Original Article

Reproducibility of Nocturnal Blood Pressure Assessed by Self-Measurement of Blood Pressure at Home

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To assess the reproducibility of nocturnal blood pressure (BP) during sleep as measured using a self-measurement device at home, we obtained repeated nocturnal home BP at 0200 h and quality of sleep assessment from a diary in 556 subjects (71% women, 62.4±11.1 years) in the general population. We used an Omron device (HEM-747IC-N, Omron Healthcare Co., Ltd., Kyoto, Japan), with which the time and frequency of monitoring can be preset and the readings stored. The mean±SD of the difference between test-retest BP measurements was 0.7±15.1 mmHg systolic and 0.2±9.7 mmHg diastolic with a mean interval of 5.9 days. The absolute differences were greater than 10 mmHg in 261 (46.9%) subjects for systolic and 145 (26.0%) subjects for diastolic. There was no evidence of regression to the mean in nocturnal measurements over at least three nights (n=390, p>0.22). The differences (the first minus the second measurement) were large in subjects who experienced sleep disturbance only in the first (n=64, 2.3±13.6 mmHg and 1.6±9.6 mmHg for systolic and diastolic, respectively) or second sessions (n=56, −4.1±16.4 mmHg and −2.5±11.4 mmHg) compared with the subjects without sleep disturbance (n=66, 1.5±17.8 mmHg and 0.8±10.3 mmHg) and those with sleep disturbance (n=370, 0.9±14.5 mmHg and 0.2±9.3 mmHg) in both sessions. In conclusion, the reproducibility of single nocturnal BP as assessed using a self-measurement device at home was not good, especially for subjects who experienced different quality of sleep in each session. To evaluate nocturnal BP using a self-measurement device, estimation of quality of sleep is indispensable. (*Hypertens Res* 2007; 30: 707–712)

***Key Words*: self measurement, reproducibility, general population, nocturnal blood pressure, Omron HEM-747IC-N**

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Introduction

In most individuals, the highest blood pressure is observed during the daytime and the lowest during the nighttime (*1*). However, blood pressure remains elevated throughout the night under pathophysiological conditions (*2*), including autonomic failure (*3*) and sleep apnea (*4*), and in some elderly hypertensives (*5*). Several cross-sectional studies have shown that target-organ damage is frequently observed in those with a diminished nocturnal decline in blood pressure (*6–8*). Non-dipping is also considered to be associated with greater cardiovascular risk (*9*). In addition, diurnal blood pressure variation predicts cardiovascular end points (*10*, *11*). To date, non-invasive ambulatory blood pressure monitoring has been the only method for assessing nocturnal blood pressure during sleep. However, we have developed a home blood pressure measuring device to monitor nocturnal blood pressure during sleep (*12*). The objective of this study was to assess the reproducibility of nocturnal blood pressure during sleep as measured using this device.

Methods

Study Population

The study protocol was approved by the Institutional Review Board of Tohoku University School of Medicine, Sendai, Japan, and by the Department of Health of the Ohasama Town Government. Informed consent was obtained from each subject. This report is based on the data from subjects who participated in the home blood pressure measurement project of the general population of Ohasama (*13*), Iwate Prefecture, Japan. The characteristics of this area and the details of that study have been described previously (*13*). Ohasama had a total population of 6,746 in 2004. Among them, 5,771 subjects were aged 20 or over. Those hospitalized, mentally ill, with dementia, or bedridden were excluded from the study. We also excluded individuals who worked outside the town. Of the remaining 2,191 eligible individuals, 2,136 subjects gave their written informed consent and participated in the home blood pressure measurement projects. We then excluded 1,291 subjects without values for nocturnal blood pressure during sleep, 166 subjects who did not keep a diary documenting quality of sleep, and 123 subjects who did not measure nocturnal blood pressure during sleep twice. Thus the number of subjects statistically analyzed totaled 556.

Blood Pressure Monitoring Devices

We obtained home blood pressure using the HEM-747IC-N device (Omron Healthcare Co., Ltd., Kyoto, Japan), which is a fully automatic unit based on the cuff-oscillometric method, generating a digital display of blood pressure readings (*12*). This device has integrated circuit memory and a clock, on which the time and frequency of monitoring home blood pressure can be preset. The memory chips also allow the storage of up to 60 readings, with time and date stamps on the measurements, which can be downloaded to a physician's computer. This device is the same as the previously validated (*14*) Omron HEM 735C except that the latter did not incorporate an integrated circuit memory. In the present study, we programmed the HEM-747IC-N device to obtain only a single blood pressure reading at 0200 h (*12*), since the nadir of the nocturnal blood pressure was observed at around 0200 h in the population of the Ohasama study (*15*). Such a measurement at a fixed clock time could eliminate the transition period in the evening, during which blood pressure rapidly changes. In addition, in the morning, the subject is only asked to recall the quality of sleep for a single measurement from the previous night; on the other hand, it is impossible to evaluate the quality of sleep during ambulatory blood pressure monitoring, since one cannot recall the quality of sleep for individual measurements obtained every 30 min. A minimal demand on subjects, *i.e.*, only a single measurement at 0200 h is also thought to improve compliance with blood pressure measurement. The requirement of multiple measurements of nocturnal blood pressure on each occasion creates too large a burden for subjects, which lowers compliance.

Blood Pressure Measurements

Public health nurses instructed subjects how to measure their morning, evening and nocturnal blood pressure during sleep. To measure nocturnal blood pressure during sleep, the subjects were asked to remove tight or restrictive clothing, apply the cuff of the HEM-747IC-N device to the upper arm at bedside, and keep their arm covered by the cuff during their sleep. Then, the device automatically measured blood pressure at the programmed clock time (0200 h) and stored the reading into the memory chip. Thus, the procedure for the self-measurement of nocturnal home blood pressure is simple and easy for most participants. The subjects were also asked to record the quality of sleep on a diary card after waking. On the diary card, subjects were asked to select one of the following options for each nocturnal blood pressure measurement; "no sleep disturbance and no awareness of measurement" or "serious or mild sleep disturbance with an awareness of measurement." Measurements of home blood pressure in the morning were made every morning within 1 h of waking, before breakfast or taking any drugs, with the subject seated and having rested for at least 2 min (*16–18*). Home blood pressure in the evening was obtained once every evening just before going to bed (*16–18*).

Classification of Subjects by Quality of Sleep

We evaluated the quality of sleep based on the diary card recordings. We defined the "sleeping" (S) state as "no sleep disturbance and no awareness of measurement" and the

Table 1. Clinical Characteristics across Groups Classified by Quality of Sleep

Variables	Whole subjects (n=556)	Group AA* (n=370)	Group SS* (n=66)	Group SA* (n=56)	Group AS* (n=64)	p-value
Women (%)	70.7	71.3	69.7	64.3	73.4	0.69
Age (years)	62.4±11.1	62.2±10.9	63.1±11.6	61.7±12.3	63.3±11.0	0.81
Home blood pressure in the morning						
Number of measurements	25.1±4.4	25.0±4.5	25.0±4.8	25.3±3.7	25.4±4.5	0.93
Systolic (mmHg)	128.9±16.6	129.0±16.6	131.5±18.9	127.0±13.1	128.6±17.0	0.53
Diastolic (mmHg)	75.2±9.3	75.0±9.4	76.4±9.9	76.3±8.2	74.4±8.7	0.45
Home blood pressure in the evening						
Number of measurements	24.5±4.7	24.5±4.7	24.8±3.3	23.9±4.7	24.5±5.5	0.72
Systolic (mmHg)	121.7±15.6	122.0±15.8	124.8±19.1	121.0±10.3	119.7±14.0	0.29
Diastolic (mmHg)	69.6±8.7	69.3±8.6	71.1±10.2	71.2±6.9	68.4±8.5	0.18
Antihypertensive medication (%)	27.9	26.0	34.9	30.4	29.7	0.47

Values are mean±SD. p-values are for overall differences across groups classified by quality of sleep. *Group AA: "awaking" state at both sessions; Group SS: "sleeping" state at both sessions; SA Group: "sleeping" state at first session and "awaking" state at second session; Group AS: "awaking" state at first session and "sleeping" state at second session.

"awaking" (A) state as "serious or mild sleep disturbance with an awareness of measurement." We then classified the subjects into four groups on the basis of quality of sleep at each session: Group AA (n=370, 66.5%), subjects in the "awaking" state at both sessions; Group SS (n=66, 11.9%), subjects in the "sleeping" state at both sessions; Group SA (n=56, 10.1%), subjects in the "sleeping" state at the first session and in the "awaking" state at the second session; and Group AS (n=64, 11.5%), subjects in the "awaking" state at the first session and in "sleeping" state at the second session.

Statistical Analysis

For database management and statistical analysis, we used SAS software, version 9.1 (SAS Institute, Cary, USA). We compared the mean of the difference (the first minus the second nocturnal blood pressure) using the paired t-test. Reproducibility of nocturnal blood pressure during sleep was studied using a Bland Altman plot (*19*). We also calculated Pearson's correlation coefficients between the first and second measurements. Variables among the four groups classified on the basis of quality of sleep were compared by ANOVA or χ^2-test. Values are expressed as the means±SD. Values of $p<0.05$ were considered statistically significant.

Results

Clinical Characteristics

The 556 participants included 393 (70.7%) women, as well as 155 (27.9%) patients who were taking blood pressure lowering drugs. In the overall study population, the mean±SD of age was 62.4±11.1 years. The morning blood pressure averaged 128.9±16.6 mmHg systolic and 75.2±9.3 mmHg diastolic and the evening blood pressure averaged 121.7±15.6 mmHg systolic and 69.6±8.7 mmHg diastolic. The numbers of measurements were 25.1±4.4 in the morning and 24.5±4.7 in the evening. Table 1 shows the clinical characteristics of the subjects across the four groups classified on the basis of quality of sleep. There were no significant differences in clinical characteristics among the four groups.

Reproducibility of Nocturnal Home Blood Pressure

The recordings of nocturnal blood pressure during sleep were repeated with a mean interval of 5.9 days. The reproducibility of nocturnal blood pressure during sleep was studied using a Bland-Altman plot (Fig. 1). In the total subject population, the mean differences between the two sessions were 0.7 mmHg (p=0.31) systolic and 0.2 mmHg (p=0.64) diastolic, and the SD of the differences of nocturnal blood pressure during sleep was 15.1 mmHg systolic and 9.7 mmHg diastolic. The absolute differences between the two recordings were greater than 10 mmHg in 261 (46.9%) and 145 (26.0%) subjects for systolic and diastolic readings, respectively. Pearson's correlation coefficient between repeated measurements was 0.67 for systolic and 0.55 for diastolic (both $p<0.001$).

We then performed subgroup analyses (Table 2). In Groups AA and SS, the nocturnal blood pressure during sleep was comparable between the two sessions (mean difference≤1.5 mmHg; $p\geq0.22$) and moderately correlated ($r\geq0.55$) for both systolic and diastolic blood pressure. Conversely, we observed considerable differences in Group SA (−4.1 mmHg, p=0.07 for systolic; −2.5 mmHg, p=0.11 for diastolic) and Group AS (2.3 mmHg, p=0.18 for systolic; 1.6 mmHg, p=0.18 for diastolic). No subgroup showed reliable reproducibility in the SD of the difference (≥13.6 mmHg systolic and ≥9.3 mmHg diastolic).

We also conducted subgroup analysis according to noctur-

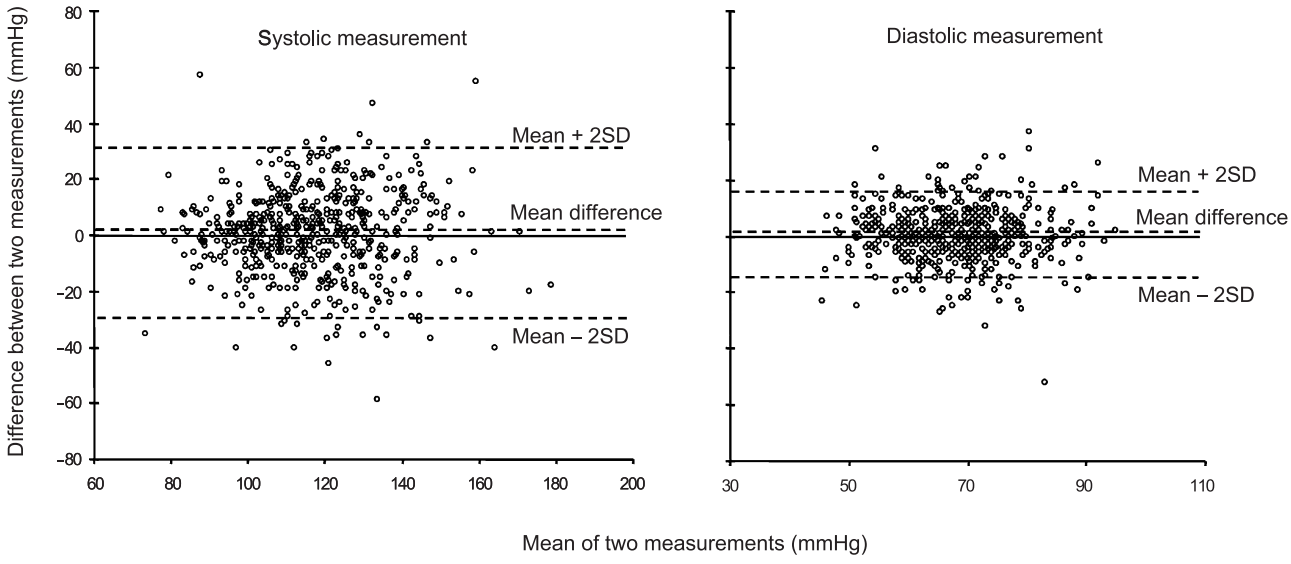

Fig. 1. *Bland-Altman plots of nocturnal home blood pressure at two sessions.*

Table 2. Agreement of Nocturnal Home Blood Pressure Values Obtained at the First and Second Sessions

Subject (No. of subjects)	Nocturnal home blood pressure (mmHg)		Difference (mmHg)	*p*-value	Correlation coefficient
	First session	Second session			
Whole subjects (*n*=556)					
Systolic pressure	117.1±18.7	116.5±18.6	0.7±15.1	0.31	0.67
Diastolic pressure	68.1±10.3	67.9±10.3	0.2±9.7	0.64	0.55
Group AA* (*n*=370)					
Systolic pressure	118.4±18.7	117.5±18.8	0.9±14.5	0.22	0.70
Diastolic pressure	68.9±10.1	68.7±10.4	0.2±9.3	0.62	0.59
Group SS* (*n*=66)					
Systolic pressure	115.4±22.0	114.0±20.0	1.5±17.8	0.50	0.64
Diastolic pressure	66.5±11.1	65.7±10.7	0.8±10.3	0.54	0.55
Group SA* (*n*=56)					
Systolic pressure	111.0±14.7	115.1±17.4	−4.1±16.4	0.07	0.49
Diastolic pressure	66.3±10.7	68.7±10.9	−2.5±11.4	0.11	0.45
Group AS* (*n*=64)					
Systolic pressure	116.5±17.3	114.2±16.6	2.3±13.6	0.18	0.68
Diastolic pressure	66.8±10.0	65.2±7.9	1.6±9.6	0.18	0.44

Values are mean±SD. *p*-values are for differences in nocturnal home blood pressure between first and second sessions. Correlation coefficients are between nocturnal home blood pressure at first and second sessions. *See Table 1.

nal blood pressure level. We defined nocturnal hypertension as an average of the measurements of the two sessions of at least 120 mmHg systolic and/or 75 mmHg diastolic based on the proposed reference value of nighttime ambulatory blood pressure (*20*). The SD of the difference of systolic/diastolic nocturnal blood pressure were 17.6/10.7 mmHg in the 250 subjects with nocturnal hypertension, and were significantly larger than those in the 306 subjects without nocturnal hypertension (12.8/8.8 mmHg, $p \leq 0.001$). The mean differences between the two sessions were small, irrespective of the presence of nocturnal hypertension (≤0.8 mmHg, *p* for the difference between with and without nocturnal hypertension ≤0.82, *p* for the difference between first and second session ≤0.30).

Among the 556 study participants, 390 participants (mean age, 63.6±10.2; 71.0% women) measured nocturnal home blood pressure three times (three nights) with intervals of approximately 5 days (5.3±4.2 days between the first and second measurements, 5.3±4.3 days between the second and third measurements). We did not find any evidence of regression to the mean among these three nocturnal measurements;

the differences among measurements were within 1 mmHg for both systolic and diastolic blood pressures ($p>0.22$).

Discussion

In the present study, we assessed the reproducibility of self-measured blood pressure performed once during sleeping period using a fully automatic home blood pressure device (HEM-747IC-N). Among the whole subject population, the mean of the difference between the first and second session was comparable at a 5.9-days interval; however, the SD of the difference was large. Nearly half of the subjects had a systolic difference of more than 10 mmHg. The observed reproducibility in nocturnal blood pressure was poor, especially in the subjects who experienced good sleep without awareness of measurement only at one session.

To the best of our knowledge, no studies have assessed the test-retest reproducibility of nocturnal blood pressure during sleep by self-measurement. To date, the reproducibility of the measurement of blood pressure during the sleeping period has been performed by ambulatory blood pressure monitoring, which has more reproducible results compared with the present study (*21–25*). The SD of the difference for nighttime or asleep ambulatory blood pressure ranges from 7 mmHg (*25*) to 15 mmHg (*23*) systolic and from 4 mmHg (*22*) to 8 mmHg (*21*) diastolic. The possible reasons why the reproducibility in the present study was poorer than in previous studies using ambulatory recordings (*21–25*) are outlined below. First, our study population consisted mainly of older subjects (62.4 ± 11.1 years), whereas those in the previous studies were younger (<49 years old) (*21–25*). Furthermore, in the Ohasama project, the hypertensive subjects being treated (27.9% of the study subjects) did not discontinue antihypertensive treatment, whereas those in the previous studies ceased antihypertensive treatment (*25*) or were untreated hypertensive subjects (*22–24*), except for one population study (*21*). Second, the limited reproducibility may be partly explained by an insufficient number of readings. In the present study, we measured blood pressure only once at 0200 h during sleep for two nights. On the other hand, ambulatory blood pressure monitoring provides multiple measurements. Mancia *et al*. (*25*) tested the hourly reproducibility of ambulatory blood pressure and showed that the hourly reproducibility increased by increasing the number of hourly readings from a single reading to three or four readings in an hour. Thus, multiple measurement of nocturnal blood pressure during sleep may result in an increase in reproducibility. There are two approaches to multiple measurements, *i.e.*, multiple measurements within a single night, as in ambulatory blood pressure monitoring, or those taken over several nights at a certain time. Our results suggest that single measurement of nocturnal blood pressure is insufficient. Although there is no general consensus on how many measurements are needed to obtain the best assessment of nocturnal blood pressure without disturbing the quality of sleep, long-term and repetitive measurement may be preferable for reliable reproducibility. In this respect, compliance or adherence with home nocturnal blood pressure measurement is an important issue. Reproducibility may be influenced by these approaches, and therefore, they need to be tested in future studies.

In the present study, Groups AS and SA tended to have poorer reproducibility compared with the other groups. This result may be partly due to differences in the quality of sleep across the two sessions. Somers *et al*. (*26*) reported nocturnal blood pressure and sleep stages with quantitative analysis of sleep by polysomnographic recordings. A decline in blood pressure was observed during non–rapid-eye-movement (non-REM) sleep compared with measurements obtained during quiet wakefulness (*26*). However, during REM sleep there was a marked increase in blood pressure (*26*). We also previously showed that nocturnal blood pressure with sleep disturbance is significantly higher than that without sleep disturbance in 134 hypertensive patients, although we relied on a questionnaire to analyze the quality of sleep (*12*).

The present study must be interpreted within the context of its potential limitations. First, in our present analysis, as in our previous study (*12*), quality of sleep was based on qualitative analysis by questionnaire and the stages of sleep and REM sleep were not detected. Second, middle-aged or older women made up the majority of the present participants and to some extent this imbalance in the sex and age distribution may limit the external validity of our findings. Third, automatic measurement of nocturnal blood pressure during sleep may induce anxiety in some patients. In conclusion, the present study found that the short-term reproducibility of single measurement of nocturnal blood pressure during sleep was limited, especially in subjects who experienced good sleep only at one session. Therefore, to evaluate nocturnal blood pressure using a self-measuring device, estimation of quality of sleep during measurement is indispensable. Further studies with multiple measurements will be required in order to validate nocturnal blood pressure assessment by self-measurement of blood pressure at home.

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