Assessment of antihypertensive treatment and risk factors for rehospitalizations of patients with primary arterial hypertension hospitalized for cardiac reasons

Ocena leczenia nadciśnienia tętniczego i czynników ryzyka ponownych hospitalizacji pacjentów z pierwotnym nadciśnieniem tętniczym hospitalizowanych z przyczyn kardiologicznych

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Abstract

Introduction. The aim of this study is comparison and evaluation of the results of antihypertensive treatment in patients with primary arterial hypertension and identification of risk factors for cardiovascular rehospitalisation in this group of patients.

Material and methods. 299 people (206 women and 93 men) diagnosed with primary arterial hypertension were included in the observational study. Patients' medical data was analyzed, including laboratory tests, transthoracic echocardiography, and 24-hour automatic blood pressure measurements. One year after hospitalization, the patients were interviewed by phone to assess blood pressure, pharmacotherapy, and cardiovascular events. The collected data was analyzed statistically.

Results. Overweight and dyslipidemic patients constituted the majority of the analyzed group. In the group of men, mean diastolic blood pressure values were significantly higher than in women. A comparison of the results of transthoracic echocardiography showed that women had significantly higher values of A wave and the E/E' ratio. One year after hospitalization, most of the patients complied with the recommendations and achieved mean blood pressure values < 140/90 mm Hg. As many as 18.7% of patients required rehospitalization for cardiovascular reasons within one year of follow-up.

Conclusions. The antihypertensive drug therapy in the study population differed from the recommendations in the European Society of Cardiology/European Society of Hypertension guidelines for the management of hypertension. Increased echocardiographic parameters of left ventricular diastolic dysfunction were associated with worse outcomes of antihypertensive treatment. Age and blood pressure below 120/70 mm Hg increased the risk of rehospitalization in the study population.

Key words: hypertension, diastolic dysfunction, pharmacotherapy, rehospitalization

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Introduction

Epidemiological data confirm that hypertension (HA) has become a common chronic disease which prevalence in the adult population in Poland is around 35% [1]. The percentage of polish patients suffering from HA is significantly higher than the world average which was 24.1% in men and 20.1% in women in 2015 [2]. Despite the significant progress in the pharmacotherapy of HA and the widespread access to combination drugs, patients' and regular use of medications still pose a significant problem. It is estimated that only about 25–30% of patients with HA in developed countries adhere to therapeutic recommendations. Obtained data indicate that the percentage of patients following the recommendations is in Poland even lower (5–15%) [3]. Almost half of the patients discontinue treatment within one year from its commencement. Even though it is a significant clinical problem, it also has serious economic consequences. According to estimates, the costs associated with cardiovascular diseases in European Union countries amount to approx. 169 billion EUR per year [4]. According to calculations, the increase in the percentage of patients adhering to treatment from 49% to 70% in only 5 European countries would enable us to save 332 million EUR over 10 years [5]. The upgrading of compliance is believed to offer the greatest potential for improvement in the context of effective and cost-effective blood pressure control [7].

The aim of this study is to compare and assess the results of antihypertensive treatment in patients with essential hypertension, as well as to compare the effect of the treatment used on blood pressure values, evaluate the compliance, and identify risk factors for cardiovascular rehospitalization in patients with HA.

Material and methods

This observational study comprised 299 people (206 women and 93 men) diagnosed with primary hypertension and hospitalized for cardiovascular reasons (in blinded). Exclusion criteria were as follows: no previous antihypertensive treatment and lack of ambulatory blood pressure measurement and/or lack of transthoracic echocardiography. The process of data collection was divided into two stages. During the first stage, relevant information was extracted from patients' medical case records. The following data were collected in this study: age, sex, body mass index (BMI) calculated using the formula:

$$BMI = weight [kg]/height [m]^2,$$

the history of comorbidities (i.e. chronic coronary syndrome, status post myocardial infarction, left ventricular hypertrophy, heart failure, ventricular arrhythmia, supraventricular extrasystoles, atrial fibrillation and flutter, peripheral vascular disease, status post stroke/transient ischemic attack, lipid disorders, type 2 diabetes mellitus, chronic kidney disease) and cardiological interventions (i.e. percutaneous coronary intervention, coronary artery bypass graft surgeries, pacemaker implantation, cardioverter-defibrillator implantation), blood pressure values and heart rate in-office measurements on admission to the hospital ward. Additionally, the following results of blood tests: blood counts, lipid profile (total cholesterol, low-density lipoprotein, high-density lipoprotein, triglycerides), thyroid hormones (thyroid stimulating hormone, free triiodothyronine, free thyroxine), biochemical parameters assessing kidney function (uric acid, urea, creatinine, estimated glomerular filtration rate calculated using MDRD formula:

$$eGFR = 186.3 \times creatinine\ level^{-1.154} \times age^{-0.203} \times \times [1.212\ for\ black\ populations] \times [0.742\ for\ women]$$

were collected. 24-hour ambulatory blood pressure monitoring values measured with the ABPM Tonoport V device (GE Healthcare, Berlin, Germany) were also retrieved. The following data were analyzed in this study: participants' in-hospital mean systolic and mean diastolic blood pressure during the day, night and in 24 h recording, as well as the minimum and maximum in-hospital systolic and diastolic blood pressure during the day and night. ABPM cuff with appropriate size was used on a non-dominant limb. This device measured blood pressure and heart rate every 15 minutes during the day and every 30 minutes during the night (from 10:00 p.m. to 7:00 a.m.). Erroneous measurements (extreme values of heart rate, systolic and diastolic blood pressure) were automatically rejected. Transthoracic echocardiography was performed using Vivid E95 apparatus (GE Healthcare, Horten, Norway). The dimensions of the heart chambers, left ventricular volume and left ventricular ejection fraction (calculated using biplane Simpson's method), values of global peak systolic longitudinal strain, left atrial volume (LAV) with the left atrial index (LAVI), left ventricular mass index, interventricular septum (IVS) thickness, end-diastolic left ventricular posterior wall thickness, maximal early mitral inflow velocity (E), the velocity of inflow wave associated with left atrial contraction (A), E/A ratio, the ratio of early transmitral flow velocity to early diastolic velocity of the mitral annulus (E/E') were also assessed in this study. Information on pharmacotherapy used in the treatment of hypertension, lipid disorders, and antiplatelet and anticoagulant therapy was also obtained.

One year after the hospitalization, a telephone survey was conducted with patients participating in this study (second stage). They answered the following questions:
— Are your blood pressure values measured at home lower than 120/70 mm Hg?
— If not, are your blood pressure values measured at home lower than 140/90 mm Hg?
— Have your blood pressure values remained at the same level since your last stay in the ward?
— Do you still use the medications prescribed on discharge from the ward?

— Do you always use the prescribed drugs in accordance with recommendations?
— Have you been hospitalized for cardiovascular diseases since your last stay in the ward?

Informed consent was obtained from all individual participants included in the study. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Polish Mother's Memorial Hospital Research Institute, Lodz, Poland (Date 27.11.2018/No. 102/2018). The Project is financed by the Polish National Agency for Academic Exchange under the Foreign Promotion Programme.

Statistical analysis

Quantitative variables are presented as mean, standard deviation, median, minimum and maximum. The chi-square test was used to evaluate whether the compared groups of patients are of the same size and whether there are any statistically significant associations between the nominal variables. To demonstrate significant statistical differences between two independent groups of patients, the Mann-Whitney U test was used; McNemar test was utilized to determine if there are differences on nominal dependent variables between two related groups. The analysis of variance was performed to test for any statistically significant associations between the variables; the observed statistically significant relationships were further in-depth examined using the analysis of simple main effects. Logistic

regression analysis was used to evaluate particular statistically significant factors, i.e. those influencing the frequency of hospitalizations and individual blood pressure values (< 120/70 mm Hg and < 140/90 mm Hg). The statistical analysis of the collected data was performed using IBM SPSS Statistics 25 package. The p < 0.05 was considered statistically significant.

Results

All recruited patients were included in the analysis. Women were in majority in the entire study group (n = 206 [68.9%]; p < 0.001) and in the subgroup of 268 patients over the age of 40 years (n = 194 [72.4%]; p < 0.001). The median age for women and men was 64 and 60 years, respectively. The youngest patient was 18 years old, and the oldest was 90 years old. Women were significantly older than men (p < 0.001) in this study. The majority of enrolled patients (n = 232; 78.9%) had a BMI above 25 kg/m^2 (p < 0.001). Women did not differ significantly from men in terms of BMI (p = 0.12). Table 1 presents data on selected comorbidities and cardiological interventions in the study group. Patients with hyperlipidemia were also in majority of the study group. Diabetes mellitus and supraventricular extrasystoles were more prevalent in women. The parameters of kidney function were also compared between men and women. Significantly higher concentrations of uric acid and creatinine as well as the estimated glomerular filtration rate

Table 1. The summary of medical history of study participants

Medical history	Number of patients		Statistical test results
	n	%	
Chronic coronary syndrome	101	33.9	χ^2 (1) = 30.93; p < 0.001
Status post myocardial infarction	28	9.4	χ^2 (1) = 197.49; p < 0.001
Percutaneous coronary interventions	24	8	χ^2 (1) = 210.71; p < 0.001
Status post coronary bypass surgery	9	3	χ^2 (1) = 264.08; p < 0.001
Left ventricular hypertrophy	77	26.2	χ^2 (1) = 66.67; p < 0.001
Heart failure	75	25.1	χ^2 (1) = 74.25; p < 0.001
Ventricular arrhythmia	78	26.7	χ^2 (1) = 68.39; p < 0.001
Supraventricular extrasystoles	93	31.1	χ^2 (1) = 42.71; p < 0.001
Paroxysmal atrial fibrillation/atrial flutter	35	11.7	χ^2 (1) = 175.39; p < 0.001
Persistent and permanent atrial fibrillation/atrial flutter	17	5.7	χ^2 (1) = 234.87; p < 0.001
Status post pacemaker implantation	5	1.7	χ^2 (1) = 278.34; p < 0.001
Status post cardioverter-defibrillator implantation	1	0.3	χ^2 (1) = 293.01; p < 0.001
Peripheral vascular disease	84	28.1	χ^2 (1) = 57.4; p < 0.001
Status post stroke/transient ischemic	23	7.7	χ^2 (1) = 214.08; p < 0.001
Lipid disorders	170	57	χ^2 (1) = 5.92; p = 0.02
Type 2 diabetes mellitus	57	19.1	χ^2 (1) = 114.47; p < 0.001
Chronic kidney disease	17	5.7	χ^2 (1) = 233.88; p < 0.001

Table 2. The results of 24-hour ambulatory blood pressure monitoring of male and female participants

Variable	M		Me		SD		Min		Max		The result of statistical test
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	
Mean systolic blood pressure — day [mm Hg]	129	131.19	127	130.3	11.42	9.58	102	109	155.8	155.7	U = 7726.5; p = 0.07
Mean diastolic blood pressure — day [mm Hg]	74.87	79.25	75	79.3	9.41	8.77	41	52.4	103.2	98	**U = 6223.5; p < 0.001**
Mean systolic blood pressure — night [mm Hg]	121.18	122.17	120.3	122.6	13.5	10.91	86.8	99	168	149	U = 8109.5; p = 0.31
Mean diastolic blood pressure — night [mm Hg]	66.63	71.38	66	72	8.15	8.73	45.8	53	90	90	**U = 5911.5; p < 0.001**
Mean systolic blood pressure — 24 hours [mm Hg]	126.25	129.03	124	127.75	12.16	9.73	101.4	111.2	156	151	U = 2107.5; p = 0.17
Mean diastolic blood pressure — 24 hours [mm Hg]	71.59	76.22	70	77.5	8.46	9.29	52	51.1	96.2	91	**U = 1691; p = 0.003**
Minimum systolic blood pressure — day [mm Hg]	104.07	104.8	103.5	106	12.36	12.52	63	79	137	121	U = 749; p = 0.57
Minimum diastolic blood pressure — day [mm Hg]	56.74	59.6	57	57	9.93	10.2	40	40	87	79	U = 714.5; p = 0.37
Maximum systolic blood pressure — day [mm Hg]	152.94	153.07	150.5	150.5	19.24	12.91	117	132	220	182	U = 790; p = 0.85
Maximum diastolic blood pressure — day [mm Hg]	92.46	96.07	92	96	12.53	10.98	63	73	120	118	U = 670.5; p = 0.19
Minimum systolic blood pressure — night [mm Hg]	100.89	103.73	99.5	103.5	12.57	13.89	79	69	135	131	U = 676; p = 0.21
Minimum diastolic blood pressure — night [mm Hg]	52.72	57.37	50.5	56.5	8.5	10.02	40	40	78	79	**U = 577; p = 0.03**
Maximum systolic blood pressure — night [mm Hg]	137.63	142.43	136.5	141.5	15.13	14	109	114	167	173	U = 699.5; p = 0.19
Maximum diastolic blood pressure — night [mm Hg]	78.5	87.67	78.5	88	10.85	10.84	57	67	108	119	**U = 435.5; p < 0.001**

M — mean; Max — maximum; Me — median; Min — minimum; SD — standard deviation

(eGFR) were observed in men (p < 0.05). 24-hour blood pressure monitoring was performed during the hospital stay (Table 2). There were no significant differences in the values of systolic blood pressure and heart rate between males and females. The collected data indicate that males had higher diastolic blood pressure than females (p < 0.001).

Considerably higher mean diastolic pressure measured during the day, mean diastolic pressure measured during the night, mean diastolic pressure in 24 h monitoring, minimum and maximum diastolic blood pressure during the night were observed in men. The analysis of echocardiographic results of all patients revealed that women

Table 3. The results of echocardiographic examination of male and female participants

Variable	M		Me		SD		Min		Max		The result of statistical test
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	
A [cm/s]	83.23	74.14	82.5	74	20.38	19.12	26	30	160	125	**U = 3930.5; p = 0.003**
GLS [%]	−19.55	−17.1	−19.5	−18	2.84	3.84	−24.9	−22.2	−12	−4.5	**U = 312.5; p = 0.004**
LA dimension [mm]	39	41.9	38	41	6.59	8.43	27	24	74	68	**U = 6463; p = 0.005**
LAV [mL]	67.12	80.01	60	68.5	30.48	36.49	18	32	263.5	220	**U = 5217.5; p = 0.002**
IVS [mm]	10.1	10.71	10	10	1.69	1.72	6	7	15	16	**U = 7046.5; p = 0.02**
LVPWd [mm]	9.57	10.19	9	10	1.71	1.66	5	5	15	16	**U = 6975; p = 0.003**
LVMI [g/m^2]	89.83	100.72	87.5	93	24.4	29.32	39	58	153	216	**U = 2277.5; p = 0.04**
Mean E/E'	9.76	8.05	8.9	7.95	3.98	3.36	4	0.5	31.2	15.4	**U = 2486.5; p = 0.02**

A — maximum velocity during atrial contraction; E/E' — the ratio of early transmitral flow velocity to early diastolic velocity of the mitral annulus; GLS — global longitudinal strain; IVS — interventricular septum; LA — left atrium; LAV — left atrium volume; LVMI — left ventricular mass index; LVPWd — end-diastolic left ventricular posterior wall thickness; Max — maximum; Me — median; Min — minimum; SD — standard deviation; sM — average

had higher values of maximum velocity during atrial contraction (A) and the ratio of early transmitral flow velocity to early diastolic velocity of the mitral annulus (E/E'). The remaining statistically significantly differences regarded parameters that had higher values in men. The variables for which the differences were statistically significant are presented in Table 3.

Pharmacotherapy

The evaluation of drugs used by patients was performed before the hospitalization in the ward, and then upon the discharge (new recommended drugs). Pharmacotherapy in the treatment of hypertension, hyperlipidemia as well as antiplatelet/anticoagulant agents were compared in this study. Significantly more patients used certain groups of drugs after their discharge from the hospital compared to the period before hospitalization. Table 4 summarizes the frequency of use of each drug group before and after the hospitalization.

Follow-up results

One year after the hospitalization, an attempt was made to contact all patients by phone. Each patient was asked the same survey questions (Table 5). We managed to contact and obtain answers from 230 patients, i.e. 76.9% of study participants (p < 0.001): 158 (68.7%) women and 72 (31.3%) men (χ^2 (1) = 0.02; p = 0.51). Sixty-nine patients did not participate in the survey for the following reasons: failure to contact the patient by phone (54 patients), lack of consent to participate in the survey (14 people), and

the patient's death (1). More than 77% of the respondents reported blood pressure values (home measurements) below 140/90 mm Hg, while 30% reported blood pressure values below 120/70 mm Hg. The majority of patients used the drugs prescribed on discharge from the ward and they always adhere to recommendations. Also, the blood pressure values of most patients have remained at the same level since their last stay in the ward. The comparison of blood pressure (BP) in subgroups of men and women did not reveal any statistically significant differences.

Rehospitalizations

The study assessed factors that could potentially have an impact on the need for hospitalization for cardiovascular causes in patients with arterial hypertension. Out of 230 patients participating in the phone survey, 43 patients (18.7%) required another hospitalization for cardiovascular reasons within a year from their last stay. The frequency of hospitalizations did not differ significantly between the groups set on the basis of answers to the questions concerning blood pressure values in home and office measurements. Nineteen (27.5%) patients with blood pressure below 120/70 mm Hg, 18 (14.4%) patients with blood pressure in the range of 120–140/70–90 mm Hg and 6 (16.7%) patients with blood pressures exceeding 140/90 mm Hg (p = 0.08) required rehospitalization. However, a statistically significant difference in the risk of rehospitalization was observed only between the group of patients with BP values below 120/70 mm Hg and those with values higher than 120/70 mm Hg (19 [27.5%] vs.

Table 4. Groups of drugs used by patients in the study group (two-time points)

Drug group	Number of patients using a drug from a given group				P-value
	On the admission to the ward		Upon discharge from the ward		
	n	%	n	%	
Beta-blockers	174	58.2	214	71.6	< 0.0001
Angiotensin converting enzyme inhibitors	123	41.1	154	51.5	< 0.001
AT1-receptor blockers	71	23.7	95	31.8	< 0.001
Loop diuretics	46	15.4	60	20.1	0.006
Thiazide diuretics	29	9.7	27	9	0.75
Thiazide-like diuretics	71	23.7	70	23.4	0.88
Potassium-sparing diuretics	38	12.7	45	15	0.12
Calcium antagonists	90	30.1	137	45.8	< 0.0001
Alpha blockers	17	5.7	29	9.7	0.003
Alpha2 receptor agonists	1	0.3	5	1.7	0.22
Methyldopa	3	1	2	0.7	1
Antiplatelet/anticoagulant agents	146	48.8	174	58.2	< 0.001
Statins	117	39.1	175	58.5	< 0.001
Other lipid-lowering drugs	8	2.7	13	4.3	0.18

Table 5. The results of a phone survey including a group of 230 patients

Question	Women		Men		Statistical significance
	n	%	n	%	
Are your home blood pressure values lower than 120/70 mm Hg?	49	31	20	27.8	$\chi^2(1) = 0.25$; $p = 0.37$
— if the first answer is negative:					
Are your home blood pressure values lower than 140/90 mm Hg?	85	78	40	76.9	$\chi^2(1) = 0.02$; $p = 0.52$
Have your blood pressure values remained at the same level since the last stay in the ward?	98	62	50	69.4	$\chi^2(1) = 1.19$; $p = 0.17$
Do you still use the drugs prescribed on discharge from the ward?	111	70.3	53	74.6	$\chi^2(1) = 0.47$; $p = 0.3$
Do you always use the prescribed medications in agreement with recommendations?	145	91.8	65	92.9	$\chi^2(1) = 0.08$; $p = 0.51$
Have you been hospitalized for cardiovascular diseases since your last stay in the ward?	29	18.4	14	19.4	$\chi^2(1) = 0.04$; $p = 0.49$

24 [14.9%]; $\chi^2(1) = 5.07$; $p = 0.02$). We did not observe any significant difference in BMI between the group of patients rehospitalized for cardiovascular reasons and the group of subjects who did not require hospitalization ($U = 3595.5$; $p = 0.35$). The rehospitalized persons were significantly older ($p = 0.02$), they had higher blood urea ($p = 0.02$) and creatinine levels ($p = 0.049$) as well as lower eGFR ($p = 0.02$). Only values of mean diastolic blood pressure during the day (in 24-hour blood pressure monitoring during hospitalization) were significantly lower in patients requiring rehospitalization compared to those who did not ($p = 0.04$). In the group of patients requiring rehospitalization, also the following echocardiographic parameters: A, LAV, LAVI, IVS, E/E' were significantly higher than in the group of non-hospitalized patients. Data are summarized in Table 6. Rehospitalized patients were significantly more likely to take antiplatelet/anticoagulant medications. This difference was probably due to the fact that this group comprised more patients with the chronic coronary syndrome who used antiplatelet therapy on a daily basis. Moreover,

Table 6. The results of the analysis of the relationship between rehospitalization and echocardiography parameters in the study group

Variable	M		Me		SD		Min		Max		Statistical significance; p-value
	1	2	1	2	1	2	1	2	1	2	
E [cm/s]	75.37	84.82	75	84	17.6	27.9	36	44	131	187	U = 2012; p = 0.07
A [cm/s]	78.15	88.75	77	90	19.85	18.87	30	53	160	121	**U = 1575.5; p = 0.005**
E/A	1.02	0.99	0.95	0.94	0.35	0.33	0.45	0.5	2.56	1.71	U = 1912; p = 0.8
GLS [%]	−18.73	−19.39	−19.3	−19.4	2.97	3.16	−9.9	−13.3	−23.7	−24.7	U = 254.5; p = 0.77
LA dimension [mm]	40.43	42.03	38	40	15.93	7.94	24	30	229	61	U = 2818; p = 0.07
LAV [mL]	69.25	82.21	62.5	70	31.63	42.3	25	18	263.5	220	**U = 2628.5; p = 0.04**
LAVI [mL/m^2]	38.11	46.65	34	39	16.39	22.56	19.43	10	153.2	113.3	**U = 1781; p = 0.01**
IVS [mm]	10.05	10.76	10	11	1.58	1.81	6	8	16	16	**U = 2685; p = 0.03**
LVPWd [mm]	9.55	9.98	10	10	1.69	1.67	5	7	16	13	U = 3147; p = 0.16
LVMI [g/m^2]	91.23	95.35	89	87	24.05	35.09	39	50	142	216	U = 1415; p = 0.96
Mean E/E'	8.83	10.6	8.2	10.7	3.19	4.82	0.6	0.5	22.3	23.4	**U = 968 5; p = 0.03**

1 — patients who were not rehospitalized; 2 — patients who were rehospitalized; A — maximum velocity during atrial contraction; E — maximum velocity of early mitral inflow; E/A — velocity ratio of early mitral inflow and mitral inflow during atrial contraction; E/E' — the ratio of early transmitral flow velocity to early diastolic velocity of the mitral annulus; GLS — global longitudinal strain; IVS — interventricular septum; LA — left atrium; LAV — left atrium volume; LAVI — left atrial volume index; LVMI — left ventricular mass index; LVPWd — end-diastolic left ventricular posterior wall thickness; M — mean; Max — maximum; Me — median; Min — minimum; SD — standard deviation

there were more patients with left ventricular hypertrophy in this group. A logistic regression analysis was performed to assess factors increasing the risk of rehospitalization in studied groups of HA patients. A combined analysis of variables revealed a statistically significant association only between IVS and the rehospitalization risk (95% CI: 1.06–2.44; OR 1.61; p = 0.03). However, when three factors with the greatest impact on the frequency of hospitalization were included in the analysis (serum creatinine, blood pressure < 120/70 mm Hg, and age), the following variables showed a significant association: age (95% CI: 1.09–12.79; OR 3.73; p = 0.04) and blood pressure below 120/70 mm Hg (95% CI: 1.09–4.44; OR 2.2; p = 0.03).

Discussion

The majority of enrolled patients had a BMI above 25 kg/m^2. This is consistent with observations that overweight and obesity influence the development of HA. Potential mechanisms associated with hypertension in people with excess body weight include the activation of the renin–angiotensin–aldosterone system, increased activity of the sympathetic nervous system, and physical compression of the kidneys [7]. A meta-analysis of the results of 25 randomized clinical trials conducted by Neter et al. [8] confirmed that the loss of each kilogram was associated with a decrease in systolic and diastolic blood pressure by about 1 mm Hg. The authors underline that the reduction of excessive body weight is particularly beneficial for patients taking antihypertensive drugs. At the same time, the findings of Paduszyńska et al. [9] provide evidence that the choice of adequate pharmacotherapy for hypertension enables the control of systolic and diastolic blood pressure, regardless of the BMI value. In this study, we observed that in some patients arterial hypertension was accompanied by other comorbidities. Available literature data confirm that the presence of HA is associated with such diseases as heart failure, renal failure, coronary heart disease, and stroke [10]. In this study, more than 75% of patients had BMI exceeded 25 kg/m^2, more than 50% of them suffered from hyperlipidemia, and about 20% had type 2 diabetes mellitus. Considering the above, a large proportion of patients participating in our study met the criteria for the diagnosis of metabolic syndrome [11]. Left ventricular hypertrophy,

which is associated with arterial hypertension and predisposes to arrhythmias, was observed in more than a quarter of patients [12].

Mean systolic blood pressure increases gradually with age in both sexes, however, in women the incidence of hypertension rises significantly after menopause. This is related to hormonal changes in the course of menopause, resulting in the activation of the renin-angiotensin system and the sympathetic nervous system, as well as in the increase in BMI, obesity, and changes in the distribution of adipose tissue [13]. Data from clinical trials confirm the lack of differences between men and women in the efficacy of antihypertensive drugs [14]. In the present study, we also did not observe any significant discrepancies. In this study, we analyzed the effects of advancing age. Patients over the age of 65 years more frequently used beta-blockers, angiotensin-converting enzyme inhibitors (ACE-I), loop and potassium-sparing diuretics, antiplatelet/anticoagulants, and statins due to the higher incidence of comorbidities in this group. Adjusting pharmacotherapy to the clinical condition of the patient contributed to the lack of significant differences in the effectiveness of antihypertensive treatment assessed in the follow-up.

According to the current guidelines, the use of antihypertensive combination drugs is recommended [15]. According to the data from 2016, only 12% of patients in Poland were administered antihypertensive combination drugs [16]. In our study group, this percentage was higher, but still, combination products were used only by about 20% of participants. The comparison of combination drug use in the period before the admission to hospital and in the period after the discharge from the ward did not reveal any significant changes. Infrequent administration of such drugs may be associated with the fact that the reimbursement is obtained only when they replace the therapy with monopreparations. Data from the NATPOL study cited by Wilimski et al. [17] confirm that ACE-I is the most commonly prescribed group of drugs. In Poland, in 2002, 59% of patients with hypertension were treated with ACE-I, 40% with beta-blockers, 34% with calcium channel blockers, and 24% with diuretics. Czarnecka et al. [18] based on their research reached similar conclusions. In our study, the percentage use of particular drug groups was higher, with beta-blockers being the most frequently administered group. The higher use of these drugs in our study in comparison to the aforementioned research can be explained by the prevalence and the type of comorbidities observed in our patients. 30% of patients in the study group were diagnosed with the chronic coronary syndrome, approx. 25% with heart failure, approx. 15% with atrial fibrillation/flutter, and approx. 10% had a myocardial infarction. In turn, frequent use of diuretics is in agreement with the current European Society of Cardiology (ESC)/European Society of Hypertension (ESH) recommendations [19] concerning the

treatment that should be based on combinations of active substances from various groups.

The obtained results indicating good control of blood pressure after one year of follow-up (mirrored by BP values below 140/90 in-home measurements) in 84% of participants are much higher than those observed in other population studies. In the NATPOL 2011 population study, the proper control of arterial hypertension was achieved by 23% of persons, and in the earlier NATPOL PLUS 2002 and WOBASZ, I studies it oscillated around 10–15% [20]. According to the data cited by Wożakowska-Kapłon et al. [21], the effectiveness of HA treatment was estimated to be ~42%. It should be emphasized that in the present study as many as 92% of patients declared that they were always taking medications in accordance with the recommendations, while the therapy recommended at discharge from the ward was continued by less than 72% of them. Changes in the treatment correspond to the answers to the question about the stabilization of blood pressure values (BP control was confirmed by 64% of surveyed patients).

In this study, we observed a statistically significant association between persistent blood pressure values below 120/70 mm Hg and more frequent hospitalizations. As it was mentioned above, in our study group, patients with systolic blood pressure < 120 mm Hg had a higher E/E' ratio. This parameter is an important predictor of the occurrence of cardiac events. In the study performed by Sharp et al. [22], a unit rise in the E/E' ratio was associated with a 17% increment in the risk of a cardiac event (HR 1.17; CI: 1.05–1.29; p = 0.003) after adjusting for covariates (HR 1.17; CI: 1.05–1.29; p = 0.003).

Echocardiographic parameters: LAV and LAVI are also important for the risk of rehospitalization. These parameters describing the size of the left atrium, positively correlate with E/E' ratio values [23], and this relationship was also observed in our study. E/E' and LAVI values are higher in HA patients compared to healthy subjects [24]. Cacciapuoti et al. [25] reported significantly higher LAVI values in the study group compared to the control group (47 ± 5 mL/m^2 vs. 23 ± 4 mL/m^2). Left atrial enlargement is an early sign of the development of hypertension with cardiac involvement and it reflects the severity of left ventricular diastolic dysfunction. Both LAV and LAVi indicate an increased cardiovascular risk [26]. The results obtained in our study are consistent with those described in the aforementioned studies. In both groups of patients with arterial hypertension, LAV and LAVI values were higher than those observed in healthy subjects. Moreover, higher values of these parameters were observed in the group of patients requiring rehospitalization, which may confirm their prognostic value in the assessment of cardiovascular risk. In our study group, the thickness of IVS was associated with the risk of rehospitalization. In the above-mentioned study, Cacciapuoti et al. [25] observed a statistically significant

difference in IVS thickness between healthy subjects and patients with arterial hypertension (10 ± 4 mm vs. 13.5 ± ± 5 mm; p < 0.01). It should be underlined that in our study, IVS thickness was more similar to the values observed in healthy people. The comparison of echocardiographic parameters between patients requiring rehospitalization within one year from the last discharge and those who did not need it revealed that the first group was characterized by a greater tendency to develop left ventricular diastolic dysfunction. Such LV impairment predisposes to the progression of heart failure and increases the risk of cardiac events.

It is also worth mentioning that we found a link between rehospitalization and higher urea and creatinine values as well as lower eGFR (analysis of individual factors effects). This relationship did not remain statistically significant after the addition of a larger number of parameters influencing hospitalization risk to the analysis. Literature data confirm that renal function deteriorates in the course of arterial hypertension [27]. It should be emphasized that in patients treated with antihypertensive therapy, no significant positive correlation between urea concentration and blood pressure is observed [28]. This may explain the reason why in this study, patients who were rehospitalized and had higher urea and creatinine values were more likely to have blood pressure below 120/70 mm Hg. The results of HOT (Hypertension Optimal Treatment) study demonstrated that serum creatinine concentration exceeding 1.5 mg/dL significantly increased the risk of death (RR 2.86; CI: 2.10–3.89; p < 0.001), including deaths related to cardiovascular events (RR 3.24; CI: 2.13–4.94; p < 0.001) [29]. The importance of eGFR as an indicator of cardiovascular risk depends on the population studied. The relationship between eGFR and cardiovascular risk is significant in high-risk groups, while in the other groups it is weak or absent [30]. Recent studies have also provided evidence that pharmacotherapy can result in a reduction in GFR. The decline in GFR is greater in patients whose antihypertensive treatment was intensified [31]. It is possible that the worse prognosis observed in patients in whom antihypertensive treatment results in systolic blood pressure drops below 120 mm Hg could be also associated with the simultaneous deterioration of renal function related to poorer perfusion. Renal function also worsens with age; it should be emphasized that in our study more advanced age significantly increased the frequency of rehospitalizations.

In the present study, age and blood pressure below 120/70 mm Hg were found to be the most important independent factors of rehospitalization. The results of clinical trials and meta-analyses demonstrate the benefits of lowering blood pressure. A meta-analysis by Thomopoulos et al. [32] revealed that the reduction in systolic and diastolic blood pressure decreased the relative risk

of cardiovascular events and death. This relationship was present in case of a decrease in systolic blood pressure (SBP) below 140 mm Hg and below 130 mm Hg. Moreover, the relative risk in the group with SBP below 130 mm Hg (mean 126 mm Hg) was lower than in the group with BP values in the range of 130–139 mm Hg. Similarly, a reduction in diastolic BP to ≤ 89–80 mm Hg was associated with a decrease in relative risk. At the same time, it was reported that the risk reduction gradually decreased with the lowering of blood pressure [32]. What is important, a subsequent meta-analysis of the same team demonstrated that significant SBP reduction was associated with disproportionately high discontinuation rates outweighing the potential benefits of reducing the risk of cardiovascular events. [33]

The results of the meta-analysis by Ettehad et al. [34] indicate the benefits of lowering SBP below 130 in all patients, regardless of the baseline risk level.

Limitations

Threshold BP values for hypertension vary in relation to the measurement method. It should be emphasized that home and ABPM measurements are more reliable for the assessment of cardiovascular risk than office measurements, however, the guidelines specify the target blood pressure values in relation to the last one. During the follow-up stage, patients were asked whether their BP measured at home and at the physician's office was below 120/70 mm Hg, or below 140/90 mm Hg (if the answer to the first question was negative). We used a cut-off value for office BP which is also the reference for establishing target values. Although the ESC/ESH guidelines endorse age-related target values, we used the same cut-off values for all patients in order to unify and simplify the phone survey as much as possible. Due to the fact that the follow-up was carried out in the form of a phone survey, ABPM results were not obtained. Sixty-nine patients did not participate in the survey, therefore we were unable to fully evaluate the entire group of patients participating in this study. This could have an impact on the observed percentage of people declaring adherence to medical recommendations. The study group was heterogeneous due to the presence of various comorbidities, which can affect the obtained results. However, this mirrors the situation that physicians face in real clinical practice.

Conclusions

The results of this study showed the discrepancies between physicians' recommendations concerning antihypertensive therapy and the current ESH/ESC guidelines for the pharmacotherapy of arterial hypertension. This may be associated with the individual approach of physicians to patients struggling with HA and other comorbidities, as

well as with the limited reimbursement of combination preparations in Poland. It should also be emphasized that patients' compliance is more important for the effectiveness of the treatment of arterial hypertension than the use of a specific group of drugs.

In this study, we observed that gender did not significantly affect the efficacy of hypertension pharmacotherapy and the prognosis in the 1-year follow-up, while the increase in parameters of left ventricular diastolic dysfunction (E/E', LAV and LAVI) was associated with worse treatment outcomes in patients with HA. Moreover, age and mean blood pressure values below 120/70 mm Hg were independent factors of cardiovascular rehospitalization among patients with hypertension, in 1-year follow-up.

Conflict of interest

The authors declare no conflict of interest.

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Streszczenie

Wstęp. Celem niniejszej pracy jest porównanie i ocena wyników leczenia hipotensyjnego pacjentów z pierwotnym nadciśnieniem tętniczym oraz identyfikacja czynników ryzyka ponownej hospitalizacji z przyczyn sercowo-naczyniowych w tej grupie chorych.

Materiał i metody. Do badania obserwacyjnego włączono 299 osób (206 kobiet i 93 mężczyzn) z rozpoznaniem pierwotnego nadciśnienia tętniczego. Przeanalizowano dane medyczne pacjentów, w tym badania laboratoryjne, wyniki przezklatkowej echokardiografii i 24-godzinnych automatycznych pomiarów ciśnienia tętniczego. Rok po hospitalizacji przeprowadzono wywiad telefoniczny z pacjentami w celu oceny wartości ciśnienia tętniczego, farmakoterapii i zdarzeń sercowo-naczyniowych. Zebrane dane poddano analizie statystycznej.

Wyniki. Pacjenci z nadwagą i dyslipidemią stanowili większość analizowanej grupy. W grupie mężczyzn średnie wartości rozkurczowego ciśnienia tętniczego były istotnie wyższe niż wśród kobiet. Porównanie wyników echokardiografii przezklatkowej wykazało, że kobiety miały istotnie wyższe wartości prędkości maksymalnej przedsionkowej fali napływu mitralnego (fala A) i stosunku prędkości maksymalnych wczesnorozkurczowej fali napływu mitralnego oraz wczesnorozkurczowej fazy ruchu pierścienia mitralnego (E/E'). Po roku od hospitalizacji większość pacjentów stosowała się do zaleceń i uzyskała średnie wartości ciśnienia tętniczego < 140/90 mm Hg. Aż 18,7% pacjentów wymagało rehospitalizacji z przyczyn sercowo-naczyniowych w ciągu rocznej obserwacji.

Wnioski. Farmakoterapia hipotensyjna w badanej populacji różniła się od zaleceń zawartych w wytycznych ESC/ESH dotyczących postępowania w nadciśnieniu tętniczym. Podwyższone parametry echokardiograficzne dysfunkcji rozkurczowej lewej komory były związane z gorszymi wynikami leczenia hipotensyjnego. Wiek i ciśnienie tętnicze poniżej 120/70 mm Hg zwiększały ryzyko rehospitalizacji w badanej populacji.

Słowa kluczowe: nadciśnienie tętnicze, dysfunkcja rozkurczowa, farmakoterapia, rehospitalizacje

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