

Prevalence and predisposing conditions for atrial fibrillation in hospitalised patients with hypertension

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Abstract

Background: Hypertension, due to its prevalence, is a common and independent risk factor for atrial fibrillation (AF). High blood pressure causes structural and functional changes in the myocardium, leading to an increased risk of arrhythmia. This risk is higher when hypertension is accompanied by concomitant diseases that contribute to the development of AF.

Aim: To estimate prevalence of AF and predisposing factors for AF in patients with hypertension hospitalised in our cardiology unit.

Methods: This retrospective analysis included 4459 patients hospitalised in the Clinical Department of Cardiology in 2009–2010. Hypertension was identified in 2512 (56.3%) patients. The study group consisted of 685 (27.3%) patients with hypertension and concomitant AF, and the control group included 1827 (63.7%) hypertensive patients without AF. We analysed clinical data including AF type, coexisting diseases and left ventricular ejection fraction evaluated by echocardiography.

Results: Mean patient age in the study group was 74 years compared to 67 years in the control group. Most patients in the study group had either paroxysmal (46%) or permanent AF (45.5%). The following rates of coexisting diseases were found in the study and control groups: heart failure (HF) 54.3% vs. 31.4%, respectively ($p < 0.001$), ischaemic heart disease (IHD) 44.4% vs. 25.2% ($p < 0.001$), diabetes 28.3% vs. 24.2% ($p = 0.126$), hypercholesterolaemia 25.4% vs. 30.4% ($p = 0.067$), stroke 10% vs. 3% ($p = 0.0028$), hyperthyroidism 4.7% vs. 1.9% ($p = 0.0002$), hypothyroidism 5.1% vs. 2.1% ($p = 0.0001$), and euthyroid goitre 5.3% vs. 2.1% ($p < 0.0001$). Multivariate logistic regression analysis identified the following factors that significantly affected the occurrence of AF in patients with hypertension: hypothyroidism (hazard ratio [HR] 3.27), IHD (HR 2.75), hyperthyroidism (HR 2.55), euthyroid goitre (HR 2.13), previous myocardial infarction (HR 1.96), and HF (HR 1.66).

Conclusions: Among hospitalised patients with hypertension, AF is present in a significant proportion of patients. Conditions predisposing to this arrhythmia in hypertensives include HF, IHD, thyroid diseases, and previous myocardial infarction. There was no evidence that diabetes, abnormal lipid profile, and impaired kidney function affected AF rate among patients with hypertension.

Key words: hypertension, atrial fibrillation, risk factors

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INTRODUCTION

Atrial fibrillation (AF) is the most common type of supraventricular tachyarrhythmia. Its prevalence doubles in each decade of life after 50 years of age, reaching 10% in octogenarians. Hypertension is a common independent risk factor for AF. The relative risk of AF in patients with hypertension is on average 1.4–2.1, and thus it is a moderately strong risk factor for AF compared to such conditions as heart failure (HF) or valvular heart dis-

ease, with the relative risk of AF in the ranges of 6.1–17.5 and 2.2–8.3, respectively [1]. However, due to its large prevalence, hypertension has major importance as a risk factor for AF, particularly among the elderly. An increase in systemic blood pressure leads to left ventricular hypertrophy, prolongation of the relaxation time, myocardial fibrosis, and atrial dilatation [2]. With this myocardial remodelling due to hypertension, other conditions also predispose to AF, including HF, valvular heart dis-

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Table 1. Causes of hospital admission in the study population

Cause of hospital admission	All patients (n = 2512)	Hypertensives with AF (study group, n = 685)	Hypertensives without AF (control group, n = 1827)
Acute coronary syndrome	567 (22.6%)	100 (14.6%)	467 (25.6%)
Implantation/reimplantation of a pacemaker, ICD, or CRT device	526 (20.9%)	184 (26.9%)	342 (18.7%)
Elective coronary angiography	411 (16.4%)	49 (7.2%)	362 (19.8%)
Heart failure	451 (17.9%)	135 (19.6%)	316 (17.3%)
Symptomatic AF	64 (2.5%)	64 (9.4%)	0
Electrical cardioversion	49 (1.9%)	49 (7.1%)	0
Uncontrolled hypertension	269 (10.7%)	39 (5.7%)	230 (12.6%)
Other	175 (7.1%)	65 (9.5%)	110 (6.0%)

AF — atrial fibrillation; ICD — implantable cardioverter-defibrillator; CRT — cardiac resynchronisation therapy

ease (mostly involving the mitral valve), ischaemic heart disease (IHD), elevated heart rate, diabetes, thyroid diseases, respiratory diseases, obesity, alcohol abuse, and smoking.

The aim of our study was to estimate prevalence of AF and identify coexisting conditions predisposing to this arrhythmia in patients with hypertension hospitalised in our cardiology unit.

METHODS

This retrospective analysis included 4459 patients hospitalised in the Clinical Department of Cardiology in 2009–2010. Hypertension was identified in 2512 (56.3%) patients. The diagnosis of hypertension in hospital was defined as the use of antihypertensive drugs or elevated blood pressure values, with mean blood pressure (calculated from at least 2 measurements done on at least 2 separate days of hospital stay) ≥ 140 mm Hg systolic and/or 90 mm Hg diastolic. The study group consisted of 685 hypertensive patients with concomitant AF (27.3%), and the control group includes 1827 hypertensives without AF (63.7%). We analysed medical records containing full clinical data. HF was diagnosed based on typical history and physical examination findings along with laboratory evidence of myocardial dysfunction. IHD was diagnosed based on typical history and/or previous acute coronary syndrome. Hypercholesterolaemia was defined as total cholesterol level above 190 mg/dL and low-density lipoprotein (LDL) cholesterol level above 115 mg/dL or previously initiated lipid-lowering treatment. The diagnosis of thyroid disease was based on history. Diabetes was defined as fasting serum glucose level above 125 mg/dL on 2 separate occasions, serum glucose level above 199 mg/dL in a random sample with clinical symptoms of diabetes or at 2 h of the oral glucose tolerance test, or previously initiated glucose-lowering treatment. Left ventricular ejection fraction (LVEF) was evaluated by echocardiography using the Simpson method or visually. Glomerular filtration rate was estimated using the Modification of Diet in Renal Disease (MDRD) study formula.

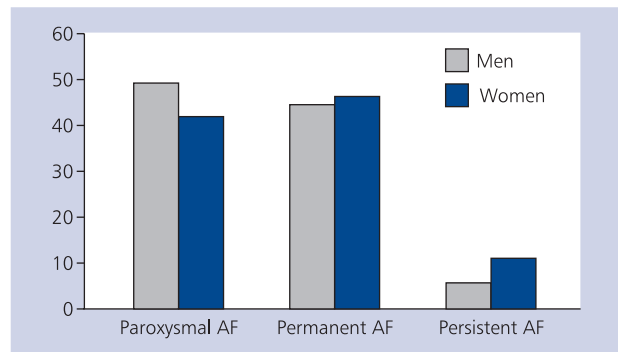


Figure 1. Atrial fibrillation (AF) type by gender in the study population

Statistical analysis

For the purpose of statistical analysis, we calculated mean values with standard deviations, medians with interquartile ranges, and minimum and maximum values for quantitative variables, and frequencies with percentages for qualitative variables. We used multivariate logistic regression analysis to estimate hazard ratios. $P < 0.05$ was considered statistically significant. Calculations were performed using the MedCalc software, version 11.5.1.0.

RESULTS

Hypertension was identified in 2512 (56.3%) hospitalised patients included in the present analysis. Reasons for hospital admission of these hypertensive patients are shown in Table 1. AF was found in 685 (27.3%) patients with hypertension. Among these hospitalised hypertensive patients, the most common types of this arrhythmia were paroxysmal AF (314 patients, 46%) and permanent AF (312 patients, 45.5%). Patients with persistent AF comprised the remaining 8.5% of the study group. Figure 1 shows occurrence of these 3 types of AF by gender.

Median age in the overall population of hospitalised hypertensives was 68 years, and 45.5% of patients were women, as

compared to 49.9% among hypertensives with AF. Median age of hypertensives with AF was 74 years (women 76 years, men 71 years) compared to 67 years in the control group (Fig. 2).

Rates of coexisting diseases in both groups are shown in Table 2. In the study and control groups, New York Heart Association (NYHA) class II HF was present in 276 (40.3%) vs. 1007 (55.1%) patients, respectively, NYHA class III HF in

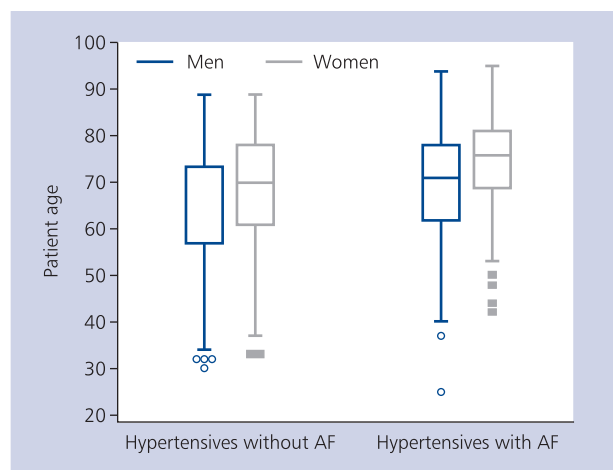


Figure 2. Mean age of women and men in the study population depending on the presence or absence of atrial fibrillation (AF)

323 (7.1%) vs. 702 (38.4%) patients, and NYHA class IV HF in 86 (12.6%) vs. 118 (6.5%) patients.

IHD was more common among hypertensives with AF (Table 2), and concomitant IHD was associated with a nearly 3-fold increase in risk of AF among hypertensives (Table 3). Previous myocardial infarction (MI) was noted in 92 (13.4%) patients in the study group, including 59 (64.1%) men, compared to 141 (7.7%) patients in the control group. In the latter group, similarly to hypertensives with AF, previous MI was also noted more frequently among men (67.4% vs. 32.6%). Acute MI was more common among hypertensives with AF ($p = 0.0324$), more frequently in men ($p = 0.0019$), while similar gender difference was not seen in the control group ($p = 0.0913$).

Among patients with AF, hypercholesterolaemia was less frequent than in the control group (Table 2). Rates of hypercholesterolaemia among men and women were similar in both groups, as this condition was found in 88 (25.7%) women and 86 (25.1%) men in the study group, and 234 (29.3%) women and 321 (31.2%) men in the control group.

Thyroid disease was more common among patients with AF. Hazard ratios (HR) for the occurrence of AF in patients with hypertension were 2.55 for hyperthyroidism, 3.27 for hypothyroidism, and 2.13 for euthyroid goitre (Table 3).

Mean glomerular filtration rate was 55.2 ± 17.9 mL/min/1.73 m² in the study group compared to 63.2 ± 26.2 mL/min/1.73 m² in the control group ($p < 0.001$). In multivariate

Table 2. Concomitant diseases, laboratory results, and left ventricular ejection fraction (LVEF) in the study and control groups

Parameter	Hypertensives with atrial fibrillation (n= 685)	Hypertensives without atrial fibrillation (n=1827)	P
Median age [years]	74 (25–95)	67 (30–89)	< 0.0001
Women/men	342 (49.9%)/343 (50.1%)	798 (43.7%)/1029 (56.3%)	0.089
Ischaemic heart disease	304 (44.4%)	460 (25.2%)	< 0.001
Previous myocardial infarction	92 (13.4%)	141 (7.7%)	0.0324
Heart failure	372 (54.3%)	574 (31.4%)	< 0.001
Diabetes type 2	194 (28.3%)	442 (24.2%)	0.126
Previous stroke	72 (10%)	54 (3%)	0.0028
Hypercholesterolaemia	174 (25.4%)	555 (30.4%)	0.067
Hyperthyroidism	32 (4.7%)	34 (1.9%)	0.0002
Hypothyroidism	35 (5.1%)	38 (2.1%)	0.0001
Euthyroid goitre	36 (5.3%)	38 (2.1%)	< 0.0001
Haemoglobin (women)	12.7 ± 1.5	13.0 ± 4.3	0.101
Haemoglobin (men)	13.6 ± 1.8	13.7 ± 1.6	0.382
Total cholesterol [mg/dL]	165.9 ± 44.8	180.7 ± 50.1	< 0.001
LDL cholesterol [mg/dL]	98.8 ± 37.8	109.1 ± 44.4	< 0.001
HDL cholesterol [mg/dL]	44.2 ± 15.7	46.7 ± 20.4	0.235
Triglycerides [mg/dL]	132.4 ± 77.4	145.2 ± 92.9	0.003
Glomerular filtration rate	55.2 ± 17.9	63.2 ± 26.2	< 0.001
LVEF	48.6 ± 11.9	48.7 ± 16.3	0.858

Table 3. Multivariate logistic regression analysis to identify factors affecting the development of atrial fibrillation in patients with hypertension

Variable	Regression coefficient	Standard error of regression coefficient	Hazard ratio	95% confidence interval	P
Hypothyroidism	1.1853	0.3141	3.2718	1.7677–6.0560	0.0002
Ischaemic heart disease	1.0127	0.1267	2.7530	2.1476–3.5292	< 0.0001
Hyperthyroidism	0.9381	0.3430	2.5552	1.3044–5.0054	0.0062
Euthyroid goitre	0.7586	0.3448	2.1354	1.0863–4.1979	0.0278
Previous myocardial infarction	0.6752	0.1972	1.9646	1.3348–2.8915	0.0006
Heart failure	0.5081	0.0717	1.6622	1.4442–1.9132	< 0.0001
Hyperlipidaemia	0.0707	0.1427	1.0733	0.8113–1.4199	0.6203
Age	0.0332	0.0064	1.0338	1.0209–1.0469	< 0.0001
Left ventricular ejection fraction	0.0134	0.0051	1.0136	1.0034–1.0238	0.0088
Haemoglobin [g/dL]	0.0048	0.0171	1.0049	0.9716–1.0392	0.7768
Triglycerides [mg/dL]	–0.0005	0.0007	0.9995	0.9980–1.0009	0.4803
LDL cholesterol [mg/dL]	–0.0021	0.0029	0.9978	0.9921–1.0035	0.4510
Total cholesterol [mg/dL]	–0.0038	0.0026	0.9962	0.9909–1.0014	0.1535
Glomerular filtration rate	–0.0083	0.0037	0.9917	0.9844–0.9991	0.0275
Diabetes	–0.0752	0.1383	0.9275	0.7073–1.2163	0.5863

analysis, however, renal dysfunction was not found to increase significantly the risk of AF in patients with hypertension (Table 3).

Mean LVEF by echocardiography was 49% in both groups. Men showed significantly lower LVEF both in the study group ($50.7 \pm 9.7\%$ vs. $46.4 \pm 13.4\%$; $p < 0.0001$) and the control group ($50.1 \pm 12.2\%$ vs. $47.6 \pm 18.8\%$; $p = 0.0035$). Mean LVEF was 46% in NYHA II class HF patients, 42% in patients with NYHA III class HF, and 35% in patients with NYHA IV class HF.

Overall, the mean number of antihypertensive drugs prescribed at hospital discharge to patients with hypertension was 2.2 ± 0.6 .

DISCUSSION

Hypertension, along with IHD, is a major common cause of AF [3]. In a population of patients with AF, hypertension was identified as the underlying etiologic factor in 69.2% of cases [4]. In our study, the proportion of hypertensives among all hospitalised patients (56.3%) was reduced compared to that found in the same age group in the general population [5]. It seems that the proportion of patients with hypertension among those hospitalised in cardiological units may be often underestimated due to the fact that both patients with IHD (30.5% of our study population) and patients with HF (37.4% of our study population) generally receive antihypertensive medications. In a study by Kawecka-Jaszcz et al. [6], hypertension was diagnosed at hospital discharge in 56% of patients in the Krakow Program for Secondary Prevention of Ischaemic Heart Disease but at the same time it was estimated the rate of

undiagnosed hypertension among patients with IHD was 20%. Similar results were reported by Bachórzewska-Gajewska et al. [7] who found hypertension in 61% of 1395 patients admitted to a general medicine and cardiology hospital unit.

In our study population, approximately one fourth of hypertensive patients (27.3%) had AF, mostly of the paroxysmal or permanent type. In a study by Morillas et al. [8], AF was diagnosed in 10.3% of 1028 hypertensive patients above 65 years of age. Median age of patients with AF in our study was 74 years. Men comprised half of these patients with AF and were on average 5 years younger than women with AF. Patients without AF were on average 7 years younger compared to patients with this arrhythmia. These findings are in agreement with the results reported by Walker and Bennett [9] who used data from the Ingenix Research Data Mart database to characterise American patients with the diagnosis of AF. The analysis by Walker and Bennett [9] included 116,969 patients aged above 40 years who mostly had permanent (65%) or paroxysmal (35%) AF.

In our study population, permanent or paroxysmal AF were the most common forms of this arrhythmia, with persistent AF present in only 6% of men and 10% of women with AF. This proportion seems low in comparison to approximately 18% of patients with persistent AF in the prospective, multicentre, international registry of patients newly diagnosed with non-valvular AF and at least one additional risk factor for stroke, Global Anticoagulant Registry in the Field (GARFIELD) which is the largest currently ongoing AF registry in the world [10]. Perhaps patients with persistent AF, if clinically stable, are treated on an outpatient basis and referred at a varying

rate to hospital for cardioversion, and our study included only hospitalised patients.

The most common coexisting condition in hypertensive patients with AF was HF. It was found in more than half of patients (54.3%) in the study population, and its severity was usually NYHA class II or III. Grzybczak et al. [11] followed 152 patients with systolic HF for 5 years and showed that HF was causally related to the development of AF in 35% of patients. In a German AF registry that included 9582 patients, hypertension was found in 69.2% of patients, and HF in 29% of patients. However, the population studied in that registry was younger than in our study, as the mean age was 68.4 ± 11 years [4]. In the above mentioned FAPRES study, HF was noted in 39% of patients with hypertension and AF [8]. In our study, however, no significant difference in LVEF was found between hypertensives with or without AF. Normal mean LVEF suggests that our patients might have had HF with preserved ejection fraction (HFPEF) which is as common as HF with reduced ejection fraction [12]. Rusinaru et al. [13] showed that AF was present in 36% of patients with HFPEF and was associated with increased mortality during a 5-year follow-up compared to patients with sinus rhythm (47% vs. 36%; $p = 0.03$).

Similarly to HF, IHD was found in nearly half of our patients with hypertension and AF (44.4%). Similar results were reported by Pedersen et al. [14] who showed that IHD was present in 44% of patients with AF. They also showed worse outcomes in patients with AF and IHD, with increased mortality as compared to patients without IHD.

Diabetes is more common among hypertensives compared to the general population so a higher rate of AF may be expected in this patient group. In a retrospective analysis including more than 800,000 subjects, diabetes was found to be an independent risk factor for the development of AF (HR 2.13; 95% confidence interval 2.10–2.16) [15]. However, such a relationship was not confirmed in the Framingham study and diabetes was not included as a risk factor for AF in the risk score derived from that study [16]. In our study, we also did not find diabetes to be more common among patients with hypertension and AF compared to hypertensives without AF.

Both hypertension and AF are established causes of stroke. In our study, stroke rate among patients with AF was increased more than three times compared to patients without AF. Hypertension is associated with a 2.5-fold increase in the risk of stroke compared to normotensives [17]. Among patients with non-valvular AF, stroke risk is increased 2.7-fold compared to patients in sinus rhythm, yielding a 5% annual stroke incidence [18]. The risk of stroke in our study population did not depend on the AF type, which is consistent with the results of a metaanalysis of 5 prospective studies [19].

In our study, patients without arrhythmia had significantly more dyslipidaemia compared to patients with AF, and the rate of hypercholesterolaemia among the latter (29%) was found to be relatively low. These results might have been related to

more frequent outpatient visits of patients with arrhythmia, resulting in the initiation of lipid-lowering therapy before admission, usually with the use of statins. As we were unable to evaluate lipid profile before initiation of lipid-lowering therapy and/or hospitalisation, fully objective evaluation and assessment of this factor was not possible, constituting a study limitation. Our findings are in agreement with the results reported by Schnabel et al. [20] who did not confirm a relationship between hypercholesterolaemia and a higher risk of this arrhythmia. However, other authors showed a relation between arrhythmia and elevated lipid levels, particularly with the presence of intracardiac thrombi [21].

In our study population, thyroid disease was identified in 15% of patients with AF, more frequently compared to patients without AF and more frequently among women compared to men. Rates of hyperthyroidism, hypothyroidism, and euthyroid goitre were similar. In a Danish cohort of 40,628 patients with hyperthyroidism, AF was found in 8.3% of subjects. Hyperthyroidism was more common in women (84.9%), and one third of all patients with hyperthyroidism and AF was above 70 years of age [22].

In multiple studies, renal dysfunction was found to be a factor associated with an increased risk of AF (HR 1.4–1.9) [23, 24], which is plausible from a pathophysiological point of view. Chronic kidney disease leads to increased volemia, resulting in volume overload and left ventricular hypertrophy, and ultimately increased atrial pressure and atrial remodelling. Pulmonary vein remodelling is another important factor predisposing to the development of AF in this patient population [25]. In our study, patients with hypertension and AF had significantly lower glomerular filtration rate compared to patients without AF. In multivariate analysis, however, renal function was not shown to be a factor affecting AF rate among hypertensives. Similar results were reported in the FAPRES study which used the same approach to evaluate renal function as in our study [8]. Both our study and the FAPRES study, however, did not evaluate albuminuria which may be a limitation of our study.

Our study was a single-centre assessment of AF rate among hospitalised patients with hypertension. We believe that this issue warrants broader multicentre evaluation of the prevalence of AF and factors predisposing to this arrhythmia in hypertensives.

CONCLUSIONS

Among hospitalised patients with hypertension, AF is present in a significant proportion of patients. Conditions predisposing to this arrhythmia in hypertensives include HF, IHD, thyroid diseases, and previous MI. There was no evidence that diabetes, abnormal lipid profile, and impaired kidney function affected AF rate among patients with hypertension.

Conflict of interest: none declared

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Częstość występowania i czynniki predysponujące do migotania przedsionków u hospitalizowanych pacjentów z nadciśnieniem tętniczym

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Streszczenie

Wstęp: Nadciśnienie tętnicze, ze względu na rozpowszechnienie, jest częstym i niezależnym czynnikiem ryzyka migotania przedsionków (AF). Wzrost wartości ciśnienia tętniczego powoduje zmiany strukturalne i czynnościowe w mięśniu sercowym, które zwiększają ryzyko wystąpienia arytmii. Ryzyko to jest większe, gdy z nadciśnieniem tętniczym współistnieją schorzenia sprzyjające rozwojowi AF.

Cel: Celem pracy była ocena częstości występowania AF i czynników predysponujących do rozwoju arytmii w grupie chorych z nadciśnieniem tętniczym hospitalizowanych na Oddziale Kardiologii.

Metody: Analizą retrospektywną objęto 4459 pacjentów hospitalizowanych w latach 2009–2010 na Klinicznym Oddziale Kardiologii. Wyodrębniono 2512 (56,3%) osób z nadciśnieniem tętniczym. Grupę badaną (685 chorych; 27,3%) stanowili pacjenci z nadciśnieniem tętniczym ze współistniejącym AF, a grupę kontrolną (1827 chorych; 63,7%) pacjenci z nadciśnieniem tętniczym bez AF. Analizowano dane kliniczne z uwzględnieniem postaci AF, schorzeń współistniejących oraz frakcji wyrzutowej lewej komory w badaniu echokardiograficznym.

Wyniki: Średnia wieku w grupie badanej wyniosła 74 lata, natomiast w grupie kontrolnej 67 lat. U chorych z AF występowała głównie napadowa (46%) lub utrwalona (45,5%) postać arytmii. Schorzenia współistniejące w grupie badanej i kontrolnej występowały z następującą częstością: niewydolność serca: 54,3% vs. 31,4% ($p < 0,001$), choroba wieńcowa: 44,4% vs. 25,2% ($p < 0,001$), cukrzyca: 28,3% vs. 24,2% ($p = 0,126$), hipercholesterolemia: 25,4% vs. 30,4% ($p = 0,067$), udar mózgu: 10% vs. 3% ($p = 0,0028$), nadczynność tarczycy: 4,7% vs. 1,9% ($p = 0,0002$), niedoczynność tarczycy: 5,1% vs. 2,1% ($p = 0,0001$), wole w eutyreozie: 5,3% vs. 2,1% ($p < 0,0001$). Wyniki wieloczynnikowej analizy regresji logistycznej czynników wpływających na wystąpienie AF u pacjentów z nadciśnieniem tętniczym są następujące: niedoczynność tarczycy: współczynnik ryzyka (HR) 3,27, choroba niedokrwienna serca: HR 2,75, nadczynność tarczycy: HR 2,55, wole w eutyreozie: HR 2,13, stan po zawale serca: HR 1,96, niewydolność serca: HR 1,66.

Wnioski: W grupie hospitalizowanych pacjentów z nadciśnieniem tętniczym AF występuje u znacznej części chorych. Schorzeniami predysponującymi do wystąpienia arytmii w grupie osób z nadciśnieniem tętniczym są: niewydolność serca, choroba wieńcowa, choroby tarczycy i przeżyty zawal serca. Nie wykazano, by cukrzyca, zaburzenia profilu lipidowego i upośledzona funkcja nerek wpływały na częstość występowania AF w grupie chorych z nadciśnieniem tętniczym.

Słowa kluczowe: nadciśnienie tętnicze, migotanie przedsionków, czynniki ryzyka

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