Original Article

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Comparing effect of definition of diurnal periods by diary, fixed periods, and actigraphy on ambulatory blood pressure parameters in a Chinese population

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Background: Reliable measurement of daytime and night-time blood pressure (BP), and degree of BP dipping during sleep during ambulatory blood pressure monitoring (ABPM) requires an accurate definition of sleep time (diurnal definition). However, superiority of any diurnal definition on ABPM remains unclear. The present study compared mean daytime and night-time SBP and DBP using different methods for diurnal definition: patient's diary, wide-defined and narrow-defined fixed periods, and actigraphy, in a Chinese population with diagnosed essential hypertension. We hypothesize that BP values from actigraphy are different from BP obtained by other methods and associated with end-organ damage (i.e. impaired renal function, proteinuria, left ventricular hypertrophy).

Methods: From April 2017 to October 2019, 203 Chinese patients diagnosed with hypertension were recruited prospectively from Lek Yuen Clinic and 179 completed a 48-h ABPM study, wearing a validated actigraph and completed a sleep diary. Presence of end-organ damage was retrieved from the computerized clinical management system. The differences in the mean BP values provided by different diurnal definition were compared using paired *t* tests and Bland–Altman plots. The prevalence of elevated BP, dipping status categories, overall percentage agreement and the Kappa statistic were calculated by pairwise comparisons between different diurnal definitions. The reproducibility was also estimated and logistic regression was used to examine the relationship between BP values from different diurnal definitions and end-organ damage.

Results: Mean daytime and night-time BP values were similar regardless of the definition used (mean difference <2 mmHg). Kappa statistics and overall percentage agreement found excellent agreement between different definitions to diagnose elevated daytime BP (Kappa ranged from 0.80 to 0.91) and night-time BP (Kappa ranged from 0.74 to 0.89). Good agreement to diagnose nondipping was also detected (Kappa ranged from 0.65 to 0.78). Furthermore, ABPM values were most reproducible when diurnal periods were defined by patient's diary (intra-class correlation coefficient = 0.82–0.93). Daytime and night-time BP values obtained using different diurnal definitions did not differ in their association to end-organ damage.

Conclusion: Differing definitions of diurnal periods provide similar mean BP values among a Chinese hypertensive population and have good agreement for diagnosis of elevated BP and dipping status. In individual patients, clinicians should be aware that different definitions of diurnal periods can lead to a 3–5 mmHg difference in patient's BP values and may affect the diagnosis of elevated BP in patients with BP close to diagnostic thresholds. The current study supports using the patient's diary to define diurnal periods, which provided the best reproducibility.

Keywords: actigraphy, ambulatory blood pressure, diary, diurnal periods, fixed periods

Abbreviations: ABPM, ambulatory blood pressure monitoring; BA, Bland and Altman; BP, blood pressure; CI, confidence interval; CMS, clinical management system; HT, hypertension; LOA, limit of agreement; OR, odd ratio; SD, standard deviation

INTRODUCTION

To obtain accurate and prognostic blood pressure (BP) parameters, such as night-time BP and nondipping from ambulatory blood pressure monitoring (ABPM), an accurate diurnal definition (awake and asleep time for the patient) is needed [1]. Currently, several methods are used to define these diurnal periods: patient's self-reported diary, wide-fixed predefined periods, narrow-fixed

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predefined periods and actigraphy [2]. However, there have been only five relevant studies that directly compared some of these diurnal definitions and found conflicting results [3–7]. Importantly, no previous studies have compared between all four commonly used definitions. Furthermore, these studies included adolescents, mostly healthy participants with no hypertension complications, and therefore, had limited generalizability to patients with hypertension [3–5]. Similarly, only one study was conducted in Asian population, which compared patient diary with narrow fixed time definition without the use of actigraphy [6]. Ethnic differences are important as racial differences in sleep duration, amount of deep sleep and 24-h BP pattern are well described and can affect BP and dipping status on ABPM [8,9]. Furthermore, there have been no previous studies investigating the relationship between differences in diurnal definition and presence of end-organ damage [3–7]. Therefore, superiority of any diurnal definition used on ABPM cannot be confirmed and different diurnal definitions are still used by clinicians and in research [10,11]. Clinically, the latest international guidelines suggest ABPM parameters to be defined by patient's diary but did not mention actigraphy, which is potentially more objective in the estimation of sleep periods [12].

The primary objective for the current study is to compare mean daytime and night-time SBP and DBP obtained by using different diurnal definitions (patients' diary, wide-defined and narrow-defined fixed periods, and actigraphy) in a Chinese population with diagnosed essential hypertension. For secondary objectives, this study compared between different diurnal definitions on: dipping status and degree of dipping, the diagnosis of elevated daytime and night-time BP and nondipping (as defined by <10% drop in BP during sleep), reproducibility of these parameters by comparing data from first and second 24-h intervals on a 48-h consecutive ABPM and the association with end-organ damage [including impaired renal function (as defined by estimated glomerular filtration rate of <60 ml/min per 1.73 m^2), and presence of proteinuria and left ventricular hypertrophy]. We hypothesize that BP parameters calculated from actigraphy would be more objective and have higher reproducibility and closer association to end-organ damage.

METHODS

This study was approved by the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (NTEC-2018-0144). Consent was obtained from all participants and the study adhered to the principles of the Declaration of Helsinki.

Participants

From April 2017 to October 2019, Chinese patients diagnosed with hypertension were recruited prospectively by doctors and via posters from Lek Yuen Clinic, which is a large government-funded primary care clinic in Shatin, Hong Kong. The study's exclusion criteria were: severe hypertension, which was defined as a clinical SBP at least 180 mmHg and/or a DBP at least 110 mmHg, because of the need for urgent assessment/treatment; the inability to provide consent; pregnancy; night-time workers, because of reversed ABPM patterns; occupational drivers because of inability to hold arm still during measurements; patients using anticoagulants to avoid bruising because of repeated BP measurements; and patients with atrial fibrillation.

Sample size

Assuming a difference of less than 5 mmHg in SBP according to different diurnal definitions, a typical standard deviation of SBP on ABPM of 10 mmHg and by using a type I and type II error of 5 and 20%, respectively, at least 34 patients were needed, and therefore, our sample size of 179 patients was adequate.

Ambulatory blood pressure measurements, patient's diary, actigraphy

We used the ApneABP monitor (Meditech, Westwood, Massachusetts USA), which uses the same algorithm as the internationally validated ABPM-4 device (www.strideBP.org). In accordance with international guidelines, ABPM was conducted on participants' nondominant arms, performed on usual working days (Monday to Friday), and the BP was measured every 30 min for 48 h. A 48-h ABPM report was considered acceptable if at least 70% of the readings were valid overall [13]. A 48-h ABPM allowed us to investigate reproducibility by comparing the BP data from the first 24 h and second 24 h. Invalid or missed readings were automatically discarded by the ABPM. The reports were not edited. Furthermore, all patients completed a sleep diary and also wore a validated actigraph (GT9X-BT; ActiGraph, LLC, Pensacola, Florida, USA) during the 48-h monitoring period.

Automated clinic blood pressure measurement

Automated clinic blood pressure measurement (AOBP) was conducted by the validated WatchBP office (Microlife AG, Heerbrugg, Switzerland) and by a trained research nurse (who validated the first reading, which was discarded). AOBP measurements was conducted in a separate quiet room. Three further readings were obtained at 1 min intervals and the mean BP values were calculated for the analyses.

Presence of end-organ damage

In Hong Kong, patients with hypertension receive yearly screening for renal damage, including serum creatinine level (impaired renal function was defined as estimated glomerular filtration rate <60 ml/min per 1.73 m^2) and spot urine protein-to-creatinine or albumin-to-creatinine level to detect proteinuria. Furthermore, they received 12-lead electrocardiogram to detect the presence of left ventricular hypertrophy [as diagnosed by the case doctor but usually is by voltage criteria, i.e. sum of S wave in V1 and R wave in V5 or V6 $\geq$3.5 mV (35 mm)] every 2–3 years. These data were recorded and retrieved from the computerized clinical management system (CMS).

Other data collection

To reduce recall bias, demographic data (age, sex) and antihypertensive drug use were retrieved from the CMS. Body weight and height were collected by a trained nurse.

Statistical analyses

Participants' demographic data were presented as numbers with percentages and means with standard deviation (SD) for categorial and continuous data, respectively. For the primary outcome, the differences in the mean SBPs and DBPs provided by different diurnal definitions were compared using paired *t* tests. Wide-fixed predefined periods were: daytime 0700 to 2300 h (16 h) and night-time: 2300 to 0700 h (8 h). Narrow-fixed predefined periods for daytime were 0900 to 2100 h (12 h) and night-time: 0100 to 0600 h (5 h).

For the secondary analysis, pairwise systematic differences of daytime and night-time SBP/DBP between the different definitions were assessed using Bland–Altman plots. Dipping status was defined by night-time to daytime SBP ratio and was categorized into four groups: extreme dipping ($\leq$0.80), normal dipping (>0.80 to $\leq$0.90), nondipping (>0.90 to $\leq$1.00) and reverse dipping (>1.00) [13]. Furthermore, daytime, night-time and 24-h hypertension were defined by BP of at least 135/85 mmHg, at least 120/70 mmHg and at least 130/80 mmHg, respectively. White-coat hypertension were defined by the presence of elevated AOBP BP ($\geq$135/85 mmHg) and normal daytime ABPM BP and masked hypertension were defined by normal AOBP BP and elevated daytime ABPM BP. The prevalence of elevated daytime and night-time BP, dipping status categories, overall percentage agreement and the Kappa statistic were calculated by pairwise comparisons between different diurnal definitions. The proportion of white-coat and masked hypertension according to different diurnal definitions on ABPM was compared using paired proportion tests.

The reproducibility of mean daytime and night-time BP values, and elevated daytime and night-time BP, nondipping status, and degree of dipping between first and second day were estimated using the intra-class correlation coefficient [95% confidence interval (CI)] via two-way random effect models, paired *t*-tests, the Kappa statistic (95% CI) and McNemar's chi-square test for categorical measures. Poor, moderate, good and excellent interclass correlation coefficients were defined as values of less than 0.50, at least 0.50 to less than 0.75, at least 0.75 to less than 0.90, and at least 0.90, respectively [14]. Logistic regression was used to determine the relationship between BP values from different diurnal definitions and end-organ damage.

As clinical BP remains widely used for diagnosis and management of hypertension, the correlation between daytime ABPM BP (using different diurnal definitions) and AOBP was examined. The agreement of detection of elevated BP between daytime ABPM BP (using different diurnal definitions) and AOBP was also examined the McNemar's (using the threshold of 135/85 and 130/80 mmHg, representing the European and American guidelines thresholds for both AOBP and ABPM, respectively) [12,15].

All statistical analyses were performed using R Statistical Software (version 3.5.2; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Participants' characteristics

From 203 participants recruited, a total of 179 participants were included in the final analysis. Participants were excluded because of incomplete 48-h ABPM ($n=14$), invalid ABPM records ($n=5$), incomplete or absent actigraphy data ($n=3$), suboptimal BP control ($n=1$), absence of diary data ($n=1$). The majority of participants were female (63.7%), had never smoked (84.8%), did not have diabetes mellitus (28.5%) and were receiving antihypertensive drug treatment (85.0%). Around one-fifth and one-third had end-organ damages (21.3%) and had elevated daytime SBP on 48-h ABPM (35.8%), respectively (Table 1). Correlation between sleep time estimated by actigraphy and patients' diary was poor ($\beta=0.195$, $P=0.066$).

Comparison of blood pressure values obtained by different diurnal definition

Regardless of the definition used, mean daytime and night-time BP values were similar (Tables 2–5). For example, mean daytime SBP defined by wide-defined fixed period was 131.66 ± 9.58 mmHg compared with narrow-defined fixed period (132.20 ± 9.97 mmHg) and actigraphy (131.83

TABLE 1. Participants' characteristics

Parameters	Numbers (%) or mean (SD)
Male	65 (36.3%)
Age (years)	66.86 (10.52)
BMI (kg/m^2)	26.14 kg/m^2 (3.78)
Creatinine level (mmol/l)	73.56 (20.76)
Presence of end-organ damages	37 (21.3%)
Presence of proteinuriaMean ACR (mg/mmol)	34 (19.1%)6.59 (29.41)
History of LVH on ECG	2 (1.1%)
Renal damage	7 (4.0%)
Antihypertensive drug use	
Any antihypertensive(s)	119 (85.0%)
Diuretics	11 (7.9%)
Beta-blockers	30 (21.4%)
CCB	88 (62.9%)
ACEI	14 (10.0%)
ARB	53 (37.9%)
Smoking	
Current smoker	5 (2.8%)
Ex-smoker	22 (12.4%)
Never smoker	151 (84.8%)
Presence of DM	51 (28.5%)
Mean LDL (mmol/l)	2.58 (0.85)
Mean HDL (mmol/l)	1.46 (0.43)
Mean TC (mmol/l)	4.70 (0.94)
Mean TG (mmol/l)	1.49 (0.80)
Mean HbA1c (%) (only collected for patients with DM) ($n=51$)	6.94 (0.87)
Elevated LDL ($\geq$3.4 mmol/l)	37 (20.8%)
Low HDL (<1.0 mmol/l)	11 (6.1%)
Elevated TC ($\geq$5.2 mmol/l)	57 (31.8%)
Elevated TG ($\geq$1.7 mmol/l)	63 (35.2%)
Mean clinic SBP (mmHg)	132.28 (12.88)
Mean clinic DBP (mmHg)	74.74 (9.11)
Elevated clinic BP	79 (57.2%)
Mean 48 h SBP (mmHg)	126.86 (8.52)
Mean 48 h DBP (mmHg)	70.76 (7.69)
Elevated 48 h BP	113 (63.1%)
Total 48 h sleep time by actigraphy (hours)	11.56 (4.55)
Total 48 h sleep time by diary (hours)	14.77 (3.22)
Total *n*	**179**

ACEI, angiotensin-converting-enzyme inhibitors; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; DM, diabetes mellitus; ECG, electrocardiogram; HbA1c, Hemoglobulin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVH, left ventricular hypertrophy; TC, total cholesterol; TG, triglyceride.

TABLE 2. Mean daytime SBP between different definitions of diurnal periods on ambulatory blood pressure monitoring

	Fixed time wide	Fixed time narrow	Actigraphy	Diary
SBP value, mean (SD)	131.66 (9.58)	132.20 (9.97)	131.83 (9.30)	132.37 (9.67)
N	179	179	179	177
P value of difference between measurement method				
	Fixed time wide	Fixed time narrow	Actigraphy	Diary
Fixed time wide	NA			
Fixed time narrow	**<0.001**	NA		
Actigraphy	0.286	0.086	NA	
diary	**<0.001**	0.329	**0.001**	NA

SD, standard deviation. Bold data signifies $P < 0.05$.

TABLE 3. Mean daytime DBP between different definitions of diurnal periods on ambulatory blood pressure monitoring

	Fixed time wide	Fixed time narrow	Actigraphy	Diary
DBP value, mean (SD)	74.20 (9.00)	74.64 (9.17)	74.16 (8.84)	74.56 (9.03)
N	179	179	179	177
P value of difference between measurement method				
	Fixed time wide	Fixed time narrow	Actigraphy	Diary
Fixed time wide	NA			
Fixed time narrow	**<0.001**	NA		
Actigraphy	0.698	**<0.001**	NA	
Diary	**<0.001**	0.748	**<0.001**	NA

SD, standard deviation. Bold data signifies $P < 0.05$.

TABLE 4. Mean night-time SBP between different definitions of diurnal periods on ambulatory blood pressure monitoring

	Fixed time wide	Fixed time narrow	Actigraphy	Diary
SBP value, mean (SD)	123.75 (9.55)	122.66 (9.91)	121.88 (9.74)	122.82 (9.59)
N	179	179	179	177
P value of difference between measurement method				
	Fixed time wide	Fixed time narrow	Actigraphy	Diary
Fixed time wide	NA			
Fixed time narrow	**<0.001**	NA		
Actigraphy	**<0.001**	**0.002**	NA	
Diary	**<0.001**	0.787	**<0.001**	NA

SD, standard deviation. Bold data signifies $P < 0.05$.

±9.30 mmHg), while using patient's diary was 132.37 ±9.67 mmHg (Table 2).

Intraindividual blood pressure differences according to different diurnal definition

The largest and the smallest intra-individual difference in daytime SBP/DBP was observed between narrow-defined fixed period and actigraphy [95% limit of agreement (LOA): −5.17 to 5.90 mmHg for SBP and −3.04 to 4.00 mmHg for DBP] and between the two definitions of fixed periods (95% LOA: −3.41 to 2.34 mmHg for SBP and −2.26 to 1.38 mmHg for DBP), respectively (Supplementary Figure 1, http://links.lww.com/HJH/C14).

Meanwhile, the largest intra-individual differences in night-time SBP and DBP were observed between narrow-defined fixed period and actigraphy [95% LOA: −5.57 to 7.12 mmHg (SBP)] and between wide-defined fixed period and actigraphy [95% LOA: −3.70 to 5.12 mmHg (DBP)], respectively. The 95% LOA was narrowest between wide-defined fixed period and diary (−3.51 to 5.61 mmHg for SBP and −2.29 to 3.75 mmHg for DBP) (Supplementary Figure 2, http://links.lww.com/HJH/C15). Most Bland–Altman plots did not show systematic trend at different BP levels and the largest beta-coefficient value was −0.039.

Agreement to diagnose elevated blood pressures, dipping status, white-coat and masked hypertension according to different diurnal definitions

Kappa statistics and overall percentage agreement found strong agreement between different definitions to diagnose elevated daytime BP (Kappa ranged from 0.80 to 0.91) and night-time BP (Kappa ranged from 0.74 to 0.89) (Table 6). Lower, but good agreement, between different diurnal definitions to diagnose nondipping were also detected (Kappa ranged from 0.65 to 0.78) (Supplementary Table 1, http://links.lww.com/HJH/C17).

Different diurnal definitions also provided similar proportion of white-coat and masked hypertension; an exception was comparison between actigraphy and fixed wide definition when elevated BP was defined as at least 130/80 mmHg ($P = 0.023$) (Supplementary Table 2, http://links.lww.com/HJH/C18).

TABLE 5. Mean night-time DBP between different definitions of diurnal periods on ambulatory blood pressure monitoring

	Fixed time wide	Fixed time narrow	Actigraphy	Diary
DBP value, mean (SD)	68.63 (7.69)	68.08 (7.66)	67.36 (7.49)	67.97 (7.70)
N	179	179	179	177
P value of difference between measurement method				
	Fixed time wide	Fixed time narrow	Actigraphy	Diary
Fixed time wide	NA			
Fixed time narrow	**<0.001**	NA		
Actigraphy	**<0.001**	**<0.001**	NA	
Diary	**<0.001**	0.285	**<0.001**	NA

ABPM, ambulatory blood pressure monitoring; NA, not applicable; SD, standard deviation. Bold data signifies $P < 0.05$.

Reproducibility of blood pressure parameters by different diurnal definition

In general, intra-class correlation coefficients and kappa statistics found good-to-excellent reproducibility of ABPM (between first and second 24 h) regardless of the diurnal definition used (Table 7). Results defined by diary had the best reproducibility. Furthermore, there were statistically significant differences between first and second day BP values when diurnal periods were defined by both wide-defined and narrow-defined fixed periods.

Association between blood pressure parameters from different diurnal definition and presence of end-organ damage

Daytime and night-time BP values obtained using different diurnal definitions had similar association with end-organ damage (Supplementary Table 3, http://links.lww.com/HJH/C19). For example, night-time SBP, which is the strongest predictive BP parameter to cardiovascular outcomes, were similarly associated with the presence of proteinuria regardless of definition methods [Supplemental Table 3d, http://links.lww.com/HJH/C19; wide-definition fixed period: odds ratio (OR) 1.06, 95% CI 1.02–1.11; narrow-definition fixed period: OR 1.05, 95% CI 1.01–1.09; actigraphy: OR 1.05, 95% CI 1.01–1.09; diary: OR 1.06, 95% CI 1.02–1.11].

Association between dipping from different diurnal definition and presence of end-organ damage

Nondipping was associated to the presence of LVH and eGFR to a similar extent, regardless of diurnal definitions (Supplementary Table 3h–I, http://links.lww.com/HJH/C19).

TABLE 6. Prevalence, Kappa statistic and overall agreement for diagnosis of elevated daytime and night-time blood pressure using different diurnal definitions

	Overall (%)	No No (%)	No Yes (%)	Yes No (%)	Yes Yes (%)	Kappa statistic (95% confidence interval)	Overall percentage agreement (95% confidence interval)
Elevated daytime BP							
Fixed period (wide-defined) Fixed period (narrow-defined)	38.5 40.8	58.1	3.4	1.1	37.4	0.91 (0.84–0.97)	0.96 (0.92–0.99)
Fixed period (wide-defined) Actigraphy	38.5 39.1	58.7	2.8	2.2	36.3	0.89 (0.83–0.96)	0.95 (0.92–0.98)
Fixed period (wide-defined) Diary	38.5 38.4	57.6	4	4	34.5	0.83 (0.75–0.92)	0.92 (0.88–0.96)
Fixed period (narrow-defined) Actigraphy	40.8 39.1	55.3	3.9	5.6	35.2	0.8 (0.71–0.89)	0.91 (0.86–0.95)
Fixed period (narrow-defined) Diary	40.8 38.4	56.5	2.8	5.1	35.6	0.83 (0.75–0.92)	0.92 (0.88–0.96)
Actigraphy Diary	39.1 38.4	58.8	1.7	2.8	36.7	0.91 (0.84–0.97)	0.95 (0.92–0.99)
Elevated nighttime BP							
Fixed period (wide-defined) Fixed period (narrow-defined)	69.8 65.9	29.1	1.1	5	64.8	0.86 (0.78–0.94)	0.94 (0.90–0.97)
Fixed period (wide-defined) Actigraphy	69.8 65.4	26.8	3.4	7.8	62	0.75 (0.64–0.85)	0.89 (0.84–0.94)
Fixed period (wide-defined) Diary	69.8 68.4	28.2	1.1	3.4	67.2	0.89 (0.82–0.97)	0.95 (0.92–0.99)
Fixed period (narrow-defined) Actigraphy	65.9 65.4	28.5	5.6	6.1	59.8	0.74 (0.64–0.84)	0.88 (0.83–0.93)
Fixed period (narrow-defined) Diary	65.9 68.4	28.2	5.1	3.4	63.3	0.81 (0.71–0.9)	0.92 (0.87–0.96)
Actigraphy Diary	65.4 68.4	28.2	5.6	3.4	62.7	0.79 (0.7–0.89)	0.91 (0.87–0.95)

$n = 174$.

TABLE 7. Reproducibility of mean daytime and night-time blood pressure, elevated blood pressure, nondipping status and degree of dipping between ambulatory blood pressure monitoring periods 1 and 2 using times derived from wide-defined and narrow-defined fixed periods, actigraphy and patients' diary

	Fixed period (wide-defined) ($n = 179$)	Fixed period (narrow-defined) ($n = 179$)	Actigraphy ($n = 179$)	Diary ($n = 177$)
	Intra-class correlation coefficient (95% confidence interval)			
Mean daytime SBP	0.79 (0.72–0.84)**	0.75 (0.66–0.81)**	0.84 (0.79–0.88)	0.85 (0.80–0.88)
Mean night-time SBP	0.78 (0.71–0.83)	0.75 (0.67–0.80)	0.77 (0.70–0.83)	0.82 (0.76–0.86)
Mean daytime DBP	0.90 (0.86–0.93)**	0.87 (0.81–0.91)**	0.93 (0.91–0.95)	0.93 (0.90–0.94)*
Mean night-time DBP	0.83 (0.78–0.87)*	0.77 (0.71–0.83)*	0.81 (0.75–0.86)*	0.86 (0.81–0.89)
	Kappa statistic (95% confidence interval)			
Elevated daytime BP	0.55 (0.42–0.67)**	0.57 (0.46–0.68)**	0.61 (0.49–0.73)	0.67 (0.56–0.78)
Elevated night-time BP	0.65 (0.53–0.77)	0.52 (0.39–0.65)	0.53 (0.39–0.66)	0.68 (0.56–0.8)
Nondipping status (two groups)	0.43 (0.28–0.57)	0.33 (0.18–0.47)	0.45 (0.31–0.6)	0.47 (0.33–0.61)
Degree of dipping (four groups)	0.40 (0.29–0.50)	0.36 (0.26–0.46)	0.44 (0.33–0.55)	0.52 (0.41–0.62)

BP, blood pressure.
*Indicates *P* value 0.05 or less using McNemar's chi-square test for paired proportions or paired *t*-test as appropriate.
**Indicates *P* value 0.01 or less using McNemar's chi-square test for paired proportions or paired *t* test as appropriate.

However, only nondipping as defined by wide fixed-time (OR 5.94, 95% CI) 1.69–37.75) and diary (OR 3.15, 95% CI 1.24–9.71) were associated with the presence of proteinuria (Supplementary Table 3g, http://links.lww.com/HJH/C19).

Relationship between automated clinic blood pressure measurement and daytime ambulatory blood pressure monitoring

The correlation between daytime ABPM and AOBP (clinic BP) was similar regardless of different diurnal definitions (0.47–0.49 and 0.69–0.7 for SBP and DBP, respectively) (Supplementary Figure 3, http://links.lww.com/HJH/C16). The agreement between AOBP and ABPM to detect elevated daytime BP were poor regardless of diurnal definitions and thresholds (Supplementary Table 4, http://links.lww.com/HJH/C20).

DISCUSSION

This was the first Chinese study that has compared the effect of different definitions on ABPM parameters using all four commonly used diurnal definitions. Our results suggest that, regardless of diurnal definition, the mean daytime and night-time SBP and DBP values were similar at population level. Good agreement between different diurnal definitions on the diagnosis of elevated BP and dipping status was also reflected by moderate-to-excellent Kappa values (Table 6). Different diurnal definitions provided similar proportion of white-coat and masked hypertension (Supplementary Table 2, http://links.lww.com/HJH/C18). However, BP values can change in individual patients because of the use of different diurnal definitions by up to 8 mmHg and may impact on the diagnosis of elevated BP. For example, 95% LOA of night-time BP between wide-definition fixed time and actigraphy was −4.33 to 8.07 mmHg. Furthermore, the current study also suggest that ABPM values were most reproducible when diurnal periods were defined by patient's diary (intra-class correlation coefficient = 0.82–0.93). Lastly, contrary to our hypothesis, BP values obtained by different diurnal definitions were associated with the presence of end-organ damage to a similar extent; BP values obtained from actigraphy did not show superiority.

Our findings are in agreement with previous studies, although our study has provided further important clinical data, especially in the Chinese population. Although, Eissa *et al.* found that actigraphy was superior in determining dipping status than diary method, Booth *et al.* commented that all definitions provided similar dipping results [3,4]. Furthermore, Booth *et al.* [3] also found that similar mean BP values could be obtained by ABPM regardless of the diurnal definition used, and reported superior agreement between patients' diary and actigraphy, which was not found in the current study. Furthermore, contrary to the findings of Booth *et al.* [3], our findings show ABPM parameters defined by patient's diaries had highest reproducibility. Slusniene *et al.* [7] conducted similar study in 69 patients with elevated BP (BP >135/85 mmHg) and found similar BP values regardless of the definition used (narrow fixed time, actigraphy and diary) but one-fifth of dipping status changed when defined by actigraphy. Finally, the Li *et al.* [6] study was the only prior Chinese study that found similar SBP/DBP values from only diary and narrow fixed time methods but did not include comparison to actigraphy. Differences between our findings and previous studies could be because of different population characteristics, with previous studies including mostly healthy western population with no end-organ damage. Furthermore, this was the first study that included two commonly used definitions (wide-defined and narrow-defined) of fixed periods. We also conducted 48-h ABPM, comparing BP values from the first and second day and thereby minimized influence of BP because of change in the environment (e.g. weather).

Research and clinical implications

For research, our findings do not support the need for actigraphy, which is more expensive, to detect diurnal periods in clinical trials as very similar mean BP values and dipping status can be obtained by using fixed-time or diary methods. In fact, diary method provides the best reproducibility of BP values. Furthermore, our results found that BP values obtained by different diurnal definitions were associated similarly with end-organ damage, possibly because of our modest sample size. Due to very similar BP values obtained by different diurnal definitions, a very large sample

size would be needed to determine the most 'accurate' diurnal definition to predict end-organ damage, and this could be achieved by analysis of large cohort studies.

Furthermore, clinicians should be aware that different definitions of diurnal periods can lead to a 3–5 mmHg difference in patient's BP levels and this may affect the diagnosis of elevated BP in patients with BP close to diagnostic thresholds. In fact, at an overall agreement of around 90% for most of our results (Table 6), around 10% of the diagnosis of elevated BP will change according to different diurnal definitions. For example, up to 20 patients (10.7%) had change of diagnosis of elevated BP when different diurnal definitions were used (Supplementary Table 5, http://links.lww.com/HJH/C21). Although further studies will be needed to determine the best way to define diurnal periods, the current study supports the use of patient's diary, which provided the best reproducibility. The choices of diurnal definition could also be situational as patient's diary would require good patient adherence, whereas actigraphy can be expensive and would require extra resources for analysis. Furthermore, fixed-time definitions may not reflect the sleeping time well in some patients (e.g. shift-workers).

Strength and limitations

Our study is the first Chinese study that included patients with hypertension with/without end-organ damage; had an adequate sample size to compare four different definitions of diurnal periods (self-reported diary, wide-fixed predefined periods, narrow-fixed predefined periods and actigraphy); and explored the association between BP parameters from different diurnal definition and the presence of end-organ damage.

However, it also had some limitations and while sample size was adequate for our primary outcome, it was not adequate for detecting the association between BP parameters from different diurnal definitions and presence of end-organ damage. Second, because of the cross-sectional nature, causal relationship (e.g. with end-organ damage) cannot be established. Furthermore, comparing BP values from first and second day in a 48-h ABPM was not the most commonly used method to define reproducibility but we would argue this had limited BP fluctuation because of external environmental changes. Moreover, LVH was defined by ECG, which is less sensitive than echocardiogram to detect LVH. Last, we have excluded patients with very high BP (i.e. SBP $\geq$180 mmHg or DBP $\geq$100 mmHg) because of safety concerns and the external validity of our results to these patients were not known. However, we would argue that diagnosis of suboptimal BP and thereby corresponding management will be similar regardless of the diurnal definition used.

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Conflicts of interest

There are no conflicts of interest.

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