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Intensity of cardiovascular and behavioral risk factors in masked and stable arterial hypertension in young subjects

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Abstract

Objective. To study the intensity of cardiovascular behavioral and other risk factors of masked arterial hypertension (MHTN) and stable arterial hypertension (SHTN) in young subjects (students of medical university). **Design and methods.** A full-design screening study included 423 young men and women aged 20–27, mean age 22. 59 % were women and 41 % — men. All subjects underwent clinical examination: physical examination — height, weight, body mass index (BMI), waist and hip circumferences, questionnaires to assess behavioral risk factors and history of the complaints; laboratory and instrumental screening: fasting serum creatinine, lipid profile (total cholesterol, triglycerides, high density lipoproteins, low density lipoproteins), 30-second breath-hold test, standard 12-lead electrocardiography (ECG); echocardiography and 24-hour blood pressure monitoring in HTN subjects (with MHTN and SHTN). **Results.** MHTN was detected in 12.3 % subjects, SHTN — in 9 %; 78.7 % were normotensives. Subjects with SHTN were overweight — BMI 28.4 (27.4; 29.7) kg/m^2. In MHTN subjects, waist and circumferences tended to increase: 77.2 (65.1; 82) and 98 (93.2; 104) cm, respectively. MHTN patients demonstrated higher office systolic blood pressure as compared to normotensives: 120 (110; 130) versus 108.5 (100; 118) mm Hg. However, they had lower BP compared to subjects with SHTN — 139 (132.3; 140) mm Hg. Family history of early cardiovascular diseases was detected in all MHTN patients (100 %), as well as in 50 % SHTN individuals and in 56 % normotensives. The highest prevalence of behavioral risk factors was found in a group of subjects with MHTN, as compared to those with SHTN and normotensives. **Conclusions.** Subjects with MHTN and SHTN have prevalent indicators of behavioral and other risk factors for HTN, which form its phenotype. The development of MHTN and SHTN in young subjects is associated with the severity of clinical, genetic and behavioral risk factors.

Key words: masked arterial hypertension, risk factors for hypertension, young subjects, 30-second breath-hold test

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Выраженность кардиоваскулярных и поведенческих факторов риска при маскированной и стабильной артериальной гипертензии у лиц молодой возрастной группы

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Резюме

Цель исследования — изучить выраженность кардиоваскулярных и поведенческих факторов риска при маскированной артериальной гипертензии (МАГ) и стабильной артериальной гипертензии (АГ) у лиц молодой возрастной группы (студентов медицинского университета). **Материалы и методы.** Проведено сплошное скринирующее исследование 423 молодых лиц мужского и женского пола в возрасте от 20 до 27 лет, средний возраст — 22 года, из которых 59 % составляли женщины и 41 % — мужчины. Все лица прошли общеклиническое обследование: физикальный осмотр — оценку роста, массы тела, индекса массы тела, окружности талии (ОТ), окружности бедер (ОБ), анкетирование по выявлению и оценке поведенческих факторов риска, данных жалоб и анамнеза; лабораторно-инструментальный скрининг: определение тощакового уровня креатинина, липидный спектр (уровни общего холестерина, триглицеридов, липопротеинов высокой плотности, липопротеинов низкой плотности), тест с 30-секундной задержкой дыхания, электрокардиографию в 12 стандартных отведениях. Суточное мониторирование артериального давления (АД) и доплерэхокардиографическое исследование проводились у лиц со стабильной и маскированной формами АГ. **Результаты.** МАГ выявлялась в 12,3 % случаев, стабильная АГ — в 9 %; 78,7 % составили нормотензивные лица. При оценке антропометрических показателей избыточная масса тела — ИМТ 28,4 (27,4; 29,7) кг/м^2 — определялась у лиц со стабильной АГ. У лиц с МАГ определялась тенденция к большему значению ОТ и ОБ: 77,2 (65,1; 82) и 98 (93,2; 104) см соответственно. Анализ уровней офисного АД указывал на более высокое офисное систолическое артериальное давление у лиц с МАГ (120 (110; 130) мм рт. ст.) по сравнению с нормотензивными лицами — 108,5 (100; 118) мм рт. ст., но более низкие по сравнению с лицами со стабильной АГ — 139 (132,3; 140) мм рт. ст. Наследственная отягощенность по ранним сердечно-сосудистым заболеваниям определялась у всех лиц с МАГ (100 %), а также у 50 % лиц со стабильной АГ и у 56 % нормотензивных лиц. Наиболее высокая распространенность поведенческих факторов риска определялась у лиц с МАГ по сравнению с лицами со стабильной АГ нормальным уровнем АД. **Выводы.** Лица с МАГ и стабильной

АГ имеют превалирующие показатели по поведенческим особенностям и факторам риска развития АГ, формирующим фенотипическое проявление данного заболевания. Развитие у лиц молодого возраста МАГ и стабильной АГ ассоциировано с выраженностью кардиоваскулярных и поведенческих факторов риска.

Ключевые слова: маскированная артериальная гипертензия, факторы риска развития артериальной гипертензии, лица молодого возраста, тест с 30-секундной задержкой дыхания

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Introduction

Current medical position in society and the state involves the change from reactive medicine to the so-called "4Ps" medicine — predictive, prophylactic (preventive), personalized, and participatory (with the active participation of the patient). So, it aims at the wider implementation of preventive measures, diagnosis at preclinical stages of the disease and identification of patients at risk (with risk factors, RF) [1]. This area of medical services for prevention and improvement of management of chronic non-communicable diseases (NCD) is currently the most popular and relevant in view of their high prevalence, related mortality and a great economic burden.

Cardiovascular pathology (cardiovascular continuum) holds the leading position among non-communicable diseases. In 2015, The World Health Organization reported the highest mortality related to cardiovascular disease (CVD), reaching 17.5 million people each year [2, 3]. In addition, widespread behavioral risk factors (RFs) also have impact on mortality rates. In 2010, approximately 1.7 million annual cardiovascular deaths were associated with the excessive salt consumption [4], and 6 million deaths annually — with active and passive smoking [5].

One of the most common cardiovascular diseases is arterial hypertension (HTN), reaching 43.4% among middle-aged males and females according to the study ESSE-Russian Federation 2012–2014. [6].

Young people until recently are usually referred the group of low cardiovascular risk. However, in recent decades high rate of hypertension among young people has been established, and in particular, the prevalence of masked hypertension (MHTN) reaches 17% [7–8]. Unexpectedly high numbers forced medical community to re-evaluate the problem. Thomas Pickering, and a number of his followers focused their research on MHTN regarding frequent target organ damage and a high cardiovascular risk in young patients compared to symptomatic HTN [7–10]. Some authors focused on the cause of the MHTN and its early complications in young people, and found associations with the habits changing, life style and food preferences [7–10].

Taking into account the basics of the "4Ps" medicine [1] and epidemiology of NCD and, in particular, cardiovascular disease with predominant HTN, preventive examinations and predictive algorithms are the most promising approaches for their prevention, prediction and management.

The aim of our research was the assessment of the severity of cardiovascular and behavioral risk factors of MHTN and stable HTN in young individuals (students of a medical university).

Design and methods

We screened 423 young males and females aged 20–27 years (mean age — 22 years old, 59% females and 41% males). All studied subjects were senior students of medical university, who were aware about the CVD, risk factors, as well as preventive measures.

The study was conducted at the Saratov State Medical University named after V.I. Razumovsky and was carried out in accordance with the standards of Good Clinical Practice and the Declaration of Helsinki. All participants provided written informed consent.

Exclusion criteria were the following: verified concomitant diseases, diabetes mellitus, congenital abnormalities, athletes, pregnant women receiving hormone replacement therapy and oral contraceptives, as well as subjects with isolated office HTN ("white coat" hypertension).

Enrolled subjects were informed about the planned examination and received individualized recommendations on the lifestyle modification before the examination. For 72 hours before the test all of participants had abstained from alcohol and, if possible, medications, apart from emergency medications. Intense exercise, smoking and stimulants, tonics and other factors that contribute to high blood pressure (BP) were restricted for at least 2 hours before the examination.

All subjects underwent examination, which included physical examination with assessment of anthropometric parameters — height, weight, body mass index (BMI), waist circumference (WC), hip circumference (HC), a survey on the identification and assessment of cardiovascular and behavioral risk factors, complaints and medical history. Laboratory screening included creatinine levels, lipid profile (total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein), 12-lead electrocardiography. Ambulatory blood pressure monitoring and doppler echocardiography were performed in patients with stable and masked HTN.

Office systolic blood pressure (SBP) and diastolic BP (DBP) was assessed by auscultatory method in accordance with European recommendations for the management of hypertension ESC / ESH in 2013 [11]. Stable HTN was diagnosed according to the European guidelines for [11] the management of hypertension of ESH / ESC 2013.

Individuals without known BP and with office BP <140/90 mm Hg underwent a test with a voluntary 30-second breath-hold and ABPM to identify MHTN [12–14]. According to the methodology, as well as the information given in advance, participants had not taken any medications for 72 hours before the test, neither had they taken stimulating beverages, or had performed intense exercise, or had smoked and had had exposure to any other factors contributing to the BP increase for 2 hours before the test. Just before the test they had rested for 30 minutes in a sitting position. Breath-holding (apnea) test was conducted according to the known methodology [12–14]: office BP was measured at least twice in a sitting position before the test, then 30-second breath-holding was performed using a nose clip (the participants were informed not to take a deep breath before breath-holding). The test result with a voluntary 30-second breath-holding was considered positive for BP ≥ 140/90 mm Hg and negative for BP <140/90 mm Hg.

The next day after the breath-holding test all participants (either with positive or negative result) 24-hour ABPM was performed in an outpatient setting for verification, confirmation / exclusion of HTN diagnosis. ABPM was performed during usual daily activities. During ABPM BP was measured at 15-minute intervals during the day and at 30-minute intervals during the night. The following parameters were analysed: average 24-hour BP and 24-hour BP variability, average daytime and nocturnal SBP and DBP, and average daytime and nocturnal variability of SBP and DBP. HTN was diagnosed according to the following standard criteria — average daytime SBP ≥ 135 mm Hg, or average daytime DBP ≥ 85 mm Hg, or average nocturnal SBP ≥ 120 mm Hg, or average nocturnal DBP ≥ 70 mm Hg [11].

MHTN was diagnosed based on the existing Recommendations for the management of hyper-

tension of the ESC / ESH 2013: a combination of normal office BP (< 140/90 mm Hg) and elevated BP according to ABPM [11], as well as positive breath-holding test [12–14].

Importantly, all subjects with a positive test of 30-second breath-holding demonstrated elevated ABPM indices — average 24-hour SBP ≥ 135 mm Hg, or average daytime DBP ≥ 85 mm Hg, or average nocturnal SBP ≥ 120 mm Hg, or average nocturnal DBP ≥ 70 mm Hg.

Statistical analysis was performed using the software "Statistica 7.0", "Microsoft Office Excel Professional + 2010". The distribution type was tested by the Kolmogorov-Smirnov test. The mean values of quantitative variables are presented as median and quartiles. Statistical hypotheses were tested using H test Kruskal-Wallis, ANOVA rank analysis and the median test.

Results and discussion

Among included subjects (n=423), the number of young women slightly exceeded the number of men (59 and 41 %, respectively). The average age of males and females was comparable comprising 22 (21, 22) years old.

Intragroup distribution according to the BP level and the presence / absence of various HTN forms (masked and stable) was the following: MHTN was detected in 12.3 %, stable HTN — in 9 %, and 78.7 % subjects were normotensive. The groups were comparable by age. The rate of detected MHTN among young people was comparable with the other published data [7–14], although the study population included senior students of medical university who are already aware of both CVD risk factors and HTN forms. Mancia G. et al. (2009) studied a sample of 2051 people, and found MHTN in 8.9 %, while PAMELA project (n=3200) showed MHTN rate as 9 % [10].

Overweight was defined only in patients with stable HTN, BMI was 28.4 (27.4; 29.7) kg/m^2

Table 1

ANTHROPOMETRIC CHARACTERISTICS OF THE GROUPS

Parameter	Normotensives	Persons with MHTN	Persons with stable HTN	p
Age, years	22 (21; 22)	22 (21; 22)	21.5 (20.8; 22.3)	0.4558
Weight, kg	61 (50; 74.25)	62 (51; 75.8)	89 (87.9; 92.25)	0.0072
BMI, kg/m^2	20.4 (19.0; 24.3)	20.7 (19.2; 23)	28.4 (27.4; 29.7)	0.0092
WC, cm	73.5 (64.8; 77.5)	77.2 (65.1; 82)	97 (95.88; 99)	0.0041
HC, cm	95.5 (90; 101)	98 (93.2; 104)	111 (105.5; 116.3)	0.0217

Note: MHTN — masked hypertension; HTN — arterial hypertension; BMI — body mass index; WC — waist circumference; HC — hip circumference. Results are given as median, quartiles [25–75 percentile]. Kruskal-Wallis test, and ANOVA rank analysis were applied to assess the intergroup differences.

Table 2

OFFICE BLOOD PRESSURE AND HEART RATE IN THE STUDIED GROUPS

Parameter	Normotensives	Persons with MHTN	Persons with stable HTN	p
Office SBP mm Hg	108.5 (100; 118)	120 (110; 130)	139 (132.3; 140)	0.0180
Office DBP, mm Hg	70 (61.5; 71.25)	79 (78; 80)	85 (78; 90)	0.0059
HR, beats/min	66 (62; 70)	74 (66; 86)	76 (70; 83)	0.0333

Note: MHTN — masked hypertension; HTN — hypertension; BP — blood pressure; HR — heart rate. Results are given as median, quartiles [25–75 percentile]. Kruskal-Wallis test, and ANOVA rank analysis were applied to assess the intergroup differences.

(p = 0.0092) (Table 1). Patients with MHTN and normotensive individuals did not show any signs of metabolic syndrome or obesity, however, waist and hip circumferences tended to be higher in MHTN: WC = 77.2 (65.1. 82) cm, HC = 98 (93. 2; 104) cm (Table 1). In 2009, Mancia G. and colleagues also showed more pronounced metabolic disorders among subjects with the latent form of HTN compared to normotensive ones [10].

Importantly, higher levels of office SBP were found in patients with MHTN compared to normotensive individuals (p = 0.0180), but lower values compared to those with stable HTN (Table 2). In addition, patients with MHTN tended to have higher DBP and heart rate (HR) compared to normotensives, but lower than patients with stable HTN. However, the differences were not significant (Table 2).

Several studies demonstrated a wide range of BP o patients with MHTN varying from "normal BP" to "high normal BP" [7–10].

Neither dyslipidemia, nor decrease in glomerular filtration rate were found in the studied cohort. However, higher lipid levels were shown in subjects with MHTN and stable HTN compared to normotensives, but the differences were non-significant. Low-density lipoprotein cholesterol was higher in patients with stable HTN and patients with MHTN, but lower than in normotensive individuals: 2.17 (1.85; 2.34); 2.3 (1.99; 2.85) and 2.1 (1.8. 2.32) mmol / L, respectively (Table 3.).

Gender analysis of lipid profile showed higher (but non-significant) values in males with MHTN, compared to females. Mancia G. and Ohkubo T. also showed a trend towards higher rates of lipid profile in MHTN and stable HTN [8, 10].

During interview regarding family CVD history (according to the ESC / ESH 2013 criteria of the European Guidelines for the management of hypertension), early CVD in male relatives under the age of 55 years and in females under 65 years were considered [11].

The history of early CVD was defined in participants' parents and, in particular, in patients with MHTN. During the survey family history of early CVD, in particular, in subjects with MHTN (100 %), as well as every second patients with stable HTN and 56 % normotensive subjects.

Behavioral and lifestyle factors [4–6] play an important role in the predisposition to HTN, which led to their high rate in the studied groups (Table 4).

Half of all young subjects with MHTN (50 %) use tobacco since 15–16 years old (early age of smoking onset), which is significantly higher than in patients with stable HTN (25 % cases) and 3.5 times higher than in normotensives (14 %) (Table 4). Male students with MHTN smoke more often than females (52 % of all men with MHTN vs. 30 % of all women with MHTN). Similar rates were shown by T. Pickering and a number of authors: 35 % among subjects with

Table 3

LABORATORY PARAMETERS IN THE STUDIED GROUPS

Parameter	Normotensives	Persons with MHTN	Persons with stable HTN	p
TC, mmol / l	4 (3.6; 4.3)	4.1 (3.71; 4.54)	4.15 (3.85; 4.65)	0.6919
TG, mmol / l	1.095 (0.89; 1.3)	1.04 (0.9; 2.15)	1.02 (0.9; 1.11)	0.1805
HDL, mmol / l	1.35 (1.3; 1.5)	1.25 (0.96; 1.42)	1.24 (1.22; 1.27)	0.0806
LDL, mmol / l	2.1 (1.8; 2.32)	2.17 (1.85; 2.34)	2.3 (1.99; 2.85)	0.6109
Creatinine, mmol / l	78.5 (70.5; 84)	75.3 (73; 82)	71.5 (70.75; 74.5)	0.2191

Note: MHTN — masked hypertension; HTN — hypertension; BP — blood pressure; HR — heart rate; TC — total cholesterol; TG — triglycerides; HDL — high-density lipoproteins; LDL — low density lipoproteins. Results are given as median, quartiles [25–75 percentile]. Kruskal-Wallis test, and ANOVA rank analysis were applied to assess the intergroup differences.

Table 4

BEHAVIORAL RISK FACTORS, INCLUDING EATING BEHAVIOR IN STUDIED GROUPS

Risk factors	Normotensives	MHTN	Stable HTN
Early smoking onset, %	14	50	25
Adding salt in the cooked food, %	25	50	50
More frequent consumption of canned food and sausage with high salt content (once per day or twice per week)	18	54	59
Frequent consumption of alcoholic beverages (up to 2–3 times a week), %	7	10	21
Nocturnal sleep, hours	7	6	3.8

Note: MHTN — masked hypertension; HTN — hypertension. Results are given as median, quartiles [25–75 percentile].
MHTN — masked hypertension; HTN — hypertension. Results are given as median, quartiles [25–75 percentile].

MHTN and 34.4% among those with stable HTN ($p<0.001$) [9]. However, Ohkubo T. et al. (2005) found the highest rate of smoking among patients with stable HTN (26%) compared to those with MHTN (22%) and normotensive individuals (19%) [8].

Analysis of eating habits showed a number of differences. Importantly, 100% of participants were students, who usually are characterized by non-compliance with the principles of good nutrition and eating behavior contributing to the rapid development of metabolic disorders. 50% of all subjects with MHTN and 50% of those with stable HTN confirmed that they add salt into the cooked food. More than half of the students with MHTN (54%) and stable HTN (59%), as compared to normotensive individuals (18%) reported daily consumption of sausages, canned foods, which are known additional sources of salt and affect HTN development. Importantly, both males and females with MAH reported diet violation (Table 4). The role of excessive salt consumption both as pure salt and in a latent form (sausage, canned food) in the development of MHTN has been repeatedly discussed and confirmed. Michikawa T. et al (2009) recently has shown that in families where food is cooked by women with acquired change in the threshold of salt sensitivity (i.e. pu too much salt), men are more likely to suffer from masked and stable HTN [15].

Subjects with stable HTN (21%) reported 2-times more often alcohol consumption 2–3 times per week (which is a sympathoadrenal trigger of HTN cascade) compared with those with MHTN (10%), and 3-fold more frequent compared to normotensives (7%) (Table 4).

In addition, such risk factor as nocturnal sleep deprivation, primarily due to nocturnal work and night shifts was found often. Sleep duration was 1.5 times lower in students with stable HTN (3.8 hours) compared to those with MHTN (6 hours) and 2 times lower than in normotensive persons (Table 4).

All students were physically active, but there were intergroup differences regarding the intensity of physical activity. Individuals with MHTN experienced low physical activity more often (more than half, 53%) compared with normotensive individuals (23%) and students with stable HTN (55%). The level of physical activity of medium intensity in all subjects was comparable in patients with normal BP (52%), with MHTN (41%) and stable HTN (40%). The subjects with MHTN (6%) and stable HTN (5%) reported lower rate of intense physical activity.

Conclusions

Young individuals (students of a Medical University) with MHTN and stable HTN demonstrate cardiovascular and behavioral risk factors of different severity that contribute to the early

development of HTN with a variety of clinical manifestations.

Young people with stable HTN are overweight as opposed to students with MHTN and normotensives.

Young people with MHTN have more frequent family history of early CVD onset; males show early smoking onset compared to those with stable HTN and normotensives.

Patients with stable HTN often have unhealthy lifestyle, including insufficient nighttime sleep (3.8 hours) due to nocturnal work and night shifts. In addition, young subjects with stable HTN consume alcoholic beverages 2–3 times more often than those with MHTN and normotensives.

Half of students with MHTN and HTN did not comply with healthy nutrition, characterized by daily consumption of sausages and canned food, which are an additional source of salt which contributed to HTN development.

Considering high rate of HTN, and high prevalence of cardiovascular behavioral risk factors among young people, including students of a medical university, preventive measures based on the use of predictive, personalized, and participatory approaches should be widely implemented.

Conflict of interest
The authors declare no conflict of interest.

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