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# Predictors of Resistance Hypertension and Achievement of Target Blood Pressure Levels in Patients with Resistant Hypertension

*Yuriy Mykolayovych Sirenko, Oksana Leonidivna Rekovets and Olena Oleksandrivna Torbas*

## Abstract

Uncontrolled arterial pressure is associated with a fourfold increase in the risk of developing cardiovascular events compared to patients with hypertension who have reached the target blood pressure level. The aim of this study is to evaluate the characteristics of patients with resistant arterial hypertension undergoing inpatient treatment at the Department of Symptomatic Hypertension and assess the prevalence of true resistant hypertension in a cohort of patients who take 3 and more antihypertensive agents, the clinical predictors of resistant hypertension. The study included 1146 patients with resistant AH who received 3 or more antihypertensive drugs with the level of office blood pressure at admission ≥140/90 mm Hg. Patients were followed by the next examinations: body height and body measurements, office blood pressure, echocardiography, sleep apnea determination, blood biochemical analysis, determination of levels of TTH, T3, T4, blood renin, blood aldosterone, metanephrine urine, and cortisol. Our data showed that 31% of patients who received 3 or more antihypertensive drugs had true resistant hypertension. Fixed combinations were taken by 71.9% of patients. We have found which factors were significantly associated with the treatment regimen with ≥3 or 4 drugs. Also we have demonstrated predictors for blood pressure reduction.

**Keywords:** resistant hypertension, pharmacology, predictors of resistance hypertension, target blood pressure, anti-hypertensive drugs

## 1. Background

The prevalence of resistant hypertension is very different according to different studies. In an analysis of National Health and Nutrition Examination Survey (NHANES) participants being treated for hypertension, only 53% were controlled to 140/90 mm Hg [1]. In Framingham Heart Study participants, only 48% of treated patients were controlled to 140/90 mm Hg, and less than 40% of elderly participants (75 years of age) were at a goal blood pressure [2]. Among higher-risk populations and, in particular, with application of the lower goal blood

pressures recommended in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) for patients with diabetes mellitus or chronic kidney disease (CKD), the proportion of uncontrolled patients is even higher. Of NHANES participants with chronic kidney disease, only 37% were controlled to 130/80 mm Hg3, and only 25% of participants with diabetes were controlled to 130/85 mm Hg [1, 3].

An estimated 10–30% of hypertensive patients are resistant to treatment defined as uncontrolled blood pressure (BP) with the use of ≥3 medications, including a diuretic [4–10]. A large number of studies have demonstrated that patients with resistant hypertension compared with patients with controlled hypertension have significantly a higher rate of target organ damage; increased cardiovascular risk, including coronary heart disease, chronic kidney disease, congestive heart failure, and stroke; and a significantly poorer prognosis than those of nonresistant hypertensive patients [3, 11].

Poor medical adherence, poor blood pressure measuring technique, and white-coat effect are relevant challenges to figuring out the real burden of resistant hypertension [11].

Previous studies have shown that obesity is associated with resistant AH [12]. In addition, other studies have shown that diabetes is associated with a resistant hypertension [13, 14]. Studies show that resistant AH is associated with an increase in age, female gender, Negroid race, the presence of diabetes mellitus, obesity, chronic kidney disease, and left ventricular hypertrophy [1, 10, 15–19]. For early detection of resistant AH, aggressive therapy can reduce both cardiovascular morbidity and mortality. However, the exact prevalence of resistant AH is not known precisely because of its variety of definitions and diversity of study sites [20, 21].

Increased blood pressure is one of the most important risk factors for stroke [4, 6, 22], and uncontrolled hypertension increases this risk [1, 23]. The prevalence of hypertension in Asian countries is almost the same as in most developed countries; many Asian patients have uncontrolled hypertension compared with developed countries [24]. For example, in developed countries, blood pressure monitoring is about 52–60%, but in Malaysia, for example, this figure is 26% [2, 11, 24–26]. In Ukraine, blood pressure control in the urban population is 14% and in rural populations 8% [27, 28].

In the current study, we have assessed the prevalence of true resistant hypertension in a cohort of patients who take 3 and more antihypertensive agents, the clinical predictors of resistant hypertension.

## 2. Material and methods

The study included 1146 patients with resistant AH who received 3 or more antihypertensive drugs who were hospitalized in 2011–2015 at the Department of Symptomatic Hypertension at the Institute of Cardiology of Ukraine, Kyiv. The level of office blood pressure when admitted to the office when receiving 3 or more AH drugs was ≥140/90 mm Hg. The average systolic blood pressure (SBP)/diastolic blood pressure (DBP) was 174,60 ± 0,64/100,50 ± 0,38 mm Hg.

Inclusion criteria. The inclusion criteria are as follows: (1) men and women aged between 18 and 80 years old and (2) patients treated with 3 and more antihypertensive drugs. The diagnosis of RH was made after treatment with three antihypertensive drug classes at maximum tolerated doses for at least 6 months. The study did not include patients with acute myocardial infarction or cerebrovascular accidents less than 3 months, acute renal failure, decompensated liver disease (level of AST, ALT above 3 times upper limit of normal), pregnancy, or lactation.

Anthropometric measurements. Weight and height, measured by anthropometric scales, will be used to calculate the body mass index (BMI) using the formula

| Parameters | Value |
|---|---|
| Men, n (%) | 423 (36,91%) |
| Women, n (%) | 723 (63,09%) |
| Height, m | 1,7 ± 0,01 |
| Weight, kg | 87,7 ± 0,61 |
| Age, years | 57,9 ± 0,37 |
| BMI, kg/m$^2$ | 31,0 ± 0,19 |
| Office SBP mm Hg at hospitalization | 174,6 ± 0,64 |
| Office DBP mm Hg at hospitalization | 100,5 ± 0,38 |
| Office SBP mm Hg on discharge from hospital | 131,3 ± 0,40 |
| Office DBP mm Hg on discharge from hospital | 80,1 ± 0,65 |
| Index of apnea-hypopnea, events /h, (n = 75) | 18,8 ± 2,11 |
| AO, sm | 3,4 ± 0,05 |
| LA, sm | 3,9 ± 0,06 |
| Left ventricle end-systolic dimension, sm | 3,5 ± 0,08 |
| Left ventricle end-diastolic dimension, sm | 5,5 ± 0,13 |
| Left ventricle end-systolic volume, mL | 48,3 ± 0,68 |
| Left ventricle end-diastolic volume, mL | 126,3 ± 1,17 |
| Inter ventricular septum thickness, sm | 1,2 ± 0,01 |
| Left ventricle posterior wall thickness, sm | 1,1 ± 0,01 |
| EF, % | 60,6 ± 0,23 |
| Left ventricular mass index, g/m$^2$ | 138,2 ± 1,43 |
| K, mmol/l | 5,1 ± 0,49 |
| Na, mmol/l | 144,0 ± 0,30 |
| Bilirubin, μmol/l | 14,1 ± 0,21 |
| Creatinine, μmol/l | 87,2 ± 0,58 |
| CKD-EPI, ml/min/1.73 m$^2$ | 82,7 ± 0,96 |
| ALT, U/l | 47,5 ± 3,39 |
| AST, U/l | 27,1 ± 0,71 |
| Fasting glucose, mmol/l | 6,0 ± 0,08 |
| Uric acid, mmol/l (n = 850) | 336,2 ± 3,62 |
| Triiodothyronine (T3), microU/l (n = 94) | 4,6 ± 1,16 |
| Thyroxin (T4), microU/l (n = 111) | 3,2 ± 0,67 |
| Thyroid hormone (TTH), microU/l (n = 231) | 2,2 ± 0,15 |
| Metanephrine urine, microG/24 h (n = 95) | 124,5 ± 7,10 |
| Renin, ng/l (n = 89) | 155,2 ± 79,73 |
| Aldosterone, ng/l (n = 118) | 29,4 ± 2,90 |
| Aldosterone-renin ratio, c.u. (n = 75) | 3,3 ± 0,68 |
| Cortisol, ng/l (n = 21) | 108,0 ± 30,73 |
| Total cholesterol, mmol/l | 5,5 ± 0,04 |
| Triglycerides, mmol/l | 1,6 ± 0,04 |
| HDL cholesterol, mmol/l | 1,3 ± 0,02 |
| LDL cholesterol, mmol/l | 3,3 ± 0,07 |
| VLDL cholesterol, mmol/l | 0,7 ± 0,02 |
| IA (index of atherogenicity), c.u. | 3,3 ± 0,07 |

**Table 1.**
*Clinical and demographic characteristics of the examined patients (n = 1146).*

BMI = weight (kg)/height squared (m²). BMIs of 18.5–26.9 kg/m² are considered eutrophic values, while individuals with BMIs of 27.0–29.9 kg/m² are overweight and ≥30 kg/m² are obese.

All patients will undergo electrocardiography, echocardiography, and office-measured SBP and DBP; an oscillometric device will be used to calculate the average of the three measurements. Biochemical and imaging tests. Blood samples will be drawn from all patients at the first visits after fasting for 12 h to measure serum total cholesterol, high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), very low-density lipoprotein cholesterol (VLDLc), triglycerides (TG), glucose, creatinine, sodium, and potassium; blood renin, aldosterone and aldosterone/renin ratio, metanephrines in urine, blood cortisol level, T3, T4, and TTH were determined in some patients. CKD-EPI was calculated. If needed, CT with intravenous contrast renal arteries and adrenal glands (for exclusion, secondary hypertension) and sleep apnea determination were performed on some patients (**Table 1**).

Statistical processing of the results was performed on a personal computer after creating databases in Microsoft Excel systems. The mean of the patients examined was determined using the analysis package in Microsoft Excel. All other statistical calculations were performed using SPSS 21.0. ANOVA to calculate the following parameters: the arithmetic mean value, M; the SD from the arithmetic mean value of m; and coefficient of reliability, p. The difference was considered reliable at a value of $p < 0.05$. The reliability of the difference between the groups was determined by the independent t-test for the mean. Correlation analysis was performed after determining the character of the distribution for Spearman.

## 3. Results

We examined 1146 patients who received 3 or more antihypertensive drugs. The mean age was 57,9 ± 0,37 years. The average body weight is 87,7 ± 0,61 kg. The average body mass index was 31,0 ± 0,19 kg/m². Average baseline office SBP and DBP were 174,6 ± 0,64 and 100,5 ± 0,38 mm Hg accordingly.

Most of the patients received 3 antihypertensive drugs: 51.4%. 48.6% of the patients take four to six drugs. Most of them take four drugs, 37.1%, 9.1% five drugs, and 2.4% six drugs.

The frequency of appointment of different classes of antihypertensive agents in the examined patients is presented in **Table 2**. In the structure of the appointments of antihypertensive drugs (AHD), ACE inhibitors were prescribed more often, 65.5%; calcium antagonists, 69.9%; and diuretics (loop, thiazide, and thiazide like), 91,8%. Beta-blockers were taken by 75.6% of patients and blockers to AT II receptor, 33.5%. Aldosterone receptor blockers were taken by 12.8% of patients and central activity drugs, 18.6%. Statins were taken by 63.8% of patients. Among those receiving combined therapy, most (71.9%) take fixed combinations. Attention was given to the low frequency of aldosterone receptor blockers received (12.8%), which was due to the fact that the study was conducted predominantly until the year 2015, when there was scientific evidence of the need for their use as the fourth drug.

For further analysis, we divided our patients according to the amount of drugs that they received. Although 3 or more antihypertensive drugs are used in the determination of resistant hypertension, we divided our patients into two groups: the first, those who took 3 drugs, and the second, those who took 4 or more drugs. A comparison of demographic characteristics and blood pressure levels in these groups is presented in **Table 3**.

| Antihypertensive class | % |
|---|---|
| Angiotensin-converting enzyme inhibitors | 65,5 |
| Angiotensinogen receptor blockers | 33,5 |
| Calcium channel blockers | 69,9 |
| Diuretics (thiazide, loops, thiazide like) | 91,8 |
| β-Blockers | 75,6 |
| Mineralocorticoid receptor antagonists | 12,8 |
| Central-acting agonists | 18,6 |
| α-Blockers | 2,6 |
| Fixed combination | 71,9 |
| Acetylsalicylic acid | 68,3 |
| Statins | 63,8 |

**Table 2.**
*Frequency of appointment of antihypertensive drugs of different classes among patients with resistant arterial hypertension (n = 1146).*

| Parameters | Value | | P |
|---|---|---|---|
| | **3 drugs (n = 591)** | **≥4 drugs (n = 555)** | |
| Men/women, n (%) | 231 (39,0)/360 (60,8) | 192 (34,6)/363 (65,4) | NS |
| Age, years | 57,2 ± 0,54 | 58,7 ± 0,48 | NS |
| Height, m | 1,7 ± 0,01 | 1,7 ± 0,01 | NS |
| Weight, kg | 85,9 ± 0,85 | 89,3 ± 0,86 | 0,004 |
| BMI, kg/m$^2$ | 30,2 ± 0,26 | 31,6 ± 0,27 | <0,001 |
| Office SBP mm Hg at hospitalization | 170,4 ± 0,79 | 179,0 ± 1,00 | <0,001 |
| Office DBP mm Hg at hospitalization | 98,4 ± 0,48 | 102,6 ± 0,58 | <0,001 |
| Office SBP mm Hg on discharge from hospital | 129,3 ± 0,52 | 133,5 ± 0,59 | <0,001 |
| Office DBP mm Hg on discharge from hospital | 78,5 ± 0,33 | 81,8 ± 1,29 | 0,013 |
| Index of apnea-hypopnea, events/h[*] | 18,7 ± 3,07 | 18,9 ± 2,90 | NS |

*[*]The somnography was performed in 31 patients in the first group and in 44 patients in the second group.*

**Table 3.**
*Characteristics of patients, depending on the number of prescribed antihypertensive drugs (n = 1146).*

As can be seen from the table, the groups did not differ by age and sex on average, but patients taking ≥4 drugs had significantly higher body mass and BMI than the group of patients taking 3 drugs. They also had significantly higher levels of office BP, both when they arrived in the hospital and on discharge. It should be noted that in both groups the value of the apnea-hypopnea index was high but did not differ from each other.

According to laboratory tests, patients taking ≥4 drugs had significantly higher blood glucose levels—(6.20 ± 0.09) mmol—than patients taking 3 drugs, (5.90 ± 0.14) mmol (p < 0.05), and a higher level of renin plasma ((218.30 ± 15.73) vs. (31.10 ± 5.91) ng/l, (p < 0.05)). Renin-aldosterone ratio was almost twice as high

(3.90 ± 0.95 vs. 2.20 ± 0.65 U/d), although it did not differ significantly between patient groups.

Analyzing the differences between patients in both groups in the main clinical states, we found that in patients receiving 4 or more drugs, significantly more obesity (45.6 vs. 34.0%), more often secondary hypertension (5.4 against 2.5%) due to stenosis of the renal arteries (1.6 vs. 0.2%), and hyperaldosteronism (2.3 vs. 0.2%) were observed; type II diabetes mellitus was more frequent (24.7 vs. 9, 5%); pathology of the thyroid gland (12.6 vs. 8.4%) due to hypothyroidism (4.1 vs. 1.5%) and chronic kidney disease were more common (5.0 vs. 1.5%); and chronic pyelonephritis (18.9 vs. 14.0%), ischemic heart disease (IHD) (47.0 vs. 37.2%) with angina pectoris III (7.7 vs. 3.4%), and heart failure (15.0 vs. 9.3%) were observed.

In analyzing the degree of decrease in blood pressure, we found that, in general, the reduction of office blood pressure among patients receiving 3 or more drugs was for SBP (43,47 ± 0,65) mm Hg and for DBP (20,33 ± 0.74) mm Hg, p < 0.001 for both values.

The analysis of the degree of reduction of blood pressure, depending on the amount of drugs, showed that DBP between patients taking 3 and 4 or more drugs did not differ significantly, 19.88 versus 20.81 mm Hg, respectively, and office SBP significantly lowered in patients taking 4 or more drugs at 45.78 mm Hg vs. group taking 3 drugs—41.3 mm Hg, p < 0.001.

Among all patients (n = 1146), 355 (31%) did not reach the target blood pressure level. Patients who did not achieve targeted SBP (31%) had significantly higher blood pressure when inpatient. They had a significantly higher blood cortisol

|  | SBP on discharge | | DBP on discharge | |
| --- | --- | --- | --- | --- |
| Age | β = −0,089 | P < 0,001 | β = −0,196 | P < 0,001 |
| Gender | β = 0,125 | P < 0,001 | β = 0,130 | P < 0,001 |
| Weight | β = 0,106 | P = 0,004 | β = 0,127 | P < 0,001 |
| BMI |  |  | β = −0,202 | P = 0,010 |
| Arterial hypertension | β = 0,205 | P = 0,001 | β = 0,117 | P < 0,001 |
| Arterial hypertension II | β = 0,108 | P = 0,001 | β = 0,133 | P < 0,001 |
| Arterial hypertension III | β = −0,259 | P = 0,023 | β = −0,106 | P = 0,001 |
| Secondary arterial hypertension | β = −0,096 | P = 0,006 | β = −0,114 | P < 0,001 |
| Vasorenal arterial hypertension | β = −0,082 | P = 0,011 | β = −0,101 | P = 0,002 |
| Hyperaldosteronism | β = −0,103 | P = 0,022 | β = −0,071 | P = 0,027 |
| Pituitary adenoma |  |  | β = −0,089 | P = 0,006 |
| Heart failure |  |  | β = 0,146 | P < 0,001 |
| Heart failure II | β = −0,079 | P = 0,014 | β = −0,103 | P = 0,002 |
| Adrenal pathology | β = −0,065 | P = 0,043 | β = −0,070 | P = 0,029 |
| T4 | β = −0,230 | P = 0,020 | β = −0,219 | P = 0,027 |
| Interventricular septum thickness | β = 0,214 | P = 0,027 | β = 0,154 | P < 0,001 |
| HD cholesterol | β = −0,230 | P = 0,001 | β = −0,198 | P = 0,003 |
| Calcium channel blockers | β = −0,140 | P < 0,001 | β = −0,080 | P = 0,013 |
| Central-acting agonists | β = −0,214 | P < 0,001 | β = −0,137 | P < 0,001 |
| Mineralocorticoid receptor antagonists | β = −0,101 | P = 0,002 | β = −0,096 | P = 0,005 |
| Acetylsalicylic acid | β = 0,169 | P < 0,001 | β = 0,197 | P < 0,001 |

**Table 4.**
*Factors influencing the reduction of blood pressure on discharge from the hospital (n = 1146).*

level (155.0 ± 44.0 vs. 35.9 ± 20.8 ng/l) and the highest left ventricular mass index (147.5 ± 3.46 vs. 135.3 ± 1.74 g/m$^2$), and obesity (42.9 vs. 37.5%), kidney abnormality (2.7 vs. 0.8%), obliterative lower extremity atherosclerosis (2.0 vs. 0.2%), structural alterations in the adrenal gland (3.0 vs. 1.2%), nephropathy (1.3 vs. 0.2%), and higher heart failure (HF in the 16.9 vs. 8.5%) were more common.

When we performed a regression analysis, we found that the decrease in office systolic and diastolic blood pressure depended on age, sex, and body weight. Thus, office SBP/DBP was worse in men; patients with a younger age; patients with greater body mass, with hypertension III degree, and with secondary hypertension, especially with hyperaldosteronism and vasorenal hypertension, adrenal pathology, heart failure, lower T4 hormone levels, more low levels of HDL cholesterol, and a larger thickness of interventricular septum thickness; and patients receiving less calcium antagonists, centrally acting drugs, and aldosterone antagonists. Data are presented in **Table 4**.

**Table 5** presents the results of a regression analysis for the detection of predictors of resistance hypertension in patients receiving 3 or more antihypertensive drugs. The predictors for blood pressure reduction were male sex, left ventricular mass index, interventricular septum thickness, left ventricle posterior wall thickness, hypothyroidism, the presence of chronic kidney disease, CKD-EPI level, blood creatinine levels, the presence of heart failure, the presence of secondary hypertension, hyperaldosteronism, pituitary adenoma, and vasorenal hypertension.

| Variables | Predictors of failure to reach the target BP | |
|---|---|---|
| Gender | β = 0,119 | P < 0,001 |
| Left ventricular mass index | β = 0,139 | P = 0,001 |
| Inter ventricular septum thickness | β = 0,169 | P = 0,002 |
| Left ventricle posterior wall thickness | β = 0,147 | P < 0,001 |
| Arterial hypertension | β = 0,085 | P = 0,009 |
| Arterial hypertension II | β = 0,090 | P = 0,005 |
| Arterial hypertension III | β = 0,077 | P = 0,018 |
| Secondary arterial hypertension | β = 0,075 | P = 0,020 |
| Vasorenal arterial hypertension | β = 0,107 | P = 0,001 |
| Hyperaldosteronism | β = 0,064 | P = 0,049 |
| Pituitary adenoma | β = 0,068 | P = 0,036 |
| Pathology of the thyroid gland | β = 0,102 | P = 0,002 |
| Hypothyroidism | β = 0,069 | P = 0,031 |
| Mixed goiter | β = 0,072 | P = 0,024 |
| Heart failure II | β = 0,125 | P < 0,001 |
| Chronic kidney disease | β = 0,076 | P = 0,018 |
| Creatinine | β = 0,108 | P = 0,028 |
| CKD-EPI | β = 0,135 | P = 0,025 |
| Office SBP mm Hg at hospitalization | β = 0,368 | P < 0,001 |
| Office DBP mm Hg at hospitalization | β = 0,238 | P < 0,001 |
| Calcium channel blockers | β = −0,116 | P = 0,001 |
| Central-acting agonists | β = −0,146 | P < 0,001 |
| Fixed combinations | β = 0,098 | P = 0,003 |
| Acetylsalicylic acid | β = 0,103 | P = 0,002 |

**Table 5.**
*Predictors of resistance hypertension in patients receiving 3 or more antihypertensive drugs (n = 1146).*

## 4. Discussion

Our data showed that in patients who received 3 or more antihypertensive drugs in 31%, the goal blood pressure (<140/90 mm Hg) was not reached, meaning it was true resistant hypertension. This is possible somewhat more than in other studies, but we have a specialized department, which is directed precisely by patients who failed to reach the target levels of blood pressure at the outpatient stage.

Among our patients with resistant arterial hypertension, 3 antihypertensive drugs were received by 51.4% of patients, 4 antihypertensive drugs were taken by 37.1% of patients, 5 antihypertensive drugs were taken by 9.1% of patients, and 6 antihypertensive drugs were taken by 2.4% of patients.

In our study ACE inhibitors were more often prescribed in 65.5% of patients, calcium antagonists in 69.9% of patients, and diuretics in 91.8% of patients. Beta-adrenergic blockers were administered to 75.5% of patients, receptor blockers to AT II to 33.5% of patients, and aldosterone receptor blockers to 12.8% of patients. Fixed combinations were taken by 71.9% of patients.

In our study patients who did not achieve targeted SBP (31%) had significantly higher blood pressure when inpatient. They had a significantly higher blood cortisol level (155.0 ± 44.0 vs. 35.9 ± 20.8 ng/l) and the highest left ventricular mass index (147.5 ± 3.46 vs. 135.3 ± 1.74 g/m$^2$), and obesity (42.9 vs. 37.5%), kidney abnormality (2.7 vs. 0.8%), obliterative lower extremity atherosclerosis (2.0 vs. 0.2%), structural alterations in the adrenal gland (3.0 vs. 1.2%), nephropathy (1.3 vs. 0.2%), and more often heart failure (16.9 vs. 8.5%) were more common.

In our study, patients taking ≥4 drugs had significantly higher blood glucose levels—(6.20 ± 0.09) mmol/l—than patients taking 3 drugs, (5.90 ± 0.14) mmol/l ($p < 0.05$), and the highest level of renin plasma ((218.30 ± 15.73) vs. (31.10 ± 5.91) ng/l ($p < 0.05$)). Renin-aldosterone ratio was almost twice as high (3.90 ± 0.95 vs. 2.20 ± 0.65 U/d), although it did not differ significantly between patient groups.

Yook Chin Chia and Siew Mooi Ching studied the prevalence and predictors of resistance to hypertension in Southeast Asia [24]. The prevalence of resistant hypertension in the primary examination in their study was 8.8%. Their data also show that patients with chronic kidney disease were 2.9-fold more likely to develop resistant AH than in patients without CKD. This is consistent with the findings in other studies [25, 29]. In our study, CKD-EPI and CKD were predictors of resistance hypertension.

The authors explain this by the fact that in patients with CKD, there is increased sensitivity to salt, resulting in a delay in sodium and fluid, which leads to more complex control of blood pressure [24]. Patients in the Yook Chin Chia study were aged 66.9 years. In our study, patients were more younger, 57,9 ± 0,37. Resistant hypertension in Yook Chin Chia study was negatively related to age, which the authors explain with the effect of survival of patients who were treated compared with those patients who already had complications from uncontrolled hypertension. In our study, office SBP/DBP was worse in younger age patients.

Many studies have shown that most patients with hypertension need 2 or more drugs to achieve the target blood pressure [2, 30–34]. The average number of AH drugs used in their study was 2. They also showed poor monitoring of blood prossure among those taking only 2 drugs; even in those who received 3 drugs, the level of blood pressure control was less than 50%. However, in general, the use of diuretics in their study was low.

Holmqvist et al. studied the adherence to treatment in patients with resistance to hypertension, which controlled or did not control blood pressure and what factors contributed to nonadherence to treatment. 5846 patients received treatment with 3 or more AH drugs for 2 years [26]. Patients who achieved target blood pressure

levels were older in age and among them those with diabetes were fewer. Initially, patients had an adherence above 80%. During the first year of treatment, the adherence decreased by 11%, regardless of whether it was controlled or not controlled. The highest adherence was observed only in patients with diabetes mellitus and hypertension, in which the authors explain the structuring of the treatment of such a patient.

Resistant hypertension is associated with significant adverse effects, including an increased risk of cardiovascular events and death as well as a decrease in the quality of life [22, 24]. The exact mechanisms underlying the development of resistant hypertension remain unclear, although several mechanisms were proposed [8, 9, 35, 36]. An increase in fluid content and an increase in the level of aldosterone play a crucial role in the development of resistance hypertension, whereas enhanced activation of the sympathoadrenal system significantly contributes to refractory hypertension [14, 20, 34].

In conclusion, the predictors for blood pressure reduction were male sex, left ventricular mass index, interventricular septum thickness, left ventricle posterior wall thickness, the presence of chronic kidney disease, CKD-EPI level, blood creatinine levels, and the presence of heart failure.

## Disclosure

None.

## Author details

Yuriy Mykolayovych Sirenko, Oksana Leonidivna Rekovets and
Olena Oleksandrivna Torbas*
FI "NSC" Institute of Cardiology named after M.D. Strazhesko NAMS of Ukraine,
Kyiv, Ukraine

*Address all correspondence to: olenatorbas@gmail.com

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