Journal of Cardiology 61 (2013) 222–226

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Comparison of demographic, clinical, laboratory parameters between patients with sustained normotension, white coat hypertension, masked hypertension, and sustained hypertension

Baris Afsar (MD)*

Department of Medicine, Division of Nephrology, Konya Numune State Hospital, Konya, Turkey

ARTICLE INFO

Article history:
Received 1 October 2012
Received in revised form 8 November 2012
Accepted 20 November 2012
Available online 5 January 2013

Keywords:
Ambulatory blood pressure
Masked hypertension
Metabolic syndrome
White coat hypertension
Sustained hypertension

ABSTRACT

Background: After measurement of office blood pressure (BP) and ambulatory BP monitoring (ABPM), 4 groups of patients were identified namely: (i) sustained normotensive patients (BPs are normal both clinically and by ABPM); (ii) white coat hypertensive patients (clinical BP were above limits, but ABPM were normal); (iii) masked hypertensive patients (clinical BP were normal, but ABPM were high); (iv) sustained hypertensive patients (both office and ABPM were high). The exact pathophysiologic mechanisms of these conditions are not exactly known. Besides in the literature there are only few studies that compare the 4 groups of patients together. Thus the study was carried out to compare patients with sustained normotension (SNT), white coat hypertension (WCHT), masked hypertension (MHT), and sustained hypertension (SHT).

Methods: All patients underwent history taking, physical examination, laboratory analysis, and ABPM. They were referred to the cardiology department for echocardiographic evaluation.

Results: In total 85 patients with SNT, 112 patients with WCHT, 31 patients with MHT, and 81 patients with SHT were included. Going from SNT to SHT, body mass index ($p < 0.0001$), waist circumference ($p < 0.0001$), fasting blood glucose ($p = 0.002$), and uric acid ($p = 0.029$) rose progressively. Presence of metabolic syndrome was also highest in SHT and lowest in SNT ($p < 0.0001$).

Conclusion: Most of the metabolic risk factors were higher in patients with MHT and SHT when compared to SNT and WCHT. Studies are needed to determine whether metabolic risk factors play a causative role for the development of MHT and SHT.

Introduction

Measurements of blood pressure (BP) were initially based on auscultatory method with a mercury or aneroid sphygmomanometer. However, high BP variability with these methods led to development of new methods including ambulatory BP monitoring (ABPM). Accumulating evidence suggests that ABPM predicts cardiovascular mortality and morbidity or end-stage renal disease better than office BP measurements which is probably due to the lower variability of BP measurements by these methods owing to multiple measurements and standardization of the circumstances in which BP is measured. Based on this background, ABPM and office BP were used to identify 4 groups of patients, namely: (i) sustained normotensive patients (BPs were normal both clinically and by ABPM); (ii) white coat hypertensive patients (clinical BPs were above limits, but ABPM were normal); (iii) masked hypertensive patients (clinical BPs were normal, but ABPM were high); (iv) sustained hypertensive patients (both office and ABPM were high) [1].

Although in the literature many studies were performed in patients with white coat, masked, and sustained hypertension, only few studies compared the 4 groups of patients together [2,3]. Despite extensive research, these studies did not certainly tell whether some conditions such as white coat hypertension has prognostic significance [4,5]. Additionally some of these studies were performed in patients who were already taking antihypertensive medication. There is no doubt that more research is needed regarding sustained normotension (SNT), white coat hypertension (WCHT), masked hypertension (MHT), and sustained hypertension (SHT). Thus the present study was conducted to compare demographic, laboratory, and clinical parameters among patients with hitherto treated SNT, WCHT, MHT, and SHT.

Materials and methods

The study had a cross-sectional design. The study was in accordance with the declaration of Helsinki; informed consent was

* Correspondence address: Ferhuniye Mah., Hastane Cad., Konya Numune State Hospital, Department of Nephrology, 42060 Konya, Turkey. Tel.: +90 332 235 45 00; fax: +90 332 235 67 86.
E-mail address: afsarbrs@yahoo.com

0914-5087/$ – see front matter
http://dx.doi.org/10.1016/j.jjcc.2012.11.003

obtained from all patients before enrollment. A local ethics committee approved the study. The study included people attending for the first time a nephrology outpatient clinic. Patients with secondary hypertension, liver disease, symptomatic heart failure, neurologic disorders or deficits, and pulmonary, autoimmune, endocrine (including type 1 and type 2 diabetic patients), malignant diseases, and patients with urinary tract infection were not included in the study. Patients with serum creatinine >1.4 mg/dL were not included. None of the patients had a history of acute coronary syndrome, myocardial infarction, angina pectoris, or coronary revascularization procedure. Patients had no history of stroke, carotid revascularization procedure, ischemic leg ulcer, peripheral revascularization, or amputation. On 12-lead electrocardiogram, all patients had normal sinus rhythm and no conduction disturbances.

None of the patients were shift workers and none of them reported alcohol intake. Body mass index (BMI) was calculated as the ratio of dry weight in kilograms to height squared (in square meters).Waist circumference (WC) was measured midway between the lower rib margin and the iliac crest.

Twenty-four-hour urine specimens were collected to determine creatinine clearance after spot urine examination. If the urinary creatinine excretion of the two consecutive specimens differed by more than 10%, another 24-h collection was made to assess the adequacy of collection.

The definition of SNT, WCHT, MHT and SHT were as follows, respectively:

office systolic and diastolic BP <140/90 mmHg and mean daytime ABP <135/85 mmHg;
office systolic and diastolic BP ≥140/90 mmHg and mean daytime ABP <135/85 mmHg;
office systolic and diastolic BP <140/90 mmHg and mean daytime ABP ≥135/85 mmHg; and
office systolic and diastolic BP ≥140/90 mmHg and mean daytime ABP time BP ≥135/85 mmHg [6].

Office blood pressure measurement

Office BP measurements were performed using a mercury sphygmomanometer. Adequate size cuffs (standard cuff of 23 cm × 12 cm or a large cuff of 34 cm × 15 cm) according to arm circumference were applied round the non-dominant arm. First and fifth phases of Korotkoff sounds were taken as the systolic and diastolic BP, respectively. The measurements were taken after the patients had rested for 10 min in sitting position, with the arm comfortably placed at the heart level. Two measurements were taken at 5-min intervals. Each set of two measurements was averaged to give the office systolic and diastolic BP.

Ambulatory blood pressure measurement

Ambulatory 24-h BP monitoring was performed on each patient's non-dominant arm using a SpaceLabs (Redmond, WA, USA) 90207 oscillometric monitor concomitantly with ultrasonography (within 1 week). The accuracy of the device was checked against the standard auscultatory method to ensure that the difference in BP measurements between methods did not exceed +5 mmHg. The device was set to obtain BP readings at 20-min intervals during the day (07:00 AM–11:00 PM) and at 30-min intervals during the night (11:00 PM–07:00 AM). Each ambulatory BP monitoring dataset was first automatically scanned to remove artifactual readings according to preselected editing criteria. Data were edited by omitting all readings of zero, all heart rate readings <20 or >200, diastolic BP readings >150 and <40 mmHg, systolic BP readings >240 and <70 mmHg, and all readings where the differences between systolic and diastolic BPs was less than 10 mmHg. Readings were evaluated if the percentage of successful readings was above 90%. The following ABPM parameters were evaluated: average ambulatory daytime systolic and diastolic BP levels (awake period), average ambulatory nighttime systolic and diastolic BP levels (asleep period), average ambulatory 24-h systolic and diastolic BP levels, and mean ambulatory daytime, nighttime, and 24-h arterial BPs. Average ambulatory daytime, nighttime, and 24-h heart rates were also determined. All subjects were instructed to rest or sleep between 11:00 PM and 7:00 AM (nighttime) and to continue their usual activities between 7:00 AM and 11:00 PM (daytime). Patients were asked to remain still at the time of measurement and to note in a diary the occurrence of unusual events or poor sleep. "Nocturnal dipping" was defined as a reduction of >10% (when compared with the daytime values) in the systolic and/or diastolic BP levels at night. Left ventricular hypertrophy was evaluated by electrocardiography using Sokolow–Lyon voltage (sum of the amplitude of the S wave in lead V1 and the R wave in lead V5 or V6 >35 mm) [7].

Besides these procedures, patients were referred to measure ecocardiographic parameters.

Echocardiography was performed with a commercially available ultrasound system (Acuson Sequoia C256, Mountain View, CA, USA) using a broadband transducer (3V2c). Two-dimensional, M-mode, color measurements were recorded. Interventricular septum thickness and ejection fraction were measured. The peak velocities of early (E) and late (A) diastolic filling, and their ratio (E/A), were also measured for all patients for the detection of diastolic dysfunction.

Additionally presence of metabolic syndrome (MetS) was diagnosed based on Adult Treatment Panel (ATP) III criteria that defined MetS as a constellation of risk factors of metabolic origin, of which three or more indicate that an individual has MetS. The 5 possible risk factors include abdominal obesity, as evidenced by a waist circumference >102 cm in men and >88 cm in women, triglyceride levels ≥150 mg/dL, high-density lipoprotein cholesterol levels <40 mg/dL in men and <50 mg/dL in women, blood pressure ≥130/85 mmHg, and a fasting glucose level ≥110 mg/dL [8].

Statistics

All values are expressed as mean ± standard deviation or as a percentage (%). Data were analyzed using the program SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL, USA). The normality of data was tested using the Kolmogorov–Smirnov test. Parameter differences among the 4 groups were evaluated using the one-way ANOVA Test for normally distributed variables and Kruskal–Wallis test for non-normally distributed variables. For post hoc analysis of normally distributed variables Tukey's *b* test was used. For post hoc analysis of non-normally distributed variables Benferroni corrected Mann–Whitney *U*-test was used. For the comparison of categorical variables, Chi-square test or Fisher's exact test was used as appropriate. Lastly multiple multivariate logistic regression analyses related with WCHT, MHT and SHT (as dependent variables). A value of $p < 0.05$ was accepted as statistically significant.

Results

Initially 340 patients were included. Four patients were excluded due to atrial fibrillation. One patient with renal artery stenosis, 2 patients with hypothyroidism, and 1 patient with hyperthyroidism, 6 patients with type 2 diabetes, 1 patient with type 1 diabetes, and 4 patients with urinary tract infection were excluded; 12 patients with creatinine >1.4 mg/dL were also excluded. The study was conducted in the remaining 309 patients. Patients were

Table 1
The comparative demographic, clinical, and laboratory parameters among the 4 groups of patients.

	Group I (*N* = 85)	Group II (*N* = 112)	Group III (*N* = 31)	Group IV (*N* = 81)	*p*-Value
Age (years)[a]	$47.8 \pm 12^{II,III,IV}$	56.8 ± 11.7^{I}	60.7 ± 10.2^{I}	59.1 ± 9.9^{I}	<0.0001[**]
Gender (male/female) (*N*)	58/27	83/29	19/12	47/34	0.110[***]
Body mass index (kg/m^2)[a]	$25.9 \pm 3.0^{III,IV}$	$26.2 \pm 2.5^{III,IV}$	$27.9 \pm 4.7^{I,II,IV}$	$29.8 \pm 2.9^{I,II,III}$	<0.0001[**]
Waist circumference (cm)	$86.6 \pm 5.7^{III,IV}$	$87.3 \pm 3.6^{III,IV}$	$92.9 \pm 8.7^{I,II}$	$93.1 \pm 7.6^{I,II}$	<0.0001[**]
Smoker/non-smoker (*N*)	$25/60^{IV}$	$33/79^{IV}$	14/17	$38/43^{I,II}$	0.029[***]
Dipper vs. non-dipper (*N*)	56/29	68/44	23/8	48/33	0.439[***]
Metabolic syndrome (present/absent) (*N*)	$3/82^{II,III,IV}$	$28/84^{I,IV}$	$9/22^{I,IV}$	$46/35^{I,II,III}$	<0.0001[***]
Fasting blood glucose (mmol/L)[a]	$5.17 \pm 0.70^{II,III,IV}$	5.78 ± 1.47^{I}	5.93 ± 1.86^{I}	6.22 ± 2.21^{I}	0.002[**]
Blood urea nitrogen (mmol/L)[a]	5.11 ± 1.57	5.5 ± 1.61	5.68 ± 1.82	5.75 ± 1.86	0.089[**]
Creatinine (μmol/L)[a]	74.3 ± 18.6^{IV}	74.1 ± 16.8^{IV}	81.3 ± 20.3	$81.6 \pm 18.6^{I,II}$	0.027[**]
Albumin (g/L)[a]	43.9 ± 3.5	44.2 ± 5.0	45.1 ± 3.8	44.7 ± 3.8	0.450[**]
Hemoglobin (g/L)[a]	140.7 ± 32.3	138.2 ± 11.0	138.6 ± 14.6	138.9 ± 11.9	0.845[**]
Sodium (mmol/L)[a]	140.5 ± 8.37	139.4 ± 3.44	1401 ± 3.07	140.3 ± 5.27	0.485[**]
Potassium (mmol/L)[a]	4.31 ± 0.32	4.31 ± 0.37	4.42 ± 0.43	4.37 ± 0.39	0.291[**]
Calcium (mmol/L)[a]	2.31 ± 0.10	2.33 ± 0.09	2.30 ± 0.14	2.33 ± 0.11	0.280[**]
Phosphorus (mmol/L)[a]	1.11 ± 0.16	1.12 ± 0.16	1.06 ± 0.15	1.12 ± 0.18	0.368[**]
Uric acid (μmol/L)[a]	303.9 ± 89.8^{IV}	312.9 ± 77.3	328.9 ± 83.9	341.4 ± 94.6^{I}	0.029[**]
Alanine amino transferase (μkat/L)[a]	0.41 ± 0.22	0.40 ± 0.17	0.42 ± 0.13	0.38 ± 0.15	0.481[**]
Aspartate amino transferase (μkat/L)[a]	0.36 ± 0.22	0.36 ± 0.14	0.40 ± 0.14	0.34 ± 0.11	0.370[**]
Total cholesterol (mmol/L)[a]	5.18 ± 0.93	5.35 ± 1.06	5.39 ± 0.89	5.41 ± 1.21	0.445[**]
LDL-cholesterol (mmol/L)[a]	3.05 ± 0.77	3.12 ± 0.84	3.29 ± 0.76	3.22 ± 0.95	0.589[**]
HDL-cholesterol (mmol/L)[a]	1.35 ± 0.33	1.41 ± 0.31	1.37 ± 0.31	1.34 ± 0.32	0.393[**]
Triglyceride (mmol/L)[a]	1.42 ± 0.68	1.59 ± 0.69	1.66 ± 0.82	1.68 ± 0.82	0.060[**]
Spot urine proteinuria present/absent (*N*)	3/82	6/106	3/28	11/70	0.064[***]
Thyroid stimulating hormone (mU/L)[a]	1.65 ± 1.10	1.53 ± 1.33	1.13 ± 0.67	1.61 ± 1.24	0.210[**]
Hs-Crp (mg/L)[a]	3.79 ± 3.05	4.45 ± 4.10	4.94 ± 3.93	5.11 ± 4.23	0.220[**]
Creatinine clearance (ml/min)/1.73 m^2[a]	$90.8 \pm 22.6^{III,IV}$	85.4 ± 19.6	76.2 ± 18.0^{I}	80.6 ± 19.2^{I}	0.001[**]

SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Hs-Crp, high-sensitivity C-reactive protein.
[a] Mean ± standard deviation.
[**] *p*-Value is based on one way ANOVA test.
[***] *p*-Value is based on Chi-square test or Fisher's exact test as appropriate.
Groups with significant differences according to the post hoc Tukey's *b* test and Benferroni corrected Mann–Whitney *U*-test test was shown in superscript roman.

divided into 4 groups according to the clinical and ambulatory BP measurements as defined above:

Group I (*N* = 85) was composed of patients with SNT;
Group II (*N* = 112) was composed of patients with WCHT;
Group III (*N* = 31) was composed of patients with MHT;
Group IV (*N* = 81) was composed of patients with SHT.

The comparative demographic, clinical, and laboratory parameters among the 4 groups of patients are given in Table 1. The comparative clinical and ambulatory BPs are shown in Table 2. Among 309 patients, 243 underwent echocardiography (others refused to do so). The comparison of electrocardiographic and echocardiography findings among the 4 groups of patients is given in Table 3.

Additional subgroup analysis was performed in patients who were extreme nocturnal dippers and reverse dippers. Extreme nocturnal dipping was defined as reduction in average SBP and DBP at night ≥20% when compared to daytime. Reverse dipping was defined as higher nocturnal average SBP and DPB in comparison with daytime values [9]. Among 309 patients, 177 patients were dippers, 67 were non-dippers, 18 were extreme dippers, and 47 were reverse dippers. Comparison of laboratory variables among these 4 groups of patients showed that only uric acid levels were different among the groups (297.4 ± 88.0 μmol/L, 350.9 ± 79.7 μmol/L, 310.5 ± 75.5 μmol/L, and 356.9 ± 70.8 μmol/L in dippers, in non-dippers, in extreme dippers, and in reverse dippers, respectively, $p < 0.0001$). Post hoc analysis revealed that uric acid levels were different between dippers and non-dippers ($p < 0.0001$) and between dippers and reverse dippers ($p < 0.0001$).

Table 2
The comparative office and ambulatory blood pressure and heart rate parameters among the 4 groups of patients.

	Group I (*N* = 85)	Group II (*N* = 112)	Group III (*N* = 31)	Group IV (*N* = 81)	*p*-Value
Office SBP (mmHg)[a]	$122.6 \pm 9.7^{II,IV}$	$151.3 \pm 16.8^{I,III,IV}$	128.8 ± 9.4^{II}	$159.4 \pm 21.6^{I,II}$	<0.0001[**]
Office DBP (mmHg)[a]	$76.8 \pm 6.78^{II,IV}$	$93.7 \pm 9.60^{I,III}$	$79.3 \pm 6.99^{II,IV}$	$96.8 \pm 9.44^{I,III}$	<0.0001[**]
Average ambulatory SBP (mmHg) (daytime)[a]	$118.8 \pm 7.6^{III,IV}$	$122.2 \pm 7.9^{III,IV}$	$143.2 \pm 7.6^{I,II}$	$146.3 \pm 13.8^{I,II}$	<0.0001[**]
Average ambulatory DBP (mmHg) (daytime)[a]	$73.2 \pm 5.7^{III,IV}$	$72.0 \pm 6.7^{III,IV}$	$79.1 \pm 7.3^{I,II,IV}$	$83.9 \pm 10.9^{I,II,III}$	<0.0001[**]
Average ambulatory SBP (mmHg) (nighttime)[a]	$108.3 \pm 11.1^{III,IV}$	$113.5 \pm 11.2^{III,IV}$	$129.2 \pm 16.3^{I,II}$	$132.6 \pm 17.5^{I,II}$	<0.0001[**]
Average ambulatory DBP (mmHg) (nighttime)[a]	65.6 ± 7.9^{IV}	65.4 ± 8.0^{IV}	69.9 ± 8.8	$74.2 \pm 8.5^{I,II}$	<0.0001[**]
Average ambulatory SBP (mmHg) (24-h)[a]	$116.6 \pm 7.8^{III,IV}$	$120.4 \pm 7.9^{III,IV}$	$140.3 \pm 9.3^{I,II}$	$143.5 \pm 14.1^{I,II}$	<0.0001[**]
Average ambulatory DBP (mmHg) (24-h)[a]	$71.6 \pm 5.6^{III,IV}$	$70.4 \pm 6.6^{III,IV}$	$77.3 \pm 7.1^{I,II}$	$81.3 \pm 8.6^{I,II}$	<0.0001[**]
Mean ambulatory arterial BP (mmHg) (daytime)[a]	$88.4 \pm 5.9^{III,IV}$	$88.7 \pm 6.4^{III,IV}$	$100.3 \pm 4.9^{I,II,IV}$	$104.6 \pm 9.3^{I,II,III}$	<0.0001[**]
Mean ambulatory arterial BP (mmHg) (nighttime)[a]	$79.9 \pm 8.5^{III,IV}$	$81.5 \pm 8.3^{III,IV}$	$89.7 \pm 10.3^{I,II}$	$93.7 \pm 9.1^{I,II}$	<0.0001[**]
Mean ambulatory arterial BP (mmHg) (24-h)[a]	$85.0 \pm 6.2^{III,IV}$	$85.8 \pm 6.3^{III,IV}$	$96.1 \pm 6.1^{I,II,IV}$	$100.2 \pm 7.9^{I,II,III}$	<0.0001[**]
Mean ambulatory heart rate (beats/min) (daytime)[a]	75.5 ± 9.92	73.7 ± 13.8	74.1 ± 9.2	75.3 ± 9.2	0.713[**]
Mean ambulatory heart rate (beats/min) (nighttime)[a]	64.5 ± 8.1	66.3 ± 10.4	65.0 ± 7.9	67.7 ± 9.3	0.448[**]
Mean ambulatory heart rate (beats/min) (24-h)[a]	73.4 ± 7.9	72.2 ± 10.1	72.1 ± 9.3	73.7 ± 8.6	0.843[**]

SBP, systolic blood pressure; DBP, diastolic blood pressure.
[a] Mean ± standard deviation.
[**] *p*-Value is based on one way ANOVA test.
Groups with significant differences according to the post hoc Tukey's *b* test are shown in superscript roman.

Table 3
Comparison of electrocardiographic and echocardiographic findings among the 4 groups of patients.

	Group I ($N=59$)	Group II ($N=95$)	Group III ($N=25$)	Group IV ($N=64$)	p-Value
Left ventricular hypertrophy (based on electrocardiography) present/absent (N)	7/78[III,IV]	14/98[III,IV]	9/22[I,II]	27/54[I,II]	<0.0001***
Interventricular septum thickness (mm)[a]	1.06 ± 0.14[II,III,IV]	1.18 ± 0.22[I,IV]	1.23 ± 0.12[I]	1.27 ± 0.14[I,II]	<0.0001**
Ejection fraction (%)[a]	59.6 ± 5.2	58.3 ± 8.1	58.1 ± 8.5	56.7 ± 8.5	0.235**
Diastolic dysfunction (present/absent) (N)	10/49[II,III,IV]	31/64[I,III,IV]	15/10[I,II]	41/23[I,II]	<0.0001***
E/A ratio	1.27 ± 0.20[II,III,IV]	1.17 ± 0.29[I,III,IV]	0.93 ± 0.24[I,II]	0.88 ± 0.22[I,II]	<0.0001***

[a] Mean ± standard deviation.
** p-Value is based on one way ANOVA test.
*** p-Value is based on Chi-square test.
Groups with significant differences according to the post hoc Tukey's b test are shown in superscript roman.

Comparison of categorical variables including gender, smoking status, electrographically determined ventricular hypertrophy, spot urine proteinuria, and presence of MetS demonstrated no difference among groups. Lastly, comparison of echocardiographic parameters including interventricular septum thickness, ejection fraction, E/A ratio, and presence of diastolic dysfunction were not different among these patients.

Additional multiple multivariate logistic regression analyses were performed to investigate the independent parameters including gender, age, smoking status, BMI, presence of metabolic syndrome, presence of spot urine proteinuria, presence of diastolic dysfunction, interventricular septum thickness, ejection fraction, fasting blood glucose, uric acid, high-sensitivity C-reactive protein, and creatinine clearance related with WCHT, MHT, and SHT (as dependent variables). The results showed that WCHT was related with age (odds ratio: 1.054, 95%CI: 1.004–1.106, $p=0.034$) and with smoking status (odds ratio: 2.829, 95%CI: 1.222–6.552, $p=0.015$). MHT was associated only with creatinine clearance (odds ratio: 0.960, 95%CI: 0.924–0.997, $p=0.036$). Finally, SHT was independently associated with being male (odds ratio: 4.184, 95%CI: 1.445–10.869, $p=0.003$), BMI (odds ratio: 1.247, 95%CI: 1.088–1.430, $p=0.002$), and presence of MetS (odds ratio: 3.555, 95%CI: 1.275–8.771, $p=0.014$).

Discussion

The current study demonstrated that most of the metabolic and clinical characteristics were different in patients with SNT, WCHT, MHT, and SHT. Additionally the comparison of the prevalence of MetS was firstly carried out among the 4 groups of patients.

Although various studies have been performed in these subjects debate is going on regarding the clinical significance of these conditions. For example, it is still not clear whether presence of WCHT portends future risk for cardiovascular complications. While some studies suggested WCHT as a risk factor [10,11], others showed that patients with WCHT had favorable prognosis [12–14]. Thus the prognostic significance of WCHT remains controversial [5]. Besides these conflicting issues, there are few studies comparing these 4 groups of patients. In one of these studies, 4 groups of patients were compared longitudinally with respect to cardiovascular mortality and stroke. The authors showed that patients with WCHT were similar to patients with SNT. However, risk was significantly higher for subjects with MHT and SHT [2]. In another study, it was shown that the incidence and risk of cardiovascular death showed a progressive increase from subjects in which in-office and out-of-office BPs were both normal to subjects with WCHT, MHT, and in-office and "out-of-office" HT, independent of age and gender [3].

Although these studies were valuable, no detailed comparison was performed with regard to demographic, laboratory, and clinical findings. Thus the current study was performed to highlight these issues.

One of the important findings of the present study was the progressive rise of various metabolic risk factors including BMI, WC, fasting blood glucose, and uric acid going from SNT to SHT. Also the prevalence of MetS was lowest in patients with SNT and highest in patients with SHT. These findings raise the probability that metabolic risk factors may play a role for the development of MHT and SHT. Indeed Mancia et al. demonstrated that serum glucose and BMI has been associated with the development of SHT [11]. In another study, it was also demonstrated that BMI and WC were higher in patients with SHT when compared to normotensive patients [15]. Even patients with WCHT have been found to have increased risk for the presence of MetS when compared to patients with SNT [16]. Why are these metabolic risk factors related with MHT and SHT? Although the current study did not aim to explore pathophysiologic relationships some speculations can be made. It is already known that excess weight leads to both structural and functional abnormalities in many systems of the body, as well as a higher risk of death from all causes, including cardiovascular diseases, and increases parallel to the range of moderate to severe weight excess in all age groups [17]. It was also found that the prevalence of SNT was significantly higher in underweight cases than normal weight and overweight cases [18]. Thus, the dominant underlying risk factor for the MetS appears to be already existing excess weight or a trend toward excess weight, which is probably the main cause of insulin resistance, dyslipidemia, IGT, and elevated BP [19].

Abdominal obesity a key element of MetS, initiates increased sympathetic outflow, increased arterial resistance, and ultimately the development of increased BP by many pathways that are still poorly understood [20]. Visceral adiposity has been found also to induce increased large artery stiffness in both younger and older persons [19]. Additionally, recent evidence demonstrated that pericardial fat tissue was related to MetS, coronary artery disease, and diastolic dysfunction [21]. It was also shown that epicardial fat tissue was associated with hypertension [22]. Thus, the relationship between MetS and WCHT, MHT, and SHT may be explained in the context of epicardial fat tissue. Increased serum uric acid levels going from SNT to SHT may also be responsible for the present findings regarding the increased prevalence of MetS as going from SNT to SHT since uric acid itself, independent of other factors, was suggested to be responsible for derangement of metabolism and blood pressure [23]. Another potential explanation for the high incidence of MetS in SHT may be the activation of renin–angiotensin–aldosterone system (RAAS). Mechanisms involved in activation of the RAAS in obesity include sympathetic stimulation, synthesis of adipokines in the RAAS by visceral fat, and hemodynamic alterations [24]. Activation of the RAAS and the sympathetic nervous system—as well as physical compression of the kidneys by visceral adiposity which impairs normal pressure natriuresis, increases renal tubular sodium reabsorption, and causes volume expansion and hypertension [25]. Last but not the least the relationship between MetS and SHT may be explained in the context of salt sensitivity. Indeed it was shown that

salt sensitivity has been associated with hypertension and the MetS [26]. Thus all aforementioned factors may explain the increased prevalence of MetS as going from patients with SNT to SHT.

The electrocardiographically determined left ventricular hypertrophy and echocardiographically determined interventricular septum thickness were found to be higher in MHT and SHT when compared to SNT and WCHT which were in accord with the literature. Previous studies have also demonstrated that patients with MHT are more likely to have left ventricular hypertrophy than normotensive subjects, assessed in terms of left ventricular mass [27–29], posterior wall thickness [30], or the prevalence of left ventricular hypertrophy [31]. Thus it was suggested that MHT patients had similar cardiovascular prognosis comparable to those of true hypertensive patients and patients with MHT and SHT are not fundamentally different from each other, but represent a different phenotypic expression of high BP [32,33]. Of note there was no difference regarding spot urine proteinuria as a measure of target organ damage. However the prevalence of proteinuria in the whole population is low overall and the lack of association between HT subtypes and proteinuria may be due to this low prevalence.

This study has some limitations that deserve mention. Firstly, since the study is cross-sectional, cause and effect relationships cannot be suggested. Secondly, the measurements were made only once, raising the question of reproducibility. Thus serial measurements would be better for the interpretation of results. Thirdly, the results could not be generalized to other patients such as those with diabetes and taking medications since these patients were excluded. Fourthly, calculation of left ventricular mass index was not specifically concerned. Lastly, although it was accepted that conventional (clinic/office) BP measurements and ABPM were adequate for classification of patients as WCHT, MHT, etc. [34], it would be better if home or self blood pressure monitoring data were available for the patients.

In conclusion this is one of the few studies to compare patients with SNT, WCHT, MHT, and SHT with respect to various demographic, clinical, and laboratory parameters. Most of the metabolic risk factors were higher in patients with MHT and SHT when compared to SNT and WCHT. Studies are needed to determine whether metabolic risk factors play a causative role for the development of MHT and SHT.

References

[1] Bobrie G, Clerson P, Ménard J, Postel-Vinay N, Chatellier G, Plouin PF. Masked hypertension: a systematic review. J Hypertens 2008;26:1715–25.
[2] Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, Hashimoto J, Totsune K, Hoshi H, Satoh H, Imai Y. Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama Study. J Am Coll Cardiol 2005;46:508–15.
[3] Mancia C, Facchetti R, Bombelli M, Grassi G, Sega R. Long-term risk of mortality associated with selective and combined elevation in office, home, and ambulatory blood pressure. Hypertension 2006;47:846–53.
[4] Angeli F, Reboldi G, Verdecchia P. Masked hypertension: evaluation, prognosis, and treatment. Am J Hypertens 2010;23:941–8.
[5] Mancia G, Parati G. Ambulatory blood pressure monitoring and organ damage. Hypertension 2000;36:894–900.
[6] O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, Mengden T, Myers M, Padfield P, Palatini P, Parati G, Pickering T, Redon J, Staessen J, Stergiou G, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003;21:821–48.
[7] Konno T, Shimizu M, Ino H, Fujino N, Hayashi K, Uchiyama K, Kaneda T, Inoue M, Fujita T, Masuta E, Funada A, Mabuchi H. Differences in diagnostic value of four electrocardiographic voltage criteria for hypertrophic cardiomyopathy in a genotyped population. Am J Cardiol 2005;96:1308–12.
[8] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486–97.
[9] O'Brien E, Sheridan J, O'Malley K. Dippers and non-dippers. Lancet 1988;2:39.
[10] Nakashima T, Yamano S, Sasaki R, Minami S, Doi K, Yamamoto J, Takaoka M, Saito Y. White-coat hypertension contributes to the presence of carotid arteriosclerosis. Hypertens Res 2004;27:739–45.
[11] Mancia G, Bombelli M, Facchetti R, Madotto F, Quarti-Trevano F, Polo Friz H, Grassi G, Sega R. Long-term risk of sustained hypertension in white-coat or masked hypertension. Hypertension 2009;54:226–32.
[12] Verdecchia P, Porcellati C, Schillaci G, Borgioni C, Ciucci A, Battistelli M, Guerrieri M, Gatteschi C, Zampi I, Santucci A. Ambulatory blood pressure: an independent predictor of prognosis in essential hypertension. Hypertension 1994;24:793–801.
[13] Khattar RS, Senior R, Lahiri A. Cardiovascular outcome in white-coat versus sustained mild hypertension: a 10-year follow-up study. Circulation 1998;98:1892–7.
[14] Pickering TG, Coats A, Mallion JM, Mancia G, Verdecchia P. Blood pressure monitoring: task force V: white-coat hypertension. Blood Press Monit 1999;4:333–41.
[15] Björklund K, Lind L, Zethelius B, Andrén B, Lithell H. Isolated ambulatory hypertension predicts cardiovascular morbidity in elderly men. Circulation 2003;107:1297–302.
[16] Helvacı MR, Kaya A, Seyhanli M, Yalcin A. White coat hypertension in definition of metabolic syndrome. Int Heart J 2008;49:449–57.
[17] Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath Jr CW. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999;341:1097–105.
[18] Helvaci MR, Ozcura F, Kaya H, Yalcin A. Funduscopic examination has limited benefit for management of hypertension. Int Heart J 2007;48:187–94.
[19] Franklin SS, Barboza MG, Pio JR, Wong ND. Blood pressure categories, hypertensive subtypes, and the metabolic syndrome. J Hypertens 2006;24:2009–16.
[20] Hall JE, Kuo JJ, de Silva AA, de Paula RB, Liu J, Tallam L. Obesity-associated hypertension and kidney disease. Curr Opin Nephrol Hypertens 2003;12:195–200.
[21] Konishi M, Sugiyama S, Sugamura K, Nozaki T, Matsubara J, Akiyama E, Utsunomiya D, Matsuzawa Y, Yamashita Y, Kimura K, Umemura S, Ogawa H. Accumulation of pericardial fat correlates with left ventricular diastolic dysfunction in patients with normal ejection fraction. J Cardiol 2012;59:344–51.
[22] Sengul C, Cevik C, Ozveren O, Duman D, Eroglu E, Oduncu V, Tanboga HI, Can MM, Akgun T, Dindar I. Epicardial fat thickness is associated with non-dipper blood pressure pattern in patients with essential hypertension. Clin Exp Hypertens 2012;34:165–70.
[23] Puddu P, Puddu GM, Cravero E, Vizioli L, Muscari A. The relationships among hyperuricemia, endothelial dysfunction, and cardiovascular diseases: molecular mechanisms and clinical implications. J Cardiol 2012;59:235–42.
[24] Thethi T, Kamiyama M, Kobori H. The link between the renin–angiotensin–aldosterone system and renal injury in obesity and the metabolic syndrome. Curr Hypertens Rep 2012;14:160–9.
[25] Hall JE, Henegar JR, Dwyer TM, Liu J, Da Silva AA, Kuo JJ, Tallam L. Is obesity a major cause of chronic kidney disease? Adv Ren Replace Ther 2004;11:41–54.
[26] Rocchini AP, Key J, Bondie D, Chico R, Moorehead C, Katch V, Martin M. The effect of weight loss on the sensitivity of blood pressure to sodium in obese adolescents. N Engl J Med 1989;321:580–5.
[27] Hernandez del-Rey R, Armario P, Martin-Baranera M, Sanchez P, Almendros MC, Coca A, Pardell H. Cardiac damage in hypertensive patients with inverse white coat hypertension. Hospitalet study. Blood Press 2003;12:89–96.
[28] Liu JE, Roman MJ, Pini R, Schwartz JE, Pickering TG, Devereux RB. Cardiac and arterial target organ damage in adults with elevated ambulatory and normal office blood pressure. Ann Intern Med 1999;131:564–72.
[29] Sega R, Trocino G, Lanzarotti A, Carugo S, Cesana G, Schiavina R, Valagussa F, Bombelli M, Giannattasio C, Zanchetti A, Mancia G. Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension. Data from the general population (PAMELA study). Circulation 2001;104:1385–92.
[30] Sakaguchi K, Horimatsu T, Kishi A, Ohnishi Y, Koike T, Fujisawa T, Maeda M. Isolated home hypertension in the morning is associated with target organ damage in patients with type 2 diabetes. J Atheroscler Thromb 2005;12:225–31.
[31] Pierdomenico SD, Lapenna D, Bucci A, Di Tommaso R, Di Mascio R, Manente BM, Caldarella MP, Neri M, Cuccurullo F, Mezzetti A. Cardiovascular outcome in treated hypertensive patients with responder, masked, false resistant, and true resistant hypertension. Am J Hypertens 2005;18:1422–8.
[32] Bobrie G, Chatellier G, Genes N, Clerson P, Vaur L, Vaisse B, Menard J, Mallion JM. Cardiovascular prognosis of "masked hypertension" detected by blood pressure self-measurement in elderly treated hypertensive patients. JAMA 2004;291:1342–9.
[33] Verberk WJ, Thien T, Kroon AA, Lenders JW, van Montfrans GA, Smit AJ, de Leeuw PW. Prevalence and persistence of masked hypertension in treated hypertensive patients. Am J Hypertens 2007;20:1258–65.
[34] O'Brien E, Asmar R, Beilin L, Imai Y, Mancia G, Mengden T, Myers M, Padfield P, Palatini P, Parati G, Pickering T, Redon J, Staessen J, Stergiou G, Verdecchia P, et al. Practice guidelines of the European Society of Hypertension for clinic, ambulatory and self blood pressure measurement. J Hypertens 2005;23:697–701.