



# Non-invasive haemodynamic assessments among hypertensive patients in a routine family doctor's office

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## Abstract

**Introduction and objective.** Difficult-to-control blood pressure can be attributed to a mismatch between the haemodynamic type of hypertension and the drug class used in treatment. Impedance cardiography may be a useful tool for enabling the individualization of antihypertensive therapy. The aim was to investigate the distribution of haemodynamic types of HT among hypertensive patients in an outpatient clinic.

**Materials and method.** This was a prospective, observational study of patients with primary hypertension at an outpatient clinic. A 10-minute ICG examination was performed in 189 consecutive patients (118 men and 71 women). Patients were divided into groups based on whether their hypertension was well-controlled (140/90 mmHg, n=95). They were also stratified according to haemodynamic states.

**Results.** Patients with poorly controlled blood pressure compared to patients with well controlled blood pressure had a high haemodynamic output in 6.3% vs. 2.1% (p=0.153), and high vascular resistance in 41.1% vs. 27.7% (p=0.037), and balanced haemodynamic states in 52.6% vs. 70.2% (0.80 beats/min) and fluid retention (p<0.01).

**Conclusions.** Half of the examined patients did not achieve the therapeutic goals for hypertension treatment. Differences in haemodynamic state of well and poor controlled hypertension groups suggests the usefulness of impedance cardiography-targeted hypertension treatment.

## Key words

cardiovascular diseases, blood pressure, arterial hypertension, impedance cardiography, hemodynamic indices, hemodynamic state

## INTRODUCTION

Hypertension (HT) is one of the most common cardiovascular disease worldwide. It is estimated to affect over 30% of the world's population, with rates rising significantly in the elderly population [1, 2, 3]. Currently, HT is the most frequent reason for patient visits to family care physicians in the USA [4]. Despite national health promotion programs and progress in anti-hypertensive drug development, HT remains a major risk factor for morbidity and mortality worldwide [5, 6] and most patients treated for HT do not achieve appropriate blood pressure control [1]. The main causes of poor control of HT are poor adherence to prescribed medicines, white-coat phenomenon, clinician inertia, insufficient use of combination treatment, lifestyle factors (excessive alcohol consumption, and high sodium intake), as well as the intake of substances that increase blood pressure or act antagonistically to antihypertensive drugs, and the complexity of current treatment strategies [7]. Efforts have

been made to improve the treatment of resistant hypertension [8] and to improve arterial blood pressure control by the use of modern technologies [9]. In a meta-analysis from 2021, professionally-led interventions have been effective and led to an almost 5 mmHg decrease of SBP [10], which inspires optimism for the future actions. Additionally, the choice of fourth-line antihypertensive pharmacotherapy is usually based on physician preference and experience, while the necessary treatment may be related to the haemodynamic type of hypertension [11, 12]. A profile with high vascular resistance and hyperkinetic/hyperdynamic circulation are the basic hypertensive states. A balanced state is recognized in the case of combination of the haemodynamic parameters, even though all of them might fit within the normal values. Fluid retention might also influence blood pressure levels. Difficulty with controlling a patient's blood pressure can often be attributed to a mismatch between drug class and the hypertensive state present in a patient [13].

The current European Society of Cardiology (ESC) guidelines recommend an individualization of the therapy based on evaluation of a patient's risk factors [7, 14]. In-office manual blood pressure measurements do not show the underlying circulatory system pathology or haemodynamic

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aberrations, such as increased systemic vascular resistance, fluid retention or cardiac output. According to the guidelines, there are five basic antihypertensive drug classes: angiotensin-converting-enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB) and calcium channel blockers (CCB), which are classified as vasodilators (therefore should be prescribed in high vascular resistance type of HT), and beta-blockers (BB) reduce contractility of the heart muscle (recommended in high output type of HT). Furthermore, diuretics should be admitted in the case of fluid retention. Impedance cardiography (ICG) examination learning curve is short and can be performed by a nurse or technician (the procedure is similar to ECG test). ICG is a non-invasive, reliable, operator-independent and reproducible technique for the measurement of haemodynamic states in patients with HT and cardiac failure [15]. It is an easy to use method which allows for the evaluation of haemodynamic parameters, and has been validated with invasive monitoring methods [16, 17]. Previously published studies have shown that ICG allows for more targeted choice, titration and monitoring of antihypertensive medication, but were not conducted in primary care outpatient clinic [18, 19].

The current study shows the distribution of haemodynamic profiles between the patients with well controlled and poorly controlled hypertension as the basis for introducing ICG-guided hypertension treatment.

## OBJECTIVE

The aim of the study was to investigate the distribution of haemodynamic types of HT among hypertensive patients in an outpatient clinic.

## MATERIALS AND METHOD

A total of 189 consecutive patients who had been previously diagnosed and treated for primary hypertension visiting family doctor's office were included in the study. The study group consisted of 118 men and 71 women. All patients underwent a 10-minute ICG examination in a sitting position in standard blood pressure measurement conditions according to ESC guidelines. The blood pressure was taken in two-minute intervals. Values achieved in the last two intervals were analyzed. The exclusion criteria were as follows: an acute coronary syndrome within two previous months, an exacerbation of heart failure, diagnosed secondary hypertension, need for haemodialysis, severe aortic stenosis, and pregnancy. For non-invasive haemodynamic measurements the Niccom (Non-Invasive Continuous Cardiac Output Monitor by Medis) device was used. The following parameters were measured or calculated: Body Mass Index [BMI], Blood Pressure [BP], Heart Rate [HR], Cardiac Index [CI], Systemic Vascular Resistance Index [SVRI], Thoracic Fluid Content [TFC], Heather Index [HI], Stroke Volume [SV], Stroke Index [SI], Left Cardiac Work [LCW], Left Cardiac Work Index [LCWI]. The echocardiography findings and laboratory tests were also collected.

For further analysis patients were divided into two groups according to effectiveness of blood pressure control: the well-controlled HT (wcHT) (BP<140/90mmHg, n=94) and the poorly-controlled HT (pcHT) (BP≥140/90mmHg, n=95).

The data were analyzed according to the haemodynamic states seen in hypertensive patients, as published by Krzesiński [20]. To make it clear, three main HD states are presented: High Output (CI ≥4.2 L/min/m<sup>2</sup> and SVRI < 2580 dyn x s x cm<sup>-5</sup> x m<sup>2</sup>), High Vascular Resistance (SVRI ≥ 2580 dyn x s x cm<sup>-5</sup> x m<sup>2</sup> and CI < 4.2 L/min/m<sup>2</sup> and SVRI < 2580 dyn x s x cm<sup>-5</sup> x m<sup>2</sup>). Additionally, subjects with (TFC women > 24, men > 34 l/kOhm) or without (TFC women ≥ 24, men ≥ 34 l/kOhm) fluid retention and high HR (≥ 80/min) were also defined within these three subpopulations.

This was a retrospective and single-center study conducted according to the Declaration of Helsinki, and the protocol was reviewed and approved by the local Ethics Committee. All patients gave written informed consent for participation.

**Statistical analysis.** Student t-test and Mann-Whitney U test were used for quantitative variables. The normality of distribution was assessed by Shapiro-Wilk W test. The qualitative variables were compared by the means of Pearson's  $\chi^2$  test. The statistical significance of  $\alpha=0.05$  was set. The STATISTICA 12 by StatSoft and Microsoft Excel were used to perform statistical analysis.

## RESULTS

The characteristics of the 189 hypertensive patients is presented in Table 1.

The wcHT patients presented with significantly lower BP, HDL concentration, SVRI and LCWI, compared to pcHT subjects. Both groups were similar in terms of age, gender and BMI. The incidence of DM, CAD, measured ejection fraction and retinopathy showed no statistically significant difference between groups.

The difference in hemodynamic state between the groups is clearly visible. In the pcHT group there is higher HR, CI (no statistical significance, a small number of patients), TFC and SVRI observed more often compared to wcHT group (Tab.2).

A high resistance profile was found more often in the pcHT group, which suggests that low doses of vasodilators were used.

Within the pcHT group, six patients had high output, four of whom had high TFC values (66.6%). At the same time, in the wcHT group, a high output and high TFC values were observed in two individuals. Within patients with a high resistance profile, there was a significant difference in the rates of fluid retention – high TFC value was found in 48.7% (n=19) of patients with pcHT and 42.3% (n=11) of patients with wcHT. When data of patients with a balanced haemodynamic profile were analyzed, high TFC values were found more often in the pcHT than in wcHT group (56% – 28 patients vs. 48.4% – 32 patients), suggesting that low doses of diuretics were used (Tab. 3).

Analyzing particularly the groups of drugs used, a significant difference in effectiveness was found only for CCB. Most patients (59.8%) received two or three drugs (Tab. 4).

**Table 1.** Characteristics of 189 hypertensive patients in two groups according to hypertension (HT) control

	Overall	BP $\geq$ 140/90mmHg (pcHT)	BP<140/90mmHg (wcHT)	p
n	189	95	94	
Ag [years]	59.9 $\pm$ 13.3	60.9 $\pm$ 13.4	58.9 $\pm$ 13.2	0.338
Male [%]	62.4	62.1	62.8	0.925
BMI [kg/m <sup>2</sup> ]	29.7 $\pm$ 5.0	29.8 $\pm$ 5.4	29.6 $\pm$ 4.6	0.595
HR [beats/min]	68.6 $\pm$ 11.0	69.4 $\pm$ 11.4	67.9 $\pm$ 10.6	0.468
SBP [mmHg]	138.8 $\pm$ 20.3	152.7 $\pm$ 18.2	124.9 $\pm$ 10.2	<0.001*
DBP [mmHg]	83.3 $\pm$ 11.9	89.2 $\pm$ 12.2	77.3 $\pm$ 8.1	<0.001*
CI [L/min/m <sup>2</sup> ]	3.09 $\pm$ 0.64	3.2 $\pm$ 0.63	3.0 $\pm$ 0.6	0.032*
SI [ml/m <sup>2</sup> ]	47.0 $\pm$ 15.5	48.0 $\pm$ 15.2	46.0 $\pm$ 15.7	0.244
TFC [1/kOhm]	30.4 $\pm$ 5.9	30.9 $\pm$ 6.1	29.9 $\pm$ 5.6	0.341
SVRI [dyn x s x cm <sup>-5</sup> x m <sup>2</sup> ]	2446 $\pm$ 587	2549 $\pm$ 579.5	2343 $\pm$ 579	0.005*
LCWI [kg x m/m <sup>2</sup> ]	3.9 $\pm$ 1.1	4.4 $\pm$ 1.1	3.4 $\pm$ 0.8	<0.001*
Glucose concentration [mg/dl]	110.0 $\pm$ 32.2 (n=121)	106.8 $\pm$ 28.8 (n=57)	112.8 $\pm$ 35.0 (n=64)	0.307
Total cholesterol level [mg/dl]	206.5 $\pm$ 48.0 (n=129)	214.5 $\pm$ 44.7 (n=63)	198.8 $\pm$ 50.1 (n=66)	0.063*
Triglycerides [mg/dl]	140.1 $\pm$ 74.0 (n=127)	132.7 $\pm$ 64.5 (n=62)	147.1 $\pm$ 81.9 (n=65)	0.405
LDL [mg/dl]	128.6 $\pm$ 45.5 (n=126)	132.7 $\pm$ 38.0 (n=61)	124.8 $\pm$ 51.6 (n=65)	0.115
HDL [mg/dl]	52.4 $\pm$ 14.1 (n=127)	55.7 $\pm$ 15.7 (n=61)	49.5 $\pm$ 11.7 (n=66)	0.036*
eGFR [ml/(min x 1.72m <sup>2</sup> )]	79.5 $\pm$ 20.8 (n=129)	79.5 $\pm$ 19.2 (n=61)	79.5 $\pm$ 22.2 (n=68)	0.996
Duration of HT [years]	10.2 $\pm$ 8.9	10.7 $\pm$ 9.5	9.7 $\pm$ 8.3	0.682
DM [%]	23.5	20.9	26.1	0.407
CAD [%]	25.0	23.7	26.5	0.570
Mean EF [%]	62.6 $\pm$ 8.1 (n=116)	62.7 $\pm$ 5.4 (n=57)	62.6 $\pm$ 10 (n=59)	0.209
Hypertensive retinopathy	52 (80%) (n=65)	24 (75%) (n=32)	28 (84.8%) (n=33)	0.321

wcHT - well-controlled hypertension group; pcHT - poorly controlled hypertension group; BMI - Body Mass Index; SBP - Systolic Blood Pressure; DBP - Diastolic Blood Pressure; HR - Heart Rate; CI - Cardiac Index; SVRI - Systemic Vascular Resistance Index; TFC Thoracic Fluid Content; HI - Heather Index; ACI - Acceleration Index; SI - Stroke Index; DM - Diabetes Mellitus; HT - Hypertension; CAD - Coronary Artery Disease; EF - Ejection Fraction; n - number of examined patients; \* p<0.05.

**Table 2.** Basic elevated hemodynamic parameters in the group of well and poorly controlled hypertension (HT)

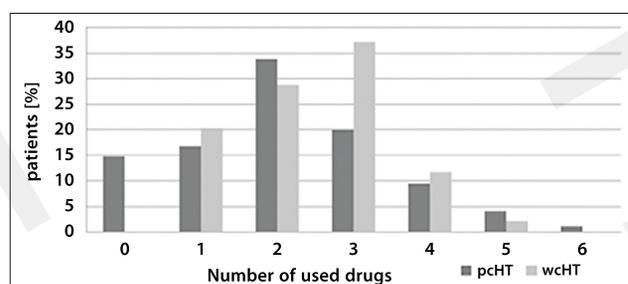
	BP $\geq$ 140/90mmHg (pcHT)	BP<140/90mmHg (wcHT)	p
n	n=95	n=94	
HR $\geq$ 80 [1/min]	16 (16.8%)	10 (10.6%)	<0.01*
CI $\geq$ 4,2 [L/min/m <sup>2</sup> ]	6 (6.3%)	2 (2.1%)	0.56
TFC M $\geq$ 34, K $\geq$ 24 [1/kOhm]	51 (53.7%)	45 (47.9%)	<0.01*
SVRI $\geq$ 2580 [dyn x s x cm <sup>-5</sup> x m <sup>2</sup> ]	39 (41.1%)	30 (31.9%)	<0.01*

wcHT - well controlled hypertension group; pcHT - poorly controlled hypertension group; HR - Heart Rate; CI - Cardiac Index; SVRI - Systemic Vascular Resistance Index; TFC - Thoracic Fluid Content; \* p<0.05.

**Table 3.** Haemodynamic profiles in the group of well and poorly controlled hypertension

	BP $\geq$ 140/90mmHg (pcHT) [%]	BP<140/90mmHg (wcHT) [%]	p
n	95	94	
CI<4,2 [L/min/m <sup>2</sup> ]			
SVRI $\geq$ 2580 [dyn x s x cm <sup>-5</sup> x m <sup>2</sup> ]	40 (42.1%)	26 (27.7%)	0.037*
<b>High Resistance</b>			
CI<4,2 [L/min/m <sup>2</sup> ]			
SVRI<2580 [dyn x s x cm <sup>-5</sup> x m <sup>2</sup> ]	49 (51.6%)	66 (70.2%)	0.009*
<b>Balanced</b>			
CI $\geq$ 4,2 [L/min/m <sup>2</sup> ]			
SVRI<2580 [dyn x s x cm <sup>-5</sup> x m <sup>2</sup> ]	6 (6.3%)	2 (2.1%)	0.153
<b>High Output</b>			

wcHT - well controlled hypertension group; pcHT - poorly controlled hypertension group; CI - Cardiac Index; SVRI - Systemic Vascular Resistance Index; \* p<0.05.

**Figure 1.** Antihypertensive drugs used in two groups (n=189): poorly vs. well controlled hypertension**Table 4.** Pharmacotherapy in the group of 189 hypertensive patients

	ACE-I	ARB	CCB	Any vasodilator	BB	Diuretics	Alpha-blockers (doxazosin)
BP<140/90mmHg (wcHT) n=94	52 (55.3%)	25 (26.6%)	46 (48.9%)	83 (88.3%)	58 (61.7%)	44 (46.8%)	7 (7%)
BP $\geq$ 140/90mmHg (pcHT) n=95	47 (49.5%)	25 (26.3%)	30 (31.6%)	75 (78.9%)	49 (51.6%)	38 (40%)	10 (5.1%)
p	0.421	0.965	0.015*	0.082	0.160	0.345	0.459

wcHT - well controlled hypertension group; pcHT - poorly controlled hypertension group; ACE-I - ACE-inhibitors; ARB - angiotensin receptor blocker; CCB - calcium channel blockers; BB - beta-blockers; ACE-I - any vasodilator and/or ARB and/or CCB and/or doxazosin; \* p<0.05

## DISCUSSION

Although hypertension is treated mainly by family physicians, despite the large number of different antihypertensive medications and the relative ease of monitoring the disease, many patients continue to have poor control of their blood pressure [21]. In the current study, almost 50% of patients were in the poor HT control group. However, ICG has not yet been approved as a first-line tool for the identification and stratification of hypertension. This study analyzes the haemodynamic parameters in hypertensive patients using ICG during routine visits to a family doctor with the aim of determining the haemodynamic states in hypertensive patients in a primary care setting. There is no easy way to discern between the possible hypertensive state of a patient performing standard physical examination without using ICG. The use of ICG-guided treatment is easy to evaluate and enables tailored antihypertensive therapy to a specific haemodynamic type of HT, such as high vascular resistance, high output (another term used in the literature is hyperkinetic/hyperdynamic), fluid retentive and balanced (where there is no dominant haemodynamic disorder), thanks to which it may facilitate the selection of drugs. Using tailored pharmacotherapy may result in lower doses used, and thus increased compliance caused by fewer side-effects may result in better HT control.

The usefulness of ICG as a method for the development of targeted treatment of hypertension has been demonstrated in numerous studies. Xiajuan et al. used ICG to assess the relationship between systolic blood pressure and the haemodynamic parameters in a population in Shanghai [22]. Hypertensive patients in the study had a higher systemic vascular resistance index, which is confirmed by the results of the current study. However, data from hypertensive patients analyzed by Xiajuan et al. had significantly lower values of cardiac index ( $2.6 \pm 1.0$  L/min/m<sup>2</sup>) compared to normotensive patients ( $2.8 \pm 0.8$  L/min/m<sup>2</sup>). In the current study, patients in the pcHT group had a higher cardiac index, compared to those in the wcHT group ( $3.2 \pm 0.63$  vs  $3.0 \pm 0.6$  L/min/m<sup>2</sup>). One important reason for this difference may be that Xiujuan et al. analyzed patients with and without hypertension, while the current study focused on patients with well controlled and poorly controlled hypertension.

In a study conducted by Abdelhammed et al, 136 patients with hypertension were observed in which it is interesting to note that there were also noticed higher values of CI in the well-controlled HT group (RR120–140/80–90mmHg), compared to not controlled HT group, and ranged from  $2.39 \pm 0.69$  L/min/m<sup>2</sup> (RR<120/80mmHg) –  $2.70 \pm 0.7$  L/min/m<sup>2</sup> (RR 120–140/80–90mmHg). In the current study, CI values were higher compared to Abdelhammed (mean  $3.09 \pm 0.64$  vs  $2.56 \pm 0.61$  L/min/m<sup>2</sup>). TFC also differed in the current study, and was higher than in Abdelhammed study [23].

In a study by Aoka et al, the patients were allocated to either a high resistance group (67%), high output group (16%) or a balanced group (17%), based on their haemodynamic profiles. In the current study, patients with pcHT were stratified into these groups, as well as with rates of 42.1%, 6.3%, and 51.6%, respectively (Tab. 3). In this case, the lower rates of high output may be explained by the average duration of HT, which was 10 years, and 51.6% of the pcHT population had already had beta-blocker treatment introduced (Tab. 4).

The effectiveness of ICG in the development of targeted hypertension treatment has been proven to be superior when compared to standard treatment guidelines in two studies performed by Krzesiński et al. In one study, increased vascular resistance seemed to be the dominant mechanism of hypertension [20, 24]. Smith et al. evaluated 164 patients with essential hypertension and obtained better office BP control in their ICG-guided group [25]. In another prospective, randomized and controlled trial, Taler et al. used ICG-based therapy in 104 resistant hypertensives and also achieved a higher frequency of goal office BP in ICG-guided group [18]. Fadl Elmula et al., in a small sample of patients with resistant HA, reported a better BP lowering effect of pharmacotherapy adjusted to the individual haemodynamic profile [26].

In the current study, over 50% of patients with chronic hypertension had poorly controlled blood pressure and did not reach their therapeutic goal. There was a significant difference in haemodynamic profiles between the patients with well controlled and poorly controlled hypertension. This suggests that the pharmacologic therapies were not tailored to the pathology in each patients' haemodynamic profile. CCB were used more often in the wcHT compared to pcHT group (48.9% vs 31.6%;  $p=0.015$ ) (Tab. 4.) Among the wcHT patients, high SVRI was less frequently observed (31.9% vs 41.1%;  $p<0.01$ ) (Tab. 2.). This difference supports the reliability of ICG: more CCB (vasodilators) – lower SVRI. Thus, the study has presented information on the usefulness and accuracy of impedance cardiography in a primary care setting.

### Strengths and limitations

The major strength of the study is that it was conducted on a population of patients treated in an outpatient setting and therefore reflects the haemodynamic state of the cardiovascular system of an average patient managed in the office of a family doctor. In addition to the haemodynamic profile, the drugs used by the patients and the effectiveness of their therapy were determined, and thus demonstrating the possibility of targeted hypertension treatment.

The limitations include the relatively small number of patients participating in the study and the fact that the studied population had various comorbidities (diabetes, coronary artery disease) in addition to hypertension. Also, the test was conducted with the patients in sitting position, which differed from the methodology of other researchers. Analysis of a visit-to-visit trend would have been useful, but there was only one ICG test of a single patient performed. Lastly, the patients came from only a single outpatient clinic; therefore, the pharmacotherapy used may differ from that in other clinics.

## CONCLUSIONS

Half of the examined patients did not achieve the therapeutic goals for hypertension treatment. Differences in haemodynamic state of well controlled and poorly controlled hypertension groups suggests the usefulness of impedance cardiography-targeted hypertension treatment.

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