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Discordance between ambulatory versus clinic blood pressure according to global cardiovascular risk group

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Background/Aims: The detection of white coat hypertension (WCH), treated normalized hypertension, and masked hypertension (MH) is important to improve the effectiveness of hypertension management. However, whether global cardiovascular risk (GCR) profile has any effect on the discordance between ambulatory blood pressure (ABP) and clinic blood pressure (CBP) is unknown.
Methods: Data from 1,916 subjects, taken from the Korean Multicenter Registry for ABP monitoring, were grouped according to diagnostic and therapeutic thresholds for CBP and ABP (140/90 and 135/85 mmHg, respectively). GCR was assessed using European Society of Hypertension 2007 guidelines.
Results: The mean subject age was 54.1 ± 14.9 years, and 48.9% of patients were female. The discordancy rate between ABP and CBP in the untreated and treated patients was 32.5% and 26.5%, respectively (p = 0.02). The prevalence of WCH or treated normalized hypertension and MH was 14.4% and 16.0%, respectively. Discordance between ABP and CBP was lower in the very high added-risk group compared to the moderate added-risk group (odds ratio [OR], 0.649; 95% confidence interval [CI], 0.487 to 0.863; p = 0.003). The prevalence of WCH or treated normalized hypertension was also lower in the very high added-risk group (OR, 0.451; 95% CI, 0.311 to 0.655).
Conclusions: Discordance between ABP and CBP was observed more frequently in untreated subjects than in treated subjects, and less frequently in the very high added-risk group, which was due mainly to the lower prevalence of WCH or treated normalized hypertension.

Keywords: Risk assessment; Blood pressure monitoring, ambulatory; Masked hypertension; White coat hypertension; Hypertension

INTRODUCTION

Arterial blood pressure (BP) is regulated by neuronal, vascular, and renal mechanisms and can vary substantially according to temperature, physical activity, emotional stress, food intake, and the use of drugs including alcohol

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and caffeine. BP measured by ambulatory blood pressure monitoring (ABPM) is generally considered to be more effective at predicting cardiovascular events than the measurement in a clinic [1]. Studies have confirmed that for both treated and untreated hypertensive patients, ambulatory blood pressure (ABP) is a more powerful predictor of cardiovascular events than clinic blood pressure (CBP) [2-4].

In clinical practice, however, the most important application of ABPM is to detect white coat hypertension (WCH) and masked hypertension (MH). Diagnostic thresholds based on cardiovascular outcomes have been reported in many studies [2,3,5-7]. In the recently published United Kingdom National Institute for Clinical Excellence (NICE) guidelines, the routine use of ABPM for the diagnosis of hypertension was recommended [8], and therapeutic thresholds for ABPM were also suggested. The current thresholds for diagnosis and treatment are around 135/85 mmHg, and this same threshold is applied for all spectrums of global cardiovascular risk (GCR) groups determined by a risk stratification process [8].

The most important rationale for the routine use of ABPM in the NICE guidelines is to reduce the cost incurred by unnecessary treatment of WCH. However, the downstream cost driven by cardiovascular events resulting from neglected treatment of MH was not considered. Unlike WCH, the higher the GCR of a hypertensive subject, the greater the effectiveness of prevention related to the detection of MH.

The role of ABPM in high-risk patients might be different from that in low-risk patients [9]. In addition, the clinical implication of a discordant diagnosis; i.e., WCH or MH diagnosed by ABPM, can differ among GCR groups. Considering the absolute risk, detection of WCH and/or MH may be more cost-effective in the higher GCR group [10]. However, there have been few reports regarding the prevalence of such discordant diagnoses according to GCR group, or the clinical implications of the risk stratification process in terms of the clinical usefulness of ABPM.

In the present cross-sectional study, the association between GCR profile and ABP CBP discordance was investigated in a multicenter clinical cohort in Korea.

METHODS

Subjects

A total of 2,215 patients were enrolled in this study from 1 August 2009 to 31 December 2010. Of these patients, data from 1,916 subjects were obtained from the Korean ABPM Registry for Evaluation of the Prognostic Threshold in Hypertension (Kor-ABP) cohort study organized by the Korean Society of Hypertension. Twenty-seven referral hospitals participated in this study, 24 of which were affiliated with one of 18 medical schools, one was a veterans' hospital, one hospital was affiliated with a Catholic foundation, and one was a medical insurance referral hospital. All investigators were cardiologists involved mainly in the field of hypertension and clinical cardiology.

A total of 2,215 patients that had undergone ABPM for the evaluation of high BP were included in this study; however, 299 patients with incomplete data, and/or a lack of informed consent were excluded. The minimum data required were demographic information, a clinical questionnaire, CBP, medical information from hospital records, and the raw ABPM data files.

Clinical and laboratory variables

The following demographic informations were included: age, gender, height, weight, abdominal circumference, smoking status, alcohol intake, extent of physical exercise, family history of hypertension and premature cardiovascular death, and past medical history including the occurrence of hypertension, diabetes, hyperlipidemia, stroke, myocardial infarction, heart failure, and cancer.

Informations taken from medical records included the presence of diabetes, hyperlipidemia, and cardiovascular diseases, as well as the time of diagnosis, mode of treatment, and prescribed medications for any of the above conditions.

Data from laboratory tests, where available, included complete blood cell count, chemistry, lipid profile, electrolytes, liver function, fasting glucose, fasting insulin, high-sensitivity C-reactive protein test, microalbuminuria, left ventricular hypertrophy measured by electrocardiogram voltage, chest X-ray, echocardiography, carotid ultrasonography, and pulse wave velocity.

CBP and ABPM data

CBP was measured using an A&D UA-767 (A&D Co., Ltd., Tokyo, Japan), which passed European Society of Hypertension (ESH) International Protocols at all institutes. CBP is defined as the average BP of two measurements taken 1 minute apart, with 5 minutes of rest before the first measurement.

ABPM data were gathered as raw data files from the website, or typed manually when raw data files were not available. The ABPM raw data were regarded as valid only when at least 14 awake BP readings, taken from 8:00 AM to 9:00 PM, were available after omitting erroneous readings according to the following criteria: (1) systolic BP > 250 or < 70 mmHg; (2) diastolic BP > 150 or < 40 mmHg; and (3) pulse pressure > 150 or < 20 mmHg [11].

Definition of risk groups

The 10-year cardiovascular event rate for the GCR groups was defined according to the 2003 ESH-European Society of Cardiology (ESC) guidelines for the management of arterial hypertension [12]. Subjects were assigned to GCR groups according to the 2007 guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the ESH and the ESC [13]. The risk group was determined by adding the various risk factors; i.e., age over 55 years for males or over 65 years for females; dyslipidemia; fasting blood glucose between 102 and 125 md/dL; obesity, defined by abdominal circumference ≥ 90 cm for males and ≥ 80 cm for females, or body mass index (BMI) ≥ 25 kg/m^2; smoking habit; and a family history of cardiovascular disease before the age of 55 years for males and 65 years for females. Dyslipidemia was defined by a history of dyslipidemia, the use of statins or other drugs for lipid abnormality, or diagnosis or data from medical records including either abnormal high density lipoprotein (HDL) or triglyceride levels, or total cholesterol ³ 190 mg/dL. Diabetes mellitus was defined by past history or current diagnosis [13]. Patients with three or more of the following: impaired fasting blood glucose without diabetes mellitus, abdominal obesity, triglyceride levels ≥ 150 mg/dL, low HDL levels, BP ≥ 130/85 mmHg, or a history of hypertension were considered to have metabolic syndrome [14].

GCR profiles were classified as groups with average, low added, moderate added, high added, and very high added risk [13]. Treated subjects with clinic systolic BP below 140 mmHg and diastolic BP below 90 mmHg were classified as grade 1 hypertensive.

Definition of thresholds for controlled hypertension

Controlled hypertension by CBP was defined as systolic BP below 140 mmHg and diastolic BP below 90 mmHg. Controlled hypertension by ABP was defined as a daytime systolic BP below 135 mmHg and a daytime diastolic BP below 85 mmHg. Subjects with controlled hypertension by ABP and uncontrolled hypertension by CBP were described as having 'treated normalized hypertension' [15]. The study protocol was approved by the Clinical Research Ethics Committees of all hospitals involved in the study.

Statistical analyses

All data are expressed as mean ± standard deviation. The statistical significance of the differences in the mean values was evaluated using analysis of variance. Chi-square and Fisher exact tests were used to determine the statistical significance of differences between groups. The various diagnostic categories were evaluated between CBP and ABP using McNemar test. Reliability analyses for inter-rater reliability and internal consistency using the κ test and Cronbach's α were performed to determine the consistency of the two BP measurement methods.

Multiple logistic regression analysis was performed to examine the association between GCR group and the various BP categories and with incorrect categorization, by adjusting age, gender, clinic systolic BP, and antihypertensive medication. The group with moderate added risk was used as the reference point. Statistical significance was defined as a 95% confidence interval (CI) and a $p < 0.05$. All data processing and analyses were performed using SPSS version 20.0 (IBM Co., Armonk, NY, USA).

RESULTS

General characteristics of the study subjects

The age of the participants was 54.1 ± 14.9 years (n = 1,916), BMI was 24.7 ± 3.4 kg/m^2, and 48.9% of patients were female. The clinic systolic BP was 142.9 ± 20.5 mmHg, and the clinic diastolic BP was 88.5 ± 14.6 mmHg. The clinic heart rate was 75.8 ± 13.8 beats per minute. ABPM devices used in this study were A&D (50.3%), Tonoport V

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(GE Medical Systems, Freiburg, Germany) and other GE devices (38.5%), Del Mar (7.6%; Avionics, Irvine, CA, USA), Spacelabs (3.5%; Spacelabs Medical, Issaquah, WA, USA), and Mobil O graph (0.1%; I.E.M., Stolberg, Germany). The indications for ABPM were the diagnosis of hypertension (59.3%), assessment of the efficacy of anti-hypertensive treatment (38.0%), symptoms of hypotension (1.6%), symptoms of autonomic dysfunction (0.8%), and diagnosis of pregnancy (0.3%). The period from midnight to 5:00 AM was defined as night. Daytime systolic BP was 136.3 ± 16.8 mmHg, and daytime diastolic BP was 85.7 ± 12.0 mmHg. Nighttime systolic and diastolic BPs were 127.6 ± 25.7 and 79.0 ± 13.5 mmHg, respectively. Heart rate was 73.3 ± 11.5 beats per minute in the day and 64.7 ± 4.7 beats per minute at night. The quality of sleep was good in 23.8% of patients, fair in 26.2%, bad in 28.4%, and very bad in 13.1% of patients. Measurement intervals were 15 (49.8%), 30 (40.8%), and 60 minutes (0.3%) in the daytime, and 15 (0.5%), 30 (77.2%), and 60 minutes (22.1 %) at night.

Among the study population, 14.3% of the subject were current smokers, 36.5% of the subject were current drinkers, 67.4% of the subject exercised less than three times per week, and 48.3%, 19.4%, and 3.2% of patients had family histories of hypertension, diabetes mellitus, and premature cardiac death, respectively.

Diabetes mellitus and dyslipidemia were present in 11.6% and 65.7% of patients, respectively. Coronary artery disease was present in 7.9% of patients and 8.7% of patients had a stroke previously. Metabolic syndrome could be assessed in only 910 subjects due to a lack of data, but 34.3% of these patients had metabolic syndrome without diabetes mellitus.

As shown in Table 1, the prevalences of optimal BP, normal BP, high normal BP, grade 1 hypertension, grade 2 hypertension, and grade 3 hypertension were 3.0%, 5.6%, 6.4%, 53.6%, 20.7%, and 10.7%, respectively. Only 7.0% (n = 136) of subjects had no cardiovascular risk factors, and only 3.5% of subjects had grade 1 or hypertension without risk factor.

As shown in Tables 1 and 2, 34.1% of patients were treated with antihypertensive medication. As shown in Table 2, the treated subjects were older, more obese, and had higher CBP and lower HDL levels. The prevalence of drinking and smoking, as well as cholesterol levels, were reduced in the treated group; however, a previous history of cardiovascular disease and a higher GCR profile were more frequent.

Global cardiovascular risk profile

As shown in Table 3, the percentage of patients with average risk, low added risk, moderate added risk, high added risk, and very high added risk was 1.5%, 8.9%, 32.1%, 32.7%, and 24.8%, respectively. Most of the parameters, with the exception of heart rate, varied as a function of

Table 1. Distribution of subjects according to total cardiovascular risk profile

Variable	Blood pressure, mmHg					
	Optimal (SBP < 120 and DBP < 80)	Normal (SBP 120–129 or DBP 80–84)	High normal (SBP 130–139 or DBP 85–89)	Grade 1 HTN (SBP 140–159 or DBP 90–99)	Grade 2 HTN (SBP 160–179 or DBP 100–109)	Grade 3 HTN (SBP ≥ 180 or DBP ≥ 110)
No other risk factors	4 (0.2)	15 (0.8)	10 (0.5)	57 (3.0)	30 (1.6)	20 (1.0)
1–2 risk factors	26 (1.4)	40 (2.1)	48 (2.5)	376 (19.6)	159 (8.3)	80 (4.2)
3 or more risk factors, MS, OD, or diabetes	13 (0.7)	36 (1.9)	46 (2.4)	413 (21.6)	148 (7.7)	85 (4.4)
Established CV or renal disease	15 (0.8)	17 (0.9)	18 (0.9)	181 (9.4)	59 (3.1)	20 (1.0)
Total	58 (3.0)	108 (5.6)	122 (6.4)	1,027 (53.6)	396 (20.7)	205 (10.7)
Antihypertensive medication	-	-	-	427 (22.2)	148 (7.7)	79 (4.1)

Values are presented as number (%). All treated hypertensive patients with blood pressure below grade 1 hypertension were categorized as grade 1 hypertension.
SBP, systolic blood pressure; DBP, diastolic blood pressure; HTN, hypertension; MS, metabolic syndrome; OD, organ damage; CV, cardiovascular.

Table 2. Characteristics of the subjects according to antihypertensive medication treatment status

Characteristic	Untreated (n = 1,262)	Treated (n = 654)	*p* value
Age, yr	52.1 ± 15.3	58.0 ± 13.2	< 0.001
Female sex, %	48.0	50.5	0.95
Body mass index, kg/m^2	24.5 ± 3.4	25.1 ± 3.5	0.001
Clinic SBP, mmHg	141.6 ± 19.7	144.6 ± 21.7	0.002
Clinic DBP, mmHg	88.2 ± 14.1	88.5 ± 15.2	0.052
Daytime SBP, mmHg	135.4 ± 15.4	136.3 ± 15.9	0.441
Daytime DBP, mmHg	86.4 ± 11.9	84.3 ± 11.4	0.055
Fasting blood glucose, mg/dL	104.5 ± 28.5	109.3 ± 37.1	0.073
Total cholesterol, mg/dL	188.6 ± 40.2	181.8 ± 44.2	0.005
HDL, mg/dL	49.1 ± 13.5	46.6 ± 11.7	0.007
Triglyceride, mg/dL	139.8 ± 99.9	146.1 ± 119.3	0.144
Smoking, %	17.1	10.7	< 0.001
Drinking, %	39.5	17.2	0.004
Cardiovascular diseases history, %	11.4	25.2	< 0.001
Global cardiovascular risk groups, %			< 0.001
Average added risk	4.5	0	
Low added risk	18.1	2.9	
Moderate added risk	41.4	40.8	
High added risk	16.1	22.0	
Very high added risk	19.7	34.2	

Values are presented as mean ± SD unless other indicated. *p* values were adjusted for age.
SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high density lipoprotein.

risk category. The risk factors for cardiovascular disease increased as GCR increased.

Discordance between ABP and CBP in all subjects

For all subjects, WCH or treated normalized hypertension and MH were observed in 14.4% and 16.1% of patients, respectively. Concordant categories below and above diagnostic or therapeutic thresholds were observed in 23.7% and 45.8% of patients, respectively. Kappa was 0.360 ($p < 0.001$) with a 95% CI (0.316 to 0.403), and Cronbach's α was 0.519 ($p < 0.001$) with a 95% CI (0.474 to 0.560). The distribution of these BP categories was significantly different between untreated and treated groups ($p = 0.021$), as shown in Fig. 1.

Discordance between ABP and CBP in untreated subjects

Of the 1,262 subjects (61.5%) not on antihypertensive medication, the mean age was 52.1 ± 15.3 years and 48.0% were female. Clinic systolic BP was 141.6 ± 19.7 mmHg, and clinic diastolic BP was 88.2 ± 14.1 mmHg. Daytime systolic and diastolic BPs were 135.4 ± 15.4 and 86.4 ± 11.9 mmHg, respectively, which were lower than clinic BPs ($p < 0.001$ for both systolic and diastolic BPs) (Table 2). The categorization of hypertension by clinic and daytime BP readings is shown in Fig. 1A. Kappa was 0.323 ($p < 0.001$) with a 95% CI (0.270 to 0.375), and Cronbach's α was 0.499 ($p < 0.001$) with a 95% CI (0.441 to 0.552). The number of subjects with WCH was 188 (14.9%), and 222 subjects (17.6%) had MH, while 298 subjects (23.6%) were normotensive, and 554 subjects (43.9%) had sustained hypertension.

Discordance between ABP and CBP in treated hypertensive patients

The age of the 654 subjects (37.5%) on antihypertensive medication was 58.0 ± 13.2 years, and 50.5% were female. Clinic systolic BP was 144.6 ± 21.7 mmHg, and diastolic

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Table 3. Clinical characteristics according to total cardiovascular risk group

Characteristic	Average risk group (n = 29)	Low added-risk group (n = 171)	Moderate added-risk group (n = 614)	High added-risk group (n = 627)	Very high added-risk group (n = 475)	*p* value
Age, yr	30.8 ± 12.0	48.2 ± 16.5	50.9 ± 14.8	57.1 ± 12.7	57.6 ± 14.4	< 0.001
Female sex, %	38	53	52	49	44	0.043
Clinic SBP, mmHg	123.1 ± 9.4	127.2 ± 15.2	142.1 ± 16.8	142.5 ± 17.2	151.1 ± 26.0	< 0.001
Clinic DBP, mmHg	75.5 ± 10.1	79.5 ± 10.2	88.4 ± 11.7	88.0 ± 12.5	93.2 ± 19.2	< 0.001
Heart rate, bpm	78.0 ± 16.4	76.5 ± 13.5	76.9 ± 14.1	75.1 ± 12.8	74.5 ± 14.2	0.041
Height, cm	170.6 ± 9.1	162.7 ± 8.9	163.2 ± 9.0	162.3 ± 9.6	162.6 ± 9.7	0.458
Weight, cm	61.4 ± 9.6	60.8 ± 10.7	65.0 ± 12.0	67.5 ± 12.0	66.7 ± 12.9	< 0.001
Body mass index, kg/m^2	21.0 ± 2.1	22.8 ± 2.9	24.3 ± 3.3	25.5 ± 3.4	25.1 ± 3.6	< 0.001
Daytime SBP, mmHg	125.0 ± 11.3	129.5 ± 14.3	135.5 ± 16.8	136.3 ± 15.0	140.4 ± 19.0	< 0.001
Daytime DBP, mmHg	78.3 ± 9.99	83.6 ± 10.8	86.8 ± 11.8	84.8 ± 11.5	86.6 ± 12.9	< 0.001
Daytime heart rate, bpm	73.1 ± 7.6	73.7 ± 8.6	73.3 ± 9.6	73.7 ± 10.2	72.6 ± 11.3	0.541
Nocturnal SBP, mmHg	112.8 ± 12.1	120.8 ± 17.7	127.8 ± 35.4	126.7 ± 17.3	131.9 ± 22.1	< 0.001
Nocturnal DBP, mmHg	69.1 ± 7.9	76.1 ± 14.1	79.4 ± 13.6	78.7 ± 12.9	80.5 ± 14.1	< 0.001
Nocturnal heart rate, bpm	60.0 ± 8.7	64.3 ± 9.5	64.5 ± 10.9	65.1 ± 11.0	65.1 ± 11.6	0.138
24-Hour SBP, mmHg	121.5 ± 11.7	126.3 ± 14.3	132.4 ± 16.0	133.3 ± 14.5	137.9 ± 18.7	< 0.001
24-Hour DBP, mmHg	75.9 ± 7.0	80.7 ± 11.7	84.1 ± 11.7	83.2 ± 10.8	84.7 ± 12.6	< 0.001
24-Hour heart rate, bpm	69.7 ± 6.9	70.9 ± 8.2	70.6 ± 9.2	71.1 ± 9.9	70.3 ± 10.9	0.739
Antihypertensive medication, %	-	2.9	29.2	39.4	46.9	< 0.001
Diabetes mellitus history, %	-	-	1.1	20.6	18.5	< 0.001
Dyslipidemia history, %	-	3.5	21.1	49.1	26.3	< 0.001
Smoking, %	-	3.2	28.1	41.0	27.7	< 0.001
Obesity, %	-	16.4	34.4	56.1	47.2	< 0.001

Values are presented as mean ± SD unless other indicated.
SBP, systolic blood pressure; DBP, diastolic blood pressure.

BP was 88.5 ± 15.2 mmHg. Daytime systolic and diastolic BPs were 136.3 ± 15.9 and 84.3 ± 11.4 mmHg, respectively, which were lower than the CBPs ($p < 0.001$ for both) (Table 2). Kappa was 0.434 ($p < 0.001$) with a 95% CI (0.363 to 0.504), and Cronbach's α was 0.556 ($p < 0.001$) with a 95% CI (0.482 to 0.619). A total of 88 subjects (13.5%) showed a 'treated normalized hypertension,' and 85 subjects (13.0%) showed a reverse white-coat effect, or 'masked' uncontrolled hypertension. According to both CBP and ABP, 157 subjects (24.0%) were normotensive, and 324 subjects (49.5%) were hypertensive as shown in Fig. 1B.

Discordance between ABP and CBP according to GCR group

As shown in Table 4, the discordancy rate between ABP and CBP were different among the GCR groups. Kappa and Cronbach's α coefficients in the very high added-risk group were significantly higher than those in the other three groups (Table 4). As shown in Table 5, in a multiple logistic regression analysis adjusted by age, gender, and antihypertensive medication status, the risk of WCH was significantly lower in the very high added-risk group than in the moderate added-risk group. However, the risk of MH was significantly higher in the low added-risk group than in the moderate added-risk group. The odds ratio for discordant diagnosis was significantly lower in the very high added-risk group compared to the moderate added-risk group when adjusted for age, gender, clinic SBP, and antihypertensive medication (Table 5).

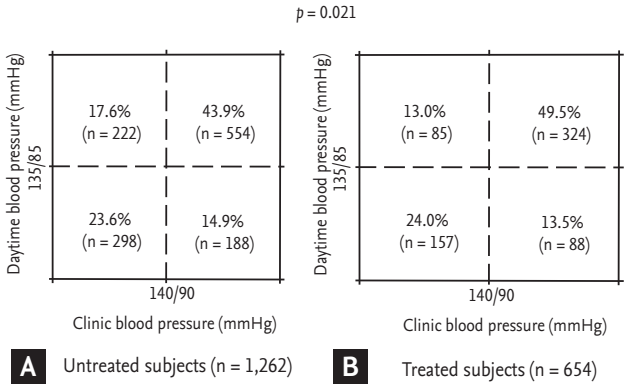

Figure 1. Prevalence of hypertension categories according to antihypertensive medication status. (A) The left upper category indicates masked hypertension and the right lower category indicates white-coat hypertension. (B) The left upper category indicates masked uncontrolled hypertension and the right lower category indicates treated normalized hypertension. The distribution was different between the treated and untreated subjects.

DISCUSSION

In this study, the discrepancy rate between CBP and ABP was shown to be affected by patient GCR profiles. About one third of hypertensive patients would have been misdiagnosed had BP been measured using CBP alone. The likelihood of observing MH was higher in the low added and average risk groups compared to the moderate risk group. However, the likelihood of observing WCH was lower in the very high added-risk group. Overall, discordance decreased as the GCR profile of a patient increased. However, the finding that MH did not decrease in the high or very high added-risk group suggests that ABPM should still be performed in the very high added-risk group to prevent cardiovascular events or to reduce downstream costs incurred by treating MH. In this study, the moderate added-risk group was set as the reference group for the logistic regression analysis because, from a clinical viewpoint, most of the average or low added-risk subjects were likely to be seen in the

Table 4. Distribution of blood pressure subtypes according to total cardiovascular risk group

Variable	Average or low added risk (n = 200)	Moderate added risk (n = 614)	High added risk (n = 627)	Very high added risk (n = 475)	*p* value
Normotension, %	51.3	19.6	21.4	21.2	
White-coat or treated normalized HTN, %	5.5	20.1	15.4	9.7	
Masked HTN, %	30.7	13.0	16.7	13.1	
Sustained HTN, %	13.1	48.3	46.9	56.1	< 0.001
κ[a]	0.216 (0.09–0.333)	0.291 (0.214–0.367)	0.314 (0.237–0.390)	0.480 (0.395–0.564)	
Cronbach's α[a]	0.386 (0.188–0.535)	0.428 (0.329–0.512)	0.481 (0.393–0.556)	0.630 (0.557–0.691)	

HTN, hypertension,
[a]95% confidence interval in the parenthesis.

Table 5. Odds ratios of the discordant classification of blood pressure subtypes according to total cardiovascular risk group

Variable	Average or low added risk (n = 200)	Moderate added risk (n = 614)	High added risk (n = 627)	Very high added risk (n = 475)
White-coat or treated normalized HTN	0.203 (0.104–0.397)	Reference	0.752 (0.556–1.018)	0.451 (0.311–0.655)
Masked HTN[a]	2.963 (2.000–4.389)	Reference	1.247 (0.903–1.724)	0.965 (0.668–1.392)
Discordance[b]	0.956 (0.671–1.361)	Reference	0.945 (0.740–1.208)	0.649 (0.487–0.863)

Discordance was defined as white-coat hypertension, treated normalized hypertension, or masked hypertension.
HTN, hypertension.
[a]Adjusted for age, gender, and the status of antihypertensive medication.
[b]Adjusted for age, gender, clinic systolic blood pressure, and the status of antihypertensive medication.

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general population, not in the clinic.

Considering the confidence interval in the κ statistics, the agreement between ABP and CBP was moderate and significantly higher in the very high added-risk group compared to the other groups. The reliability of the ABPM, as measured by the Cronbach's α statistic, was acceptable only in the very high added-risk group. These findings were unexpected since BP variability could be higher in the very high added-risk group, which would make CBP unreliable. However, the emotional stabilization that occurs from multiple clinic visits may be an explanation for the findings in this group. Further studies are needed to investigate the precise role of ABPM in the very high added-risk group despite better agreement between ABP and CBP.

The discordance between ABP and CBP was higher in untreated subjects than in treated subjects. Compared to a previous study in Korea, the prevalence of MH was higher [16], whereas it was lower than that in a Spanish study [17]. These differences may be due to the use of different diagnostic criteria, and the use of daytime versus 24-hour BP measurements [18]. Considering the markedly higher prevalence of MH in the general population, a lower GCR profile or patient selection bias could affect the prevalence of MH [19].

Taking the above findings together, the use of ABPM it is expected to reduce cardiovascular events and downstream cost by detecting and treating MH, and by preventing the treatment of WCH and treated normalized hypertension. Considering the higher risk in the high added-risk group, the role of ABPM seems to be more important even though the prevalence of MH is comparable or lower than in the other GCR groups. Such an implication seems to be consistent with a previous study showing that cardiac damage was more frequent in MH than in WCH [20]. Therefore, ABPM could be the first step in detecting and managing MH in clinical practice. In one previous study the prevalence of WCH was reported to be around 15% to 50% [21], which is higher than that in the present study. Despite this, two other studies have reported similar WCH prevalences [19,22], and only one study has reported a lower prevalence (5.7%) [16]. The term 'treated normalized hypertension' has recently been adopted to describe patients with a CBP ≥ 140/90 mmHg and an ABP below < 135/85 mmHg, which, if only the CBP was considered, could be mistaken for uncontrolled BP [15]. The lower prevalence of treated normalized hypertension in the higher GCR groups, and concern regarding overtreatment or treatment-induced hypotension, should not result in inaction by physicians treating uncontrolled hypertension. However, in resistant hypertension, the white-coat effect is reported to be associated with myocardial ischemia, making it useful to perform ABPM before prescribing four or more antihypertensive drugs, or before an invasive procedure [23-25].

The clinical implication of the present study is the importance of ABPM in high-risk hypertension patients, not because of the prevalence of WCH, but because of the combination of sustained MH prevalence and higher attributable risk. In clinical practice, ABPM, as well as risk stratification, is helpful to prevent cardiovascular events and to reduce downstream costs incurred by undertreated hypertension.

Study limitations

The present study had several limitations. GCR was assessed mainly by anthropometry, questionnaires, and medical records from a registry database. Shortcomings included the lack of more detailed biochemical data, and the lack of target organ damage evaluation. The GCR may therefore have been underestimated or somewhat different from those in the guidelines [13]. However, because information from the questionnaires and the medical records was available for most subjects, this investigation may be more representative than smaller-scale studies with more detailed evaluation.

In this study, about 50% of patients were in groups with high or very high added risk, which may be higher than in other large-scale ABPM registries, such as the Spanish ABPM registry, because the subjects in this study were registered at referral hospitals rather than at primary clinics. Therefore, the ability to generalize the results of this study may be limited, especially in a primary care setting.

In conclusion, discordance between ABP and CBP was observed more frequently in untreated subjects than in treated subjects. Discordance was lower in the very high added-risk group compared to the lower risk groups, and this was due to decreased WCH or treated normalized hypertension, not decreased MH.

KEY MESSAGE

1. About 30% of the subjects visiting hypertension clinic are misdiagnosed without using ambulatory blood pressure monitoring regardless of the antihypetensive medication status.
2. Masked hypertension or masked uncontrolled hypertension are not decreased in the patient with high or very high risk profile.
3. Ambulatory blood pressure monitoring can be important tool to decrease the downstream cost of the misdiagnosis in hypertension management especially in high risk patients.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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