



## Daytime cold exposure and salt intake based on nocturnal urinary sodium excretion: A cross-sectional analysis of the HEIJO-KYO study



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### HIGHLIGHTS

- We measured ambient temperature and nocturnal sodium excretion among 860 elderly.
- Colder daytime ambient temperature was associated with higher salt intake.
- Higher sodium excretion rate was associated with higher nighttime blood pressure.

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### ABSTRACT

Increased cardiovascular incidence in winter is partly explained by higher blood pressure due to cold exposure. Although higher salt intake induced by cold exposure has been reported in mice, the association remains unclear in humans. To investigate the association between salt intake and cold exposure in winter, a cross-sectional study was conducted among 860 elderly subjects (mean  $\pm$  standard deviation: 72.0  $\pm$  7.1 years).

We determined ambient temperature at every 10 min according to indoor temperature measured in the subjects' home, outdoor temperature, and self-administered diary logging time spent outdoors. Salt intake was estimated by nocturnal sodium excretion rate of overnight urine collection. A 1 °C lower daytime ambient temperature was significantly associated with a higher urinary sodium excretion rate by 0.07 mmol/h in the subsequent night independent of age, sex, body weight, alcohol intake, calcium channel blocker use, diabetes, household income, estimated glomerular filtration rate, daytime physical activity ( $p = 0.02$ ). After further adjustment for outdoor temperature and day length, the lowest tertile groups of ambient daytime temperature (10.1  $\pm$  2.3 °C) showed the nocturnal urinary sodium excretion rate was higher by 14.2% (7.62 vs. 6.54 mmol/h) compared with the highest tertile group (19.3  $\pm$  1.8 °C). Higher sodium excretion rate was associated with higher nighttime ambulatory blood pressure ( $p < 0.01$ ) and its lower nocturnal dipping ( $p < 0.01$ ). Significant association between higher salt intake and daytime cold exposure partly explain the mechanism of higher blood pressure in winter, and suggest that a reduction of cold exposure might be effective to decrease salt intake.

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### 1. Introduction

Higher mortality in winter than other seasons is worldwide phenomenon [1–4]. Increased mortality from ischemic heart diseases and stroke in winter [5–7] is partly explained by a higher blood pressure (BP) due to cold exposure [8,9].

As an index of cold exposure, outdoor temperature is convenient because it is usually available from meteorological office. However, it may diverse from the really-exposed temperature, because it poorly correlate with indoor temperature especially in cold climate [10]. Ambient temperatures defined as indoor temperature while the participants

stayed at home and outdoor temperature while the participants were out of their home showed the strongest association with ambulatory BP than outdoor temperature and indoor temperature [10,11].

Higher salt intake estimated using 24 h urinary sodium excretion is associated with higher BP from within-population and cross-population analyses in the INTERSALT study [12,13]. Systematic review from randomized controlled studies demonstrated effectiveness of a low-salt diet in decreasing BP [14]. Meta-analysis of prospective cohort studies including over 100,000 participants showed that higher salt intake is significantly associated with greater incidence of stroke and total cardiovascular disease (CVD) [15].

Higher salt intake induced by cold exposure was reported in mice [16,17], and it may also explain the higher BP due to cold exposure. However, the influence of cold exposure on salt intake in human has

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not reported. The association between ambient temperature and salt intake may provide important evidence to develop a suitable environment for reduction of salt intake to prevent CVD.

To quantify the association between ambient temperature and salt intake, we conducted the cross-sectional study among 880 elderly participants. We estimated salt intake from the nocturnal urinary sodium excretion because of the high correlation between 24 h and overnight sodium excretion in an Asian population [18,19].

## 2. Methods

### 2.1. Participants

From September to April in 2010, 2011, 2012, and 2013, we recruited 880 home-dwelling males and females, aged 60 years or more for HEIJO-KYO (Housing Environments and Health Investigation among Japanese Older People in Nara, Kansai Region), a prospective community-based cohort study. The study protocol has been previously described [20]. Of all 880 participants, we excluded 20 participants with missing of indoor temperature or overnight urine collection during the colder season (October–April), 860 were remained for analysis (Fig. 1). All participants provided a written informed consent and the study protocol was approved by the Nara Medical University Ethics Review Board.

### 2.2. Study protocol

The participants' characteristics, including age, gender, smoking, household income, and drinking habits, and medication use were obtained using a standardized questionnaire. After the waist circumference at the level of the umbilicus in the standing position, an overnight fasting venous sample was obtained. At noon, we started measurements of indoor temperature, ambulatory BP and actigraphy for 48 h. The participants were instructed to collect overnight urine at the second night. We revisited each participant at home to retrieve instruments and collect their diaries logging bedtime, rising time, duration in bedroom, and time spent outdoors.

### 2.3. Nocturnal urinary sodium excretion

After discarding the last void at bedtime, participants were asked to collect urine until the first morning void. The sodium concentration was measured using an ion-selective electrode method in a commercial laboratory (SRL Co. Inc., Tokyo, Japan). The total nocturnal urinary sodium excretion (mmol) and nocturnal urinary sodium excretion rate (mmol/h) were calculated from the total urine volume, the sodium concentration, and the duration of urine collection.

### 2.4. Daytime ambient temperature

Indoor temperature was measured in the living room and bedroom 60 cm above the floor. Bed temperature was measured at center of the bed 50 cm from the headboard. These temperatures were measured at 10 min intervals using a Thermochron iButtons (DS1922L; Maxim Integrated, Dallas, TX, USA) with an accuracy of  $\pm 0.5$  °C from  $-10$  °C to  $+65$  °C and a 0.0624 °C resolution. Outdoor temperature was also measured at 10 min intervals and was provided by the local meteorological office in Nara (latitude, 34° N). We defined the ambient temperature as indoor temperature (temperature in the living room or bedroom) while the participants were at living room or bedroom, and the outdoor temperature while the participants were out of their homes. The at-home and out-of-home periods were determined according to the participants' self-reported diaries logging the time spent outdoors and the time spent at living room and bedroom. The mean ambient temperature during the last daytime (rising–bedtime) before the nocturnal urine collection was calculated.

### 2.5. Ambulatory BP and physical activity

Physical activity was determined at 1 min epochs using an actigraph (Actiwatch 2; Respironics Inc., Murrysville, PA, USA) worn on the non-dominant arm. Ambulatory BP was measured using a validated device (TM-2430; A&D Co. Ltd., Tokyo, Japan) on the non-dominant arm at 30 min intervals. We calculated the mean of two days for the daytime systolic BP (blood pressure), nighttime systolic BP, and dipping [(daytime systolic BP – nighttime systolic BP) / (daytime systolic BP)  $\times 100$ ].

### 2.6. Other measurements

Venous blood samples were analyzed using a standard clinical chemical analysis to determine the concentration of creatinine, glycated hemoglobin (HbA1c), and fasting plasma glucose. Diabetes was defined based on medical history, the current administration of anti-diabetic treatment, or fasting plasma glucose of at least 126 mg/dl and HbA1c of at least 6.5% (National Glycohemoglobin Standardization Program value). The estimated glomerular filtration rate (eGFR) was calculated by the Japanese Society of Nephrology—Chronic Kidney Disease Practice Guide formula:  $eGFR \text{ (ml/min/1.73 m}^2\text{)} = 194 \times [\text{serum creatinine (mg/dl)}]^{-1.094} \times [\text{age (years)}]^{-0.287}$ . The result was multiplied by a correction factor of 0.739 for women. Data of the day length from sun rise to sunset in Nara on the measurement days were obtained from National astronomical Observatory of Japan. The habitual intake of soup and fruit were asked using self-administered questionnaire as follows: “How many cups of Miso soup and other kind of soup do you have in a week?”, “How often do you take fruit in a week?”, and “Please select your quantity of your usual fruit intake from 1) small size, 2) standard portion size, and 3) large portion size”. The product of the fruit intake frequency in a week and the size (1 to 3) was calculated.

### 2.7. Statistical analysis

For continuous variables with a normal distribution, the mean  $\pm$  standard deviation was reported. For variables not distributed normally, the median and interquartile ranges were reported. The associations of variables with the nocturnal urinary sodium excretion rate were assessed using univariate and multivariate linear regression models. Multivariate adjusted mean values among tertile groups of daytime ambient temperature were compared using ANCOVA (analysis of covariance).

We assessed associations of nocturnal urinary sodium excretion rate with daytime ambient temperature as continuous variables (Table 2) and tertile groups (Table 3).

We explored the variables as potential confounders with marginal to significant association ( $p < 0.20$ ) in the univariate model. In the

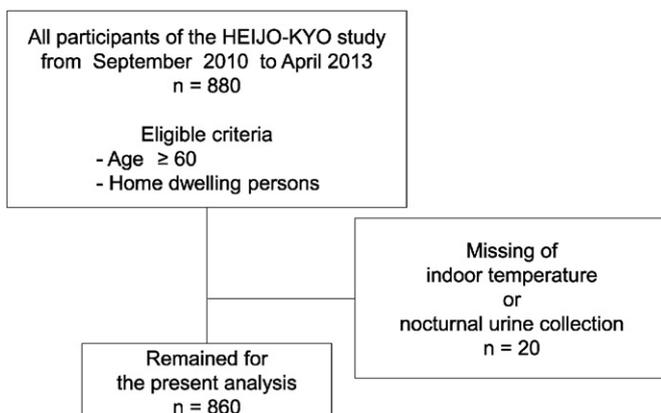


Fig. 1. Flow chart of participants.

Multivariate models, we simultaneously adjusted for potential confounders. To detect severe multicollinearity we calculated the variance inflation factors. All *p*-values were two-sided, and those <0.05 were considered statistically significant. All statistical analyses were performed using the SPSS ver. 21.0 software (SPSS, Chicago, IL, USA).

### 3. Results

The mean age among 860 participants was  $72.0 \pm 7.1$  (mean  $\pm$  SD) and 49.2% were males. Tertile groups of ambient temperature were T1 ( $10.1 \pm 2.3$  °C), T2 ( $15.0 \pm 1.1$  °C), and T3 ( $19.3 \pm 1.8$  °C), respectively. Daytime ambient temperature was significantly associated with nighttime ambient temperature, bed temperature at night, daytime outdoor temperature, and nighttime outdoor temperature. We did not find a significant difference in household income and education status across the tertile groups (Table 1).

In the univariate linear regression analysis, the daytime ambient temperature was significantly associated with the nocturnal urinary sodium excretion rate ( $\beta = -0.07$ , 95% CI:  $-0.13$  to  $-0.01$ ,  $p = 0.03$ ). On the other hand, nocturnal urinary sodium excretion rate did not show significant association with daytime outdoor temperature ( $p = 0.44$ ), nighttime outdoor temperature ( $p = 0.36$ ), nighttime ambient temperature ( $p = 0.30$ ), and bed temperature in nighttime ( $p = 0.30$ ).

In the multivariate linear regression model, the ambient temperature showed a significant inverse association with the nocturnal urinary sodium excretion rate even after adjusting for potential confounders such as age, male, body weight, alcohol intake, CCB (calcium channel blocker), and diuretics use, household income, and daytime physical

activity ( $\beta = -0.07$ , 95% CI:  $-0.13$  to  $-0.01$ ,  $p = 0.02$ ; Table 2). In this multivariate model, we did not detect severe multicollinearity with variance inflation factors of 10 and above.

Similarly, categorical analysis using tertile groups of daytime ambient temperature showed significant and inverse association with nocturnal urinary sodium excretion rate [T1: 7.49 mmol/h (95% CI: 7.06–7.92); T2: 7.01 (6.58–7.44); and T3: 6.65 (6.22–7.08);  $p$  for trend < 0.01], and total nocturnal urinary sodium excretion [T1: 62.4 mmol (58.7–66.0); T2: 58.5 (54.9–62.2); and T3: 54.3 (50.7–58.0);  $p$  for trend < 0.01; Fig. 2].

In Table 3, a significant association between tertile groups of daytime ambient temperature and nocturnal urinary sodium excretion rate stayed significant even after adjustment for all potential confounders in univariate models ( $p < 0.2$ ) plus day length (model 2,  $p = 0.006$ ). After further adjustment for outdoor temperature, a lower daytime ambient temperature by 9.2 °C (T1: 10.1 °C vs. T3: 19.3 °C) was associated with a higher sodium excretion rate by 14.2% (7.62 vs. 6.54 mmol/h; model 3). Adjustment for pressure natriuresis induced by nighttime systolic BP during urine collection did not attenuate the significant association ( $p = 0.005$ , model 4).

In stratified analysis by age groups, gender, and body weight groups, we found consistently inverse association between daytime ambient temperature and nocturnal sodium excretion rate. The higher tertile group of daytime ambient temperature is significantly associated with lower sodium excretion rate ( $p = 0.048$ ) in younger group ( $\leq 72$  years) and elder group ( $> 72$  years;  $p = 0.042$ ). As for gender, the lower ambient temperature group ( $\leq$  median: 15.07 °C) was significantly associated with higher sodium excretion ( $p = 0.025$ ) among female,

**Table 1**  
Characteristic of 860 participants by tertile groups of daytime ambient temperature.

Variables	Daytime ambient temperature <sup>a</sup> (°C)			<i>p</i> for trend
	T1 (<13.1)	T2 (13.1–16.9)	T3 ( $\geq 16.9$ )	
	n = 288	n = 287	n = 285	
<i>Environment</i>				
Ambient temperature <sup>a</sup> , mean (SD)				
Daytime	10.1 (2.3)	15.0 (1.1)	19.3 (1.8)	
Nighttime	9.0 (3.4)	12.5 (3.1)	16.4 (3.8)	<0.01
Bed temperature at night, mean (SD)	29.4 (5.2)	29.9 (4.4)	30.4 (3.8)	0.02
Outdoor temperature, °C, mean (SD)				
Daytime	5.4 (2.7)	8.7 (3.9)	13.1 (4.9)	<0.01
Nighttime	1.9 (3.1)	4.8 (3.8)	8.9 (4.9)	<0.01
Day length, min, mean (SD)	656.6 (39.6)	666.2 (46.8)	677.8 (50.6)	<0.01
<i>Basic characteristics</i>				
Age, mean (SD)	71.9 (7.4)	71.7 (6.8)	72.7 (7.1)	0.17
Male, n (%)	147 (51.0)	141 (49.1)	132 (46.3)	0.24
Body weight, kg, mean (SD)	57.2 (10.8)	57.6 (10.7)	57.7 (10.2)	0.59
Current smoker, n (%)	20 (6.9)	13 (4.5)	11 (3.9)	0.06
Alcohol intake ( $\geq 30$ g/day)	46 (16.0)	37 (12.9)	33 (11.6)	0.07
<i>Clinical characteristics</i>				
Anti-hypertensive use, n (%)	117 (40.6)	136 (47.4)	125 (43.9)	0.45
ACEI/ARBs	74 (25.7)	90 (31.4)	81 (28.4)	0.48
CCB	75 (26.0)	94 (32.8)	85 (29.8)	0.31
Diuretics <sup>d</sup>	20 (6.9)	16 (5.6)	18 (6.3)	0.74
Diabetes, n (%)	32 (11.1)	34 (11.8)	36 (12.6)	0.52
eGFR, ml/min/1.73 m <sup>2</sup> , mean (SD)	73.1 (15.3)	73.4 (14.9)	70.1 (14.4)	0.02
<i>Socio-economic status</i>				
Household income <sup>b</sup> , n (%)	114 (39.6)	115 (40.1)	116 (40.7)	0.81
Education ( $\geq 13$ years), n (%)	70 (24.3)	74 (25.8)	68 (23.9)	1.00
<i>Other covariates</i>				
Daytime physical activity, counts/min, mean (SD)	319.9 (117.8)	312.8 (106.8)	284.2 (110.3)	<0.01
Duration spent outdoor in daytime, min, median (IQR)	179 (70,346)	182 (76,354)	201 (81,335)	0.57 <sup>c</sup>

T1–T3, tertiles of daytime ambient temperature; SD, standard deviation; IQR, inter-quartile range; ACE, angiotensin converting enzyme inhibitor; ARBs, angiotensin receptor blockers; CCB, calcium channel blocker; and eGFR, estimated glomerular filtration rate.

<sup>a</sup> Ambient temperature is indoor temperature during at-home and outdoor temperature during out-of home period.

<sup>b</sup>  $\geq 4$  million yen/year.

<sup>c</sup> *p*-Value was estimated after log-transformation.

<sup>d</sup> Diuretics include thiazide, loop diuretics, and spironolactone.

**Table 2**  
Association of variables with nocturnal urinary sodium excretion rate.

Variables	Univariate model		Multivariate model <sup>b</sup>		Partial R <sup>2</sup>
	$\beta^a$ (95% CI)	p-Value	Adjusted $\beta$ (95% CI)	p-Value	
<i>Environment</i>					
Ambient temperature (per 1 °C)					
Daytime	−0.07 (−0.13, −0.01)	0.03	−0.07 (−0.13, −0.01)	0.02	0.006
Nighttime	−0.03 (−0.08, 0.03)	0.30			
Bed temperature at night (per 1 °C)	0.03 (−0.03, 0.08)	0.30			
Outdoor temperature (per 1 °C)					
Daytime	−0.02 (−0.07, 0.03)	0.44			
Nighttime	−0.02 (−0.07, 0.03)	0.36			
Day length (per 30 min)	0.02 (−0.14, 0.18)	0.82			
<i>Basic characteristics</i>					
Age (per 1 year)	0.05 (0.02, 0.09)	<0.01	0.08 (0.04, 0.12)	<0.01	0.016
Male	1.88 (1.39, 2.36)	<0.01	0.96 (0.33, 1.58)	<0.01	0.010
Body weight (per 1 kg)	0.09 (0.07, 0.12)	<0.01	0.08 (0.05, 0.11)	<0.01	0.029
Current smoker	0.63 (−0.51, 1.76)	0.28			
Alcohol intake ( $\geq 30$ g/day)	1.19 (0.47, 1.91)	<0.01	0.10 (−0.65, 0.85)	0.80	0.00007
<i>Clinical characteristics</i>					
Anti-hypertensive use	0.19 (−0.32, 0.69)	0.47			
ACEI/ARB	−0.10 (−0.65, 0.45)	0.72			
CCB	0.78 (0.24, 1.33)	<0.01	0.27 (−0.27, 0.82)	0.32	0.001
Diuretics	−0.13 (−1.17, 0.91)	0.81			
Diabetes	0.91 (0.14, 1.68)	0.02	0.53 (−0.21, 1.28)	0.16	0.002
eGFR, per 10 ml/min/1.73 m <sup>2</sup>	−0.13 (−0.29, 0.04)	0.13	0.03 (−0.13, 0.20)	0.68	0.0002
<i>Socio-economic status</i>					
Household income, $\geq 4$ million yen/year	−0.45 (−0.97, 0.08)	0.09	−0.37 (−0.88, 0.14)	0.16	0.002
Education, $\geq 13$ years	−0.19 (−0.77, 0.38)	0.51			
<i>Life style</i>					
Daytime PA (per 100 counts/min)	−0.16 (−0.38, 0.05)	0.13	0.17 (−0.05, 0.39)	0.14	0.002
Duration spent outdoor (per 1 min) <sup>c</sup>	0.016 (−0.11, 0.14)	0.81			

ACE, angiotensin converting enzyme inhibitor; ARBs, angiotensin receptor blockers; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate; and PA, physical activity.

<sup>a</sup>  $\beta$  coefficient show the difference in nocturnal urinary sodium excretion rate (mmol/h) associated with 1 unit change of each covariates.

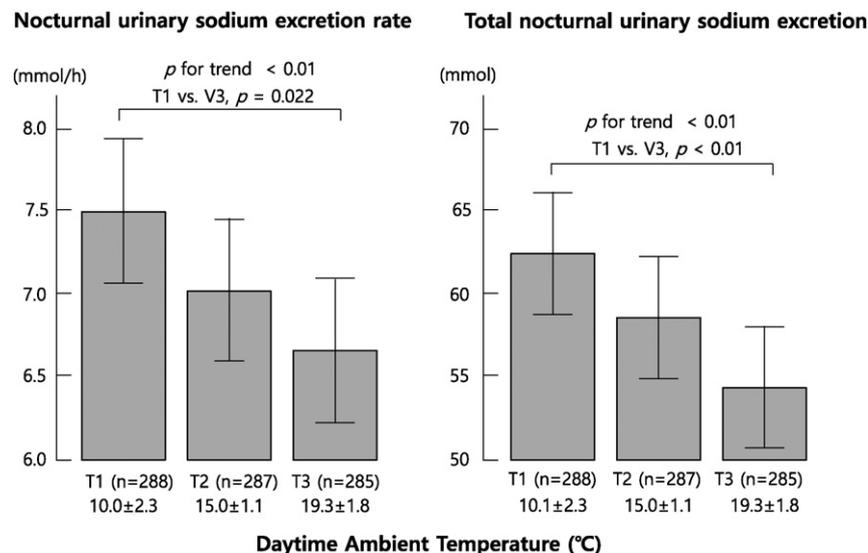
<sup>b</sup> Multivariate model simultaneously include all covariate with  $p < 0.2$  in univariate model.

<sup>c</sup> Included after log-transformation due to its skewed distribution.

and the lower tertile group of daytime ambient temperature was significantly associated with higher sodium excretion rate among male ( $p = 0.019$ ). As for obesity, the lower ambient temperature group ( $\leq 15.07$  °C) was significantly associated with higher sodium excretion ( $p = 0.028$ ) among the low weight group ( $\leq$ median: 57 kg), and the lower tertile group of daytime ambient temperature was associated with higher sodium excretion rate ( $p = 0.019$ ) among the higher weight

group ( $> 57$  kg). All these associations were independent of other potential confounders such as independent of alcohol intake, CCB administration, diabetes, eGFR, income, daytime physical activity, outdoor temperature, and day length.

Of 860, 789 participants (91.7%) answered the questions about soup and fruit intake. The mean soup intake was  $6.0 \pm 3.6$  (SD) cups in a week, and the fruit intake index was  $11.45 \pm 7.7$  with almost normal



**Fig. 2.** Nocturnal Urinary Sodium Excretion by Daytime Ambient Temperature. Error bars show 95% confidence intervals. Each column demonstrates mean values nocturnal urinary sodium excretion rate (mmol/h), and total nocturnal urinary sodium excretion (mmol) by tertile groups of daytime ambulatory temperature.

**Table 3**  
Adjusted nocturnal urinary sodium excretion rate by tertiles of daytime ambient temperature.

Models	Nocturnal urinary sodium excretion rate (95% CI)			p-Value trend	p-Value T1 vs. T3*
	T1 (10.1 ± 2.3 °C) n = 288	T2 (15.0 ± 1.1 °C) n = 287	T3 (19.3 ± 1.8 °C) n = 285		
Model 1 <sup>a</sup>	7.51 (7.09, 7.92)	6.96 (6.54, 7.37)	6.66 (6.25, 7.08)	0.005	0.016
Model 2 <sup>b</sup> (day length adjusted)	7.51 (7.09, 7.92)	6.96 (6.54, 7.37)	6.67 (6.25, 7.10)	0.006	0.019
Model 3 <sup>c</sup> (outdoor temperature adjusted)	7.62 (7.14, 8.10)	6.97 (6.55, 7.38)	6.54 (6.05, 7.03)	0.006	0.019
Model 4 <sup>d</sup> (nighttime systolic BP adjusted)	7.59 (7.12, 8.05)	7.00 (6.60, 7.41)	6.52 (6.04, 7.00)	0.005	0.017

T, tertile; BP, blood pressure; 95% CI, 95% confidence interval; CCB, calcium channel blocker; and eGFR, estimated glomerular filtration rate.

<sup>a</sup> Adjusted for all variables with  $p < 0.20$  in univariate regression model (Table 2) such as age, gender, body weight, alcohol intake, CCB administration, diabetes, eGFR, and household income, daytime physical activity.

<sup>b</sup> Adjusted for covariates in model 1 plus day length (per 30 min).

<sup>c</sup> Adjusted for covariates in model 2 plus outdoor temperature.

<sup>d</sup> Adjusted for covariates in model 3 plus nighttime systolic blood pressure.

\* After Bonferroni correction for multiple comparison.

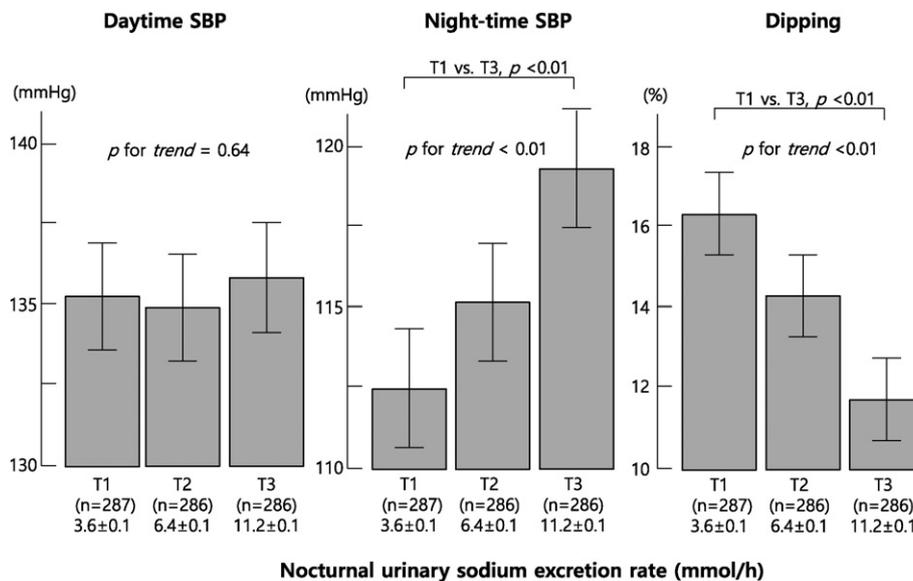
distribution. After further adjustment for hot soup intake and fruit intake in the multivariate model in the Table 2, we found consistently significant association between daytime ambient temperature and nocturnal sodium excretion rate ( $p = 0.039$ ).

Fig. 3 shows mean values of daytime systolic BP, nighttime systolic BP, and dipping by the tertile groups of the nocturnal urinary sodium excretion rate (T1:  $3.6 \pm 0.1$ , T2:  $6.4 \pm 0.1$ , and T3:  $11.2 \pm 0.1$  mmol/h) adjusted for age, gender, abdominal circumference, current smoking status, alcohol intake, anti-hypertensive medication, and daytime physical activity. Nocturnal urinary sodium excretion rate was significantly associated with nighttime systolic BP ( $p$  for trend  $< 0.01$ ) and dipping ( $p$  for trend  $< 0.01$ ). The nighttime systolic BP in the highest tertile group of the nocturnal sodium excretion rate was significantly higher than in the lowest tertile group (119.2 vs. 112.5 mm Hg,  $p < 0.001$ ). The dipping in the lowest tertile group of sodium excretion rate was significantly higher than that in the highest tertile group (16.2% vs. 11.7%,  $p < 0.01$ ). In contrast, the nocturnal urinary sodium excretion rate did not show a significant association with daytime systolic BP ( $p$  for trend = 0.64). We did not find significant association between daytime ambient temperature and nighttime systolic BP ( $p = 0.22$ ).

#### 4. Discussion

A higher salt intake is shown to be associated with a lower ambient temperature as evidenced by the higher nocturnal urinary sodium excretion rates observed. These higher nocturnal urinary sodium excretion rates were significantly associated with the lower ambient temperature in the previous day independent of potential confounders such as age, gender, body weight, alcohol intake, CCB administration, diabetes, household income, eGFR, and daytime physical activity ( $\beta = -0.07$ , 95% CI:  $-0.13$  to  $-0.01$ ,  $p = 0.02$ ).

Although Hata et al. showed higher sodium excretion rates in winter (monthly outdoor temperature: 4.8 °C) than in summer (29.1 °C) among 14 normotensive and 20 hypertensive men [21], the association between temperatures which each participants exposed and urinary sodium excretion have not yet been investigated. The findings from the present study are concordant with the experiments using rats [22] and mice [17]. Dejima et al. showed that cold exposure (7 °C–9 °C) for 6 h caused a higher salt intake during the 9 h following cold exposure [16], and the increased salt intake was accompanied by a higher concentration of noradrenaline in the kidney and plasma renin activity during



**Fig. 3.** Nocturnal urinary sodium excretion rate and ambulatory blood pressure. Error bars show 95% confidence intervals. Each column demonstrates mean values of daytime BP, nighttime BP and Dipping by tertile groups of nocturnal sodium excretion rate. Mean values were adjusted for age, gender, abdominal circumference, current smoking, alcohol intake, antihypertensive medication, and daytime physical activity.  $p$ -Values for the mean difference between T1 and T3 were estimated by Bonferroni correction.

cold exposure compared with the control group [17]. The mechanism of cold-induced salt intake is explained by the activation of the renin-angiotensin system (RAS) by noradrenaline [23] and the increase of salt intake by RAS [24]. In the present study, cold exposure at during daytime cause higher sympathetic activity and RAS activation, and may cause higher salt appetite during daytime based on previous studies. In contrast, influence of cold exposure derived from indoor temperature attenuates during bed [25]. The higher salt intake during daytime may cause higher nocturnal sodium excretion at night.

Pressure natriuresis may increase nocturnal urinary excretion [26–28]. In the present study, we found significant association between ambient temperature and nocturnal urinary sodium excretion rate even after adjusting for ambulatory BP during urine collection (model 4 in Table 3).

The strengths of the current study include the measurement of ambulatory temperature and the large-scale sample size. The ambient temperature in the present analysis was estimated from both outdoor and indoor temperatures because it allowed for a better prediction of morning BP surge and daytime ambulatory BP than crude indoor and outdoor temperatures [10,11]. Owing to the large-scale sample size, we could assess the independent association of ambient temperature and salt intake independent of a variety of potential confounders.

However, the present study has some limitations. First, we estimated salt intake through nocturnal urine collection, which is inferior to 24 h urine collection, because it provides a higher ratio of intra- to inter-individual variance than the 24-hour urine collection (2.12 vs. 1.48). [18] However, the association between the daytime ambient temperature and the subsequent nocturnal urinary sodium excretion may be acceptable. In addition, sodium excretion in the 24 h urine collection and overnight urine collection showed a high correlation among the Asian population (correlation coefficient: 0.86–0.92). [18,19] The second limitation of the present study is the lack of information regarding sodium loss from sweat. To address this, we assessed the physical activity measured using the actigraph. Third limitation lies in the way to estimate ambient temperature. We use outdoor temperature as exposed temperature while the participants go out of home. Therefore, we may have overestimated cold exposure when participants left their homes but remained in an indoor environment. Fourth, we lack information about the intake of total energy and other nutrition in the present study. Finally we recruited participants with cooperation of local-resident associations and elderly-resident clubs in six areas of Nara prefecture with non-random sampling (participation rate unclear), and the generalizability of the study may be limited. However, the proportion of study participants using anti-hypertensive and anti-hyperglycemic medications was similar to that of a large-scale national survey among 3499 elderly ( $\geq 60$  years) individuals conducted in 2010 (anti-hypertensive medication use: 40.3%; anti-diabetic treatment: 12.0%) [29].

The clinical implications of the present study can be interpreted through previous evidence regarding the influence of salt intake on BP and incidence of CVD. High salt intake can cause cardiovascular diseases (CVDs) via hypertension. Concordant with a previous study [28], we found a significant association between sodium excretion and nighttime BP. Nighttime BP has been shown to provide a superior prediction for CVD incidence compared with daytime systolic BP [30]. Salt-induced hypertension is caused by a higher extracellular volume [31], the cellular hypertrophy of arterial smooth muscle, cardiac myocytes [32], and endothelial dysfunction due to decreased endothelial nitric oxide [33, 34]. Furthermore, epidemiologic studies have shown a direct harmful effect of salt intake on stroke, left ventricular hypertrophy [35,36], the progression of renal disease, and proteinuria [37,38] independent of BP. The present study suggests that these harmful effects of salt intake may be associated with ambient temperature. A large scale prospective study showed that a 100 mmol increase in the 24 h sodium excretion is associated with a higher hazard ratio for the mortality of coronary heart disease, CVD, and all-cause mortality by 51%, 45%, and 26%, respectively [39]. We found that the nocturnal urinary sodium excretion rate was

1.08 mmol/h lower when the ambient temperature was 9.3 °C higher (model 3 in Table 3). Based on the night-to-day ratio of sodium excretion (0.79) [28] and the mean duration of urine collection in the present study ( $498 \pm 82.1$  min), 1.08 mmol/h is equivalent to approximately 30.4 mmol sodium excretion in 24 h. This meant that cold exposure by 9.3 °C is associated with a 15.5%, 13.7%, and 7.9% higher mortalities by coronary heart disease, CVD, and all-cause mortality, respectively.

In summary, we found significant cross-sectional association between lower ambient temperature and higher salt intake independent of potential confounders from community-based 860 elderly. Although our findings suggest that a reduction of cold exposure may be effective to decrease salt intake, further well-designed prospective randomized controlled studies are required.

#### Author contributions

K.S. and K.O. designed the study and conducted data collection. N.T. contributed to methods of measurement. N.K. contributed to interpretation of data. K.S. analyzed the data and prepared draft of this study and all authors reviewed it.

#### Conflict of interest

The authors have no conflicts of interest to declare.

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