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ORIGINAL ARTICLE

Usefulness of impedance cardiography in optimisation of antihypertensive treatment in patients with metabolic syndrome: a randomised prospective clinical trial

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Abstract

Background: The effective antihypertensive therapy is one of the main goals of treatment in metabolic syndrome (MS) because hypertensive patients with MS are of high cardiovascular risk. The impedance cardiography (ICG), as a modern technique of non-invasive haemodynamic monitoring, enables the evaluation of cardiac index (CI), thoracic fluid content (TFC) and systemic vascular resistance index (SVRI) and seems to be useful in clinical individual assessment of patients with MS.

Aim: To estimate the effectiveness of the antihypertensive therapy based on ICG.

Methods: The study involved 82 hypertensive patients with MS (57 men, age 45.5 ± 10.0 years), without any major chronic diseases. After the preliminary assessment including office blood pressure measurement (OBPM), ambulatory blood pressure monitoring (ABPM) and ICG, the subjects were randomised into two groups: empirical (GE) and treated with the use of haemodynamic evaluation by ICG (HD). The effect of the therapy was estimated at 3 months follow-up.

Results: After 12 weeks the HD group was characterised by lower mean BP values in OBPM and ABPM, with statistical significance for night-time SBP (120.6 ± 9.1 *vs* 115.6 ± 8.2 mm Hg, p = 0.036). The use of ICG significantly increased the reduction of BP in OBPM — SBP (GE *vs* HD: change 10.7 *vs* 18.1 mm Hg, p = 0.012), DBP (8.9 *vs* 12.2 mm Hg, p = 0.037), and ABPM: in the 24-h period SBP (10.5 *vs* 16.7 mm Hg; p = 0.013) and day-time SBP (10.5 *vs* 17.2 mm Hg, p = 0.009). More patients in the HD group reached recommended BP control in OBPM (23.5 *vs* 36.6%, p = 0.222) and ABPM (23.5 vs 43.9%, p = 0.117).

Conclusions: The antihypertensive therapy guided by ICG increased the reduction of BP in patients with MS. The assessment of haemodynamic profile by ICG guarantees better choice of antihypertensive drugs and subsequently increases the chance of recommended BP control in patients with MS.

Key words: metabolic syndrome, arterial hypertension, impedance cardiography

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INTRODUCTION

Arterial hypertension (AH) affects approximately 1/4 of the world's population and constitutes an important clinical, social and economic problem [1]. It is the main risk factor for ischaemic heart disease, heart failure, renal failure, and stroke. In more than 50% of patients AH coexists with metabolic disturbances. In Polish population AH is the most common component of metabolic syndrome (MS) [2, 3]. Due to increased cardiovascular risk, in MS patients without concomitant cardiovascular diseases strict blood pressure (BP) control is suggested with BP target values < 130/80 mm Hg [4]. Achieving this goal being a challenging task, the percentage of patients with poor BP control is disconcertingly high (in the WOBASZ trial only 10% of men and 16% of women had normal BP values) [5]. The authors of the current guidelines [6, 7] have not defined any specific algorithm for the treat-

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ment of hypertension, instead they emphasize that the guidelines are not meant to dictate the treatment and that the treatment decisions must be made based upon the independent judgement of physician and each patient individual circumstances.

The increase of BP, involved in the pathogenesis of AH, is the result of complex mechanisms and potential underlying causes include fluid retention, increased vascular resistance and hyperdynamic function of the left ventricle. Impedance cardiography (ICG) is a noninvasive and easy to use method of haemodynamic monitoring of cardiac index (CI) and other parameters that accurately characterise the contribution of above-mentioned mechanisms in the development of AH, such as thoracic fluid content (TFC), systemic vascular resistance (SVR), and heart rate (HR) [8, 9]. The results of previous clinical trials confirmed the effectiveness of ICG in individualisation of antihypertensive treatment. As noted by Taler at al. [10], ICG guaranties better choice of drugs and their dosing according to patients individual haemodynamic status. Smith at al. [11] also suggests that in hypertensive patients ICG significantly improves the effectiveness of the therapy and enables the monitoring of treatment effects. However, these authors have not provided clear recommendations on principles for the antihypertensive treatment based on haemodynamic measurements and their criterion values, which significantly reduced the chances for implementing their findings into clinical practice.

The aim of the study was to compare the effectiveness of the antihypertensive therapy with empirical method or with new treatment algorithm based on haemodynamic parameters assessed by ICG in patients with mild and moderate hypertension.

METHODS

Study population

The study population comprised patients with at least 3-month history of mild or moderate AH, defined according to European Society of Cardiology (ESC) guidelines [6], who fulfilled other criteria of MS [12] and who were admitted to the Department of Cardiology and Internal Diseases, Military Institute of Medicine, Warsaw between February 2008 and June 2009 for diagnostics of AH.

Eligible were patients who fulfilled criteria for MS, including not treated AH (BP increased for at least 3 months) and have poorly controlled AH with 1 or 2 antihypertensive agents.

Exclusion criteria included: (1) confirmed secondary AH, (2) improperly controlled AH with three or more antihypertensive medicines, (3) severe comorbidities: heart failure, cardiomyopathy, significant heart rhythm abnormalities, significant valvular disease, renal failure, chronic obstructive pulmonary disease, diabetes, polyneuropathy, peripheral vascular disease, (4) age < 18 years and > 65 years, (5) heart rhythm other than normal sinus rhythm (including permanent cardiac pacing), (6) in patients included in the study (during observation): significant violation of study protocol, drug administration other than recommended, contact made by patient before the scheduled visit due to poor treatment tolerance, including serious adverse effects connected with drug administration, and refusal to further participation in the study.

The protocol was approved by the Ethics Committee of Military Institute of Medicine (no. 3/WIM/2008). All patients gave informed written consent to participate in this study.

Study design

The study was randomised (1:1), prospective and controlled by conventional treatment. At the first visit, the initial clinical assessment was conducted including physical examination and medical interview concerning symptoms and comorbid conditions. Drug-treated patients were asked to withdraw their previous medication and advised to take a rescue dose of sublingual captopril in case of BP excursions. At the second visit (after 2 weeks) all patients underwent following examinations: interview and physical examination, ambulatory blood pressure monitoring (ABPM), ICG, ECG, echocardiography, and laboratory tests (serum electrolytes, creatinine, fasting glycaemia, lipid profile).

Participants were randomly assigned to one of two groups (using RandomBots Medusa 2.0.2 software): (a) empiric group (GE), in which treatment choice was based on clinical data and current ESC guidelines, (b) haemodynamic group (HD), in which treatment choice was based on clinical data and current guidelines considering haemodynamic parameters obtained by ICG. In both groups, the therapeutic decisions were made by independent researchers. Patients were blinded to group assignment.

The treatment effect was assessed at the third visit (after 12 weeks) based on the results of tests performed (that were similar to those conducted during the second visit, except for echocardigraphic evaluation). Short-term endpoints were: between-group differences in absolute BP values, BP reduction and BP control after 12 weeks of treatment (per protocol analysis).

Patients were instructed to contact the researcher if significant treatment-related adverse symptoms occur (e.g. poor treatment tolerance, lack of clinical effect).

Medical history and physical examination

Clinical examinations were performed during all visits according to ESC guidelines [6], with special reference to cardiovascular risk factors and symptoms suggesting secondary cause of AH as well as to end-organ damage. Office blood pressure measurements (OBPM) were performed according to ESC guidelines [6].

Ambulatory blood pressure monitoring

In all participants, 24-h BP profile was obtained by ABPM (Spacelabs 90207; Spacelabs, Medical Inc, Redmond, Wa-

shington, USA). During daytime activity, specified as the period between 6.00 and 22.00, automatic BP measurements were performed every 10 min. During night-time rest (22.00––6.00) BP values were measured every 30 min. The results were interpreted according to ESC guidelines ESC [6].

Impedance cardiography

Haemodynamic parameters were measured by ICG technique during 10-min examination (Niccomo device, Medis, Germany) in the morning hours (7.30–8.30), with the subject in horizontal position, after rest. Blood pressure measurement was performed automatically every 2 min, using arm cuff. The assessment of other haemodynamic parameters was performed by beat-to-beat method. Readings of haemodynamic parameters relevant to treatment algorithm (TFC, CI, SVRI, and HR) were taken in the 5th min of the examination and recorded in the report. All study data were archived (Niccomo® software, 1.6 version). According to SVRI, CI, HR and TFC values, haemodynamic cut-off values were defined as: (1) hyperconstrictive profile if SVRI > 2500 dyn·s·cm^{-5}·m^2, (2) hyperdynamic profile if CI > 4.2 L/min/m^2 and/or HR > > 80/min, (3) hypervolaemic profile if TFC > 34 1/kOhm for men and > 24 1/kOhm for women, (4) balanced profile if above-mentioned parameters were below previously defined threshold values. Mean BP values for entire 24-h ABPM measurement period higher than 140/90 mm Hg were regarded as additional indication for combination therapy.

Echocardiographic evaluation

The echocardiographic studies were performed in the morning (7.30–8.30), according to the recommendations of the Working Group of Echocardiography of the Polish Society of Cardiology [13] with the Vivid 7 ultrasound machine (GE-Healthcare, United States) in order to exclude significant pathologies involving cavity dimensions, myocardial contractibility and wall thickness of the left ventricle.

Treatment

Non-pharmacological treatment was conducted according to current ESC guidelines [6, 7]. Drugs used in antihypertensive pharmacological therapy have been proven effective in numerous clinical trials: lisinopril — an angiotensin converting enzyme inhibitor (ACEI), telmisartan — an angiotensin receptor blocker (ARB), hydrochlorothiazide — a thiazide diuretic, metoprolol — cardio-selective beta-blocker (BB), amlodipine — a dihydropyridine calcium blocker (CB).

In the HD group, the treatment algorithm was arbitrary adopted based on researchers' own experience and available medical literature on the pathophysiology of AH and the use of ICG in diagnostics and treatment of AH. Absolute values of CI and SVRI were determined based on available literature data [10, 11, 14]. TFC values for men and women were defined based on epidemiological data from large clinical trials [10, 11] with regard to gender-dependent algorithms used in Niccomo device. Considering reports on disadvantageous prognostic effect of accelerated HR, the resting HR > 80/min was regarded as additional indication for BB therapy [15, 16]. The first step was to select the medication based on ICG result: in patients with hyperdynamic profile BB was recommended, in patients with hypervolaemic profile — thiazide diuretic, and in patients with vasoconstrictive profile — renin–angiotensin–aldosterone (RAA) system blockers (in combination with CB if SVRI was significantly high). Appropriate drug combinations were administered when complex haemodynamic disturbances were present. In patients with significantly increased 24-h BP and indication for monotherapy according to haemodynamic assessment, the second step consisted in introduction of second antihypertensive drug according to previously defined combinations (Fig. 1). Patients with balanced haemodynamic profile received ACEI/ARB combination.

Statistical analysis

Statistical analysis was performed using the Statistica 7.0 software (StatSoft Inc.). To assess the normality of data distribution the Shapiro-Wilk test was used. All results are expressed as mean values ± SD for continuous variables and numbers and percentages for categorical variables. Comparisons of treatment effects between groups were performed with t-Student test for normally distributed data and with non-parametric tests (U-Mann Whitney, χ^2) for non-normal data. A p values < 0.05 were considered statistically significant.

RESULTS

A total of 82 patients (57 men and 25 women) aged 45.5 ± ± 10.0 years were examined. Baseline characteristics of study participants are shown in Table 1. Haemodynamic profiles were differential among studied patients, although most prevalent was the vasoconstrictive profile (45.1%). Hyperdynamic circulation and hypovolaemia were observed in 30.5% and 19.5% of patients, accordingly, and almost 1/3 of patients were characterised by balanced haemodynamic profile (32.9%). In 25.6% of patients at least 2 of above-mentioned abnormalities were present.

Seven patients were excluded from the analysis (5 resigned from control visit and 2 was diagnosed with diabetes demanding insulin therapy). The final analysis included 75 patients who fulfilled all conditions according to study protocol (Fig. 2). Almost all the patients were treated with RAA system blocker, the percentage of patients taking these drugs was similar in both groups (GE *vs* HD: 88.2% *vs* 87.8%, NS). At the same time, combination treatment was significantly more frequently used in the HD group than in the GE group (75.6% *vs* 41.2%, p = 0.002), mainly due to higher percentage of patients taking CB (25% *vs* 3.9%, p = 0.016) and BB (41.5% *vs* 17.7%, p = 0.025) in the HD group. Thiazide diu-

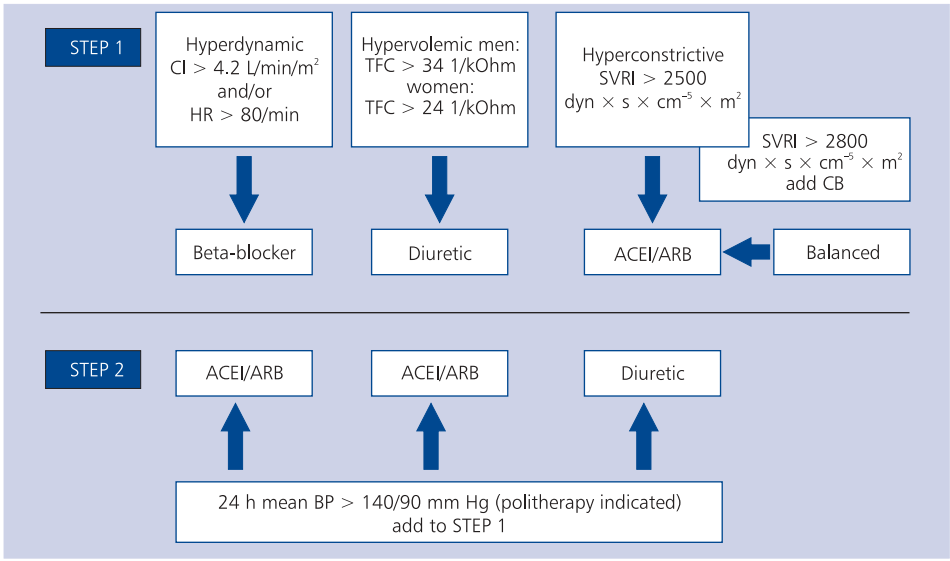

Figure 1. Treatment algorithm based on selected haemodynamic parameters (see detailed description in the text); ACEI — angiotensin converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure; CB — calcium blocker; CI — cardiac index; HR — heart rate; SVRI — systemic vascular resistance index; TFC — thoracic fluid content

Table 1. Baseline patients' characteristics

	Empiric group (EG) (n = 40)	Haemodynamic group (HD) (n = 42)	P	Whole study population (n = 82)
Males	30 (75.0%)	27 (64.3%)	0.292	57 (69.5%)
Age [years]	44.6 ± 10.4	46.3 ± 9.6	0.461	45.5 ± 10.0
BMI [kg/m²]	31.0 ± 4.4	30.1 ± 3.7	0.383	30.5 ± 4.0
SBP [mm Hg]	146.2 ± 14.6	149.9 ± 17.4	0.339	148.1 ± 16.1
DBP [mm Hg]	95.6 ± 9.7	96.4 ± 9.3	0.702	96.0 ± 9.5
Smokers	10 (25.0%)	8 (19.1%)	0.515	18 (22.0%)
Treated AH	11 (27.5%)	13 (30.1%)	0.731	24 (29.3%)
Family history of AH	29 (72.5%)	27 (64.3%)	0.424	40 (48.8%)
Left ventricular hypertrophy	10 (25.0%)	14 (33.3%)	0.449	24 (29.3%)
Symptoms				
Headaches	19 (47.5%)	24 (57.1%)	0.382	43 (52.4%)
Malaise	12 (30.0%)	12 (28.6%)	0.887	24 (29.3%)
Dizziness	4 (10.0%)	1 (2.4%)	0.149	5 (6.1%)
Vision impairment	5 (12.5%)	3 (7.1%)	0.414	8 (9.8%)
Asymptomatic	15 (37.5%)	13 (31.0%)	0.532	28 (34.1%)

BMI — body mass index; SBP — systolic blood pressure; DBP — diastolic blood pressure; AH — arterial hypertension

retic was taken by almost every third patient, similarly frequent in both groups (HD *vs* GE: 29.3% and 29.4%, accordingly, p = 0.989). No significant treatment-related adverse effects were noted.

Treatment effects in study groups

Blood pressure values obtained from both OBPM and all ABPM measurement periods were lower in the HD group, although the differences were statistically significant only for

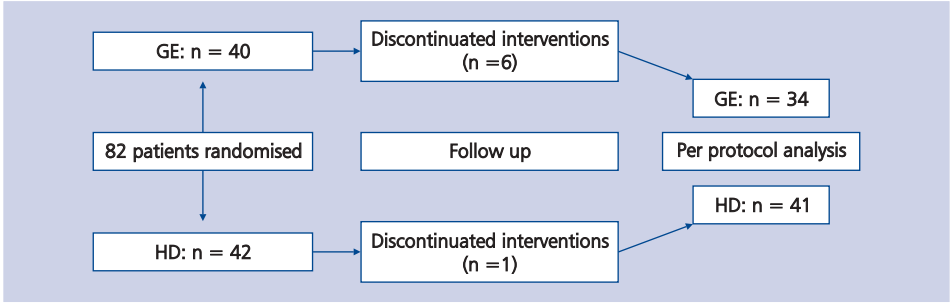

Figure 2. Patient flow chart; GE — empiric group; HD — haemodynamic group

night-time SBP. The analysis of mean BP values underlined between-group differences in the effect of treatment: mean BP reduction was significantly greater in the HD group compared with the GE group, which was most evident for OBPM (both SBP and DBP) and mean SBP values from all measurement periods and daytime ABPM (Table 2).

The assessment of the treatment's effect on haemodynamic profile revealed a significant reduction in SVRI values, that was greater (the difference was of borderline statistical significance) in the HD group (Table 2). The treatment did not influence CI and TFC values averaged for both groups.

The analysis of BP control rate showed that in the HD group the administered therapy turned out to be more effective according to both OBPM (< 130/80 mm Hg) and ABPM, although the magnitude of the differences only reflected a trend toward change in BP values (Table 3).

DISCUSSION

Although the principles for AH treatment have been discussed for many years, any explicit algorithms for antihypertensive pharmacotherapy are still not available. Therefore, current guidelines on the management of patients with AH focus on detailed diagnostics, which enables the assessment of risk factor and individualisation of treatment [6, 7]. Based on current guidelines, reports from other authors and our own experience, we have developed an algorithm for the choice of antihypertensive therapy according to selected haemodynamic parameters. Its usefulness was confirmed by thorough evaluation of treatment effects.

Characteristics of the studied population

An examination performed with ICG revealed significant variability in haemodynamic profiles in the studied population. The most frequent were vasoconstrictive features, which in considerable proportion of patients were accompanied by hypervolaemia and hyperdynamic myocardial function (mainly resting tachycardia).These finding are supported by many reports on pathomechanism of AH in patients with MS. The increase in vascular resistance may be attributed to activation of the RAA system, vascular smooth muscle remodelling, and endothelial dysfunction. Hyperdynamic circulation may be related with excessive sympathetic activity observed in MS patients, whereas subjects predisposed to hypervolaemia may also be prone to sodium retention [2, 4, 17].

When analysing haemodynamic characteristics of studied population, it should be noted that the subject included in our study were predominantly young or middle age, and that caution should be exercised when extrapolating the results to other age groups. According to other researchers' opinion [10, 11, 18], it should be expected that among older patients the percentage of disturbances related with hyperdynamic myocardial function would be significantly lower, and the number of patients with hyperconstriction and hypervolaemia would be higher.

Treatment effect comparison

Proposed therapeutic management including haemodynamic parameters increased the effectiveness of antihypertensive therapy. The analysis of BP values revealed that the hypotensive effect of treatment was stronger in the HD group, particularly for SBP values obtained by OBPM, but also for ABPM. In both groups, OBPM values < 140/90 mm Hg were achieved in more than 50% of patients, but target BP values < 130/80 mm Hg (recommended for MS patients) were markedly more frequently attained in the HD group.

Furthermore, BP control assessed based on ABPM was also better in the HD group. Although the differences did not reach the statistical significance, increase by 20% in the proportion of patients with good BP control seems to be clinically significant.

Smith et al. [11] and Taler et al. [10] evaluated the effectiveness of ICG in the management of AH, but they have not specified the management algorithm based on absolute values of haemodynamic parameters. In the CONTROL [1] trial, patients (mean age 55 years, without significant comorbid conditions, mean BP values 155/93 mm Hg) received 3-month therapy, that in the HD group was modified based on the comparison of monthly ICG measurements. Treatment based on haemodynamic evaluation was related with significantly better BP control, including greater reduction of mean

Table 2. Effect of treatment on blood pressure values and haemodynamic parameters

	Empiric group (EG) (n = 34)	Haemodynamic group (HD) (n = 41)	P
OBPM			
SBP [mm Hg], baseline	145.9 ± 14.9	150.6 ± 17.1	0.233
SBP [mm Hg], after 12 week	135.3 ± 11.8	132.5 ± 12.2	0.441
Change in SBP [mm Hg]	10.7 ± 11.9	18.1 ± 12.8	0.012
DBP [mm Hg], baseline	94.7 ± 9.4	96.5 ± 9.4	0.417
DBP [mm Hg], after 12 weeks	85.8 ± 7.4	84.3 ± 6.7	0.342
Change in DBP [mm Hg]	8.9 ± 8.8	12.2 ± 7.2	0.037
ABPM			
Entire 24-h period			
SBP [mm Hg], baseline	141.4 ± 11.3	143.6 ± 10.8	0.229
SBP [mm Hg], after 12 weeks	130.9 ± 9.2	126.9 ± 8.6	0.056
Change in SBP [mm Hg]	10.5 ± 11.9	16.7 ± 9.3	0.013
DBP [mm Hg], baseline	88.0 ± 8.1	89.3 ± 6.6	0.438
DBP [mm Hg], after 12 weeks	79.5 ± 7.1	78.4 ± 5.8	0.470
Change in DBP [mm Hg]	8.5 ± 8.3	10.9 ± 7.2	0.181
Daytime			
SBP [mm Hg], baseline	145.4 ± 11.8	148.9 ± 11.0	0.088
SBP [mm Hg], after 12 weeks	134.9 ± 10.0	131.7 ± 8.8	0.158
Change in SBP [mm Hg]	10.5 ± 11.7	17.2 ± 10.1	0.009
DBP [mm Hg], baseline	91.4 ± 8.5	93.6 ± 7.1	0.228
DBP [mm Hg], after 12 weeks	82.7 ± 8.2	82.1 ± 5.7	0.708
Change in DBP [mm Hg]	8.7 ± 8.8	11.5 ± 7.00	0.128
Night-time			
SBP [mm Hg], baseline	130.4 ± 113	130.3 ± 12.9	0.958
SBP [mm Hg], after 12 weeks	120.6 ± 9.1	115.7 ± 10.7	0.038
Change in SBP [mm Hg]	9.9 ± 13.1	14.6 ± 10.4	0.084
DBP [mm Hg], baseline	78.6 ± 9.0	78.5 ± 8.2	0.981
DBP [mm Hg], after 12 weeks	70.9 ± 7.0	67.9 ± 6.5	0.054
Change in DBP [mm Hg]	7.6 ± 9.0	10.7 ± 8.6	0.142
Impedance cardiography			
TFC (1/kOhm), baseline	27.6 ± 4.4	26.8 ± 2.9	0.484
TFC [1/kOhm], after 12 weeks	27.5 ± 4.7	26.8 ± 4.0	0.525
Change in TFC [1/kOhm]	0.1 ± 3.1	0.04 ± 3.0	0.834
CI [L/min/m^2], baseline	3.23 ± 0.58	3.28 ± 0.54	0.740
CI [L/min/m^2], after 12 weeks	3.10 ± 0.49	3.24 ± 0.47	0.215
Change in CI [L/min/m^2]	0.14 ± 0.39	0.13 ± 0.47	0.659
SVRI [dyn·s·cm^{-5}·m^2], baseline	2467.6 ± 574.1	2495.9 ± 495.9	0.287
SVRI [dyn·s·cm^{-5}·m^2], after 12 weeks	2305.4 ± 434.9	2154.9 ± 369.2	0.201
Change in SVRI [dyn·s·cm^{-5}·m^2]	162.3 ± 378.5	341.0 ± 413.3	0.064

ABPM — ambulatory blood pressure monitoring; CI — cardiac index; DBP — diastolic blood pressure; OBPM — office blood pressure measurement; SBP — systolic blood pressure; SVRI — systemic vascular resistance index; TFC — thoracic fluid content

SBP and DBP, as well as higher proportion of patients with BP < 140/90 mm Hg in the HD group (77% *vs* 57%, p < < 0.001). Similarly, in the study performed by Taler et al. [10], who examined slightly different population (mean age 66 years, resistant AH, significant percentage of patients with comorbidities), the effect of 3-month therapy was more pro-

Table 3. Effect of treatment on blood pressure control

	Empiric group (EG) (n = 34)	Haemodynamic group (HD) (n = 41)	P
OBPM			
< 140/90 mm Hg	18 (52.9%)	21 (51.2%)	0.882
< 130/80 mm Hg	8 (23.5%)	15 (36.6%)	0.222
ABPM*			
Adequate blood pressure control over all measurement periods	9 (26.5%)	18 (43.9%)	0.117
Entire 24-h period			
SBP/DBP	18 (52.9%)/18 (52.9%)	27 (65.9%)/28 (68.3%)	0.256/0.174
Daytime			
SBP/DBP	17 (50.0%)/20 (58.8%)	27 (65.9%)/29 (70.7%)	0.165/0.281
Night-time			
SBP/DBP	19 (55.9%)/17 (50.0%)	27 (65.9%)/26 (63.4%)	0.377/0.242

*Normative values: during the entire measurement period: BP < 130/80 mm Hg, during daytime activity: BP < 135/85 mm Hg, during night-time rest: BP < 120/70 mm Hg; OBPM — office blood pressure measurement; ABPM — ambulatory blood pressure monitoring; DBP — diastolic blood pressure; SBP — systolic blood pressure

nounced in the HD group, both for mean BP values (GE *vs* HD: 147/79 *vs* 139/72 mm Hg, $p < 0.01$), and good BP control defined as BP < 140/90 mm Hg (33% *vs* 56%, $p < 0.05$).

When assessing the influence of antihypertensive treatment on haemodynamic parameters, we noted significant effect only for SVRI reduction. Lack of differences between groups with respect to other haemodynamic parameters, including TFC and CI, may be attributed to different treatment regiments and averaging the results for whole groups (GE and HD). Thus, the results obtained presumably do not reflect the treatment effect in the subgroups treated with medicines having different mechanisms of action. Similar observations concerning the assessment of the effect of treatment on haemodynamic parameters were made by the authors of above-mentioned studies [11, 12].

Recapitulating the value of ICG in the treatment of AH, one should mention the meta-analysis of the above trials [10, 11], performed by Ferrario et al. [19]. Odds ratio (OR) for achieving BP control in pooled analysis was as high as 2.41 (95% CI 1.44–4.05, $p < 0.0008$), although it should be noted that it was calculated for a short period of observation.

Beneficial effect of ICG-guided antihypertensive therapy may have significant prognostic value. The results of large meta-analysis performed by Williams [20] indicate that a decrease of BP values by 4/3 mm Hg reduces the risk of stroke by 23%, the risk of coronary heart disease by 15% and the risk of overall mortality by 14%.

Administered treatment

Patients from the HD group were significantly more frequently treated with more than one antihypertensive agent. Statistically significant differences were observed for rarely used drugs, mostly in combination therapy with ACEI (CB and BB). It should be mentioned that the most frequent polytherapy in the GE group was a combination of ACEI/ARB with thiazide diuretic, what was supported by clinical experience and knowledge based on the results of large clinical trials and previous guidelines [21–23], whereas in the HD group equally frequent was the combination of ACEI/ARB with CB, which is in accordance with current guidelines on antihypertensive treatment that were created based on the results from the ACCOMPLISH study [24].

Observed differences in the frequency of polytherapy and the number of antihypertensive medications taken require a thorough commentary. First of all, it should be underlined that in the HD group detailed management algorithm significantly limited subjectivity of the treatment choice. At the same time, in the GE group, the therapy was chosen by independent researchers based on current guidelines and their own experience. In both groups, the therapeutic goal was to achieve good BP control avoiding too aggressive and rapid reduction of BP. It is worth to underline that mean BP values in the HD group were slightly higher, and it is not surprising that those patients required polytherapy more frequently than those from the GE group. It should be emphasized that taking a higher number of medications (22.6%) was related to 50% increase in BP reduction compared to the GE group, which may result from appropriate choice of antihypertensive therapy. It is not negligible that in many cases, choice of medication for patients from the GE group made by physician who was blinded to ICG result was haemodynamically accurate (consistent with the patient's haemodynamic profile), which might diminish between-group differences and lead to underestimating the benefits from the use of ICG.

Limitations of the study

The obtained results should be referred with caution to population of women with MS, because they were in the minority in our study. Furthermore, it seems that in larger study population the results would have more statistical power for the detection of clinically significant differences in favour of the HD group. Undoubtedly, of particular value would be long-term assessment of the effectiveness of ICG-guided antihypertensive treatment considering not only BP reduction but also prognosis for patients (such a study is currently ongoing at the Military Institute of Medicine).

CONCLUSIONS

Impedance cardiography is a useful and well tolerated method of evaluating patients with MS who require antihypertensive therapy. It can provide complementary data of high cognitive and clinical values. The implementation of the proposed algorithm of antihypertensive treatment based on criterion values of selected haemodynamic parameters can significantly increase BP reduction in this group of patients.

Conflict of interest: *none declared*

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Przydatność kardiografii impedancyjnej w optymalizacji leczenia hipotensyjnego chorych z zespołem metabolicznym: randomizowane, prospektywne badanie kliniczne

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Streszczenie

Wstęp: Nadciśnienie tętnicze (HT) występuje u ponad 1/4 populacji świata; jest głównym czynnikiem ryzyka choroby niedokrwiennej serca, niewydolności serca i nerek oraz udaru mózgu. W ponad 50% współistnieje ono z zaburzeniami metabolicznymi, a spośród elementów składowych zespołu metabolicznego (MS) występuje w populacji polskiej najczęściej. W obowiązujących wytycznych nie zedefiniowano jednoznacznie algorytmu leczenia HT. Podkreśla się, że podane zalecenia mają jedynie charakter wskazówek, a decyzja o wyborze terapii powinna być oparta na indywidualnej ocenie klinicznej pacjenta. Łatwą techniką monitorowania hemodynamicznego jest kardiografia impedancyjna (ICG), która wydaje się przydatna w indywidualizacji leczenia hipotensyjnego.

Cel: Celem pracy było porównanie skuteczności leczenia chorych z łagodnym i umiarkowanym HT przy zastosowaniu metody empirycznej i uwzględniającej nowy algorytm terapii oparty na parametrach hemodynamicznych ocenianych metodą ICG.

Metody: Grupę badaną stanowili chorzy z wywiadem łagodnego lub umiarkowanego HT i spełniający inne kryteria MS. Badanie miało charakter randomizowany (1:1), prospektywny i równolegle kontrolowany leczeniem konwencjonalnym. Badanych przydzielano losowo do dwóch grup: empirycznej (GE), w której sposób leczenia wybierano na podstawie danych klinicznych i obowiązujących wytycznych, oraz hemodynamicznej (HD), w której sposób leczenia wybierano na podstawie danych klinicznych i obowiązujących wytycznych, z uwzględnieniem wartości parametrów hemodynamicznych określonych metodą ICG. Algorytm terapii w grupie HD ustalono arbitralnie na podstawie doświadczeń własnych i dostępnego piśmiennictwa dotyczącego patofizjologii HT i stosowania ICG w diagnostyce i terapii HT. Wszystkich badanych przed i po wdrożeniu leczenia poddano m.in.: pomiarowi ręcznemu ciśnienia tętniczego (OBPM), ocenie dobowego profilu ciśnienia tętniczego (BP) metodą całodobowego pomiaru ciśnienia tętniczego (ABPM), ICG i badaniom laboratoryjnym. Efekt leczenia oceniano w czasie trzeciej wizyty (po 12 tygodniach). Za punkty końcowe w obserwacji krótkoterminowej uznano międzygrupowe różnice w zakresie wartości bezwzględnych BP, redukcji BP i uzyskanej kontroli BP po 12 tygodniach terapii.

Wyniki: Badaniom poddano grupę 82 chorych (57 mężczyzn i 25 kobiet) w wieku 45,5 ± 10,0 lat. W grupie HD wartości BP były niższe zarówno dla OBPM, jak i wszystkich okresów pomiarowych w ABPM, choć znamienność statystyczną uzyskano jedynie dla skurczowego BP (SBP) w okresie spoczynku nocnego (120,6 *v.* 115,6 mm Hg; p = 0,036). Analiza zmiany średnich wartości BP wykazała istotnie statystycznie większe obniżenie BP w grupie HD, zwłaszcza w zakresie OBPM: zarówno dla SBP (GE *v.* HD: 10,7 *v.* 18,1 mm Hg; p = 0,012), jak i rozkurczowego BP (DBP) (8,9 *v.* 12,2 mm Hg; p = 0,037) oraz średnich wartości SBP z ABPM: w całym okresie pomiarowym (10,5 *v.* 16,7 mm Hg; p = 0,013) oraz w okresie aktywności dziennej (10,5 *v.* 17,2 mm Hg; p = 0,009). W ocenie wpływu leczenia na profil hemodynamiczny w obu badanych grupach stwierdzono obniżenie wartości wskaźnika systemowego oporu naczyniowego, istotnie większe w grupie HD (162,3 *v.* 341,0 dyn·s·cm^{-5}·m^2; p = 0.064). W analizie odsetka uzyskania prawidłowej kontroli BP większą skuteczność zastosowanej terapii zaobserwowano również w grupie HD, zarówno dla OBPM < 130/80 mm Hg (23,5 *v.* 36,6%; p = 0,222), jak i ABPM (23,5 *v.* 43,9%; p = 0,117), choć w ocenie statystycznej różnice pojawiły się jedynie na poziomie trendów odwzorowujących zmiany BP.

Wnioski: Kardiografia impedancyjna jest przydatną i dobrze tolerowaną metodą oceny chorych z MS wymagających terapii hipotensyjnej. Dostarcza ona komplementarnych informacji o wysokiej wartości poznawczej i klinicznej, a zastosowanie zaproponowanego algorytmu leczenia hipotensyjnego opartego na kryterialnych wartościach wybranych parametrów hemodynamicznych istotnie zwiększa stopień redukcji BP w tej grupie chorych.

Słowa kluczowe: zespół metaboliczny, nadciśnienie tętnicze, kardiografia impedancyjna

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