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Clinical, laboratory and prognostic features of masked arterial hypertension in midlife working women

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Abstract

Objective. Late detection and diagnostics of masked hypertension (MHTN) triggering cardiovascular continuum is still one of the key issues in healthcare system. **Design and methods.** We examined 309 midlife women (31–57 years old) working in institutions without specified factors of occupational hazards. We excluded patients with verified pathology, taking oral contraception or hormonotherapy. MHTN was verified based on the following criteria: combination of normal office blood pressure (BP) (≤ 140/90 mm Hg), positive breathhold test and elevated BP according to the results of 24-hour BP monitoring. **Results and conclusions.** MHTN was detected in 8.7%. We defined clinical features of MHTN in examined population: absence of complaints and anamnesis of cardiovascular diseases, elevated mean haemodynamic pressure, and increased body mass index. Analysis of clinical and laboratory results showed no difference between mean parameters of lipid profile in the examined population, despite higher dyslipidemia rate among patients with hypertension and MHTN as compared to patients without hypertension ($p < 0.05$). The tendency towards elevation of fasting blood glucose and decreasing of glomerular filtration rate in patients with MHTN was not significantly different. Ten-year risk of fatal cardiovascular events (assessed by survival model based on Weibull function) in midlife working women with MHTN was comparable with women with manifest hypertension.

Key words: masked hypertension, midlife women, clinical and laboratory features, prognosis

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Клинико-лабораторные и прогностические особенности маскированной артериальной гипертензии у работающих женщин среднего возраста

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Резюме

Актуальность и цель исследования. Несвоевременное выявление и диагностика маскированной артериальной гипертензии (МАГ), запускающей сердечно-сосудистый континуум, остается одной из важных проблем в практическом здравоохранении. **Материалы и методы.** В данном случае было обследовано 309 работающих женщин среднего возраста в учреждениях без регламентированных факторов профессиональной вредности. Верификация МАГ проводилась с использованием пробы с задержкой дыхания и суточного мониторирования артериального давления. **Результаты и выводы.** Выявляемость МАГ составила 8,7%. Определены клинические особенности МАГ обследованной выборки: отсутствие жалоб и анамнестических данных сердечно-сосудистых заболеваний, повышение среднего гемодинамического давления, увеличение индекса массы тела. Анализ клинико-лабораторных данных показал, что, несмотря на более высокую частоту выявления дислипидемий среди пациентов с АГ и МАГ, чем у пациентов без АГ ($p < 0,05$), параметры липидограммы в среднем по выборкам не достигали степени статистической значимости. Тенденция к повышению тощакового уровня гликемии и снижению скорости клубочковой фильтрации у больных МАГ также не достигала степени статистической значимости. Десятилетний риск развития фатальных сердечно-сосудистых событий у женщин среднего возраста с МАГ был сравним с пациентками, имеющими манифестную АГ.

Ключевые слова: маскированная артериальная гипертензия, женщины среднего возраста, клинически-лабораторные особенности, прогноз

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Introduction

According to a collaborative study, completed in 2014 in Russia, the prevalence of hypertension (HTN) was astimated as high among women at 35–54 years old, and according to the Russian Stroke Registry in 2009–2010 years stroke morbidity in women is higher than in men — 53 and 47%, respectively [2]. At the same time low efficiency of antihypertensive treatment in women is stated. According to NHANES (National Health and Nutrition Examination Survey), target levels of blood pressure (BP) are achieved rarer in women than in men (48% vs. 60%) [3]. However, gender differences and peculiarities of antihypertensive treatment in women are not fully elucidated. This was confirmed by a study conducted by F. Turnbull in Australia in 2011, which established that general practitioners prescribed combined antihypertensive therapy to women more seldom, because they consider their cardiovascular risk to be much lower than in men [4].

The prevalence of masked HTN (MHTN) varies from 4.4 to 17%: according to the study by Muntner P. et al. it was 4.4% (2014), in "PAMELA" trial it was 9%, and in the Ohasama study (1996) it achieved 13.6% [5–7].

According to a meta-analysis, the wide range of MHTN prevalence in the population might be due to the different study design [8].

Based on the data of numerous studies assessing cardiovascular prognosis in Sweden, Belgium, Denmark, Italy, France, asymptomatic target organ damage, increased risk of persistent HTN, higher cardiovascular risk is more frequently found in patients with MHTN compared to patients with symptomatic HTN [4]. In a long-term study "OHASAMA" (1332 patients at the age of 40 years and older) the rate of strokes and deaths in the MHTN group was comparable to the one with manifest AH [7].

The timely detection of any HTN form is required considering high prevalence of MHTN, an early risk of target organ damage, a high rate of life-threatening complications (cerebrovascular and renal complications, coronary heart disease, myocardium infarction, heart failure) [10] and mortality in this gender-age group, as well as HTN features, associated with hormonal changes (pre- and post-menopausal periods, surgical menopause), which aggravate cardiovascular risk factors, women lifestyle and result in higher risk [11].

The prognostic value of MHTN remains important and disputed problem, and available evidence is based on data of heterogeneous patient group, so clinical and metabolic profile of these patients is not completely elucidated.

Therfore, the aim of our study was to investigate the frequency, clinical, laboratory and prognostic features of MHTN in working middle-aged women.

Design and methods

In a complete screening study, we enrolled middle-aged (from 31 to 57 years) employees of 2 commercial and 2 state companies without declared occupational hazard. The participation was voluntary and compliant with the Helsinki Declaration. Study response was 74% (n = 309). All patients underwent full clinical examination including office blood pressure measurements, electrocardiography, clinical examination and laboratory screening testing. To assess cardiac risk factors and their prevalence we interviewed all subjects using special questionnaire based on the main and advanced modules of STEPS (WHO, v. 2.0).

Participants of the screening study were informed in advance about visit date and received individual lifestyle recommendations for the period until the visit. It included alcohol cessation for 72 hours prior the study and on day of ambulatory blood pressure monitoring (ABPM) and drugs withdrawal whenpossible. The avoidance of intense exercise, smoking and stimulating drinks for at least 2 hours before the study and during ABPM was also recommended.

Laboratory screening included fasting glucose, creatinine, uric acid, and lipid profile assessment. Anthropometric measurements included the height, weight, waist and hips circumferences. In additional self-reported life quality using a graduated five-point scale was performed.

Based on examination participants were divided into two groups: the first one consisted of people with known HTN (hypertensive patients) and women with office blood pressure levels ≥ 140/90 mmHg (n = 56), the second group included

women with office blood pressure ≤ 140/90 mmHg who did not know about HTN presence, they were classified as "patients without HTN" according to the office blood pressure level (n = 253). Patients from second group also underwent breath-holding test (patent number 2376930) for MHTN detection [13–14] and ABPM. The data of patients with comorbidities and women who used oral contraceptives were excluded from analysis.

The breath-holding test was considered positive if BP level was more than 140/90 mmHg and negative when BP was below 140/90 mmHg [13–14].

The next day after breath-holding test patients underwent ABPM following their usual daily activities. BP was registered with 15-minute interval during daytime and with 30-minute interval at night. The following parameters were analyzed: the average BP and 24-hour BP variability, the average systolic (SBP) and diastolic blood pressure (DBP) during daytime and nighttime, and the average SBP and DBP variability in corresponding day periods [15].

The MHTN was diagnosed in accordance with the current Guidelines for the management of arterial hypertension of ESC/ESH 2013: a combination of normal office BP (≤ 140/90 mmHg) and elevated BP according to ABPM, and a positive breath-holding test indicated MHTN.

Thus, according to the examination results, including breath-holding test, several groups were formed: patients with MHTN, patients without HTN and patients with HTN.

The assessment of 10-year risk of fatal cardiovascular events (CVE) was performed using survival model based on the Weibull function [4]. For this purpose a probability of fatal cardiovascular event was calculated at the time of examination and 10 years later with an assumption that there would be no significant change in critical parameters, which were taken as weighted values based on the meta-analysis of 12 prospective cohort studies (SCORE project) [3].

A primary analytical database included individual data as qualitative and quantitative variables. Statistical analysis was conducted using STATISTICA 7.0, StatSoftInc and EXCEL Microsoft Office professional plus 2010, version 14.0.6112.5000. The distribution was assessed by Kolmogorov-Smirnov test, considering the indicators of excess and symmetry. The quantitative variables are presented as median and interquartile range (lower quartile; upper quartile). Statistical hypothesis were tested by Mann-Whitney U-test for quantitative variables and Chi-square test for categorical ones. Univariant nonparametric analysis of variance was performed in unrelated samplings; Spearman rank correlation was used to assess interrelations between the variables. Correlations equality was tested by the Fisher transformation.

Results and discussion

The relative rates of HTN and MHTN were comparable with the results of previous studies and counting18.4 % in patients with HTN, 72.9 % in patients without HTN, and 8.7 % in patients with MHTN [5–7].

There were differences in office BP between patients without HTN, patients with MHTN and patients with manifested HTN (Table 1). At the same time significant differences were relative to all patients groups. Office BP was normal in 60 % of women with MHTN and in 40 % of patients with high normal BP.

Differences in office BP levels in patients with MHTN were investigated in several studies, and many authors have attempted to identify BP reference ranges to identify MHTN. For example, A. Viera et al. proved that DBP had the greatest diagnostic valuewith the «cut-off» level at 120/82 mm Hg. In our study (Table 1), the biggest differences between the groups were found for DBP. However, SBP was significantly higher in our patients, and the average hemodynamic pressure possessed the highest sensitivity (84 %).

Clinical symptoms, including complaints, in studied patients with MHTN were lacking. Only every second woman with diagnosed MHTN had complaints, mostly of fatigue, which is known to be the main manifestation of the widespread asthenovegetative syndrome and was referred to the latter one. Headache, which is specific for HTN, was detected only in 15.7 % of patients. In the majority of cases the headaches were transient, and patients wrote it off for overwork and fatigue but not with elevated BP.

Table 1

OFFICE BLOOD PRESSURE IN WOMEN

Parameter	Patients without HTN	Patients with HTN	MHTN	Kruskall-Wallis criterion p
SBP mm Hg	115.0 (105.0; 120.0)	143.5 (140.0; 153.0)	130.0 (120.0; 136.0)	0.0001
DBP mm Hg	77.5 (70.0; 80.0)	95.0 (90.0; 100.0)	82.0 (80.0; 89.0)	0.0001
PBP mm Hg	40 (35; 40)	45 (40; 60)	40 (40; 50)	0.1086
Average BP, mm Hg	90.00 (81.67; 96.67)	109.50 (106.68; 113.34)	98.00 (93.43; 103.35)	0.0004

Note: results are presented as median and quartiles. HTN — arterial hypertension; MHTN — masked arterial hypertension; SBP — systolic blood pressure; DBP — diastolic blood pressure; PBP — pulse blood pressure; BP — blood pressure.

Table 2

ANTHROPOMETRIC, CLINICAL AND LABORATORY PARAMETERS IN EXAMINED GROUPS

Parameter	Patients without HTN (1)	Patients with HTN (2)	MHTN (3)	Kruskall-Wallis criterion p
Age, years	43.5 (31.0; 48.0)	51.5 (47.0; 57.0)	53.0 (51.0; 57.0)	0.0029
Weigh, kg	67.5 (50.0;75.0)	85.9 (80.0; 101.0)	80.0 (76.0;82.0)	0.0024
BMI, kg/m^2	24.69 (19.88; 28.44)	32.93 (29.74; 35.06)	30.07 (29.02; 30.87)	0.0059
Waist, cm	86 (62; 93)	100 (97; 104)	90 (86; 93)	0.0083
Hip, cm	101 (85; 105)	114 (109; 117)	109 (106; 118)	0.0237
HR, bpm	69 (64; 76)	67 (66; 70)	70 (62; 80)	0.6605
TCh, mg/dl	148.5 (142.0; 154.0)	183.0 (170.0; 228.0)	183.0 (169.0; 216.0)	0.0658
TG, mg/dl	66.5 (64.0; 80.0)	85.0 (63.0; 125.0)	84.5 (79.0; 100.0)	0.2030
HDL, mg/dl	52.0 (49.0; 55.0)	50.5 (48.0; 55.0)	46.5 (45.0; 51.0)	0.2131
LDL, mg/dl	107.0 (102.0; 119.0)	118.5 (116.0; 128.0)	122.0 (112.0; 132.0)	0.1281
Glucose, mmol/l	4.7 (4.4; 5.2)	5.6 (4.9; 6.0)	5.4 (4.7; 6.1)	0.0688
Creatinine, mcmol/l	75.5 (73.0; 81.0)	81.0 (74.0; 88.0)	92.5 (70.0; 97.0)	0.5855
GFR, ml/min	78.71 (69.57; 79.7)	69.17 (61.07; 74.08)	58.48 (54.2; 80.56)	0.2469
UA, mcmol/l	182.5 (170.0; 217.0)	177.5 (168.0; 189.0)	197.0 (193.0; 206.0)	0.6055

Note: results are presented as median and quartiles. HTN — arterial hypertension; MHTN — masked arterial hypertension; BMI — body mass index; HR — heart rate; bpm — beats per minute; TCh — total cholesterol; TG — triglycerides; HDL — high density lipoproteins; LDL — low density lipoproteins; GFR — glomerular filtration rate; UA — uric acid.

In our study, patients with MHTN were slightly older than patients without HTN, but there was no age difference between patients with clinical HTN and MHTN. Considering the study design, this fact just shows a higher prevalence of MHTN among elderly population.

There were significant differences in body mass index (BMI) among patients with and without HTN, while BMI in MHTN patients was 30.07 kg/m^2 being comparable to the values in patients with and without HTN (Table 2).

There were no significant differences in lipid profile parameters (Table 2), despite the higher rate of dyslipidemia in patients with HTN and MHTN, than in patients without HTN ($p < 0.05$).There was a trend towards an increase in fasting glucose

Table 3

COMPARISON OF TEN-YEAR RISK OF FATAL CARDIOVASCULAR EVENTS IN SURVEYED WOMENH

Patients group	10-year risk of fatal CVE	Kruskall-Wallis criterion	Mann-Whitney U-test, p		
			0 and 1 group	0 and 2 group	1 and 2 group
Patients without HTN (1)	0.45 (0.12; 1.34)	0.003	0.017	0.015	0.897
Patients with HTN (2)	0.68 (0.27; 1.79)				
MHTN (3)	0.76 (0.34; 1.45)				

Note: CVE — cardiovascular events; HTN — arterial hypertension; MHTN — masked arterial hypertension.

Table 4

CORRELATIONS BETWEEN PARAMETERS CONTRIBUTING TO THE 10-YEAR RISK OF FATAL CARDIOVASCULAR EVENTS IN MIDDLE-AGED WOMEN

Parameters/ Groups	Patients without HTN	Patients with HTN	MHTN
Age	0.874*	0.936*	0.922*
SBP	0.851		
TCh		0.826	

Note: only significant correlations are presented. HTN — arterial hypertension; MHTN — masked arterial hypertension; SBP — systolic blood pressure; TCh — total cholesterol; * — non-significant differences, $p > 0.05$.

level and a reduction of glomerular filtration rate in patients with MHTN, but no significant differences were found (Table 2).

Taking into account the clinical importance of manifested HTN, MHTN and the role of HTN in the development of cardiovascular diseases and their complications in screened women [1, 7], 10-year risk of fatal CVE was analyzed (Table 3).

The findings appeared to be highly important: the risk of fatal CVE in middle-aged women with MHTN was comparable to the risk in women with manifested HTN (0.76 % and 0.68 %, respectively).

Considering the age differences in patients with MHTN, we conducted a correlation analysis to assess the primary impact of criterion parameters on the 10-year risk of fatal CVE (Table 4).

Herewith, in general sample there were no significant difference in correlation coefficients of 10-year risk of fatal CVE with age, total cholesterol and SBP ($p = 0.056$, 0.051 and 0.051, respectively).

Conclusions

1. MHTN is detected in 8.7 % of middle-aged working women without complaints and anamnesis of cardiovascular diseases.

2. There are several clinical and laboratory features in middle-aged women with MHTN compared to patients without HTN: an increase in average BP and BMI, higher rates of dyslipidemia and hyperglycemia, elevated levels of uric acid and creatinine.

3. MHTN in middle-aged women is associated with the higher risk of fatal CVE, comparable to the risk in age-matched patients with manifested HTN.

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Conflict of interest
The authors declare no conflict of interest.

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