Association between timing of hot water bathing before bedtime and night-/sleeptime blood pressure and dipping in the elderly: a longitudinal analysis for repeated measurements in home settings

Running title: Bath timing and asleep BP

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Abstract

Hot water bathing-a Japanese traditional practice-has not been evaluated for its association with night- and sleep-time blood pressure (BP) in large populations. In this longitudinal analysis, bathing parameters and ambulatory BP were repeatedly measured for 2 nights in 758 Japanese elderly individuals. Participants were divided into 3 groups according to tertile values of time soaked in the bathtub (Duration: tertile value, 11 and 15 min), time from bathing-end to bedtime (Time before bedtime: tertile value, 42 and 106 min), and temperature of hot water in the bathtub (Water temp: tertile value, 40.3 and 41.2 °C). Participants' mean age was 70.9 years, and mean night- and sleep-time systolic BP (SBP) and dipping were 115.1±16.1, 114.2±16.2 mmHg, and 14.2%±8.8%, respectively. Multivariable mixed-effect linear regression models adjusted for potential confounding factors suggested that night-time SBP was significantly lower in the intermediate Time before bedtime group by 1.7 mmHg (95% CI, 0.2–3.1) and in the short group by 1.9 mmHg (95% CI, 0.1–3.7) than that in the long group. Dipping was significantly greater in the intermediate Time before bedtime group by 1.8% (95% CI, 0.7–2.9) and in the short group by 1.8% (95% CI, 0.6–3.1) than that in the long group. These associations were consistent regarding sleep-time SBP. Conversely, Water temp and Duration did not significantly associate with any ambulatory BP parameter. Remarkably, Time before bedtime significantly prolonged with increases in tertiles of Water temp (P for trend=0.006). In conclusion, the findings of this study revealed that Japanese hot water bathing, especially the short time from bathing-end to bedtime, was associated with lower night- and sleep-time BP and greater dipping in an elderly population.

Keywords: bathing, night-time blood pressure, sleep-time blood pressure, dipping, hot water, passive body heating

Introduction

Blood pressure (BP) of humans varies with circadian physiology and behavior. Night-time BP is lower than daytime BP in normotensive and hypertensive individuals (Millar–Craig MW et al., 1978; Shaw DB et al., 1963). Reportedly, night-time BP and nocturnal BP fall (dipping) accurately predict the cardiovascular outcomes and all-cause mortality than that of office blood pressure and daytime BP, where cardiovascular risk increases from the normal range of night-time systolic BP (SBP) of 110 mmHg (Banegas JR et al., 2018; Dolan E et al., 2005; Ingelsson E et al., 2006; Staessen JA et al., 1999). In addition, sleep-time BP predicts future cardiovascular disease (Hermida RC et al., 2018). Some risk factors increasing night- and sleep-time BP are suggested, such as diabetes, chronic kidney disease, and sleep disordered breathing; however, environmental factors are yet to be entirely elucidated (Ayala DE et al., 2013; Drawz PE et al., 2016; Ejaz AA et al., 2004; Kario K et al., 1998; Parati G et al., 2014; Saeki K et al., 2014).

Hot water bathing is a Japanese traditional practice. Generally, Japanese people soak in comparatively high temperature water up to their shoulder every evening (Hayasaka S et al., 2011; Traphagan JW et al., 2004). Physiologically, arterial BP is largely affected by systemic vascular resistance (SVR) and cardiac output (CO), and experimental studies suggested passive body heating dilates the vasculature and increases the peripheral blood volume, resulting in decreased preload volume to the heart (Crandall CG & González–Alonso J. 2010; Crandall CG & Wilson TE. 2015; Lilly LS. 2015; Rowell LB. 1983). These contribute to decrease SVR and CO and lower BP. Previous studies in laboratory and home settings suggested that hot water bathing lowers systemic BP; however, these studies were limited by small sample sizes and inadequate BP measurements only before bedtime (Ohnaka T et al. 1995; Kanda K et al. 1996; Kawabe H & Saito I. 2006; Fujiwara T et al. 2017). Therefore, to date, it remains uncertain whether hot water bathing contributes to lowering night- and sleep-time BP. In the present study, we analyzed repeated measurements of bathing parameters and ambulatory BP in a Japanese elderly population.

Methods

Participants and Study Protocol

The present study analyzed data from the HEIJO-KYO cohort of 1127 community-dwelling elderly individuals (\geq 60 years); the survey had been conducted between September and April in 2010, 2011, 2012, 2013, and 2014 (Obayashi K et al., 2012). Of these, we excluded the participants who did not take a bath (n=321), participants who did not complete logging bathing/sleep diaries (n=25), and participants without data on ambulatory BP (n=23). Consequently, 758 participants were enrolled in this study. All participants provided written informed consent, and the study protocol was approved by Nara Medical University' ethics committee.

Measurement of Ambulatory BP

Ambulatory BP was measured using a validated recorder (TM-2430; A&D Co. Ltd., Tokyo, Japan) and cuff on the non-dominant arm. BP was measured at 30-min intervals for consecutive 48 h, and the session was conducted one time for each person. Daytime and night-time values were defined by standardized self-administered diary entries as out-of-bed and in-bed periods. Daytime and night-time BP measuring <10 and <5 times in a day, respectively, were excluded from the analysis. Mean values for each two days in SBP and diastolic BP (DBP) were calculated. Dipping was defined as percentage night-time SBP fall corresponding to daytime SBP. Nocturnal hypertension was defined as night-time SBP≥120 mmHg or night-time DBP≥70 mmHg (Shimamoto K et al., 2014). Simultaneously with ambulatory BP, physical activity was measured at 1-min intervals using an actigraph (Actiwatch 2; Respironics, Inc., Murrysville, PA, USA) worn on the non-dominant wrist for 2 days. Data were analyzed using the Actiware (version 5.5, Respironics Inc., Murrysville,

PA), and sleep-onset and offset were estimated automatically with default criterion. Sleeptime BP was defined as mean BP between actigraphic sleep-onset and offset.

Measurement of Bathing and Sleeping Parameters

Time-related bathing and sleeping parameters were evaluated using a standardized selfadministered diary on 2 days for time bathing-start and bathing-end, time soaked in the bathtub (Duration), time from bathing-end to bedtime (Time before bedtime), bedtime, and rising time. Temperature of hot water in the bathtub (Water temp) was measured using a logger (Thermochron iButton; Maxim integrated, Dallas, TX, USA) at 1-min intervals for 2 days. With regard to bathroom, dressing room, and bedroom, temperatures 60 cm above the floor were measured at 10-min intervals. Outdoor temperature was estimated at 10-min intervals using data from the local meteorological office in Nara (latitude, 34°N). Regarding Water temp, we extracted water temperature data between bathing-start and bathing-end from whole raw data, and data of temperature below 30 °C and data below 2.5 percentile and above 97.5 percentile due to technical errors were excluded from the analysis. Average data in 2 days on these bathing and sleeping parameters were used in the analysis.

Other Measurements

Body mass index (BMI) was calculated as body weight divided by the square of body height (kg/m^2) . Smoking and drinking status and medication use were evaluated using a self-administered questionnaire. The presence of diabetes or dyslipidemia was determined on medical history and current medication use. Venous blood samples were obtained, and estimated glomerular filtration rates (eGFR) were calculated using the formula advocated by the Japanese Society of Nephrology–Chronic Kidney Disease Practice Guide: eGFR (mL/min per 1.73 m²) = 194 × [serum creatinine (mg/dL)]^{-1.094} × [age (years)]^{-0.287}.

Statistical Analyzes

Normally distributed continuous variables were reported as mean±standard deviation (SD); non-normally distributed variables were presented as median (interquartile ranges, IQRs). Mean and median values were compared using unpaired t-tests and the Mann-Whitney U test, respectively. Proportion was compared using the Chi-squared test. Associations of hot water bathing with night- and sleep-time BP and dipping were evaluated using a two-level linear regression model consisting of participant-level variables, including age (year), gender, BMI (kg/m²), current smoking, alcohol consumption (\geq 30 g/day), antihypertensive drug use, diabetes, dyslipidemia, and eGFR (<60 mL/min/1.73 m²) and measurement day-level variables, including Duration, Time before bedtime, Water temp, daytime physical activity (counts/min), bedtime (min), and rising time (min). Regression coefficients were estimated by maximum likelihood. Participants were divided into 3 groups according to tertile values of Duration (tertile value, 11 and 15 min), Time before bedtime (tertile value, 42 and 106 min), and Water temp (tertile value, 40.3 and 41.2 °C). Trends for the association of bathing parameters (Duration, Time before bedtime, and Water temp) with night- and sleep-time SBP and dipping were evaluated using linear regression analysis. P values for the association trends of Time before bedtime with Duration and Water temp were calculated using the Jonckheere-Terpstra test. All analyzes were performed using SPSS 24.0 for Windows (IBM SPSS Inc., Chicago, IL, USA). A two-sided P < 0.05 was considered statistically significant.

Results

The mean age of 758 participants was 70.9±7.0 years; 364 participants (48.0%) were male. Mean night- and sleep-time SBP were 115.1±16.1 mmHg and 114.2±16.2 mmHg, respectively; mean dipping was 14.2±8.8%. Nocturnal hypertension was significantly associated with older age, male gender, higher BMI, higher prevalence of current smoker and lower eGFR, greater alcohol consumption, and lower daytime physical activity (**Table 1**).

Mean Duration and Water temp were 13.3±5.7 min and 40.8°C±1.3°C, respectively. Median Time before bedtime was 70.0 min (30.0–131.0) (**Table 2**). Mean Time bathing-start and bathing-end, bedtime, and rising time were 20:38±1:44, 21:04±1:44, 22:37±1:11, and 6:46±0:57, respectively. Mean temperatures in bathroom, dressing room, bedroom and outdoor were 16.5°C±4.4°C, 13.6°C±4.1°C, 12.4°C±4.4°C, and 4.9°C±4.9°C, respectively. Day-to-day correlations of bathing and sleeping parameters were moderately high (intraclass correlation coefficient, 0.68–0.89).

In the mixed-effect linear regression models (**Table 3**) when compared with the long Time before bedtime group, night-time SBP was significantly lower in the intermediate group by 1.9 mmHg (95% confidence interval, 0.4–3.5 mmHg) and in the short group by 2.1 mmHg (0.4–3.9 mmHg). Consistently, sleep-time SBP was significantly lower in the intermediate Time before bedtime group by 2.1 mmHg (0.5–3.6 mmHg) and in the short group by 2.4 mmHg (0.5–4.2 mmHg) than that in the long group. Dipping was significantly greater in the intermediate Time before bedtime group by 1.9% (0.7–3.0%) and in the short group by 1.9% (0.7–3.1%) than that in the long group. In contrast, Duration and Water temp did not significantly associate with night- and sleep-time SBP and dipping. Sensitivity analysis, excluding thirty-four data (2.2%) on BP measurements less than 70% readings in a day, indicated similar results that night-time SBP was significantly lower in the intermediate Time before bedtime group by 1.8 mmHg (0.3–3.3 mmHg) and in the short group by 1.8 mmHg (0.1–3.6 mmHg) than that in the long group. In addition, similar results were observed regarding sleep-time SBP and dipping (data not shown).

Multivariable models adjusted for potential confounding factors suggested consistent results that night-time SBP was significantly lower in the intermediate Time before bedtime group by 1.7 mmHg (0.2–3.1 mmHg) and in the short group by 1.9 mmHg (0.1–3.7 mmHg) than that in the long group (**model 2**, **Table 4**). Similarly, sleep-time SBP was significantly lower in the intermediate Time before bedtime group by 1.9 mmHg (0.3–3.4 mmHg) and in the short group by 2.2 mmHg (0.3–4.0 mmHg) than that in the long group. Dipping was significantly greater in the intermediate Time before bedtime group by 1.8% (0.7–2.9%) and in the short group by 1.8% (0.6–3.1%) than that in the long group. The associations between covariates and night- and sleep-time SBP were suggested in supplemental table 1.

Median Time before bedtime in the low, intermediate, and high Water temp groups were 63.8, 70.0, and 91.0 min, respectively. Time before bedtime significantly prolonged with increases in tertiles of Water temp (P for trend=0.006) (**Figure 1A**). In contrast, median Time before bedtime in the short, intermediate, and long Duration groups were 76.0, 67.3, and 75.5 min, respectively, and no significant differences of association trends were observed between Duration and Time before bedtime (**Figure 1B**).

Discussion

Our study revealed that timing of hot water bathing before bedtime was significantly associated with lower night- and sleep-time BP and enhancement of nocturnal BP dipping in a large elderly population. However, time soaked in the bathtub and temperature of hot water in the bathtub did not significantly associate with both night- and sleep-time BP and dipping.

Our observations were consistent with previous studies and add novel evidence that bathing before bedtime relates to lower night- and sleep-time BP in large samples. A home setting study of 158 volunteers suggested that evening SBP decreased by 4.1 mmHg at 30 min after hot water bathing and that, thereafter, SBP decreased by 3.2 mmHg at 60 min after bathing (Kawabe H & Saito I. 2006). Effect sizes of these BP-lowering effect correspond to 0.25 SD and 0.20 SD of BP before hot water bathing, respectively. In contrast, no significant BP-lowering effects were observed at 120 min after hot water bathing. Another study of 48 hypertensive patients suggested similar results that average SBP decreased by 6.3 mmHg during 120 mins after hot water bathing and that BP decline became smaller after that (Fujiwara T et al. 2017). Regarding studies measuring night-time BP, an observational study of 28 hypertensive patients suggested no significant decreases in night-time BP after hot water bathing compared with no bathing nights (Ishikawa J et al. 2016). This study did not investigate Time before bedtime as a bathing parameter. In our study, shorter groups with Time before bedtime within 106 mins exhibited a significantly lower night-time BP than the long Time before bedtime group ranging from 107 to 431 mins.

Previous solid evidence supports our data on the association between hot water bathing and lower BP during sleep. Physiologically, SVR and CO are core factors for consisting BP. It is well recognized that passive body heating dilates the vasculature and decreases SVR. In addition, cutaneous vasodilation causes the shift of blood volume from central to peripheral

(Deschamps A & Magder S. 1990; Ganio MS et al. 2012). This blood volume increase in peripheral organs leads to a decrease in cardiac preload, resulting in decreased CO (Bundgaard-Nielsen M et al., 2010; Wilson TE et al., 2009). Notably, reducing heat loss is an important factor to continue vasodilation (Crandall CG et al. 2008). Body temperature after hot water bathing reportedly depends on room temperature spent after bathing (Hashiguchi N et al., 2002; Kanda K et al. 1996). Indoor temperature is too low to reduce heat loss, e.g. bedroom temperature as 12.4 °C, although body temperature may stay high when entered bed in short time after bathing. Thus, our results were reasonable that the association between bathing and lower BP was observed when time from bathing-end to bedtime is shorter. On the contrary, regarding temperature of hot water in the bathtub and time soaked in the bathtub, no significant associations with night- or sleep-time BP were observed. The magnitude of body heating is influenced by the intensity and duration of heating, although our data indicated that higher temperature of hot water in the bathtub was associated with prolonged time from bathing-end to bedtime but not time soaked in the bathtub. Another possible mechanism underlying the association of hot water bathing with night-and sleep-time BP includes better sleep quality induced by bathing. A recent systematic review suggested that water-based passive body heating improved self-rated sleep quality and shortened sleep-onset latency, depending on the conditions of body heating (Haghayegh S et al. 2019). Previous studies suggested body heating improved sleep initiation and maintenance measured subjectively and objectively (Kanda K et al. 1999; Mishima Y et al., 2005; Oshima–Saeki C et al., 2017; Sung EJ et al., 2000). Further, we reported that better sleep was associated with lower night-time BP (Oume M et al., 2018).

Our data could be clinically interpreted using data on previous studies. A meta-analysis of population-based prospective studies of 9.6 years followed-up indicated that a 1 mmHghigher night-time SBP corresponds to a 1.4 % increase in the risk of cardiovascular death regardless of normal night-time SBP (Boggia J et al., 2007). Thus, a 1.9 mmHg decrease in night-time SBP observed in group with shorter time from bathing-end to bedtime corresponds to a 2.7 % decrease in the risk of cardiovascular death. Further, a recent study of 2315 middle-aged Finnish males suggested that high frequency of sauna bathing reduced cardiovascular risk and all-cause mortality (Laukkanen T et al. 2015). Our results may partly explain this sauna bathing effect on cardiovascular risk. Future researches investigating the effects of body temperature at bedtime on night- and sleep-time BP and cardiovascular risk are needed.

Advantages of our study include the large sample size, which permits adjustment for a number of potential confounders; previous related studies faced limitations here. Another strength includes a longitudinal design using repeated bathing and ambulatory BP measurements, and mixed-effect linear regression models were used to evaluate the longitudinal association between hot water bathing and night- and sleep-time BP. The present study has several limitations as follows. First, our study participants were not randomly selected, possibly leading to selection bias, although some data on BMI and eGFR were similar to data surveyed nationwide (Japanese Ministry of Health, Labour and Welfare. 2017). Second, body temperatures, such as skin or core body temperature, were not considered. Further study measuring changes in these body temperatures by hot water bathing is warranted. Third, data on bathing were measured only over 2 nights, leading to misclassification of the bathing status, although moderately high night-to-night correlations were suggested in the present study. Forth, the data were only available from 758 participants (67.3%), possibly affecting the validity of the statistical results. As described in supplemental table 2, participants without bathing seemed to be older and have higher night-time BP than the present study participants. This may be related to the associations of hot water bathing with night-time BP. The BP-lowering effects of hot water bathing were reportedly greater in

elderly individuals than youngers because of decreased autonomic nerve functions in elderly individuals (Nagasawa Y et al., 2001). Fifth, we measured physical activity during BP measurement on the non-dominant wrist because the dominant wrist shows overcounts for physical activity by minor activity with trunk still, e.g. writing, cooking, and brushing teeth (Middelkoop HA et al., 1997). However, this does not follow the current guideline (Hermida RC et al., 2013).

In conclusion, our study revealed that timing of hot water bathing significantly associated with lower night- and sleep-time BP and enhanced nocturnal BP dipping in a large elderly population. These were independent of important risk factors of higher night- and sleep-time BP including aging, smoking, diabetes, renal dysfunction, and physical inactivity. In addition, these associations between hot water bathing and lower BP during sleep were observed when time from bathing-end to bedtime is shorter, although time soaked in the bathtub and temperature of hot water in the bathtub did not significantly associate with both night- and sleep-time BP and dipping.

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Conflict of Interest

KS and KO received research grant from YKK AP Inc.; Ushio Inc.; Tokyo Electric Power Company; EnviroLife Research Institute Co., Ltd.; Sekisui Chemical Co., Ltd.; LIXIL Corp.; and KYOCERA Corp. The other authors reported no conflicts of interest.

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Figure Legends

Figure 1

Box plots of Time before bedtime according to tertiles of Water temp (A) and Duration (B). Time before bedtime are presented as medians and 25th and 75th percentiles (boxes), and 10th and 90th percentiles (whiskers). P values for association trend are calculated using the Jonckheere–Terpstra test. Time before bedtime, time from bathing-end to bedtime; Water temp, temperature of hot water in the bathtub; Duration, time soaked in the bathtub.

	Nocturnal	Nocturnal hypertension		
	With $(n = 350)$	Without $(n = 408)$	Р	
Demogratic parameters				
Age, mean, years	72.0 (7.1)	69.9 (6.8)	< 0.001	
Gender, number, male	198 (56.6%)	166 (40.7%)	< 0.001	
BMI, mean, kg/m ²	23.5 (3.0)	22.9 (3.2)	0.017	
Current smoker, number	26 (7.4%)	8 (2.0%)	< 0.001	
Alcohol consumption (≥30 g/day), number	65 (18.6%)	50 (12.3%)	0.010	
Clinical parameters				
Antihypertensive drug use, number	167 (47.7%)	167 (40.9%)	0.07	
Diabetes, number	28 (8.0%)	36 (8.8%)	0.68	
Dyslipidemia	96 (27.4%)	134 (32.8%)	0.11	
eGFR (<60 mL/min/1.73 m ²), number	73 (21.2%)	58 (14.4%)	0.015	
Daytime physical activity, mean, count/min	294.8 (102.8)	323.4 (104.8)	< 0.001	
Ambulatory BP				
Daytime SBP, mean, mmHg	141.7 (12.0)	128.2 (12.2)	< 0.001	
Daytime DBP, mean, mmHg	83.0 (7.4)	77.0 (7.0)	< 0.001	
Night-time SBP, mean, mmHg	128.3 (12.1)	103.8 (8.8)	< 0.001	
Night-time DBP, mean, mmHg	83.0 (7.4)	61.3 (5.1)	< 0.001	
Sleep-time SBP, mean, mmHg	127.1 (12.3)	102.7 (8.7)	< 0.001	
Sleep-time DBP, mean, mmHg	73.0 (6.7)	60.7 (5.2)	< 0.001	
Dipping, mean, %	9.1 (7.8)	18.6 (7.1)	< 0.001	

Table1. Basic and clinical characteristics accoring to night- and sleep-time BP levels (n = 758)

Data are expressed as means with standard deviation. BMI, body mass index; eGFR, estimated glomerular filtration rate; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

icient
CI
.72
.80
.84
.84
.83
.78
.74
.87
.89
.90
.73

Table 2.	Summary	of bathing	and sleep	parameters in	758 p	participants
	and the second sec					

Data are expressed as means with standard deviation and medians with interquartile range. Time before bedtime, time from bathing-end to bedtime; Water temp, temperature of hot water in bathtub; Duration, time soaked in bathtub.

*test after natural log-transformation.

	Т	Time before bedtime (range, min)				
	Short (1-41)	Intermediate (42-106)	Long (107–431)	$P_{\rm trend}$		
No. of data	511	500	505			
Night-time SBP						
Difference, mmHg (95% CI)	-2.1 (-3.9, -0.4)	-1.9 (-3.5, -0.4)	Reference	0.030		
Р	0.019	0.016				
Sleep-time SBP						
Difference, mmHg (95% CI)	-2.4 (-4.2, -0.5)	-2.1 (-3.6, -0.5)	Reference	0.016		
Р	0.011	0.009				
Dipping						
Difference, % (95% CI)	1.9 (0.7, 3.1)	1.9 (0.7, 3.0)	Reference	0.006		
Р	0.003	0.001				
		Water temp (range, °C)				
	Low (34.9-40.2)	Intermediate (40.3-41.2)	High (41.3-44.5)			
No. of data	482	485	485			
Night-time SBP						
Difference, mmHg (95% CI)	Reference	-0.5 (-2.1, 1.0)	0.3 (-1.4, 2.1)	0.74		
Р		0.50	0.27			
Sleep-time SBP						
Difference, mmHg (95% CI)	Reference	-0.5 (-2.1, 1.1)	0.04 (-1.8, 1.9)	0.58		
Р		0.56	0.97			
Dipping						
Difference, % (95% CI)	Reference	0.3 (-0.9, 1.4)	-0.7 (-1.9, 0.6)	0.31		
Р		0.63	0.30			
		Duration (range, min)				
	Short (2–10)	Intermediate (11-15)	Long (16-41)			
No. of data	427	527	562			
Night-time SBP						
Difference, mmHg (95% CI)	Reference	-0.8 (-2.5, 0.8)	-1.0 (-3.0, 1.0)	0.33		
Р		0.33	0.32			
Sleep-time SBP						
Difference, mmHg (95% CI)	Reference	-0.9 (-2.6, 0.8)	-1.3 (-3.3, 0.8)	0.38		
Р		0.30	0.22			
Dipping						
Difference, % (95% CI)	Reference	-0.01 (-1.2, 1.2)	0.4 (-0.9, 1.8)	0.51		
Р		0.99	0.52			

Table 3. Differences in night- and sleep-time SBP and dipping according to tertiles of bathing parameters

SBP, systolic blood pressure; CI, confidence interval. Time before bedtime, time from bathing-end to bedtime; Water temp, temperature of hot water in bathtub; Duration, time soaked in bathtub.

	Time before bedtime (range, min)			
	Short (1-41)	Intermediate (42-106)	Long (107–431)	
Adjusted model 1				
Night-time SBP				
Difference, mmHg (95% CI)	-1.9 (-3.6, -0.1)	-1.7 (-3.1, -0.2)	Reference	
Р	0.038	0.028		
Sleep-time SBP				
Difference, mmHg (95% CI)	-2.1 (-3.9, -0.3)	-1.9 (-3.4, -0.3)	Reference	
Р	0.023	0.018		
Dipping				
Difference, % (95% CI)	1.8 (0.5, 3.0)	1.7 (0.6, 2.9)	Reference	
Р	0.005	0.002		
Adjusted model 2				
Night-time SBP				
Difference, mmHg (95% CI)	-1.9 (-3.7, -0.1)	-1.7 (-3.1, -0.2)	Reference	
Р	0.035	0.025		
Sleep-time SBP				
Difference, mmHg (95% CI)	-2.2 (-4.0, -0.3)	-1.9 (-3.4, -0.3)	Reference	
Р	0.020	0.017		
Dipping				
Difference, % (95% CI)	1.8 (0.6, 3.1)	1.8 (0.7, 2.9)	Reference	
Р	0.004	0.001		
Adjusted model 3		and a second		
Night-time SBP				
Difference, mmHg (95% CI)	-1.8 (-3.6, -0.03)	-1.6 (-3.1, -0.1)	Reference	
Р	0.047	0.034		
Sleep-time SBP				
Difference, mmHg (95% CI)	-2.1 (-3.9, -0.2)	-1.8 (-3.3, -0.2)	Reference	
Р	0.027	0.023		
Dipping				
Difference, % (95% CI)	1.8 (0.6, 3.0)	1.8 (0.7, 3.0)	Reference	
Р	0.004	0.002		

Table 4.	Adjuted	differences in night- and slee	p-time SBP and	dipping acco	ording to Tir	ne before bedtime

SBP, systolic blood pressure; CI, confidence interval. eGFR, estimated glomerular filtration rate. Time before bedtime, time from bathing-end to bedtime.

model 1: adjusted for age, gender, body mass index, and smoking/drinking status.

model 2: adjusted for age, gender, body mass index, and smoking/drinking status. antihypertensive drug use, diabetes, dyslipidemia, and eGFR.

model 3: adjusted for age, gender, body mass index, and smoking/drinking status. antihypertensive drug use, diabetes, dyslipidemia, eGFR, daytime physical activity, bedtime, and rising time.

Supplemental table 1	Association between	1 covariates and	night- and sleen-time S	SRP
Suppremental table 1.	Association between	i covai lates anu	mgnt- and steep-time .	JDI

Covariates		Night-time SBP					
	Unadjusted β	95% CI	Р	Adjusted β	95% CI	Р	
Age	0.56	0.40, 0.72	< 0.001	0.60	0.43, 0.77	< 0.001	
Gender	4.03	1.76, 6.30	< 0.001	1.02	-1.55, 3.59	0.44	
BMI	0.65	0.28, 1.02	0.001	0.66	0.27, 1.04	0.001	
Current smoker	4.45	-1.07, 9.97	0.11	6.66	1.20, 12.1	0.017	
Alcohol consumption	2.54	-0.65, 5.72	0.12	0.67	-2.69, 4.02	0.70	
Antihypertensive drug use	3.72	1.43, 6.01	0.001	1.78	-0.63, 4.19	0.15	
Diabetes	3.36	-0.75, 7.47	0.11	0.76	-3.25, 4.77	0.71	
Dyslipidemia	-2.03	-4.52, 0.45	0.11	-3.46	-6.00, -0.92	0.008	
eGFR	4.50	1.50, 7.51	0.003	1.41	-1.60, 4.42	0.36	
Bedtime	-0.004	-0.02, 0.01	0.54	0.01	-0.01, 0.02	0.25	
Rising time	0.01	-0.01, 0.02	0.22	0.002	-0.01, 0.02	0.75	
Daytime physical activity	-0.01	-0.02, -0.01	0.001	-0.01	-0.01, 0.003	0.22	
			Sleep-	time SBP			
	Unadjusted β	95% CI	Р	Adjusted β	95% CI	Р	
Age	0.57	0.41, 0.73	< 0.001	0.60	0.42, 0.77	< 0.001	
Gender	4.24	1.95, 6.53	< 0.001	1.08	-1.51, 3.67	0.41	
BMI	0.67	0.3, 1.04	< 0.001	0.67	0.29, 1.05	< 0.001	
Current smoker	4.69	-0.85, 10.23	0.10	6.93	1.46, 12.4	0.013	
Alcohol consumption	2.44	-0.79, 5.67	0.14	0.39	-2.99, 3.78	0.82	
Antihypertensive drug use	3.88	1.57, 6.19	0.001	1.95	-0.48, 4.38	0.12	
Diabetes	3.51	-0.62, 7.64	0.10	0.88	-3.14, 4.90	0.67	
Dyslipidemia	-2.28	-4.78, 0.21	0.07	-3.81	-6.35, -1.26	0.003	
eGFR	5.00	1.97, 8.03	0.001	1.87	-1.16, 4.90	0.23	
Bedtime	-0.01	-0.02, 0.01	0.36	0.01	-0.01, 0.02	0.37	
Rising time	0.009	-0.01, 0.02	0.19	0.003	-0.01, 0.02	0.72	
Daytime physical activity	-0.02	-0.02, -0.01	< 0.001	-0.01	-0.01, 0.003	0.23	

SBP, systolic blood pressure; BMI, body mass index; eGFR, estimated glomerular filtration rate.

Inclusion $(n = 758)$	Exclusion ($n = 369$)	Р
70.9 (7.0)	74.3 (6.8)	< 0.001
364 (48.0%)	166 (45.0%)	0.34
23.2 (3.1)	22.9 (3.0)	0.17
34 (4.5%)	22 (6.0%)	0.28
115 (15.2%)	48 (13.0%)	0.33
333 (43.9%)	170 (46.1%)	0.50
64 (8.4%)	43 (11.7%)	0.085
230 (30.3%)	112 (30.4%)	0.99
131 (17.5%)	76 (20.8%)	0.19
310.2 (104.8)	275.8 (98.8)	< 0.001
134.4 (13.9)	136.6 (14.5)	0.019
79.8 (7.8)	79.4 (7.9)	0.44
115.1 (16.1)	117.2 (16.1)	0.051
67.0 (8.4)	66.6 (8.4)	0.40
114.2 (16.2)	115.7 (16.2)	0.17
66.4 (8.5)	65.8 (8.6)	0.28
14.2 (8.8)	14.1 (9.2)	0.80
	Inclusion $(n = 758)$ 70.9 (7.0) 364 (48.0%) 23.2 (3.1) 34 (4.5%) 115 (15.2%) 333 (43.9%) 64 (8.4%) 230 (30.3%) 131 (17.5%) 310.2 (104.8) 134.4 (13.9) 79.8 (7.8) 115.1 (16.1) 67.0 (8.4) 114.2 (16.2) 66.4 (8.5) 14.2 (8.8)	Inclusion $(n = 758)$ Exclusion $(n = 369)$ 70.9 (7.0)74.3 (6.8)364 (48.0%)166 (45.0%)23.2 (3.1)22.9 (3.0)34 (4.5%)22 (6.0%)115 (15.2%)48 (13.0%)333 (43.9%)170 (46.1%)64 (8.4%)43 (11.7%)230 (30.3%)112 (30.4%)131 (17.5%)76 (20.8%)310.2 (104.8)275.8 (98.8)134.4 (13.9)136.6 (14.5)79.8 (7.8)79.4 (7.9)115.1 (16.1)117.2 (16.1)67.0 (8.4)66.6 (8.4)114.2 (16.2)115.7 (16.2)66.4 (8.5)65.8 (8.6)14.2 (8.8)14.1 (9.2)

Supplemental table 2. Basic and clinical characteristics according to inclusion criteria

Data are expressed as means with standard deviation. BMI, body mass index; eGFR, estimated glomerular filtration rate; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.





