Hypertension Research (2017) 40, 405–410

www.nature.com/hr

ORIGINAL ARTICLE

Relationship between 24-h urine sodium/potassium ratio and central aortic systolic blood pressure in hypertensive patients

Moo-Yong Rhee[1,2], Sung-Joon Shin[3], Namyi Gu[2,4], Deuk-Young Nah[5], Byong-Kyu Kim[5], Kyung-Soon Hong[6], Eun-Joo Cho[7], Ki-Chul Sung[8], Sim-Yeol Lee[9] and Kwang-Il Kim[10]

Studies evaluating the relationship between measured 24-h urine sodium (24HUNa), potassium (24HUK) and aortic blood pressure (BP) are rare, and no such study has been performed with an Asian population. We evaluated the relationship between 24HUNa, 24HUK, casual BP, 24-h ambulatory BP and aortic BP by analyzing data from 524 participants with valid 24-h urine collection, 24-h ambulatory BP and central BP measurements (mean age 48.1 ± 9.8 years, 193 men). Hypertension was defined as a 24-h ambulatory BP ⩾ 130/80 mm Hg or current treatment for hypertension ($n = 219$). The participants with hypertension and high 24HUNa (mean 210.5 ± 52.0 mmol per day, range 151.0–432.0) showed higher 24-h systolic ($P = 0.037$) and diastolic BP ($P = 0.037$) and aortic systolic BP (AoSBP, $P = 0.038$) than the participants with hypertension and low 24HUNa (mean 115.7 ± 25.0 mmol per day, range 45.6–150.0), adjusted for confounders. The participants with hypertension and a high ratio of 24HUNa and 24HUK (24HUNa/24HUK, mean 4.03 ± 1.00, range 2.93–7.96) had higher AoSBP than the participants with hypertension and a low 24HUNa/24HUK ratio (mean 2.13 ± 0.54, range 0.53–2.91), adjusted for confounders ($P = 0.026$). The participants with hypertension demonstrated a significant linear relationship between AoSBP and 24HUNa/24HUK ratio that was independent of 24HUNa, according to the multiple regression analysis ($P = 0.047$). In hypertensive patients, 24HUNa/24HUK was positively and more strongly related to AoSBP compared with 24HUNa alone. The result indicates that high sodium and low potassium intake may increase the subsequent risk of cardiovascular disease by elevating AoSBP.
Hypertension Research (2017) **40,** 405–410; doi:10.1038/hr.2016.161; published online 24 November 2016

Keywords: blood pressure; potassium; sodium; urine

INTRODUCTION

Various studies have demonstrated that excessive sodium intake is associated with elevated blood pressure (BP) levels and an increased risk of cardiovascular events.[1–3] Many trials and epidemiological studies have shown that BP and cardiovascular events decrease with reduced sodium intake.[4]

Traditionally, brachial BP has been used as a surrogate marker for BP-related cardiovascular events. However, recent studies have shown that central BP has better predictive power for future cardiovascular events compared with brachial BP.[5] The early return of the reflected wave during the ventricular ejection period augments central systolic BP (SBP). Among the factors associated with the augmentation of central SBP, an increase in arterial stiffness increases aortic pulse wave velocity, with early return of the reflected wave from peripheral arteries.[6] Studies have shown that high sodium intake is associated with elevated aortic pulse wave velocity,[7–9] suggesting that high sodium intake elevates central SBP.

Several studies have shown the association between urinary salt excretion and central hemodynamics.[10–12] However, the relationship between measured (not estimated) 24-h urine sodium (24HUNa), potassium (24HUK) and central hemodynamics is unknown in Asian populations.

We evaluated the association between 24-h urinary salt excretion and central hemodynamic in the general population.

METHODS

Study population

Random samples of adults from Goyang city, with an approximate adult population of 600 000, and Paju city, with an approximate adult population of 240 000, were selected by list-assisted random digit dialing, and both listed and

[1]Cardiovascular Center, Dongguk University Ilsan Hospital, Gyeonggi-do, Republic of Korea; [2]Clinical Trial Center, Dongguk University Ilsan Hospital, Gyeonggi-do, Republic of Korea; [3]Division of Nephrology, Department of Internal Medicine, Dongguk University Ilsan Hospital, Gyeonggi-do, Republic of Korea; [4]Department of Clinical Pharmacology and Therapeutics, Dongguk University Ilsan Hospital, Gyeonggi-do, Republic of Korea; [5]Cardiovascular Center, Dongguk University Gyeongju Hospital, Gyeongbuk, Republic of Korea; [6]Department of Cardiology, Hallym University College of Medicine, Gangwon-do, Republic of Korea; [7]Department of Cardiology, Catholic University of Korea College of Medicine, Seoul, Republic of Korea; [8]Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [9]Department of Home Economics Education, Dongguk University, Seoul, Republic of Korea and [10]Department of Internal Medicine, Seoul National University Bundang Hospital, Gyeonggi-do, Republic of Korea
Correspondence: Dr M-Y Rhee, Cardiovascular Center, Dongguk University Ilsan Hospital, 27 Dongguk-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do 10326, Republic of Korea.
E-mail: mooyong_rhee@dumc.or.kr
Received 19 July 2016; revised 5 October 2016; accepted 9 October 2016; published online 24 November 2016

unlisted telephone households were included. The study was performed in 2011 in Goyang city and in 2012 in Paju city. The design of the study population selection and enrollment has been described in detail elsewhere.[13] We used the same study design in both cities. Adults between 20 and 65 years of age within the selected households were chosen through telephone interviews.

Study protocol

The participants visited the clinical trial center before 0830 hours. Urine collection began after voiding and discarding the first urine sample between 0900 and 0930 hours. All urine voided during the next 24 h was collected. The 24-h ambulatory BP was measured in parallel. The next day, the participants visited the clinical trial center before 0900 hours. The participants were asked to void the last urine sample 24 h after the first voiding. The last voided urine sample was added to the urine collection bag. After completing the 24-h urine collection, casual BP and central BP were measured. The concentrations of sodium and potassium were measured using an ion-selective electrode method (Modular DPE chemistry; Roche Diagnostics, Mannheim, Baden-Württemberg, Germany). Creatinine was measured using the Jaffe reaction (Kinetic colorimetric assay; Roche Diagnostics). For biochemical analysis, a blood sample was obtained after at least 8 h of overnight fasting. The study protocol was reviewed and approved by the Institutional Review Board of Dongguk University Ilsan Hospital. Each participant provided written informed consent.

Completeness of urine collection

The validity of the 24-h urine collection was assessed using a combination of self-reported urine loss and the 24-h urine creatinine-based determination, assuming that the urinary creatinine excretion rate was constant. If the self-reported urine sample loss was more than 100 ml, if the loss occurred more than once, or if either the urinary creatinine level was <6 mmol per day with a total urine volume of <1000 ml per day or the urinary creatinine level was <5 mmol per day, then the collected urine sample was considered to be insufficient for a 24-h collection.[14]

BP measurement

Casual BP levels were measured from both arms (with the participant in a sitting position) using a validated semiautomatic device (Watch BP Office; Microlife AG, Widnau, Switzerland) by a trained nurse.[15] BP was measured three times at 1-min intervals after 5 min of rest, and three SBP and diastolic BP (DBP) measurements from each arm were averaged. Ambulatory BP was measured for 24 h in 30-min intervals (Mobil-O-Graph; I.E.M. GmbH, Stolberg, Germany) in conjunction with the 24-h urine collection.[16] More than 70% of the expected measurements, 14 measurements during the day and 7 measurements at night, were considered to be valid measurements.[17] Hypertension was defined as an averaged 24-h SBP $\geqslant 130$ mm Hg, an averaged 24-h DBP $\geqslant 80$ mm Hg or the current use of antihypertensive medication with a previous diagnosis of hypertension.[18]

Aortic BP was measured using a validated non-invasive device (Sphygmocor; AtCor Medical, Sydney, Australia).[19,20] The participants rested for 5 min in a sitting position before the measurements were performed. Aortic BP was calculated from pressure waveforms obtained by applanation tonometry from the radial artery at the wrist and brachial BP, which was taken before the pressure waveform recordings using the generalized transfer function. A valid measurement was an operator quality index $>80\%$. Aortic pulse pressure was calculated as the difference between the aortic systolic and diastolic BP (AoSBP and AoDBP, respectively). Aortic augmentation pressure is the difference between the AoSBP and the inflection point at the end of the first systolic shoulder. The augmentation index is the ratio of the aortic augmentation pressure to the aortic pulse pressure. Given that the augmentation index is influenced by patient heart rate, an augmentation index normalized for a heart rate of 75 beats per minute (AI75) was derived.

Statistical analysis

The study population was divided into high 24HUNa ($\geqslant$151 mmol/24-h, mean 210.5 ± 52.0 mmol per day, range 151.0–432.0 mmol per day) and low 24HUNa ($<$151 mmol/24-h, mean 115.7 ± 25.0 mmol per day, range 45.6–150.0 mmol per day), according to the level of 24HUNa excretion, and high 24HUNa/24HUK ($\geqslant$2.93, mean 4.03 ± 1.00, range 2.93–7.96) and low 24HUNa/24HUK ($<$2.93, mean 2.13 ± 0.54, range 0.53–2.91), according to the 24HUNa and 24HUK ratio.

All statistical tests were two-sided, and the level of significance was set at 0.05. Continuous variables were expressed as the means $\pm$ s.d. Categorical variables were described as numbers and percentages in parenthesis. The continuous data were analyzed using Student's *t*-test for two-group comparisons, and the proportions between groups were compared using the χ^2 test. In the group comparisons of high and low 24HUNa and high and low 24HUNa/24HUK, the effects of age, gender, body mass index and antihypertensive medication were included. Multivariate linear regression analysis was performed to predict the independent effect of 24HUNa and 24HUNa/24HUK on the hemodynamic variables, including the effects of age, gender, body mass index and use of antihypertensive medications. All analyses were implemented using SPSS ver. 20 (SPSS, Chicago, IL, USA).

RESULTS

Among 707 individuals, 524 participants who had valid collections of 24-h urine, valid measurements of 24-h ambulatory BP and valid central BP measurements were included in the analysis. The demographic and clinical characteristics of the analyzed population are shown in Table 1. In total, 219 of the participants had hypertension (135 non-medicated, 84 medicated). The hypertensive individuals had a higher mean age, body mass index, prevalence of men, smokers and diabetes, 24HUNa and 24HUK. The 24HUNa/24HUK did not differ between the hypertensive and normotensive individuals. The serum creatinine, fasting blood glucose, cholesterol and triglyceride levels were higher in the hypertensive individuals than in the normotensive individuals.

Table 2 shows the hemodynamics comparison between the high-24HUNa and low-24HUNa groups. Among the entire study population, there was no difference in hemodynamics between the high- and low-24HUNa groups. In the hypertensive individuals, the high-24HUNa group had higher aortic systolic BP (AoSBP), 24-h SBP and DBP than the low-24HUNa group, with the adjusted analysis controlled for age, gender, body mass index and use of antihypertensive medication. In contrast, among the normotensive individuals, the low-24HUNa group showed higher casual DBP, 24-h DBP, AoSBP and AoDBP than the high-24HUNa group, after controlling for confounders.

As shown in Table 3, the high 24HUNa/24HUK group had higher 24-h DBP and AoSBP. Among the hypertensive individuals, the high 24HUNa/24HUK group had higher casual SBP and DBP, 24-h SBP and DBP, and AoSBP and AoDBP than the low-24HUNa/24HUK group. However, casual DBP and AoSBP showed a persistent difference, with a multivariate analysis controlled for age, gender, body mass index and use of antihypertensive medication. There was no difference in hemodynamics between the low and high 24HUNa/24HUK groups among the normotensive individuals.

Multivariate regression analysis, controlled for age, gender, body mass index, use of antihypertensive medication and 24HUNa, revealed an independent association between 24HUNa/24HUK and AoSBP (Table 4). The 24HUNa was not independently associated with AoSBP. In contrast to the aortic SBP, the 24-h SBP and DBP were not associated with 24HUNa ($P=0.420$ and 0.860, respectively) and 24HUNa/24HUK ($P=0.181$ and 0.121, respectively) in a multivariate regression analysis (table not shown).

DISCUSSION

We evaluated the association between urinary Na and K excretions and hemodynamics. This study is the first to reveal the independent association between a high ratio of urinary sodium/potassium and elevated AoSBP in Asian hypertension patients.

In our study, in hypertensive participants, there was a significant association between high 24HUNa and higher 24-h SBP, 24-h DBP and AoSBP compared with low-24HUNa. Previous studies have demonstrated an association between high sodium intake and elevated aortic pulse wave velocity.[8,9] Elevated aortic pulse wave velocity leads to elevated AoSBP through the early return of backward pressure. In addition, high 24HUNa/24HUK was associated with higher AoSBP but not with 24-h SBP and 24-h DBP. These findings indicate that AoSBP is influenced not only by high sodium intake but also by high sodium intake and/or low potassium intake. Multivariate regression analysis showed an independent and positive association between 24HUNa/24HUK and AoSBP, indicating a stronger effect of balanced sodium and potassium intake on AoSBP than sodium intake alone. Given our study results, low sodium and/or high potassium intake is an important strategy to avoid the elevation of central aortic BP and eventually cardiovascular events, because elevated central aortic BP is strongly associated with future cardiovascular events.[5]

Along with high dietary sodium intake, a well-known environmental factor, low potassium intake has been shown to be related to hypertension.[21–23] However, in the present study, 24HUK levels were higher in hypertensive individuals than that in normotensive individuals. Moreover, there was no relationship between the 24HUK and BP parameters (data not shown). The lack of such a relationship contrasts with the results of a previous study of a Korean population.[24] Although the reason is unclear, the lack of a relationship between 24HUK and BP may be explained by the different sodium and potassium intake estimation methods (24-h urine collection *vs* dietary survey) and the exclusion of individuals older than 65 years of age. The difference in methods may yield bias in terms of the sodium and potassium intake levels at the population and individual levels. Using the 24-h collection method, a discrepancy in sodium and potassium intake levels has been reported when these levels were measured using the dietary survey,[25] spot urine[26,27] and overnight urine collection methods.[28] Another reason may be the blunted effect of potassium in lowering BP when sodium intake is low[29,30] because the sodium intake in our study population was relatively low compared with that in the previous study.[24]

In addition to sodium or potassium intake alone, the INTERSALT study revealed a strong negative association between urinary sodium/potassium ratio and BP.[31] One of the suggested mechanisms underlying the elevation of BP through long-term potassium intake depletion is a cellular potassium deficit and sodium retention by the

Table 1 Characteristics of study population

Parameters	*All*	*Normotensives*	*Hypertensives*	P-*values*
n	524	305	219	
Age, years	48.1±9.8	45.1±9.6	52.1±8.5	<0.001
Gender				
Men, *n* (%)	193 (36.8)	79 (25.9)	114 (52.1)	<0.001
Women, *n* (%)	331 (63.2)	226 (74.1)	105 (47.9)	
BMI, kg m^{-2}	23.9±3.3	23.1±3.1	25.1±3.2	<0.001
Weight, kg	63.2±11.3	60.4±10.5	67.0±11.4	<0.001
Height, cm	162.1±8.1	161.5±8.1	163.1±7.9	0.029
Smoker, *n* (%)	123 (23.5)	59 (19.6)	64 (29.6)	0.009
Drinking, *n* (%)	188 (35.9)	98 (41.9)	90 (50.6)	0.090
Diabetes, *n* (%)	35 (6.7)	5 (1.6)	30 (13.7)	<0.001
Casual SBP, mm Hg	116.7±12.9	110.9±10.0	124.8±12.3	<0.001
Casual DBP, mm Hg	75.0±9.7	70.4±7.0	81.5±9.2	<0.001
24-h SBP, mm Hg	116.6±11.0	110.8±7.0	124.6±10.6	<0.001
24-h DBP, mm Hg	75.9±9.8	70.3±6.1	83.7±8.7	<0.001
AoSBP, mm Hg	110.7±13.1	104.8±10.1	118.8±12.5	<0.001
AoDBP, mm Hg	76.6±10.0	72.0±7.4	83.1±9.6	<0.001
Aortic pulse pressure, mm Hg	34.2±7.8	33.0±7.0	35.8±8.7	<0.001
Augmented pressure, mm Hg	10.1±5.3	9.5±5.0	10.9±5.7	0.004
Heart rate, b.p.m.	68.9±8.6	68.7±8.3	69.2±9.1	0.459
AI75, %	25.7±10.4	25.0±10.8	26.6±9.8	0.088
24-h Urine Na, mmol/24-h	159.8±61.5	154.8±59.9	166.8±63.1	0.027
24-h Urine K, mmol/24-h	55.9±20.7	54.3±18.8	58.3±23.0	0.036
24-h urine Na/24-h urine K ratio	3.10±1.22	3.05±1.21	3.13±1.25	0.463
Serum Na, mmol l^{-1}	141.4±2.4	141.4±2.4	141.4±2.3	0.942
Serum K, mmol l^{-1}	4.25±.30	4.24±0.31	4.27±0.30	0.176
Serum Cr, mg dl^{-1}	0.76±.16	0.73±0.14	0.79±0.17	<0.001
Fasting glucose, mg dl^{-1}	97.6±19.1	93.8±10.1	103.0±26.1	<0.001
Total cholesterol, mg dl^{-1}	196.8±35.1	195.8±34.4	198.1±36.1	0.469
LDL cholesterol, mg dl^{-1}	121.4±32.8	120.5±31.8	122.5±34.3	0.498
HDL cholesterol, mg dl^{-1}	56.9±15.7	59.5±15.9	53.2±14.5	<0.001
Triglyceride, mg dl^{-1}	132.5±106.0	111.9±75.6	161.3±132.4	<0.001

Abbreviations: AI75, augmentation index normalized for a heart rate of 75 beats per minute; AoDBP, aortic diastolic blood pressure; AoSBP, aortic systolic blood pressure; BMI, body mass index; Cr, creatinine; DBP, diastolic blood pressure; HDL, high density lipoprotein; K, potassium; LDL, low density lipoprotein; Na, sodium; SBP, systolic blood pressure. Pearson's χ^2 test or the independent *t*-test was performed for the categorical data or continuous data, as appropriate.
Data are expressed as mean±s.d., or number and percent in parenthesis, as appropriates.

Table 2 Difference of hemodynamic values between high and low 24-hour urine sodium excretion

	All				*Normotensives*				*Hypertensives*			
	Low 24HUNa (<151 mmol/24-h)	*High 24HUNa (⩾151 mmol/24-h)*	P	P[a]	*Low-24HUNa*	*High 24HUNa*	P	P[b]	*Low-24HUNa*	*High 24HUNa*	P	P[a]
n	262	262			161	144			101	118		
Casual SBP	115.2±13.0	118.3±12.8	0.006	0.949	110.8±10.8	111.0±9.0	0.856	0.048	122.2±13.2	127.1±11.0	0.003	0.086
Casual DBP	74.2±9.4	75.8±9.9	0.056	0.338	70.8±7.4	69.9±6.6	0.269	0.001	79.7±9.7	83.1±8.4	0.006	0.080
24-h SBP	115.3±10.4	117.9±11.5	0.006	0.400	110.7±7.1	111.0±6.9	0.662	0.530	122.6±10.7	126.3±10.3	0.009	0.037
24-h DBP	74.8±9.0	77.1±10.5	0.008	0.983	70.4±6.0	70.3±6.2	0.914	0.046	81.9±8.7	85.3±8.5	0.004	0.037
AoSBP	109.5±13.1	111.9±13.0	0.035	0.901	105.3±10.9	104.4±9.2	0.430	0.014	116.1±13.5	121.0±11.0	0.004	0.038
AoDBP	75.9±9.8	77.4±10.3	0.083	0.307	72.4±7.7	71.4±7.0	0.222	0.001	81.3±10.2	84.7±8.8	0.010	0.086
Aortic PP	33.8±7.8	34.6±7.9	0.238	0.393	32.8±6.7	33.2±7.3	0.622	0.705	35.3±9.2	36.3±8.2	0.418	0.500
AP	10.4±5.5	9.8±5.1	0.184	0.851	10.0±4.9	9.1±5.1	0.131	0.461	11.1±6.3	10.7±5.1	0.527	0.620
AI75	27.1±10.4	24.3±10.3	0.002	0.190	26.9±10.0	23.0±11.4	0.002	0.041	27.5±11.0	25.8±8.5	0.201	0.663

Abbreviations: 24HUNa, 24-h urine sodium; AI75, augmentation index normalized for a heart rate of 75 beats per minute; AoDBP, aortic diastolic blood pressure; AoSBP, aortic systolic blood pressure; AP, augmented pressure; DBP, diastolic blood pressure; PP, pulse pressure; SBP, systolic blood pressure.
[a]Multivariate analysis controlled for age, gender, body mass index and use of antihypertensive medication.
[b]Multivariate analysis controlled for age, gender and body mass index.

Table 3 Difference of hemodynamic values between high and low Na/K ratio

	All				*Normotensives*				*Hypertensives*			
	Low 24HUNa/24HUK (< 2.93)	*High 24HUNa/24HUK (⩾ 2.93)*	P	P[a]	*Low 24HUNa/24HUK*	*High 24HUNa/24HUK*	P	P[b]	*Low 24HUNa/24HUK*	*High 24HUNa/24HUK*	P	P[a]
n	262	262			158	147			104	115		
Casual SBP	115.7±13.0	117.7±12.8	0.071	0.126	111.3±10.6	110.5±9.3	0.500	0.325	122.4±13.6	127.0±10.6	0.006	0.093
Casual DBP	74.0±9.5	76.0±9.8	0.019	0.053	70.5±7.2	70.3±6.8	0.790	0.474	79.4±10.1	83.4±7.9	0.002	0.043
24-h SBP	115.8±10.7	117.4±11.2	0.099	0.133	111.2±7.2	110.5±6.8	0.347	0.279	122.8±11.5	126.2±9.4	0.015	0.252
24-h DBP	74.9±9.9	77.0±9.7	0.015	0.040	70.0±6.3	70.7±5.8	0.364	0.779	82.2±9.8	85.0±7.5	0.018	0.424
Aortic SBP	109.5±13.2	111.8±12.9	0.039	0.028	105.2±10.7	104.5±9.4	0.560	0.714	116.1±13.8	121.2±10.5	0.002	0.026
Aortic DBP	75.6±10.0	77.6±10.0	0.019	0.057	72.0±7.7	71.9±7.1	0.966	0.663	81.1±10.6	84.9±8.3	0.003	0.077
Aortic PP	34.2±8.2	34.2±7.5	0.956	0.608	33.4±7.7	32.6±6.1	0.295	0.717	35.4±8.8	36.2±8.6	0.499	0.404
AP	10.1±5.6	10.1±5.1	0.870	0.112	9.6±5.2	9.5±4.8	0.758	0.278	10.7±6.1	11.0±5.3	0.701	0.303
AI75	25.8±10.6	25.6±10.3	0.874	0.160	25.5±10.7	24.6±11.0	0.458	0.566	26.2±10.5	27.0±9.1	0.566	0.152

Abbreviations: 24HUNa/24HUK, ratio of 24-h urine sodium and 24-h urine potassium; AI75, augmentation index normalized for a heart rate of 75 beats per minute; AoDBP, aortic diastolic blood pressure; AoSBP, aortic systolic blood pressure; AP, augmented pressure; DBP, diastolic blood pressure; PP, pulse pressure; SBP, systolic blood pressure.
[a]Multivariate analysis controlled for age, gender, body mass index and use of antihypertensive medication.
[b]Multivariate analysis controlled for age, gender and body mass index.

Table 4 Independent relationship between aortic systolic blood pressure and 24-h urinary sodium/potassium with multivariate regression analysis adjusted for determinants

Aortic SBP vs	B	*s.e.*	b	t	P
All					
Model 1					
24HUNa/24HUK	0.936	0.413	0.088	2.267	0.024
Model 2					
24HUNa/24HUK	0.930	0.413	0.087	2.251	0.025
Use of antihypertensive medication	−0.906	1.444	−0.025	−0.628	0.530
Model 3					
24HUNa/24HUK	1.278	.467	0.120	2.735	0.006
Use of antihypertensive medication	−0.849	1.441	−0.024	−0.589	0.556
24HUNa	−0.015	0.010	−0.071	−1.587	0.113
Hypertensive individuals					
Model 1					
24HUNa/24HUK	1.848	0.672	0.186	2.748	0.006
Model 2					
24HUNa/24HUK	1.569	0.655	0.158	2.396	0.017
Use of antihypertensive medication	−3.407	0.873	−0.267	−3.902	<0.001
Model 3					
24HUNa/24HUK	1.446	0.724	0.145	1.997	0.047
Use of antihypertensive medication	−3.431	0.877	−0.269	−3.913	<0.001
24HUNa	0.006	0.015	0.031	0.400	0.689

Model 1: controlled for age, gender and body mass index.
Model 2: controlled for age, gender, body mass index and use of antihypertensive medication.
Model 3: controlled for age, gender, body mass index, use of antihypertensive medication and 24-h urine sodium.
B, unadjusted regression coefficient; *b*, standardized regression coefficient; *t*, the value of the *t*-test.
24HUNa/24HUK, ratio of 24-h urine sodium and 24-h urine potassium; 24HUNa, 24-h urine sodium.

kidneys, leading to hypertension.[32] Another explanation is sodium sensitivity, which is highly prevalent in blacks.[33,34] Although there is no direct evidence, relatively low urinary potassium excretion (i.e., high 24HUNa/K) suggests the presence of sodium sensitivity, considering the high prevalence of sodium sensitivity and low urinary potassium excretion in blacks.[35] The prevalence of sodium sensitivity in Asian hypertension patients is expected to be approximately 50%.[36,37] In our study, the positive association between AoSBP and 24HUNa/24HUK existed only in hypertensive individuals, and it was not observed in normotensive individuals. Thus, the combination of relatively low potassium intake and sodium sensitivity may contribute to the elevation of central BP.

In the literature, three studies previous have evaluated the association between sodium and potassium intake with central hemodynamics.[10–12] Among these studies, only one showed a significant correlation between AoSBP and urinary sodium/potassium ratio. The other two studies did not demonstrate an independent association between AoSBP and urinary sodium/potassium ratio or sodium excretion. There were several differences between the previous studies and our own. First, we diagnosed hypertension using a 24-h ambulatory BP measurement. Unlike our study, Park *et al.*[11] did not exclude white coat hypertension because they used conventionally measured BP. Polonia *et al.*[12] did not provide the criteria they used to diagnose hypertension. Second, we collected 24-h urine samples to measure urinary sodium and potassium excretion. Park *et al.*[11] estimated 24HUNa using spot urine samples from Korean hypertension patients. The accuracy of the equations estimating 24HUNa from spot urine has been questioned,[26] although it is widely used. Thus, it is unclear whether the results of an association between aortic hemodynamics and estimated 24HUNa could be extrapolated to the measured24HUNa. Third, the mean 24HUNa in our study was 159.8 mmol/24-h, which was between the measured 24HUNa in other studies (209 mmol/24-h and 105 mmol/24-h).[10,12] The positive association between 24HUNa and central hemodynamics in populations with different means of 24HUNa suggests a significant influence of high sodium intake on central hemodynamics without the distinction of sodium intake levels. The estimated 24HUNa from Park *et al.*[11] is difficult to compare because they estimated 24HUNa from spot urine samples using an equation previously developed by Tanaka *et al.*;[38] this equation showed a significant difference between the mean estimated and measured 24HUNa values in the validation of the equation in the external population. We also showed that estimating 24HUNa from

spot urine samples, including with Tanaka's equation, tends to under- or overestimate 24HUNa according to the amount of the 24-h urine Na, differing significantly from the measured 24HUNa.[26,39] Fourth, the ethnicity of the population in our study differed from that of the Redelinghuys *et al.* study.[10] Blacks have a higher prevalence of sodium sensitivity compared with other ethnicities. The high prevalence of sodium sensitivity may contribute to a positive association of casual and ambulatory SBP with 24HUNa/24HUK in the Redelinghuys *et al.* study,[10] which was not observed in our study. Nevertheless, the linear association between AoSBP and 24HUNa/24HUK in hypertensive individuals but not in normotensive individuals in our study may be explained by sodium sensitivity, which is more prevalent in hypertensives than in normotensives.[33,37] Sodium-resistant individuals, who have no response or a negative response to high sodium intake, are more likely to be normotensive than hypertensive. Thus, the lack of an association between AoSBP and 24HUNa/24HUK in normotensive individuals may be explained by the high prevalence of sodium-resistant individuals.

One limitation of our study is its cross-sectional nature, resulting in the inability to speculate on the causality between the urinary sodium/potassium ratio and central aortic BP. The following limitations may have resulted in bias in our study results. The sodium intake was measured using a single 24-h urine collection. A single 24-h urine collection does not accurately reflect dietary sodium intake, although it is considered to be the most reliable method in population surveys.[40,41] However, multiple collections of 24-h urine samples (more than seven times) are impractical in population surveys. Moreover, an indirect method (using a generalized transfer function) was used to measure central hemodynamics.[42]

In conclusion, 24HUNa/24HUNK was positively related to AoSBP in patients with hypertension, demonstrating a stronger effect compared with 24HUNa alone. The result indicates that high sodium and low potassium intakes may increase the subsequent risk of cardiovascular disease through the elevation of central aortic BP.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This work was supported by the Research Program funded by the Ministry of Food and Drug Safety in 2011 (11162KFDA162) and 2012 (12162MFDS103).

1 He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. *BMJ* 2013; **346**: f1325.
2 Strazzullo P, D'Elia L, Kandala NB, Cappuccio FP. Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. *BMJ* 2009; **339**: b4567.
3 Aburto NJ, Ziolkovska A, Hooper L, Elliott P, Cappuccio FP, Meerpohl JJ. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ* 2013; **346**: f1326.
4 He FJ, MacGregor GA. A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. *J Hum Hypertens* 2009; **23**: 363–384.
5 McEniery CM, Cockcroft JR, Roman MJ, Franklin SS, Wilkinson IB. Central blood pressure: current evidence and clinical importance. *Eur Heart J* 2014; **35**: 1719–1725.
6 Nichols WW, Singh BM. Augmentation index as a measure of peripheral vascular disease state. *Curr Opin Cardiol* 2002; **17**: 543–551.
7 Todd AS, Macginley RJ, Schollum JB, Johnson RJ, Williams SM, Sutherland WH, Mann JI, Walker RJ. Dietary salt loading impairs arterial vascular reactivity. *Am J Clin Nutr* 2010; **91**: 557–564.
8 Avolio AP, Clyde KM, Beard TC, Cooke HM, Ho KK, O'Rourke MF. Improved arterial distensibility in normotensive subjects on a low salt diet. *Arteriosclerosis* 1986; **6**: 166–169.
9 Rhee MY, Kim JH, Na SH, Chung JW, Bae JH, Nah DY, Gu N, Kim HY. Elevation of heart-femoral pulse wave velocity by short-term low sodium diet followed by high sodium diet in hypertensive patients with sodium sensitivity. *Nutr Res Pract* 2016; **10**: 288–293.
10 Redelinghuys M, Norton GR, Scott L, Maseko MJ, Brooksbank R, Majane OH, Sareli P, Woodiwiss AJ. Relationship between urinary salt excretion and pulse pressure and central aortic hemodynamics independent of steady state pressure in the general population. *Hypertension* 2010; **56**: 584–590.
11 Park S, Park JB, Lakatta EG. Association of central hemodynamics with estimated 24-h urinary sodium in patients with hypertension. *J Hypertens* 2011; **29**: 1502–1507.
12 Polonia JJ, Magalhaes MT, Senra D, Barbosa L, Silva JA, Ribeiro SM. Association of 24-h urinary salt excretion with central haemodynamics and assessment of food categories contributing to salt consumption in Portuguese patients with hypertension. *Blood Press Monit* 2013; **18**: 303–310.
13 Rhee MY, Shin SJ, Park SH, Kim SW. Sodium intake of a city population in Korea estimated by 24-h urine collection method. *Eur J Clin Nutr* 2013; **67**: 875–880.
14 Reinivuo H, Valsta LM, Laatikainen T, Tuomilehto J, Pietinen P. Sodium in the Finnish diet: II trends in dietary sodium intake and comparison between intake and 24-h excretion of sodium. *Eur J Clin Nutr* 2006; **60**: 1160–1167.
15 Stergiou GS, Tzamouranis D, Protogerou A, Nasothimiou E, Kapralos C. Validation of the Microlife Watch BP Office professional device for office blood pressure measurement according to the International protocol. *Blood Press Monit* 2008; **13**: 299–303.
16 Wei W, Tolle M, Zidek W, van der Giet M. Validation of the mobil-O-Graph: 24 h-blood pressure measurement device. *Blood Press Monit* 2010; **15**: 225–228.
17 O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, Mengden T, Myers M, Padfield P, Palatini P, Parati G, Pickering T, Redon J, Staessen J, Stergiou G, Verdecchia PEuropean Society of Hypertension Working Group on Blood Pressure M. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens* 2003; **21**: 821–848.
18 Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, Grassi G, Heagerty AM, Kjeldsen SE, Laurent S, Narkiewicz K, Ruilope L, Rynkiewicz A, Schmieder RE, Boudier HA, Zanchetti A, Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellemans I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Erdine S, Kiowski W, Agabiti-Rosei E, Ambrosioni E, Lindholm LH, Viigimaa M, Adamopoulos S, Agabiti-Rosei E, Ambrosioni E, Bertomeu V, Clement D, Erdine S, Farsang C, Gaita D, Lip G, Mallion JM, Manolis AJ, Nilsson PM, O'Brien E, Ponikowski P, Redon J, Ruschitzka F, Tamargo J, van Zwieten P, Waeber B, Williams B. Management of Arterial Hypertension of the European Society of H, European Society of C 2007. Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007; **25**: 1105–1187.
19 Pauca AL, O'Rourke MF, Kon ND. Prospective evaluation of a method for estimating ascending aortic pressure from the radial artery pressure waveform. *Hypertension* 2001; **38**: 932–937.
20 Adji A, Hirata K, O'Rourke MF. Clinical use of indices determined non-invasively from the radial and carotid pressure waveforms. *Blood Press Monit* 2006; **11**: 215–221.
21 Krishna GG, Miller E, Kapoor S. Increased blood pressure during potassium depletion in normotensive men. *N Engl J Med* 1989; **320**: 1177–1182.
22 Krishna GG, Kapoor SC. Potassium depletion exacerbates essential hypertension. *Ann Intern Med* 1991; **115**: 77–83.
23 Adrogue HJ, Madias NE. Sodium surfeit and potassium deficit: keys to the pathogenesis of hypertension. *J Am Soc Hypertens* 2014; **8**: 203–213.
24 Noh HM, Park SY, Lee HS, Oh HY, Paek YJ, Song HJ, Park KH. Association between high blood pressure and intakes of sodium and potassium among Korean adults: Korean National Health and Nutrition Examination Survey 2007-2012. *J Acad Nutr Diet* 2015; **115**: 1950–1957.
25 Espeland MA, Kumanyika S, Wilson AC, Reboussin DM, Easter L, Self M, Robertson J, Brown WM, McFarlane M. Group TCR. Statistical issues in analyzing 24-hour dietary recall and 24-hour urine collection data for sodium and potassium intakes. *Am J Epidemiol* 2001; **153**: 996–1006.
26 Rhee MY, Kim JH, Shin SJ, Gu N, Nah DY, Hong KS, Cho EJ, Sung KC. Estimation of 24-hour urinary sodium excretion using spot urine samples. *Nutrients* 2014; **6**: 2360–2375.
27 Okuda M, Asakura K, Sasaki S, Shinozaki K. Twenty-four-hour urinary sodium and potassium excretion and associated factors in Japanese secondary school students. *Hypertens Res* 2016; **39**: 524–529.
28 Yasutake K, Horita N, Murata Y, Koyama S, Enjoji M, Tsuchihashi T. Estimated urinary salt excretion by a self-monitoring device is applicable to education of salt restriction. *Hypertens Res* 2015; **38**: 143–148.
29 Rodrigues SL, Baldo MP, Machado RC, Forechi L, Molina Mdel C, Mill JG. High potassium intake blunts the effect of elevated sodium intake on blood pressure levels. *J Am Soc Hypertens* 2014; **8**: 232–238.
30 Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D, Klag MJ. Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. *JAMA* 1997; **277**: 1624–1632.
31 Intersalt: An International Study of Electrolyte Excretion and Blood Pressure. Results for 24 hour urinary sodium and potassium excretion. Intersalt Cooperative Research Group. *BMJ* 1988; **297**: 319–328.
32 Adrogue HJ, Madias NE. Sodium and potassium in the pathogenesis of hypertension. *N Engl J Med* 2007; **356**: 1966–1978.

33 Weinberger MH, Miller JZ, Luft FC, Grim CE, Fineberg NS. Definitions and characteristics of sodium sensitivity and blood pressure resistance. *Hypertension* 1986; **8**: II127–II134.
34 Morris RC Jr, Sebastian A, Forman A, Tanaka M, Schmidlin O. Normotensive salt sensitivity: effects of race and dietary potassium. *Hypertension* 1999; **33**: 18–23.
35 Aviv A, Hollenberg NK, Weder A. Urinary potassium excretion and sodium sensitivity in blacks. *Hypertension* 2004; **43**: 707–713.
36 Kawasaki T, Delea CS, Bartter FC, Smith H. The effect of high-sodium and low-sodium intakes on blood pressure and other related variables in human subjects with idiopathic hypertension. *Am J Med* 1978; **64**: 193–198.
37 Shin SJ, Lim CY, Rhee MY, Oh SW, Na SH, Park Y, Kim CI, Kim SY, Kim JW, Park HK. Characteristics of sodium sensitivity in Korean populations. *J Korean Med Sci* 2011; **26**: 1061–1067.
38 Tanaka T, Okamura T, Miura K, Kadowaki T, Ueshima H, Nakagawa H, Hashimoto T. A simple method to estimate populational 24-h urinary sodium and potassium excretion using a casual urine specimen. *J Hum Hypertens* 2002; **16**: 97–103.
39 Rhee MY. High sodium intake: review of recent issues on its association with cardiovascular events and measurement methods. *Korean Circ J* 2015; **45**: 175–183.
40 Luft FC, Fineberg NS, Sloan RS. Estimating dietary sodium intake in individuals receiving a randomly fluctuating intake. *Hypertension* 1982; **4**: 805–808.
41 World Health Organization. Reducing Salt Intake in Populations. Report of a WHO Forum and Technical Meeting. Paris, France: World Health Organization, 2007.
42 Hope SA, Meredith IT, Tay D, Cameron JD. 'Generalizability' of a radial-aortic transfer function for the derivation of central aortic waveform parameters. *J Hypertens* 2007; **25**: 1812–1820.