Correlations between indices of dynamic components of ambulatory blood pressure and renal damage in elderly Chinese male with essential hypertension

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Objective Twenty-four-hour ambulatory blood pressure monitoring (ABPM) is an accurate method to document changes in blood pressure (BP) and is more predictive than office and home BP monitoring for cardiovascular outcomes in elderly people. We aimed to determine the relationship between ABPM indices and renal damage in elderly Chinese male patients with essential hypertension.

Methods We investigated 998 Chinese men (mean age of 78.44 ± 12.02 years) with essential hypertension. Renal function, laboratory testing, and ABPM, including ABP, BP variability, and BP circadian rhythms were investigated. Data were shown according to BP controlling status. The relationships between ABPM indices and renal damage [expressed by urine protein, urine albumin/creatinine ratio (uACR), estimated glomerular filtration rate (eGFR), blood urea nitrogen (BUN)] were assessed using multiple regression analysis.

Results After adjustments for age, common cardiovascular risk factors, and medications, uACR level was positively associated with 24-h mean systolic blood pressure (SBP), 24-h mean pulse pressure (PP), and 24-h SBP percent time of elevation. eGFR level was negatively associated with the 24-h mean SBP and 24-h mean PP. BUN level was positively correlated with the 24-h mean SBP, 24-h mean PP, and 24-h SBP percent time of elevation, whereas the BUN level was negatively associated with the 24-h DBP SD.

Conclusion The ABPM indices associated with renal damage may be regarded as an early predictive marker for renal function impairment in Chinese elderly male patients with hypertension. *Blood Press Monit* 25: 303–309 Copyright © 2020 The Author(s). Published by Wolters Kluwer Health, Inc.

Introduction

Hypertension is an age-related disease; the prevalence of hypertension may increase rapidly with age [1]. Elderly patients with hypertension often have an increased risk of impaired vascular structure or function, such as a decline in arterial elasticity, and stiffness, and a decrease in catecholamine reactivity, which would have an adverse effect on blood pressure (BP), blood pressure variability (BPV), and BP circadian rhythms [2–4]. It is accepted that 24-h ambulatory blood pressure monitoring (ABPM) is more valuable than office BP or home BP monitoring for assessing cardiovascular changes in elderly patients with hypertension [5,6]. In addition, the incidence of target organ damage (TOD) increases

sharply in elderly patients with hypertension, which is the main cause of mortality and disability in elderly patients with essential hypertension [7]. As we know, BP control is closely related to TOD, and ABPM can provide more accurate real-world parameters than office BP. To date, there have been a considerable number of clinical trials to assess the association between ABPM and cardiovascular outcomes [8]. However, most studies on the relationship between ABPM and renal function are limited by small sample sizes and relatively younger subjects [9,10]. Furthermore, few large-scale cross-sectional studies have reported the association between ABPM and impaired renal function in Asia, especially in elderly Chinese patients with hypertension [9]. Therefore, to further assess the potential value of ABPM as a predictive marker for renal function impairment in elderly patients with hypertension, we investigated the association between indices of static and dynamic components of ambulatory BP and renal damage in elderly male patients with hypertension.

Methods

Ethical approval of the study protocol

This study complied with the Declaration of Helsinki and was approved by the Scientific and Ethics Review Board of the Department of Geriatrics, Chinese PLA General Hospital (Beijing, P.R. China). All patients enrolled in the study gave written informed consent.

Patient enrolment

As the largest medical center providing health service for veteran soldiers in Beijing district, we had full access to the thorough medical profiles of these patients. Patients with a documented history of hypertension visited the outpatient department and underwent ABPM between January 2010 and December 2012 met the enrolment criteria. Anti-hypertensive medication should be maintained if it had been given before enrolment. Patients' prior medical profile was carefully reviewed to exclude secondary hypertension, active malignant disease, and end-stage renal disease [estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m^2]. Suspected or newly diagnosed hypertension was excluded. Finally, 998 male patients (mean age, 78.44 ± 12.02 years) with essential hypertension were enrolled during the recruitment period.

Data on demographic variables, laboratory indicators, medication use, medical history, and smoking habits were collected. The patients' comorbidities were obtained from medical records of current or previous diagnosis and included the following: diabetes mellitus, dyslipidemia, peripheral arterial occlusive disease (PAOD), coronary heart disease (CHD), chronic heart failure (CHF), chronic kidney disease (CKD), and cardiovascular disease (CVD).

Laboratory measurements

Following an overnight fast, serum samples were collected in tubes containing liquid EDTA, centrifuged at 4°C, and stored at −80°C before analysis. Blood urea nitrogen (BUN), serum uric acid (sUA), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), sUA, and glucose were measured using an automated Cobas6000 analyzer from Roche (Basel, Switzerland), with reagents purchased from Roche Diagnostics GmbH (Munich, Germany). Serum high-sensitivity C-reactive protein (HS-CRP) was measured by immunonephelometry with a CRP extended range flex reagent cartridge and anti-human CRP antibodies from Siemens Healthcare Diagnostics, Inc. (Deerfield, Illinois, USA). N-terminal fragment pro-B-type natriuretic peptide (NT-proBNP) was measured using a chemiluminescence immunoassay with reagents purchased from Roche Diagnostics GmbH. Serum and urine creatinine concentrations were determined using a creatinine flex reagent cartridge from Siemens Healthcare Diagnostics, Inc. (Deerfield). Along with the serum tests, the early morning midstream urine

samples were collected to test the level of albumin protein and creatinine ratio (uACR) was calculated as milligrams of albumin per gram of creatinine. The total quantity of urine protein was tested with the collection of 24-h urine specimens in the following 24 h. All participants were instructed to begin collection after discarding first-morning urine until the collection of first voided urine sample the next morning in the receptacle provided. Patients were instructed to avoid strenuous muscular activity during the collection of the 24-h urine sample. The eGFR was calculated using the Asian-modified CKD-EPI formula [11]. All testing was performed by well-trained laboratory scientists at the Chinese PLA General Hospital under blinded conditions.

Twenty-four-hour ambulatory blood pressure monitoring

ABPM was performed from 9:00 in the morning to 9:00 in the next morning using a noninvasive portable ambulatory BP monitor (A&D Company, Tokyo, Japan). Sampling was conducted once every 15 min in the daytime (6:00–22:00) and every 30 min in the night-time (22:00–6:00 the next morning). Bedtime and rise time were set according to the real sleep pattern as the patients noted. The patients were asked to maintain their daily life and work habits. When the monitoring time was >24 h and >80% of the readings were valid, the data were considered eligible. Recorded data were processed with CardioVisions (Meditech, Inc., Budapest, Hungary). Using CardioVisions, the 24-h mean systolic blood pressure (SBP), 24-h mean diastolic blood pressure (DBP), daytime SBP (defined as the mean BP during the remaining portion of the day), daytime DBP, nocturnal SBP (defined as the mean BP from the time when the patient went to bed until the time of awakening), and nocturnal DBP. The weighted SD, namely the average 24-h SBP and DBP SDs corrected for daytime and night-time duration in hours was calculated according to

the formula: $$SD = \frac{(\text{daytime SD} \times \text{daytime hours}) + (\text{night-time SD} \times \text{night-time hours})}{\text{24-h period}}$$

[12]. The statistics calculated were as follows: 24-h mean pulse pressure (PP) (the difference between the SBP and DBP); 24-h mean arterial pressure (DBP + 1/3 PP); daytime mean PP; daytime mean arterial pressure; nocturnal mean PP; nocturnal mean arterial pressure; SBP nocturnal fall rate [calculated as (daytime SBP – nocturnal SBP)/daytime SBP]; DBP nocturnal fall rate [calculated as (daytime DBP – nocturnal DBP)/daytime DBP]; hypertension time indices [an elevated time-to-total time ratio, 24-h SBP percent time elevation (PTE%), and 24-h DBP PTE%]; and hypotensive time indices [a depressed time-to-total time ratio: 24-h SBP percent time depression (PTD%, <90 mmHg), and 24-h DBP PTD% (<60 mmHg)]. We classified patients whose 24-h mean SBP/DBP less than 130/80 mmHg, daytime mean SBP/DBP less than 135/85 mmHg and night-time mean SBP/DBP less than

120/70 mmHg according to guidelines into BP controlled group and others into BP uncontrolled group [13].

Statistical analyses

Statistical analyses were performed with SPSS software (version 16.0; SPSS, Inc., Chicago, Illinois, USA). Descriptive statistics were presented as the mean ± SD for continuous variables or percentages for categorical variables. Data of non-normal distribution were expressed as median (quartile). The mean differences between controlled and uncontrolled groups were compared by independent *t*-test, and chi-square test was used to compare the classified variable. The relationship between two continuous variables was assessed by Pearson's correlation or Spearman's correlation, depending on the distribution of the variables. Multiple linear regression analysis was used to determine the relationship between ABPM indices and cardiac function, as well as renal function, in our study cohort. In the model, we entered factors associated with renal function at a $P < 0.1$, and in Enter fashion, included those variables with a $P < 0.05$. Differences with a two-sided P value <0.05 were considered statistically significant.

Results

Baseline characteristics

The characteristics of the 998 male (mean age, 78.44 ± 12.02 years) with hypertension are shown in Table 1. Of these patients, 70.1% were ≥75 years of age and 78.9% had a GFR >60 mL/min/1.73 m^2. Patients who had achieved the target BP were slightly younger and had lower serum creatinine, lower uACR, and lower proteinuria compared with those whose BP remained uncontrolled. Patients with BP controlled took more anti-hypertensive drugs like calcium-channel blockers and diuretics.

Ambulatory blood pressure monitoring measurements

ABPM parameters are shown in Table 2. Comparing with those BP uncontrolled, Patients with BP controlled not only had a lower mean BP during day and night but also had more significant nocturnal BP fall.

Correlation analysis

Univariate analysis is shown in Table 3 revealed that the uACR level was positively correlated with the 24-h mean SBP ($r = 0.351$, $P < 0.001$), 24-h mean arterial pressure ($r = 0.145$, $P < 0.001$), 24-h mean PP ($r = 0.368$, $P < 0.001$), daytime SBP ($r = 0.330$, $P < 0.001$), daytime mean arterial pressure ($r = 0.121$, $P = 0.01$), daytime mean PP ($r = 0.365$ $P < 0.001$), nocturnal SBP ($r = 0.318$ $P < 0.001$), nocturnal mean arterial pressure ($r = 0.154$, $P < 0.001$), nocturnal mean PP ($r = 0.345$, $P < 0.001$), and 24-h SBP weighted SD ($r = 0.129$, $P < 0.001$), whereas the uACR was negatively correlated with the daytime DBP ($r = -0.087$, $P = 0.05$),

Table 1 Clinical characteristics and biochemical parameters

Variable	Total (*n*=998)	Controlled (*n*=526)	Uncontrolled (*n*=472)	*P*
		Blood pressure status		
Age (years)	78.44±12.02	78.19±10.65	79.71±10.16	0.022
BMI (kg/m^2)	24.78±3.07	24.67±3.05	24.89±3.09	0.276
Laboratory parameters				
Fasting serum glucose (mmol/L)	5.55±1.22	5.51±1.27	5.59±1.16	0.322
NT-proBNP (pg/mL) [median (IQR)]	139.20 (325.9)	116.60 (239.15)	163.85 (401.10)	0.231
HS-CRP (mg/dL) [median (IQR)]	0.30 (0.70)	0.30 (0.74)	0.30 (0.68)	0.471
Total cholesterol (mmol/L)	4.13±0.87	4.10±0.81	4.17±0.92	0.177
LDL-C (mmol/L)	2.43±0.71	2.40±0.67	2.46±0.75	0.231
Blood urea nitrogen (mmol/L)	7.20±3.42	6.85±2.93	7.57±3.86	0.001
Serum creatinine (mmol/L)	99.01±66.02	93.99±52.77	104.60±77.86	0.011
eGFR (mL/min)	82.38±28.04	84.32±24.92	80.04±31.02	0.033
uACR (mg/mmol) [median (IQR)]	10.54 (32.78)	7.14 (19.24)	18.74 (71.79)	<0.0001
Serum uric acid (mmol/L)	336.99±85.17	336.2±79.66	337.88±91.01	0.756
Proteinuria (g/d) [median (IQR)]	0.08 (0.11)	0.07 (0.9)	0.09 (0.13)	0.009
Clinical characteristics, *n* (%)				
Diabetes mellitus	352 (36.2)	169 (32.9)	183 (39.87)	0.025
Coronary artery disease	596 (61.3)	293 (57.1)	283 (61.66)	0.233
Cerebro-vascular disease	473 (48.7)	227 (44.2)	246 (53.59)	0.004
Chronic kidney disease	210 (21.1)	96 (19.3)	114 (24.26)	0.022
Current smoker	378 (38.1)	197 (37.6)	181 (38.76)	0.707
Concomitant therapy				
Anti-hypertensive therapy, *n* (%)	850 (83.7)	412 (85.8)	438 (81.7)	0.071
Number of anti-hypertensive drugs	1.81±1.17	1.98±1.22	1.65±1.11	<0.001
ACEI/ARB, *n* (%)	532 (54.0)	275 (58.9)	257 (49.6)	0.004
β-blocker, *n* (%)	387 (39.3)	181 (38.8)	206 (39.8)	0.746
Calcium-channel blockers, *n* (%)	591 (60.0)	313 (67.0)	278 (53.7)	<0.001
Diuretics, *n* (%)	234 (23.8)	134 (28.7)	100 (19.3)	0.001
Statin, *n* (%)	556 (56.5)	299 (57.8)	257 (55.0)	0.376
Anti-platelet therapy, *n* (%)	703 (72.0)	330 (71.4)	373 (72.6)	0.692
Anti-diabetes therapy, *n* (%)	340 (34.1)	180 (38.1)	160 (30.4)	0.017

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; HS-CRP, high-sensitive C-reactive protein; NT pro-BNP, N-terminal fragment pro-B-type natriuretic peptide; IQR, interquartile range; LDL-C, low-density lipoprotein-cholesterol; uACR, urinary albumin-to-creatinine ratio.

Table 2 Ambulatory blood pressure monitoring parameters

ABPM parameters	Total (n=998)	Blood pressure status		P
		Controlled (n=526)	Uncontrolled (n=472)	
24-h mean SBP (mmHg)	128.54±13.10	119.39±7.22	139.05±8.51	<0.0001
24-h mean DBP (mmHg)	66.01±8.40	63.64±7.08	68.66±8.97	<0.0001
24-h mean arterial pressure (mmHg)	88.86±8.04	82.16±5.71	92.13±6.89	<0.0001
24-h mean PP (mmHg)	62.53±13.37	55.75±9.35	70.39±11.69	<0.0001
Daytime SBP (mmHg)	129.14±16.47	119.87±7.61	139.55±17.49	<0.0001
Daytime DBP (mmHg)	66.55±8.70	64.37±7.52	68.97±9.28	<0.0001
Daytime MAP (mmHg)	87.40±8.97	82.87±6.15	92.49±8.88	<0.0001
Daytime mean PP (mmHg)	62.59±16.50	55.5±9.29	70.58±19.04	<0.0001
Nocturnal SBP (mmHg)	127.81±15.78	118.02±10.95	138.79±12.90	<0.0001
Nocturnal DBP (mmHg)	64.39±9.22	61.82±7.99	67.24±9.66	<0.0001
Nocturnal mean arterial pressure (mmHg)	85.53±9.74	80.55±7.49	91.09±8.86	<0.0001
Nocturnal mean PP (mmHg)	63.42±14.28	55.50±9.29	71.55±13.30	<0.0001
24-h SBP weighted SD	13.63±3.42	12.98±2.90	14.35±3.80	<0.0001
24-h DBP weighted SD	8.06±2.00	7.98±1.80	8.18±2.17	0.118
Nocturnal SBP fall rate (%)	0.59±8.72	1.43±8.56	−0.33±8.81	0.001
Nocturnal DBP fall rate (%)	1.84±26.59	3.75±9.07	2.10±9.10	0.004
24-h SBP PTE%	36.51±24.04	19.02±12.67	56.20±17.67	<0.0001
24-h DBP PTE%	11.13±13.24	7.26±8.74	15.41±15.78	<0.0001
24-h SBP PTD%	3.32±6.352	5.86±7.78	0.46±1.39	<0.0001
24-h DBP PTD%	37.86±27.48	43.81±26.79	31.14±26.61	<0.0001

ABPM, ambulatory blood pressure monitoring; DBP, diastolic blood pressure; PTD, percent time depression; PTE, percent time elevation; SBP, systolic blood pressure.

Table 3 Association between ambulatory blood pressure monitoring indices and renal function

	uACR		BUN		eGFR		Proteinuria	
	r	P	R	P	R	P	r	P
24-h mean SBP	0.351	<0.001	0.133	<0.001	−0.113	<0.001	0.199	<0.001
24-h mean DBP	−0.070	0.090	−0.182	<0.001	0.120	<0.001	.046	0.255
24-h mean arterial pressure	0.145	<0.001	−0.056	0.077	0.021	0.510	.146	<0.001
24-h mean PP	0.368	<0.001	0.237	<0.001	−0.177	<0.001	.152	<0.001
Daytime SBP	0.330	<0.001	0.097	0.002	−0.086	0.007	.178	<0.001
Daytime DBP	−0.087	0.050	−0.194	<0.001	0.125	<0.001	.032	0.426
Daytime mean arterial pressure	0.121	0.010	−0.087	0.006	0.045	0.158	.123	0.002
Daytime mean PP	0.365	<0.001	0.217	<0.001	−0.157	<0.001	.143	<0.001
Nocturnal SBP	0.318	<0.001	0.158	<0.001	−0.143	<0.001	.179	<0.001
Nocturnal DBP	−0.040	0.350	−0.120	<0.001	0.074	0.019	.074	0.065
Nocturnal mean arterial pressure	0.154	<0.001	0.007	0.829	−0.033	0.297	.149	<0.001
Nocturnal mean PP	0.345	<0.001	0.239	<0.001	−0.191	<0.001	.135	0.001
24-h SBP wSD	0.129	<0.001	0.076	0.017	−0.057	0.073	.071	0.076
24-h DBP wSD	−0.030	0.440	−0.110	0.001	0.066	0.040	−.024	0.557
Nocturnal SBP F	−0.104	0.020	−0.115	<0.001	0.098	0.002	−.062	0.120
Nocturnal DBP F	−0.113	0.010	−0.100	0.002	0.072	0.024	−0.080	0.045
24-h SBP PTE%	0.350	<0.001	0.134	<0.001	−0.106	0.001	.185	<0.001
24-h DBP PTE%	−0.020	0.648	−0.12	<0.001	0.083	0.009	.086	0.032
24-h SBP PTD%	−0.216	<0.001	−0.041	0.200	0.028	0.373	−0.102	0.011
24-h DBP PTD%	0.083	0.055	0.174	<0.001	−0.113	<0.001	−0.049	0.219

BUN, blood urea nitrogen; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; F, fall rate; uACR, urinary albumin-to-creatinine ratio; wSD, weighted SD; PTE, percent time elevation; PTD, percent time depression; SBP, systolic blood pressure.

nocturnal SBP fall rate ($r=−0.104$, $P=0.02$), and nocturnal DBP fall rate ($r=−0.113$, $P=0.01$).

A similar analysis was conducted to determine the relationship between ABPM indices and the BUN level, proteinuria and eGFR level, and the detailed results are presented in Table 3.

Based on the multiple linear regression analysis, after adjusting for age, BMI, smoking status, laboratory indicators (including NT pro-BNP, HS-CRP, TC, LDL-C, HDL-C, sUA), comorbidities (including diabetes mellitus, dyslipidemia, PAOD, CHD, CHF, CKD, and CVD), medications (including ACEI/ARB, β-blocker, a calcium-channel blocker, loop diuretic, statin, and anti-platelets) and ABPM indices associated with independent variables at a $P<0.1$, the uACR level was positively correlated with the 24-h mean SBP ($β=0.003$, $P=0.002$), 24-h mean PP ($β=0.003$, $P=0.027$), and 24-h SBP PTE% ($β=0.000$, $P=0.001$), whereas the eGFR level was negatively correlated with the 24-h mean SBP ($β=−0.004$, $P=0.007$) and 24-h mean PP ($β=−0.011$, $P=0.012$). The BUN level was positively correlated with the 24-h mean SBP ($β=0.002$, $P=0.002$), 24-h mean PP ($β=0.001$, $P=0.008$), and 24-h SBP PTE% ($β=0.002$, $P=0.015$),

Table 4 Results of multiple linear analysis with ambulatory blood pressure monitoring indices and renal function

Indices	B	Standardized β	t	VIF	P
Proteinuria					
Constant	0.342		8.401		<0.001
Diabetes mellitus	0.002	0.214	2.552	1.336	0.003
Chronic kidney disease	0.001	0.304	4.487	1.118	0.001
Loop diuretic use	−0.012	−0.037	−1.062	1.324	0.012
Smoking	0.006	0.094	0.689	1.033	0.011
uACR					
Constant	0.515		3.279		0.001
24-h mean SBP	0.003	0.119	4.988	1.103	0.002
24-h mean PP	0.003	0.320	3.751	2.319	0.027
24-h SBP PTE%	0.000	0.223	9.041	1.201	0.001
Chronic kidney disease	0.002	0.204	7.773	1.057	<0.001
Loop diuretic use	−0.002	0.125	8.002	1.039	<0.001
Smoking	0.002	0.438	9.848	1.242	0.003
eGFR					
Constant	0.356		7.788		<0.001
Age	−0.002	−0.415	−5.452	1.150	<0.001
24-h mean SBP	−0.004	−0.370	−1.403	1.204	0.007
24-h m PP	−0.011	−0.098	−1.062	2.656	0.012
NT-proBNP	−0.004	−0.210	−6.557	1.222	<0.001
Blood urea nitrogen					
Constant	0.487		3.917		0.003
24-h mean SBP	0.002	0.150		1.433	0.002
24-h mean PP	0.001	0.137	3.321	1.123	0.008
24-h DBP weighted SD	−0.025	−0.098	−2.177	1.101	0.007
24-h SBP PTE%	0.002	0.219	1.676	3.206	0.015
NT-proBNP	0.004	0.386	2.210	2.554	0.001
Loop diuretic use	0.002	0.102	4.589	1.114	< 0.001

ABPM, ambulatory blood pressure monitoring; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal fragment pro-B-type natriuretic peptide; PTE, pressure percent time elevation; SBP, systolic blood pressure; uACR, urinary albumin-to-creatinine ratio; VIF, variance inflation factor.

whereas the BUN level was negatively correlated with the 24-h DBP weighted SD ($\beta = -0.025$, $P = 0.007$). Other indices of ABPM had no significant association with renal function (Table 4).

Discussion

Our data showed that the uACR level was positively correlated with the 24-h mean SBP, 24-h mean PP, and 24-h SBP PTE%, whereas the eGFR level was negatively correlated with the 24-h mean SBP and PP. The BUN level was positively correlated with the 24-h mean SBP, 24-h mean PP, and 24-h SBP PTE%, whereas the BUN level was negatively correlated with the 24-h DBP weighted SD. The other indices of ABPM had no significant association with renal function.

These data are the first to show that ABPM indices (ABP, BPV, BP circadian rhythms, and 24-h hypertensive or hypotensive time indices) are independently associated with the uACR, eGFR, and BUN levels in elderly Chinese men with hypertension, even after adjusted for age, common cardiovascular risk factors, co-morbidities, and medications. This novel finding adds to a growing body of evidence supporting ABPM as a useful predictor of TOD and adverse clinical outcomes in elderly patients with hypertension.

Most studies have shown that ABPM is more predictive than clinic BP for cardiovascular disease, stroke, and death, even after controlling for clinic BP [4–6,8,14–17]. Night-time ABP has been shown to provide more prognostic information than daytime ABP, with the exception of one cohort [4,5,14,17]. However, the relationship between ABP, BPV, BP circadian rhythms, and hypertensive or hypotensive time indices and renal damage has only been evaluated in a few cohorts. Nondipping has been shown to be a risk factor for the development of microalbuminuria, an increase in urinary protein excretion, and a decline in creatinine clearance [18,19]. Furthermore, in a cohort of 217 veterans with CKD followed for a median of 3.5 years, nondipping was shown to be a significant predictor for end-stage renal disease independent of clinic BP [20]. Data from the African American Study of Kidney Disease and Hypertension study indicated that a large majority of seemingly well-controlled (based on office BP) hypertensive patients have elevated BP at night; elevated nocturnal BP is associated with more severe manifestations of TOD [21]. Lurbe *et al.* [18] showed that in patients with type-1 diabetes, nondipper subjects have a higher risk of developing diabetic nephropathy. Recently, Wang *et al.* [10] reported that the nocturnal BP level and reversed dipper BP pattern are closely related to renal damage in patients with CKD. In addition, reversed dipper SBP and 24-h is DBP independently correlated with an eGFR <60 mL/min/1.73 m^2, and bedtime SBP is associated with proteinuria (>1 g/24 h). Our data demonstrated that among elderly patients with hypertension, the eGFR level was negatively correlated with the 24-h mean SBP and 24-h mean PP, whereas the BUN level was positively correlated with the 24-h mean SBP and 24-h mean PP in elderly patients with hypertension, which is

consistent with previous findings. In addition, our study revealed that the uACR level is positively associated with the 24-h mean SBP, 24-h mean PP, and 24-h SBP PTE% and the BUN level is negatively correlated with the 24-h DBP SD. This is the first study to evaluate the potential predictive value of ABPM on renal damage in elderly patients with hypertension. This is particularly relevant to nocturnal BP, 24-h mean BP, BPV, BP circadian rhythms, and hypertensive or hypotensive time indices because daytime BP is easily obtained in the clinic or at home, while nighttime BP, mean BP, BPV, BP circadian rhythms, and hypertensive or hypotensive time indices typically require ambulatory BP monitoring, which presents logistical challenges. This study is the first demonstration of the importance of ABPM indices as an early marker for renal damage in elderly hypertensive patients. In developing a strategy for BP reduction and early protection of target organs, there is increasing recognition of the importance of nocturnal BP, mean BP, BPV, and BP circadian rhythms.

CKD has been shown to be a risk factor for BP control and BP circadian rhythm abnormities [9,22]. Young *et al.* [23] reported that the elevation of SBP and PP was the highest risk of decline in kidney function in the elderly. Perhaps a plausible explanation is that vascular stiffness exacerbates the decline of GFR as well as effective blood perfusion in elderly patients. The mechanism by which CKD leads to BP circadian rhythm abnormalities, such as elevated nighttime BP, is not well understood, but is likely multifactorial and includes volume-dependent hypertension exacerbated by recumbent posture, abnormal sodium handling, and comorbidities, such as diabetes and autonomic insufficiency. Cardiac autonomic neuropathy, one aspect of autonomic insufficiency, is associated with elevated nighttime BP in patients with and without CKD [24,25]. Patients with CKD are known to have increased sympathetic activity [26]. One possible mechanism for increased nighttime BP in subjects with cardiac autonomic neuropathy is increased sympathetic activation causing increased renin release and proximal tubular sodium reabsorption [27]. Those findings revealed that the relationship between CKD and BP control and BP circadian rhythm abnormalities was causation in elderly patients with hypertension. Further prospective studies are required to assess the association between CKD severity and BP control and BP circadian rhythm abnormalities.

Although a few clinical trials have noted the relationship between renal damage and BP control and BP circadian rhythms [9,10], most studies were carried out in small sample size and relatively younger subjects [10]. Our study, a large-scale cross-sectional analysis, has provided the first systematic evaluation of the association between various ABPM indices (ABP, BPV, BP circadian rhythms, and hypertensive or hypotensive time indices) and renal damage in elderly males with hypertension. The present study suggests that the control of ABPM indices (ABP, BPV, BP circadian rhythms, and hypertensive or hypotensive time indices), excluding office BP and home BP monitoring, may be necessary for preventing TOD. Those ABPM indices associated with renal damage may be of predictive value for renal damage in elderly male patients with hypertension.

There were some limitations to the present study. First, all participants were males. Because it is the characteristic of our Geriatric Department that most patients are male, our current findings were only suitable for Chinese male patients. Second, this was an observational study. therefore, the association we observed cannot be assessed definitively. Third, we cannot exclude the possibility that ABPM indices are a consequence of renal damage in elderly patients with hypertension, as this is a cross-sectional study. At last, office BP levels were not obtained and no comparison could be done between ABPM and home BP parameters.

We are the first to report that in elderly Chinese male patients with hypertension, the uACR level is associated with the 24-h mean SBP, 24-h mean PP, and 24-h SBP PTE%. The eGFR level is associated with the 24-h mean SBP and 24-h mean PP. The BUN level is associated with the 24-h mean SBP, 24-h mean PP, 24-h DBP weighted SD, and 24-h SBP PTE% independent of common potential confounders, including age, medication use, cardiovascular comorbidities, and risk factors. The ABPM indices associated with renal damage may be regarded as an early predictive marker for renal function impairment in elderly Chinese male patients with hypertension.

Acknowledgements

Conflicts of interest
There are no conflicts of interest.

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