30 minutes for a 24-hour period with the TM-2421 device (A&D Company Limited, Tokyo, Japan). Each patient took the device home and began measurements at their convenience. ABPM data were collected on 1117 patients. Every patient's ABPM data was visually checked to detect inadequate data, including outliers, and 34 patients were determined to be invalid participants. Duplication was seen in two patients, and six patients withdrew consent. Therefore, 1075 patients were available for analysis (Supplemental Figure 1).

A simple questionnaire was completed by each patient at the time of the ABPM, and the questionnaire collected information such as the time the patient went to bed, the time the patient got up, the frequency of waking up to use the lavatory, and information about how the monitoring affected sleep. *Night-time* was defined as actual sleep time using the patient's diary. The International Continence Society defined *nocturia* as a complaint that an individual has to wake ≥1 times at night to void (23). However, there are relatively large individual differences between the frequency of night-time urination and the level of complaints. For this study, nocturia was defined as when the patient awakens for urination ≥3 times during a night (20th higher percentile). Quality of sleep was rated on a four-category scale from "as usual" to "much difficulty sleeping."

Nocturnal BP Change and Its Patterns

The degree of nocturnal BP change (NBPC) was calculated by the following equation:

$$\text{degree of NBPC} = 100 \times ([\text{mean daytime systolic pressure}] - [\text{mean nocturnal systolic pressure}])/[\text{mean daytime systolic pressure}]$$

Patients with NBPC >10% and <20% were classified as "dippers," >20% as "extreme dippers," 0% to <10% as "nondippers," and <0% as "risers." These cutoff points are based on the guidelines for ABPM by the Japanese Circulation Society (24) as well as a previous study (12).

Morning BP Change

Morning systolic BP (SBP) was the average of SBP during the first 2 hours after awakening time (four SBP readings). The lowest SBP was the average SBP of three readings centered on the lowest night-time reading. Morning BP change (MBPC) was defined as the morning SBP minus the lowest SBP.

Specification of the Season for ABPM

The season for ABPM was divided into summer and winter according to the data from the Chronological Scientific Tables by the National Astronomical Observatory of Japan. The season was determined as summer if the mean monthly temperature in the region of the participating facility was >20°C, and as winter when the temperature was <20°C.

Office BP Measurement

All of the BP measurements were performed by an automated sphygmomanometer after 5 minutes of rest. Three consecutive seated readings were recorded. In our analysis, office BP was the mean of these three readings.

Table 1. Characteristics of study participants

	Women	Men
Number of participants	393 (36.6)	682 (63.4)
Age (yr)	58.5±12.3	62.0±10.6
CKD stage		
3	169 (43.0)	302 (44.3)
4	165 (42.0)	284 (41.6)
5	59 (15.0)	96 (14.1)
eGFR (ml/min per 1.73 m^2)	28.7±12.6	28.8±11.9
BMI (kg/m^2)	22.6±4.3	23.6±3.3
Overweight (BMI ≥25)	78 (19.9)	182 (26.7)
Obesity (BMI ≥30)	23 (5.9)	29 (4.3)
Antihypertensive medicine use	343 (87.3)	632 (92.7)
Diuretic use	109 (27.7)	181 (26.5)
Office SBP, by CKD stage (mmHg)	129.8±18.6	132.1±17.8
3	127.3±17.8	129.7±17.2
4	130.7±18.8	132.7±17.8
5	134.5±19.4	137.8±18.8
Office DBP, by CKD stage (mmHg)	76.3±11.2	77.6±11.5
3	75.2±10.8	77.9±11.3
4	76.9±11.5	77.3±11.5
5	77.5±11.2	77.5±12.1
Morning BP change, by CKD stage (mmHg)	21.6±16.6	23.5±16.5
3	22.0±16.6	23.4±16.3
4	21.5±16.7	23.9±16.8
5	21.2±16.5	22.5±16.6
Diabetes mellitus[a]	128 (32.6)	253 (37.1)
Proteinuria[b]	345 (89.6)	581 (88.0)
Nocturia	50 (12.8)	154 (22.8)
Much difficulty in sleep	75 (19.1)	143 (21.2)
Examination period		
Summer	102 (26.0)	188 (27.6)
Winter	291 (74.1)	494 (72.4)

Data are *n* (%) or mean ± SD, unless otherwise indicated. The data of 1075 participants who underwent ambulatory BP monitoring were summarized. eGFR, estimated GFR; BMI, body mass index; SBP, systolic BP; DBP, diastolic BP.
[a]Diabetes mellitus was diagnosed when at least one of the following criteria was met: diabetes mellitus described as an underlying disease or complication of CKD as reported by a physician, hemoglobin A1c (National Glycohemoglobin Standardization Program) of >6.5%, or concomitant use of antihyperglycemic medications including insulin.
[b]Proteinuria was identified when the urinary albumin/creatinine ratio from spot urine was ≥30 (mg/g creatinine).

Diagnostic Criteria for Hypertension

A diagnosis of hypertension was made if the office BP was >140/90 mmHg or 24-hour average BP from ABPM was >130/80 mmHg, based on the Japanese Society of Hypertension guidelines (25).

Definitions of WCHT, MHT, and Persistent Hypertension

We classified hypertension using thresholds of office BP of 140/90 mmHg and 24-hour average BP of 130/80 mmHg. WCHT is the office BP ≥140/90 mmHg and

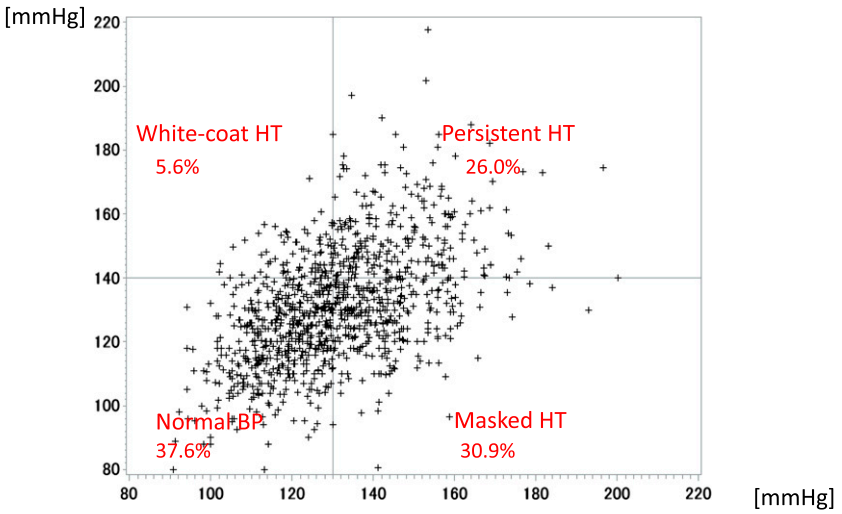

Figure 1. | **Two-dimensional scattered plot of office systolic BP and 24-hour average systolic BP**. The vertical axis shows office systolic BP, whereas the horizontal axis shows 24-hour average systolic BP. When determining the four patterns of BP shown, both systolic and diastolic pressures were taken into account. The cutoff levels for the diagnosis of hypertension (HT) were 140/90 mmHg for office BP and 130/80 mmHg for 24-hour average BP. White-coat HT, hypertensive office BP and normal 24-hour average BP; persistent hypertension, hypertensive office BP and hypertensive 24-hour average BP; normal BP, normal office BP and normal 24-hour average BP; masked HT, normal office BP and hypertensive 24-hour average BP.

Table 2. Factors associated with hypertension patterns

	BP Pattern				Total	*P* Value
	Normal BP	White-Coat Hypertension	Masked Hypertension	Persistent Hypertension		
Total participants	404 (37.6)	60 (5.6)	332 (30.9)	279 (26.0)	1075 (100.0)	
CKD stage						
3	199 (42.3)	27 (5.7)	143 (30.4)	102 (21.7)	471	0.01
4	160 (35.6)	25 (5.6)	143 (31.9)	121 (27.0)	449	
5	45 (29.0)	8 (5.2)	46 (29.7)	56 (36.1)	155	
Sex						
Women	176 (44.8)	23 (5.9)	106 (27.0)	88 (22.4)	393	0.002
Men	228 (33.4)	37 (5.4)	226 (33.1)	191 (28.0)	682	
Antihypertensive medicine use						
No	52 (52.0)	3 (3.0)	28 (28.0)	17 (17.0)	100	0.01
Yes	352 (36.1)	57 (5.9)	304 (31.2)	262 (26.9)	975	
Diuretic use						
No	305 (38.9)	41 (5.2)	234 (29.8)	205 (26.1)	785	0.39
Yes	99 (34.1)	19 (6.6)	98 (33.8)	74 (25.5)	290	
Overweight						
No	332 (40.7)	46 (5.6)	245 (30.1)	192 (23.6)	815	0.001
Yes	72 (27.7)	14 (5.4)	87 (33.5)	87 (33.5)	260	
Diabetes						
No	300 (43.2)	36 (5.2)	209 (30.1)	149 (21.5)	694	<0.001
Yes	104 (27.3)	24 (6.3)	123 (32.3)	130 (34.1)	381	
Proteinuria						
No	76 (63.9)	7 (5.9)	23 (19.3)	13 (10.9)	119	<0.001
Yes	316 (34.1)	51 (5.5)	300 (32.4)	259 (28.0)	926	
Season						
Summer	129 (44.5)	24 (8.3)	79 (27.2)	58 (20.0)	290	0.001
Winter	275 (35.0)	36 (4.6)	253 (32.2)	221 (28.2)	785	

Data are presented as *n* (%) unless otherwise indicated. Hypertension is classified into the above-listed four patterns, using thresholds of office BP of 140/90 mmHg and 24-hour average BP of 130/80 mmHg. The *P* value for general association is the general correlation between row and column, and it means a rough indication of correlation between background factors and these BP patterns. The ratio of BP patterns and background factors such as CKD stage, sex, antihypertensive medication use, diuretic use, obesity, proteinuria, diabetes, and season were analyzed.

Table 3. Factors associated with the difference between office BP and ABP: Univariate analysis

	Difference in BP (mmHg)	*P* Value
Dichotomous variables		
Men (versus women)	0.79	0.26
Overweight (BMI ≥25)	0.55	0.48
Obesity (BMI ≥30)	0.34	0.83
Antihypertensive medicine use	3.35	0.01
Diuretic use	1.53	0.04
Diabetes	2.19	0.002
Proteinuria	2.30	0.03
Nocturia	0.89	0.30
Much difficulty in sleep	0.83	0.32
Winter (versus summer)	−0.17	0.83
CKD stage 4 (versus stage 3)	1.29	0.08
CKD stage 5 (versus stage 3)	2.79	0.01
Continuous variables		
Age (10 yr)	0.87	0.003
BMI (1 kg/m^2)	0.09	0.36
eGFR (10 ml/min per 1.73 m^2)	−0.82	0.003

Simple linear regression analysis was used for univariate evaluations to detect the factors associated with the difference between office BP and 24-hour average BP calculated from ABP data. Dependent variable is absolute value of 24-hour average BP minus office BP. ABP, ambulatory BP; BMI, body mass index; eGFR, estimated GFR.

Table 4. Factors associated with the difference between office BP and ABP: Multivariate analysis

Variables	Difference in BP (mmHg)	*P* Value
Men (versus women)	0.31	0.67
Age (10 yr)	0.56	0.07
eGFR (10 ml/min per 1.73 m^2)	−0.56	0.05
Diabetes	1.70	0.02
Antihypertensive medicine use	2.61	0.03
Much difficulty in sleep	0.86	0.31
Nocturia	−0.06	0.95
Winter (versus summer)	−0.52	0.50

Multiple regression analysis was performed for multivariate evaluations including sex, other variables with *P* value <10% explored in Table 3, and patients' questionnaire variables as independent variables. As for renal function, we adopted eGFR instead of CKD stages. We did not incorporate proteinuria into this model. ABP, ambulatory BP; BMI, body mass index; eGFR, estimated GFR.

24-hour average BP of <130/80 mmHg. MHT is the office BP of <140/90 mmHg and 24-hour average BP ≥130/80 mmHg. Persistent hypertension (PHT) is the office BP ≥140/90 mmHg and 24-hour average BP ≥130/80 mmHg.

Renal Function

Serum creatinine from single blood sampling at baseline was measured at a central laboratory and estimated GFR (eGFR) was calculated by the following equations (26):

$$\text{Men}: \text{eGFR} = 194 \times (\text{age}^{-0.287}) \times (\text{serum Cre}^{-1.094})$$
$$\text{Women}: \text{eGFR} = 0.739 \times 194 \times (\text{age}^{-0.287}) \times (\text{serum Cre}^{-1.094})$$

CKD stage was defined using eGFR (60 > eGFR ≥ 30 for stage 3, 30 > eGFR ≥ 15 for stage 4, and 15 > eGFR ≥ 10 for stage 5).

Statistical Analyses

Continuous variables from two groups were compared with *t* tests, and ANOVA was used for comparisons among ≥3 groups. For multiple comparisons, tendencies were explored by ANOVA with linear contrast. For categorical variables, chi-squared tests (2×2 contingency table), or Cochran-Mantel-Haenszel tests (m×n table) were performed when there were additional categories.

Simple linear regression analysis or the chi-squared test were used for univariate evaluations to investigate the relation between ABPM parameters and patient questionnaires (night urination times and sleep quality), season for ABPM, and baseline characteristics (sex, age, body mass index [BMI], overweight, eGFR, CKD stage, antihypertensive medicine use, diuretic use, and systolic and diastolic BP). Multiple regression analyses were used for multivariate evaluations including variables with *P* values <10% explored above. All statistical analyses were performed by using the SAS software program for Windows (version 9.2; SAS Institute Inc, Tokyo, Japan).

Results

Demographics

Table 1 summarizes the patient demographics, showing that 393 participants were women (mean age, 58.5 years) and 682 were men (mean age, 62.0 years). Our results showed that 19.9% of women and 26.7% of men had a BMI ≥25, and 32.6% of women and 37.1% of men had diabetes. Approximately 90% of all participants were receiving antihypertensive medications and 27% were treated with diuretics. In addition, 43.8% had stage 3 CKD, 41.8% had stage 4 CKD, 14.4% had stage 5 CKD.

Office BP and 24-Hour Average BP

Figure 1 shows the scatter plot of office and 24-hour average systolic BP (SBP). The coefficients of correlation were 0.50 for SBP ($P<0.001$) and 0.52 for diastolic BP (DBP) ($P<0.001$). Based on office BP, 31.6% of all participants were diagnosed as having hypertension. Based on the 24-hour average BP, 56.9% were diagnosed as having hypertension. Our results showed that 30.9% of patients

Table 5. Patterns of nocturnal BP change

	Extreme Dipper	Dipper	Nondipper	Riser	Total	*P* Value
CKD stage						
Total	105	395	408	167	1075	
3	54 (11.5)	181 (38.4)	173 (36.7)	63 (13.3)	471	
4	44 (9.8)	152 (33.9)	172 (38.3)	81 (18.0)	449	
5	7 (4.5)	62 (40.0)	63 (40.6)	23 (14.8)	155	
Much difficulty in sleep						
Total	104	394	403	166	1067	
No	89 (10.5)	325 (38.3)	314 (37.0)	121 (14.3)	849	
Yes	15 (6.9)	69 (31.7)	89 (40.8)	45 (20.6)	218	0.02
Nocturia						
Total	105	393	404	166	1068	
No	95 (11.0)	347 (40.2)	301 (34.8)	121 (14.0)	864	<0.001
Yes	10 (4.9)	46 (22.5)	103 (50.5)	45 (22.1)	204	
Season						
Total	105	395	408	167	1075	
Summer	21 (7.2)	90 (31.0)	114 (39.3)	65 (22.4)	290	<0.001
Winter	84 (10.7)	305 (38.9)	294 (37.5)	102 (13.0)	785	
Antihypertensive medicine use						
Total	105	395	408	167	1075	
No	13 (13.0)	39 (39.0)	40 (48.0)	8 (8.0)	100	0.14
Yes	92 (9.4)	356 (36.5)	368 (37.7)	159 (16.3)	975	
Diuretic use						
Total	105	395	408	167	1075	
No	82 (10.5)	298 (38.0)	294 (37.5)	111 (14.1)	785	0.10
Yes	23 (7.9)	97 (33.5)	114 (39.3)	56 (19.3)	290	
Overweight						
Total	105	395	408	167	1075	
No	79 (9.7)	294 (36.1)	318 (39.0)	124 (15.2)	815	0.65
Yes	26 (10.0)	101 (38.9)	90 (34.6)	43 (16.5)	260	
Diabetes						
Total	105	395	408	167	1075	
No	73 (10.5)	277 (39.9)	265 (38.2)	79 (11.4)	694	<0.001
Yes	32 (8.4)	118 (31.0)	143 (37.5)	88 (23.1)	381	
Proteinuria						
Total	99	383	402	161	1045	
No	20 (16.8)	43 (36.1)	41 (34.5)	15 (12.6)	119	0.03
Yes	79 (8.5)	340 (36.7)	361 (39.0)	146 (15.8)	926	

Data are *n* (%) unless otherwise indicated. Nocturnal BP change is classified into four patterns according to the level of nocturnal BP decrease. The patterns of nocturnal BP change and background factors such as CKD stage, quality of sleep, nocturia, season, antihypertensive medication use, diuretic use, obesity, and diabetes. *P* value for general association is general correlation between row and column, and it means a rough indication of correlation between background factors and these BP patterns.

had MHT, 5.6% had WCHT, and 26.0% had PHT, whereas 37.6% had well controlled BP. The median interval between the office BP measurement and ABPM was 41 days (25th percentile, 0 days; 75th percentile, 154 days). We divided the patients into two groups by the 75th percentile value, and analyzed for the patterns of hypertension. However, we did not observe any difference between them (data not shown).

We evaluated the relationship between hypertension patterns and background factors (Table 2). As for the CKD stage, prevalence of normal BP decreased from 42.3% to 29.0%, and that of PHT rose from 21.7% to 36.1% with advancing CKD stage. The prevalence of WCHT was little associated with factors of clinical interest excluding diabetes and the season. The prevalence of MHT and PHT was higher in men than women and in winter than in summer. Incidence of MHT and PHT was high in patients with diabetes or overweight.

We also evaluated the difference between office BP and ambulatory BP (ABP) as a continuous variable (Tables 3 and 4), and diabetes, antihypertensive medicine use, and low eGFR accounted for the difference between them. Proteinuria was not associated significantly with the difference between office BP and ABP in another multivariate model (Supplemental Table 1).

Characteristics of NBPC

NBPC patterns were analyzed (Table 5). Prevalence of nondippers and risers was lower at stage 3 than at stages 4 and 5. Prevalence of nondippers or risers was markedly high among the patients with much difficulty sleeping (P=0.02) and among the patients with nocturia

Table 6. Factors associated with nocturnal BP change: Univariate analysis

	Difference in Nocturnal BP Change (%)	*P* Value
Dichotomous variables		
Men (versus women)	0.22	0.70
Overweight (BMI ≥25)	−0.25	0.69
Obesity (BMI ≥30)	0.33	0.80
Antihypertensive medicine use	−1.88	0.04
Diuretic use	−1.75	0.004
Diabetes	−2.56	<0.001
Proteinuria	−1.88	0.03
Nocturia	−3.99	<0.001
Much difficulty in sleep	−1.82	0.007
Winter (versus summer)	2.55	<0.001
CKD stage 4 (versus stage 3)	−1.44	0.01
CKD stage 5 (versus stage 3)	−1.18	0.15
Continuous variables		
Age (10 yr)	−0.53	0.03
BMI (1 kg/m^2)	0.04	0.56
eGFR (10 ml/min per 1.73 m^2)	0.59	0.008

Simple linear regression analysis was used for univariate evaluations to detect the factors associated with nocturnal BP change. BMI, body mass index; eGFR, estimated GFR.

($P<0.001$). In general, there are two methods to separate the daytime period and night-time period: the patient diaries and the short-window setting. In this study, we adopted the former. We checked whether the ratio of NBPC patterns changed according to these two definitions; however, there was a slight difference (data not shown).

Our results showed that 290 patients underwent ABPM in summer, whereas there were 785 patients in winter. The 24-hour average BP was higher during winter than during summer. The prevalence of nondippers or risers was higher during summer than winter.

As for other baseline factors, diabetes was a significant variable on NBPC. The prevalence of nondippers or risers was higher among diabetic patients than among nondiabetic patients.

Univariate regression analyses were also performed in an attempt to identify factors associated with NBPC as a continuous variable. Table 6 shows that the significant factors were antihypertensive medication use, diuretic use, diabetes, proteinuria, nocturia, much difficulty in sleep, season, age, and renal function (eGFR and CKD stage).

We performed multivariate regression analyses with the NBPC as a dependent variable and the above-mentioned factors as independent variables, stratifying the participants according to nocturia (Figure 2). In the nocturia-negative group, CKD stage 4 (relative to stage 3), diabetes, and season (winter) were identified as significant, and CKD stage 5 relative to stage 3, much difficulty in sleep, and diuretic use also tended to reduce the NBPC. In the nocturia-positive group, neither CKD stage nor sleep quality was a significant independent variable. Only diabetes was significant. Proteinuria was not significantly associated with NBPC in a multivariate model (Supplemental Table 2).

MBPC

We performed univariate regression analyses to clarify which factors were associated with MBPC. Age, BMI, overweight, obesity, and season were found to be significant variables (Table 7). Next, we performed multivariate regression analyses with the above-mentioned factors as independent variables (Table 8). BMI was selected as representative of obesity-related variables and eGFR as representative renal function-related variables. MBPC became larger with advancing age and higher BMI. MBPC tended to become larger in winter than summer. For patients with diabetes, MBPC is smaller than in patients without diabetes.

Discussion

Office BP and 24-Hour Average BP

The majority of participants had hypertension and proteinuria but the mean BP was normal (132/76 mmHg) and >90% of participants were treated with angiotensin converting enzyme inhibitors/angiotensin receptor blockers (22). However, the large SD of mean office BP suggested the presence of patients with relatively poorly controlled BP.

In ABPM studies, the 24-hour average BP was the first parameter to be examined (27). WCHT accounted for 5.6% of all participants. Its prevalence has been reported to be 13% (10,28) or 18% (29) among the population in general. Bangash and Agarwal performed a meta-analysis of CKD patients (six trials, reported from 2005 to 2008) and reported that the prevalence was 18.3% (10.5%–31.7%) (30) and 15% among CKD cohort (31). Compared with these previous data, the prevalence of WCHT in this study was very low. There is no consensus on the prognosis of WCHT (32). Some investigators have reported that WCHT is likely to shift to PHT (33) or that the risk for stroke does not differ between WCHT and PHT, whereas other investigators have reported that the incidence of stroke is significantly lower among patients with WCHT (34).

In this study, about 30% of all participants had MHT. The prevalence of MHT varies considerably among different reports: Ohkubo *et al.* reported 17% among the population in general (10); Bogrie *et al.* and Mancia *et al.* reported 8% (28,29) among the population in hypertensives. As for the prevalence of MHT among CKD patients, a meta-analysis by Bangash and Agarwal reported 8.3% (4.7%–31.3%) (30); Kanno *et al.* estimated 15% from The Ohasama Study data (31); and Pogue *et al.* reported 42.9% from the African American Study of Kidney Disease and Hypertension trial data (35). The percentage of MHT in this study was relatively high compared with these previous reports except for the African American Study of Kidney Disease and Hypertension. The prognosis of MHT is poor according to many reports (10,28,36–38). If the diagnosis of

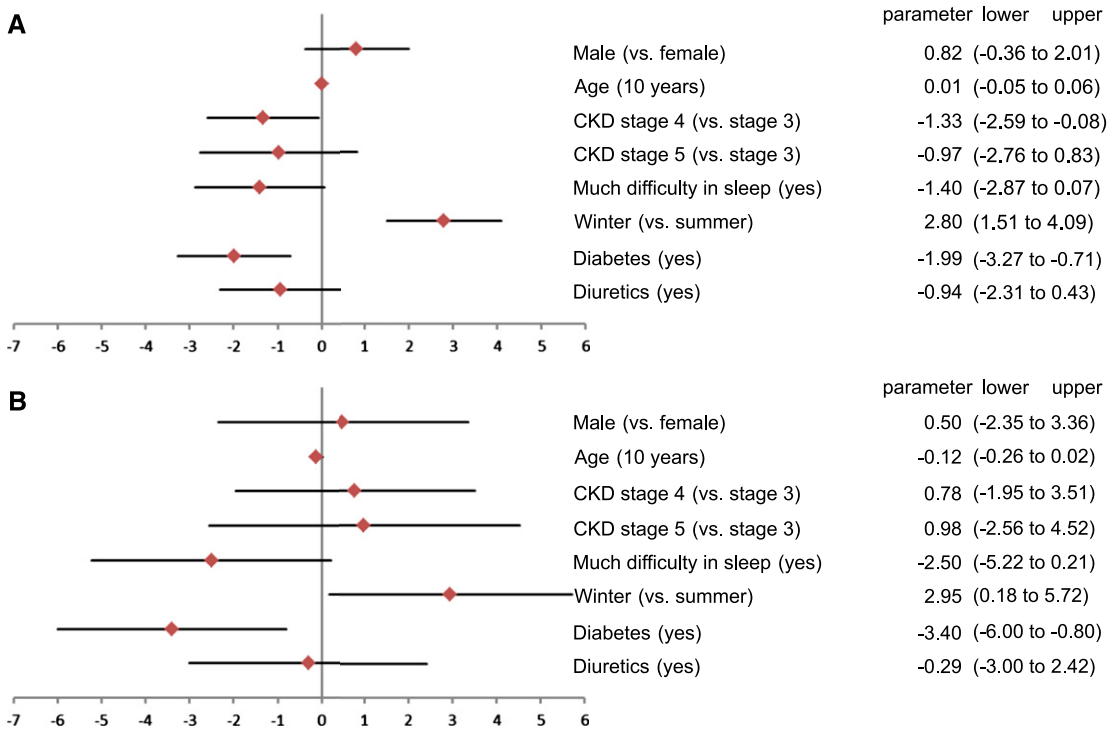

Figure 2. | Multiple regression model for the identification of factors associated with the degree of the nocturnal BP change. The degree of the nocturnal BP change was stratified according to presence/absence of nocturia. The parameter estimate (filled diamond) and its 95% confidence interval (95% CI) (solid line) are shown. The first column to the right shows the independent variables; the second column shows the parameter estimates; and the third shows the 95% CIs. The independent variables analyzed were sex (men), age (plus 10 years), CKD stage 4 (relative to stage 3), CKD stage 5 (relative to stage 3), sleep quality (poor sleep), and season (winter). (A) Linear multiple regression model for the nocturia-negative group, with the degree of the nocturnal BP change as a dependent variable. (B) Linear multiple regression model for the nocturia-positive group, with the degree of nocturnal BP change as a dependent variable.

hypertension relies only on office BP, many patients who require treatment may be overlooked. The factors that increased the difference between office BP and ABP were renal function, diabetes, and antihypertensive medicine use including diuretic use. This means that we are unable to control BP of patients with CKD, diabetes, and hypertension only by office BP. Quality of sleep, nocturia, and season did not have a large effect on the difference.

NBPC and CKD Stage

The findings of the relationship between NBPC and CKD stage were approximately equal to our predictions. The percentage of patients showing a nondipper or riser pattern was higher at stages 4 and 5 than at stage 3. However, there was no linear increase in the percentage of those two patterns with advancing CKD stages (data not shown). When evaluating NBPC as a continuous variable, we were not able to find the tendency that the degree of nocturnal fall became small with advancing CKD stage or eGFR decrease (Supplemental Table 3).

Factors Associated with NBPC

Quality of sleep has been suggested to affect the NBPC (39). Quality of sleep and the frequency of urination at night were evaluated in this study. Both appear to influence the pattern of the nocturnal BP decrease markedly. They can be collected by simple questionnaire and they are useful when interpreting NBPC and its patterns.

We also observed a seasonal effect on NBPC. The significantly higher percentage of patients showing an insufficient nocturnal BP decrease during summer than winter was contradictory to our anticipation. However, the MBPC was more marked during winter. This suggests that some of the patients who were classified as showing a sufficient nocturnal BP decrease had MBPC. The degree of MBPC was also greater during winter (19.5 mmHg in summer versus 24.0 mmHg in winter; $P<0.001$). If a goal is to achieve good BP control throughout the day, it seems essential to note the seasonal effect on diurnal BP variation.

From the multiple regression analysis with NBPC as a dependent variable and nocturia as a stratifying factor, CKD stage 4 (relative to stage 3), diabetes, and season (winter) were identified as significant variables in the nocturia-negative group, and CKD stage 5 (relative to stage 3), much difficulty in sleep, and diuretic use tended to have the same effect on NBPC (Figure 2A). However, the results differed considerably in the nocturia-positive group. Season and diabetes remained significant factors, but the influence of sleep status and CKD stage was not significant in this group (Figure 2B). When using eGFR as an independent variable instead of CKD stage, it remained significant in the nocturia-negative group (Supplemental Table 3). In this analysis, the nocturia was used as a stratifying factor rather than as an independent variable for the following reasons: the NBPC will inevitably decrease if the

Table 7. Morning BP change as a dependent variable: Univariate analysis

	Difference in BP (mmHg)	*P* Value
Dichotomous variable		
Men (versus women)	1.82	0.09
Overweight (BMI ≥25)	2.72	0.02
Obesity (BMI ≥30)	5.44	0.02
Antihypertensive medicine use	2.21	0.21
Diuretic use	0.03	0.98
Diabetes	−1.82	0.09
Proteinuria	−0.34	0.83
Nocturia	−0.98	0.45
Much difficulty in sleep	−1.91	0.13
Winter (versus summer)	4.58	<0.001
CKD stage 4 (versus CKD stage 3)	0.88	0.88
CKD stage 5 (versus CKD stage 3)	0.59	0.59
Continuous variables		
Age (10 yr)	2.07	<0.001
BMI (1 kg/m^2)	0.48	0.001
eGFR (10 ml/min per 1.73 m^2)	0.08	0.84

Morning BP change is defined as the difference between morning SBP (the average of SBPs during the first 2 hours) minus the lowest SBP (the average SBPs of three readings centered on the lowest night-time readings). Simple linear regression analysis was used for univariate evaluations to detect the factors associated with morning BP change. BMI, body mass index; eGFR, estimated GFR.

Table 8. Morning BP change as a dependent variable: Multivariate analysis

Variables	Difference in BP (mmHg)	*P* Value
Men (versus women)	0.63	0.57
Age (10 yr)	0.22	<0.001
Diabetes	−3.65	0.001
Winter (versus summer)	4.52	<0.001
BMI (1 kg/m^2)	0.56	<0.001
Much difficulty in sleep	−1.46	0.26
Nocturia	−2.29	0.10
Antihypertensive medicine use	1.76	0.34
eGFR (10 ml/min per 1.73 m^2)	0.35	0.44

Multiple regression analysis was performed for multivariate evaluations. Model includes variables with *P* value <10% explored in Table 7 and variables of clinical interest. BMI is selected as the representative of obesity-related variables such as overweight (BMI ≥25), obesity (BMI ≥30), and BMI. BMI, body mass index; eGFR, estimated GFR.

patient is getting up frequently during the night for urination, nocturia is likely to develop as CKD stages advance, and the quality of sleep is also associated with nocturia. These results suggest that this way of patient stratification was rational. The results also suggest that when interpreting the ABPM data, identifying nocturia is essential.

For reference, we evaluated multiple regression models with/without nocturia (Supplemental Table 4). In model 2, nocturia had a largest slope among independent variables. R^2 values were 0.05 (model 1) and 0.08 (model 2), that is, nocturia increased the R^2 value nearly 50%. The R^2 was very small due to wide variation of NBPC, but this result showed that nocturia was a very important variable when interpreting ABPM data.

MBPC

MBPC is smaller in patients with diabetes than in patients without diabetes. Renal function was not significant. This is probably due to various interventions to the lifestyle of patients with diabetes or advancing CKD, including drugs. In other words, a reversal of cause and effect might be happening here.

Summary

In this study, we confirmed that the prevalence of PHT was high in the CKD population and increased in association with progression of CKD. The difference in office BP and ABP was increased by diabetes, taking antihypertensive medications, and low eGFR. Various background factors such as eGFR, diabetes, antihypertensive medication use, BMI, and season accounted for abnormal BP patterns in CKD patients. A longitudinal study with use of CKD-JAC data will elucidate the relationship between nondippers, risers, MBPCs, and cardiovascular outcomes.

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Disclosures

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