or asthma, thyroid disease, peripheral artery disease, renal failure, hypercholesterolemia, history of MI, stroke or TIA, coronary revascularization, treatment with ACEIs, ARBs, diuretics except spironolactone, spironolactone, amiodarone, digoxin, and statins.

	OR	95% CI	*P*
age	0.98	0.97–0.99	<0.0001
specialty care	2.37	1.95–2.87	<0.0001
history of MI	1.41	1.14–1.74	<0.01
atrial fibrillation	1.32	1.08–1.63	<0.01
COPD or asthma	0.48	0.39–0.60	<0.0001
hypercholesterolemia	1.42	1.17–1.71	<0.001
history of coronary revascularization	1.77	1.32–2.36	<0.0001
concomitant therapy			
ACEI	1.49	1.19–1.87	<0.001
spironolactone	1.26	1.05–1.53	<0.05
digoxin	0.62	0.50–0.76	<0.0001
amiodarone	0.50	0.35–0.70	<0.0001
statins	1.57	1.28–1.93	<0.0001

Abbreviations: CI – confidence interval, OR – odds ratio, others – see TABLE 1

TABLE 3 Multivariate analysis of factors affecting the use of angiotensin-converting enzyme inhibitors

	OR	95% CI	*P*
male sex	1.38	1.12–1.70	<0.01
specialty care	1.47	1.19–1.83	<0.001
hypertension	1.97	1.60–2.50	<0.0001
valvular heart disease	0.77	0.61–0.97	<0.05
diabetes	1.46	1.14–1.89	<0.01
anemia	0.63	0.43–0.91	<0.05
concomitant therapy			
ARBs	0.02	0.01–0.05	<0.0001
β-blockers	1.49	1.19–1.88	<0.001
diuretics (without spironolcatone)	1.66	1.34–2.07	<0.0001
spironolactone	1.33	1.08–1.64	<0.01
statins	1.62	1.62–2.01	<0.0001

For details on multivariate logistic regression model see TABLE 1

Abbreviations: see TABLES 1 and 2

In our analysis, the percentage of patients with AF within the outpatient population with HF was 38% and was similar to Polish hospitalized population from the EHFS – 40%.[15] As in other analyses, the prevalence of AF in our population increased with the NYHA class.

Because the risk of AF increases with age, it is expected that the mean age of patients with AF is higher than the mean age of patients without AF. Sex difference in the prevalence of AF is particularly interesting. Although our finding of higher AF prevalence among women is in line with the results of other surveys, the origin of this relationship is unclear.[22,23] It could be explained by older mean age and greater prevalence of noncardiac diseases in women.

In fact, HF patients with AF constitute a particular subpopulation with a specific set of risk factors and concomitant diseases. This phenomenon is illustrated mainly by the lower prevalence of ischemic mechanisms, such as ischemic disease itself and a number of its typical risk factors and complications. In our survey, the subgroup of patients with AF had lower prevalence of ischemic heart disease, history of MI, and history of cardiac revascularization. This is in line with the data from the ALPHA study, in which ischemic etiology of HF (most common in the general population – 43.5%) was the least common in patients with AF – 13.5%.[24] A similar result was described in Japanese JCARE-CARD registry.[25] In our analysis, the difference was independent of

a similar burden of hypertension, diabetes, and obesity, although it could be related to age and sex differences.

What is particularly interesting is the lower rate of MI in the subpopulation of patients with AF compared with those with sinus rhythm. Generally, AF is known as a typical complication of MI, especially in patients with left ventricular systolic dysfunction, both in acute setting and after discharge. Of note, the presence of AF in this population is associated with higher long-term mortality.[26] The study by Jons et al.[27] offers a possible explanation to this finding. In the population of post-MI patients, in which β-blockers were widely used, the majority of AF events (>90%) were asymptomatic leading to underestimation of arrhythmia prevalence.[27] Another interesting finding was the lower prevalence of hypercholesterolemia in patients with AF. This observation had been described previously and could be associated with subclinical hyperthyroidism.[25] In our study, valvular disease, the most typical etiology of HF in AF patients (48.9% in the ALPHA study), was observed twice more often in the subgroup of patients with AF than in those with sinus rhythm.

On the other hand, we observed higher prevalence of some chronic noncardiac diseases such as chronic pulmonary diseases, chronic renal failure, thyroid diseases, peripheral vascular diseases, and anemia. These findings are in agreement with the previous studies[28] and can be explained by older age of AF patients or specific pathophysiological conditions. For example, chronic pulmonary diseases are associated with pulmonary hypertension and could lead to right atrium overload and arrhythmia, while higher prevalence of anemia could be a complication of antithrombotic therapy. The higher rate of anemia among patients with coexisting HF and AF is a particularly interesting result of our study, in light of the reports concerning the role of anemia in HF pathomechanisms and prognosis.[29]

In a univariate model, the presence of AF significantly affected pharmacotherapy of HF. We observed higher use of diuretics (both spironolactone and others), digoxin, amiodarone, acenocoumarol, and ARBs, and lower use of ACEIs, β-blockers, and statins in the subgroup with AF. The results concerning digoxin and diuretics were similar to the previous findings.[19,25,30,31] Although there was a significant difference in the use of ARBs, this group of drugs was generally used rarely at the time of registry.

Although the use of acenocoumarol was significantly higher among patients with AF, its prevalence (45.5%) demonstrates underuse of antithrombotic treatment. Of note, during the study (2003–2005), both HF signs and low ejection fraction were considered sufficient indications for oral antithrombotic treatment in AF, based on the American College of Cardiology/American Heart Association/European Society of Cardiology guidelines. Nevertheless, the fact of suboptimal implementation of oral antithrombotic therapy in real life has been frequently reported.[32,33] During the study, only one of the oral anticoagulants was available in Poland – acenocoumarol. The introduction of other antithrombotic drugs can improve the implementation of oral antithrombotic treatment in AF.[34,35]

Our most striking finding was the fact that drugs which improve the prognosis in HF were used less frequently in patients with AF. This observation, surprising in the case of ACEIs, seems quite illogical in the case of β-blockers. Of note, we found inconsistent data addressing this issue in the previously published studies. Although AF was the negative predictor of β-blocker use in the study by Muntwyler et al.[19] (odds ratio [OR] 0.79, 95% confidence interval [CI] 0.69–0.89), no such effect of AF on this therapy was observed in the EPICA study[30] (OR 0.6; 95% CI 0.1–2.7). As for ACEIs, Muntwyler et al.[19] observed no effect of AF on ACEI use (OR 1.03, 95% CI 0.92–1.15), while the EPICA study showed a positive correlation between AF and ACEIs (OR 1.9, 95% CI 1.0–3.6). In the JCARE-CARD registry, AF was associated with statistically significantly lower use of β-blockers in HF and lower use, but not statistically significant, of ACEIs.[25] Similar finding was reported in the Italian Network on Congestive Heart Failure Registry (published recently but covering the years 1995–1999); however, the use of β-blockers in this registry was generally very low.[31] On the other hand, in the EuroHeart Failure Survey, AF was not an independent predictor of both β-blocker and ACEI use.[36] In IMPROVEMENT-HF, which investigated various models of therapy, AF increased the chance of receiving digoxin rather than an ACEI for single drug regimens 2.4-fold and the chance of receiving digoxin rather than β-blockers combined with ACEIs 2.6-fold.[37] Another important finding that could explain our results is lower use of β-blockers and ACEIs among women and older patients.[19,23,31,37,38]

Nevertheless, in our model of multivariable logistic regression, AF did not appear to be an independent predictor of ACEI use or even positive independent predictor of β-blocker use in HF. Thus, a negative connection between AF and drug use, which had been previously shown in univariate analyses, was the consequence of confounding factors such as specific demographics, comorbidities, and concomitant therapy. One of the strongest predictors of ACEI and β-blocker use was access to specialty care (inversely associated with AF presence). The connection between specialty (cardiologist) care and prescription of drugs that can improve prognosis in HF had been described previously.[39-42]

Our analysis has several limitations. First, the data cover the years 2003–2005, which was before ARBs became popular in the management of HF[43] and before eplerenon was introduced. Furthermore, cardiac resynchronization therapy was not prevalent at the time,[44] just as there was no

alternative for acenocoumarol in oral anticoagulation. Nevertheless, our analysis still remains the largest assessment of outpatient population with coexisting HF and AF in Poland. The recently reported primary data from the Record AF registry is based on 303 patients with new diagnosis of AF, of whom only 84 had coexisting HF.[45] In another large registry of European outpatients with HF (with participation of Polish centers), 38.6% of patients had a history of AF,[17] but to the best of our knowledge, no analysis has been published so far describing this subgroup. Second, our registry did not specifically address the issue of contraindications to treatment, so the models that assessed the reasons for using ACEIs and β-blockers seem to be incomplete. For example, according to the current guidelines, ARBs should be used instead of ACEIs only in the case of ACEI intolerance, and this could not be addressed in our analysis.[46] Third, we could not determine the type of AF (paroxysmal, persistent, permanent), which might have provided interesting data given the fact that several aspects of the guidelines have been reported to be neglected in the subpopulation of patients with paroxysmal arrhythmia.[42,47]

Conclusions Patients with AF constitute a large subpopulation within the group of outpatients with HF (more than 30%). Patients with coexisting HF and AF are older, include mostly women, have lower prevalence of coronary artery disease and higher prevalence of valvular heart disease or chronic noncardiac diseases. A specific distribution of risk factors with a significant effect of noncardiac concomitant diseases may influence HF therapy. Access to specialty care may optimize treatment in this particular patient population.

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ARTYKUŁ ORYGINALNY

Epidemiologia i leczenie ambulatoryjne chorych z niewydolnością serca i współistniejącym migotaniem przedsionków

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SŁOWA KLUCZOWE

epidemiologia, leczenie, migotanie przedsionków, niewydolność serca

STRESZCZENIE

WPROWADZENIE Migotanie przedsionków (*atrial fibrillation* – AF) jest najczęstszym zaburzeniem rytmu wikłającym przebieg niewydolności serca (*heart failure* – HF). Współwystępowanie tych chorób można częściowo tłumaczyć obecnością wspólnych czynników ryzyka. Choć wpływ AF na rokowanie w HF pozostaje dyskusyjny, obecność tej arytmii wiąże się z określonymi powikłaniami i wpływa na stosowane leczenie.

CELE Celem niniejszej analizy była ocena epidemiologii i leczenia polskich chorych ambulatoryjnych ze współistniejącymi HF i AF.

PACJENCI I METODY Prezentowana analiza została przeprowadzona w ramach Narodowego Programu Profilaktyki i Leczenia Chorób Układu Sercowo-Naczyniowego POLKARD 2003–2005 i obejmowała chorych z HF leczonych w reprezentacyjnej próbie 400 ośrodków ambulatoryjnych. Dane uzyskano za pomocą badania kwestionariuszowego obejmującego dane demograficzne oraz informacje na temat współistniejących chorób i stosowanego leczenia, podawane przez chorych i lekarzy na podstawie dostępnej dokumentacji ambulatoryjnej.

WYNIKI Do badania włączono 3682 chorych z HF (średni wiek 67,1 ±11,7 roku, 58% mężczyzn). U 38% chorych współwystępowało AF. Częstość tej arytmii wzrastała wraz z klasą New York Heart Association. Stwierdzono istotne różnice między chorymi z AF i rytmem zatokowym pod względem danych demograficznych, czynników ryzyka, chorób współistniejących i stosowanego leczenia. Choć częstość stosowania inhibitorów konwertazy angiotensyny i β-blokerów była istotnie mniejsza w podgrupie z AF, analiza wieloczynnikowa wykazała, że wynika to raczej ze szczególnej demografii i chorób towarzyszących niż z samej arytmii. Opieka specjalistyczna nad chorymi wiązała się ze zwiększonym rozpowszechnieniem terapii ukierunkowanej na poprawę rokowania w HF.

WNIOSKI Chorzy z AF stanowią specyficzną podgrupę chorych z HF. Szczególny rozkład czynników ryzyka z istotnym udziałem chorób niekardiologicznych może zaburzać ukierunkowane leczenie HF w tej grupie. Wydaje się, że opieka specjalistyczna jest w stanie poprawić leczenie chorych ze współistniejącym HF i AF.

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Praca wpłynęła: 09.22.2011.
Przyjęta do druku: 11.11.2011.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2011; 121 (11): 392-399