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Association Between Estimated 24-h Urinary Sodium Excretion and Metabolic Syndrome in Korean Adults

The 2009 to 2011 Korea National Health and Nutrition Examination Survey

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Abstract: High sodium intake is 1 of the modifiable risk factors for cardiovascular disease, but in Korea, daily sodium intake is estimated to be double the level recommended by World Health Organization. We investigated the association between the estimated 24-h urinary sodium excretion (24hUNaE) and metabolic syndrome using nationwide population data.

In total, 17,541 individuals (weighted n = 33,200,054; weighted men, 52.5% [95% confidence interval, CI = 51.8–53.3]; weighted age, 45.2 years [44.7–45.7]) who participated in the Korean Health and Nutrition Examination Survey 2009 to 2011 were investigated. NCEP-ATP III criteria for metabolic syndrome were used, and sodium intake was estimated by 24hUNaE using Tanaka equation with a spot urine sample.

The weighted mean 24hUNaE values were 3964 mg/d (95% CI = 3885–4044) in men and 4736 mg/d (4654–4817) in women. The weighted age-adjusted prevalence of metabolic syndrome was 22.2% (21.4–23.0), and it increased with 24hUNaE quartile in both men and women (mean ± standard error of the mean; men: 22.5 ± 1.0%, 23.0 ± 1.0%, 26.0 ± 1.2%, and 26.0 ± 1.2%; $P = 0.026$; women: 19.4 ± 0.8%, 17.7 ± 0.8%, 19.8 ± 1.0%, and 23.0 ± 1.1%; $P = 0.002$, for quartiles 1–4, respectively). Even after adjustment for age, daily calorie intake, heavy alcohol drinking, regular exercise, college graduation, and antihypertensive medication, the weighted prevalence of metabolic syndrome increased with the increase in 24hUNaE in men and women. The weighted 24hUNaE was positively associated with the number of metabolic syndrome components after adjustment for confounding factors in men and women. In subjects without antihypertensive medication, the odds ratio for metabolic syndrome in quartile 4 of 24hUNaE compared with quartile 1 was 1.56 (1.33–1.84, $P < 0.001$) in the total population, 1.66 (1.34–2.06, $P < 0.001$) in men, and 1.94 (1.49–2.53, $P < 0.001$) in women.

In this nationwide population study, we observed a significant independent association between high sodium intake, estimated by spot urine sodium excretion, and the presence of metabolic syndrome in men and women.

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Abbreviations: 24hUNaE = 24-h urinary sodium excretion, ANCOVA = analysis of covariance, BMI = body mass index, BP = blood pressure, CI = confidence interval, CVD = cardiovascular disease, DSM = Diagnostic and Statistical Manual of Mental Disorders, eGFR = estimation of glomerular filtration rate, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein-cholesterol, KNHANES = Korea National Health and Nutrition Examination Survey, NCEP-ATPIII = the National Cholesterol Education Program Adult Treatment Panel, OR = odds ratio, SCr = serum creatinine, SD = standard deviation, SEM = standard error of the mean, TG = triglyceride, WC = waist circumference, WHO = World Health Organization.

INTRODUCTION

Metabolic syndrome is associated with an increased risk of cardiovascular disease (CVD), diabetes, chronic kidney disease, and total mortality.[1,2] The prevalence of metabolic syndrome is increasing in Korea. According to data from the Korean National Health and Nutrition Examination Surveys 1998 to 2007, the age-adjusted prevalence of metabolic syndrome increased from 24.9% to 31.3%.[3] Thus, specific modifiable risk factors for metabolic syndrome should be defined and measures to modify them emphasized.

The mean sodium intake in Korea (5158 mg/d, 12 g of salt) is 2 to 3 times higher than that recommended by the World Health Organization (WHO) (<2000 mg/d).[4,5] Excess sodium intake has a clinical impact on CVDs,[6] and accumulating evidence suggests that even modest reductions in dietary sodium reduce CVD events and the substantial associated economic burden.[7,8] Thus, many nations have developed campaigns to reduce salt intake to help prevent CVDs; such public health interventions would be even more useful in a population with a high average sodium intake.[9]

Although increasing evidence indicates an association between high sodium intake and CVDs,[6] in Korea, there are limited nationwide survey data on the association of sodium intake and metabolic syndrome. Previously, we reported that high sodium intake was associated with an increased prevalence of albuminuria, a marker for the renal component of metabolic syndrome.[10,11]

Because high salt consumption is a modifiable risk factor associated with CVDs, it is important to investigate the

population-based association between salt intake and metabolic syndrome in Korean subjects, who are known to have high salt intake. In this study, we investigated the association between salt intake, estimated using 24-h urinary sodium excretion (24hUNaE), and metabolic syndrome and its components, stratified by gender.

METHODS

Study Population

Details of the study population and methods have been published elsewhere.[11,12] Briefly, from the 28,009 participants in KNHANES 2009 to 2011 (a cross-sectional, nationally representative, and stratified survey), we considered 21,119 individuals with age 19 years and older. Among this population, 17,541 individuals who participated in the laboratory examination were finally included in the analyses (Supplementary Figure 1, http://links.lww.com/MD/A895). KNHANES is conducted regularly by the Korean Center for Disease Control using a representative population recruited using population-allocation systematic sampling with multistage stratification. Its operation and procedures have been reported before.[12] Because KNHANES is a complex probability sample survey, the survey design should be explicitly used when producing statistical estimates or undertaking statistical analysis of the KNHANES data to present an unbiased cross-sectional estimates for the entire Korean population.[13] After approval of the investigator's proposal by the Korean Center for Disease Control, a survey dataset was provided, including information about survey location, stratification by age, gender, and other factors, and sample weight for each participant. The sampling weight for each sample person created by Korean CDC reflect the reciprocal of the probabilities of selection (the primary sample units, household), an adjustment for nonresponse (household, person), and a poststratification factors such as age, sex, metropolitan area, or province category approximately equal to the total population of Korea (2005 Korean National Census Registry) to produce estimates representative of the noninstitutionalized Korean civilian population. KNHANES data include a standardized health interview using well-established questions to determine the demographic and socioeconomic characteristics of the subjects. In the present study, current smokers were defined as smokers. Heavy alcohol drinking was defined as those who drank at least 4 times/wk among the 6 answered items questioning the frequency of drinking days per a week or a month of the alcohol-related questionnaire in KNHANES V: never during recent 1 year, <1 time/mo, approximately 1 time/mo, 2 to 4 times/mo, 2 to 3 times/wk, and >4 times/wk. Physical activity was assessed in terms of intensity, duration, and frequency, and regular exercise was defined as exercising 5 or more times per week of moderate or 3 or more sessions per week of strenuous exercise, sustained for at least 30 min per session. We did not exclude the individual with depressive symptom because it was not evaluated by Diagnostic and Statistical Manual of Mental Disorders criteria. The study was approved by the Institutional Review Board of Ilsan-Paik Hospital (2015-09-003).

Definition of Metabolic Syndrome

Metabolic syndrome was defined according to the criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) guidelines.[14] The presence of any 3 of the following 5 factors is required for a diagnosis of metabolic

syndrome: waist circumference (WC) ≥ 90 cm in men or ≥ 80 cm in women, hypertriglyceridemia (triglyceride, TG ≥ 150 mg/dL), low high-density lipoprotein cholesterol (HDL-C ≤ 40 mg/dL for men and ≤ 50 mg/dL for women), elevated blood pressure (BP) (systolic BP ≥ 130 mm Hg and/or diastolic BP ≥ 85 mm Hg or current use of antihypertensive drugs), and impaired fasting glucose (fasting plasma glucose [FPG] ≥ 100 mg/dL or use of glucose-lowering medicine).

Estimating the 24hUNaE and Glomerular Filtration Rate

The 24hUNaE was estimated from the sodium and creatinine of random urine samples using Tanaka equation[15]: 24-h urinary Na excretion (mmol/d) $= 21.98 \times U_{Na}/U_{Cr} \times [-2.04 \times$ age $+ 14.89 \times$ weight (kg) $+ 16.14 \times$ height (cm) $- 2244.45]^{0.392}$. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation: GFR $= 141 \times \min (SCr/\kappa, 1)^{\alpha} \times \max (SCr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ (if female) $\times 1.159$ (if black), where SCr is the serum creatinine level in mg/dL, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1.[16]

Statistical Analysis

All data are presented as weighted means and confidence intervals (CI) or standard error of the mean (SEM) unless otherwise specified. Weighted age-adjusted comparisons of the clinical characteristics according to the quartile of the estimated 24hUNaE were made using analysis of covariance (ANCOVA) stratified by gender (Tables 1 and 2). ANCOVA was used to explore the association between quartiles of 24hUNaE and the presence of metabolic syndrome or its components (Table 2). Weighted multivariate comparisons of 24hUNaE by number of metabolic syndrome components were made using ANCOVA (Table 3). Logistic regression analyses were performed to determine the odds ratios for each quartile of the estimated 24hUNaE, with quartile 1 as the reference (Table 4). These data were analyzed using the SPSS software (ver. 21.0 for Windows; SPSS, Chicago, IL), and the level of significance was $P < 0.05$.

RESULTS

The weighted characteristics of study participants by gender are presented in Table 5. Men were more likely than women to report college graduation, current smoking, heavy alcohol drinking, and diabetes (all $P < 0.05$). The mean systolic and diastolic BP, body mass index (BMI), WC, TG, and FPG were significantly higher, whereas HDL-C was lower, in men than women. Overall, the weighted mean prevalence of metabolic syndrome was 22.2% (95% CI $= 21.4–23.0$). Metabolic syndrome was more prevalent in men than women (mean and 95% CI: 24.3% and 23.1–25.4 vs 19.9% and 18.9–20.9, respectively; $P < 0.001$). The mean 24hUNaE was 4331 mg/d in Korean adults overall, and those in men and women were 3964 mg/d (3885–4044) and 4736 mg/d (4654–4817), respectively. The weighted mean of 24hUNaE was higher in subjects with metabolic syndrome than in those without: 5812 mg/d and 5624 to 6000 versus 4469 mg/d and 4387 to 4552, respectively; $P < 0.001$.

The weighted demographic and clinical characteristics of the 17,541 participants (weighted n $= 33,200,054$) according to

TABLE 1. Age-Adjusted Weighted Clinical Characteristics of Korean Adult Men by Estimated 24-h Urine Na Excretion

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P_{trend}
24hUNaE, mg/d	−2300	2301−3570	3571−5460	5461−	
Unweighted/weighted, N	1995/4,795,677	1994/4,465,703	2003/4,356,537	1993/3,815,262	
Age, y	39.7 ± 0.4	43.2 ± 0.4	45.0 ± 0.5	$48.8 \pm 0.5^{*,†,‡}$	<0.001
College graduation, %	37.2 ± 1.4	37.3 ± 1.3	37.1 ± 1.4	$31.1 \pm 1.4^{*,†,‡}$	<0.001
Heavy alcohol drinking, %	12.9 ± 0.8	12.3 ± 0.9	13.2 ± 0.9	14.5 ± 0.9	0.401
Regular exercise, %	15.0 ± 1.0	16.3 ± 1.0	17.3 ± 1.1	17.9 ± 1.1	0.213
Total calories intake, cal/d	2344 ± 34	2443 ± 28	2448 ± 32	$2440 \pm 32^{*}$	0.084
BMI, kg/m^2	23.7 ± 0.1	24.0 ± 0.1	24.2 ± 0.1	$24.4 \pm 0.1^{*,†}$	<0.001
WC, cm	83.1 ± 0.3	84.0 ± 0.2	84.5 ± 0.3	$85.0 \pm 0.3^{*,†}$	0.001
Systolic BP, mm Hg	119.9 ± 0.4	120.1 ± 0.4	121.6 ± 0.4	$124.0 \pm 0.5^{*,†,‡}$	<0.001
Diastolic BP, mm Hg	79.6 ± 0.3	80.2 ± 0.3	80.7 ± 0.3	$81.4 \pm 0.3^{*,†}$	0.001
Antihypertensive medication, %	16.1 ± 0.7	12.6 ± 0.8	11.8 ± 0.8	$11.0 \pm 0.8^{*}$	<0.001
FPG, mg/dL	99.4 ± 0.6	98.5 ± 0.6	97.5 ± 0.5	98.6 ± 0.7	0.072
Serum TC, mg/dL	187.3 ± 1.0	187.2 ± 1.0	186.6 ± 1.0	186.0 ± 1.1	0.743
Serum TG, mg/dL	148.0 ± 3.1	157.2 ± 3.9	159.5 ± 4.1	$168.2 \pm 4.6^{*}$	0.002
Serum HDL-C, mg/dL	50.1 ± 0.3	49.5 ± 0.3	49.7 ± 0.4	49.7 ± 0.4	0.554
eGFR, mL/min per 1.73 m^2	90.9 ± 0.4	92.1 ± 0.4	93.5 ± 0.4	$95.6 \pm 0.5^{*,†,‡}$	<0.001
eGFR < 60 mL/min per 1.73 m^2, %	3.2 ± 0.4	2.8 ± 0.4	3.3 ± 0.5	$1.4 \pm 0.3^{*,†,‡}$	0.001
Component of metabolic syndrome					
High WC, %	21.8 ± 1.1	24.5 ± 1.2	28.0 ± 1.3	$28.2 \pm 1.3^{*,†}$	<0.001
High blood pressure, %	41.0 ± 1.3	39.4 ± 1.3	43.0 ± 1.4	$45.2 \pm 1.4^{*,†}$	0.013
High FPG, %	30.7 ± 1.1	29.8 ± 1.1	28.2 ± 1.2	$31.5 \pm 1.2^{‡}$	0.186
High serum TG, %	34.9 ± 1.3	35.7 ± 1.3	38.7 ± 1.3	$38.6 \pm 1.4^{*}$	0.068
Low serum HDL-C, %	17.3 ± 0.9	19.3 ± 1.1	20.3 ± 1.2	20.0 ± 1.3	0.159
Metabolic syndrome, %	22.5 ± 1.0	23.0 ± 1.0	26.0 ± 1.2	$26.0 \pm 1.2^{*,†}$	0.026

Data are expressed as means with standard error of the mean.

24hUNaE = 24-h urinary sodium excretion (estimated), BMI = body mass index, BP = blood pressure, eGFR = estimation of glomerular filtration rate, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride, WC = waist circumference.

*$P < 0.05$, quartile 4 vs quartile 1.

†$P < 0.05$, quartile 4 vs quartile 2.

‡$P < 0.05$, quartile 4 vs quartile 3.

quartiles of 24hUNaE stratified by gender are shown in Tables 1 and 2. To ensure the effect of population's age distribution, age-adjusted comparing the differences between population groups was measured. The weighted age-adjusted proportion of subjects with college graduation decreased by quartile in relation to 24hUNaE in both men and women. Whereas age, proportion of college graduation, BMI, WC, systolic and diastolic BP, serum TG, and eGFR increased with increasing 24hUNaE level across the quartiles in both men and women, the proportion of subjects with antihypertensive medication or decreased eGFR declined. The weighted age-adjusted prevalence of metabolic syndrome increased with 24hUNaE quartile in both men and women; the mean $\pm$ SEM values for quartiles 1 to 4 in men were $22.5 \pm 1.0\%$, $23.0 \pm 1.0\%$, $26.0 \pm 1.2\%$, and $26.0 \pm 1.2\%$ ($P = 0.026$), and those in women were $19.4 \pm 0.8\%$, $17.7 \pm 0.8\%$, $19.8 \pm 1.0\%$, and $23.0 \pm 1.1\%$ ($P = 0.002$), respectively. In weighted, age-adjusted comparisons for the presence of each component of metabolic syndrome, the proportion of abdominal obesity and hypertension increased significantly according to increases in 24hUNaE in men. In women, abdominal obesity, hypertension, and hypertriglyceridemia increased significantly with increasing 24hUNaE.

In the weighted age-adjusted comparison, for both men and women, the 24hUNaE of hypertensive subjects without antihypertensive medication was significantly higher than that in subjects without hypertension and in those with hypertension taking antihypertensive medication; in men, the mean $\pm$ SEM values were 4413 ± 91, 3896 ± 42, and 3707 ± 118 mg/d, respectively (all $P < 0.001$), and in women, 5564 ± 124, 4652 ± 42, and 4660 ± 125 mg/d, respectively (all $P < 0.001$).

In gender-stratified models adjusted for age, antihypertensive medication, daily calorie intake, heavy alcohol consumption, regular exercise, and college graduation, the 24hUNaE quartile was significantly associated with abdominal obesity, hypertension, and hence the presence of metabolic syndrome in both men and women (Table 6). Additionally, the proportion of subjects with hypertriglyceridemia increased with higher 24hUNaE quartiles in women. To minimize interference induced by decreased eGFR, we excluded subjects with eGFR < 60 mL/min per 1.73 m^2. The positive association between increased 24hUNaE and the proportion of subjects with metabolic syndrome remained statistically significant after the exclusion of subjects with decreased eGFR (<60 mL/min per 1.73 m^2). The weighted estimated 24hUNaE increased according to the number of metabolic syndrome components in both men and women, even after adjusting for those confounding variables (Table 3).

To further exclude any bias induced by antihypertensive medication, logistic regression analyses were performed to investigate the presence of metabolic syndrome by 24hUNaE

TABLE 2. Age-Adjusted Weighted Clinical Characteristics of Korean Adult Women by Estimated 24-h Urine Na Excretion

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P_{trend}
24hUNaE, mg/d	−2700	2701–4250	4251–6500	6501–	
Unweighted/weighted, N	2379/4,368,843	2398/4,034,431	2391/3,826,232	2388/3,537,370	
Age, y	40.3 ± 0.4	45.3 ± 0.4	49.0 ± 0.4	53.5 ± 0.5[*,†,‡]	<0.001
College graduation, %	26.6 ± 1.2	30.1 ± 1.2	26.8 ± 1.0	22.3 ± 1.0[*,†,‡]	<0.001
Heavy alcohol drinking, %	2.6 ± 0.5	2.2 ± 0.4	1.7 ± 0.3	2.8 ± 0.5	0.212
Regular exercise, %	14.1 ± 0.9	15.3 ± 0.9	15.3 ± 0.9	16.7 ± 1.0	0.281
Total calories intake, cal/d	1607 ± 16	1686 ± 20	1716 ± 17	1709 ± 18[*]	<0.001
BMI, kg/m²	22.7 ± 0.1	23.3 ± 0.1	23.4 ± 0.1	24.0 ± 0.1[*,†,‡]	<0.001
WC, cm	76.3 ± 0.2	77.9 ± 0.2	78.5 ± 0.3	80.2 ± 0.3[*,†,‡]	<0.001
Systolic BP, mm Hg	114.4 ± 0.3	115.2 ± 0.4	116.6 ± 0.4	120.0 ± 0.4[*,†,‡]	<0.001
Diastolic BP, mm Hg	73.2 ± 0.2	73.9 ± 0.3	74.6 ± 0.3	76.1 ± 0.3[*,†,‡]	<0.001
Antihypertensive medication, %	20.5 ± 0.7	16.4 ± 0.7	13.4 ± 0.8	14.6 ± 0.9[*]	<0.001
FPG, mg/dL	94.9 ± 0.4	94.2 ± 0.4	95.3 ± 0.5	95.2 ± 0.5	0.221
Serum TC, mg/dL	188.5 ± 0.9	188.5 ± 0.8	189.1 ± 0.9	189.8 ± 1.0	0.713
Serum TG, mg/dL	105.5 ± 1.6	107.7 ± 1.6	114.7 ± 2.1	122.9 ± 2.3[*,†,‡]	<0.001
Serum HDL-C, mg/dL	56.0 ± 0.3	55.9 ± 0.3	55.7 ± 0.3	55.3 ± 0.3	0.310
eGFR, mL/min per 1.73 m²	95.4 ± 0.5	97.7 ± 0.4	98.3 ± 0.4	100.7 ± 0.4[*,†,‡]	<0.001
eGFR < 60 mL/min per 1.73 m², %	3.4 ± 0.4	3.3 ± 0.3	2.4 ± 0.4	1.1 ± 0.3[*,†,‡]	<0.001
Component of metabolic syndrome					
High WC, %	19.9 ± 0.9	23.4 ± 1.0	24.2 ± 1.1	30.1 ± 1.2[*,†,‡]	<0.001
High BP, %	30.0 ± 0.8	27.8 ± 0.9	28.5 ± 0.9	33.1 ± 1.2[*,†,‡]	0.001
High FPG, %	22.6 ± 0.9	20.6 ± 0.9	22.7 ± 1.0	23.0 ± 1.1	0.248
High TG, %	18.2 ± 0.9	18.2 ± 0.9	22.0 ± 1.0	25.0 ± 1.1[*,†]	<0.001
Low HDL-C, %	33.0 ± 1.1	33.1 ± 1.1	33.6 ± 1.1	34.6 ± 1.2	0.754
Metabolic syndrome, %	19.4 ± 0.8	17.7 ± 0.8	19.8 ± 1.0	23.0 ± 1.1[†,‡]	0.002

Data are expressed as means with standard error of the mean.

24hUNaE = 24-h urinary sodium excretion (estimated), BMI = body mass index, BP = blood pressure, eGFR = estimation of glomerular filtration rate, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride, WC = waist circumference.

[*] $P < 0.05$, quartile 4 vs quartile 1.

[†] $P < 0.05$, quartile 4 vs quartile 2.

[‡] $P < 0.05$, quartile 4 vs quartile 3.

TABLE 3. Sex-Stratified Weighted Estimated 24-h Urine Na Excretion of Korean Adult by Number of Metabolic Syndrome Components

	0	1	2	3	4–5	P_{trend}
Men						
Unweighted/weighted, N	1920/4,831,945	2079/4,591,804	1843/3,777,891	1305/262,6521	838/1,615,017	
Model 1, mg/d	3545 ± 63	3844 ± 64	4172 ± 72	4387 ± 132	4410 ± 132	<0.001
Model 2, mg/d	3791 ± 64	3864 ± 60	4073 ± 69	4185 ± 130	4187 ± 143	0.004
Model 3, mg/d	3838 ± 73	3859 ± 63	4049 ± 72	4218 ± 134	4222 ± 137	0.003
Model 4, mg/d	3830 ± 73	3858 ± 63	4050 ± 75	4169 ± 104	4264 ± 140	0.003
Women, mg/d						
Unweighted/weighted, N	3157/5,917,467	2435/4,012,560	1766/2,707,804	1195/1721,380	1003/1,407,666	
Model 1, mg/d	3919 ± 51	4752 ± 76	5252 ± 96	5732 ± 126	5870 ± 155	<0.001
Model 2, mg/d	4350 ± 51	4775 ± 72	4974 ± 94	5197 ± 129	5221 ± 163	<0.001
Model 3, mg/d	4340 ± 56	4789 ± 77	4945 ± 93	5273 ± 129	5324 ± 166	<0.001
Model 4, mg/d	4344 ± 57	4782 ± 78	4934 ± 93	5283 ± 132	5369 ± 170	<0.001

Mean ± standard error of the mean.

Model 1 = no adjustment.

Model 2 = age-adjusted.

Model 3 = age, antihypertensive medication, daily calories intake, heavy alcohol drinking, regular exercise, and college graduation adjusted.

Model 4 = age, daily calories intake, heavy alcohol drinking regular exercise, and college graduation adjusted after exclusion of estimation of glomerular filtration rate < 60 mL/min per 1.73 m².

TABLE 4. Sex-Stratified Logistic Regression Analyses for the Presence of Metabolic Syndrome by Quartiles of Estimated 24-h Urine Na Excretion

	All		Men		Women	
	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*
Without antihypertensive medication						
Quartile 1	Reference		Reference		Reference	
Quartile 2	1.21 (1.03–1.43)	0.020	1.21 (0.99–1.48)	0.059	1.21 (0.91–1.63)	0.195
Quartile 3	1.44 (1.20–1.72)	<0.001	1.62 (1.31–2.01)	<0.001	1.47 (1.11–1.94)	0.007
Quartile 4	1.56 (1.33–1.84)	<0.001	1.66 (1.34–2.06)	<0.001	1.94 (1.49–2.53)	<0.001
With antihypertensive medication						
Quartile 1	Reference		Reference		Reference	
Quartile 2	0.90 (0.70–1.16)	0.413	0.88 (0.61–1.27)	0.485	0.85 (0.60–1.21)	0.376
Quartile 3	0.88 (0.69–1.13)	0.329	0.75 (0.52–1.09)	0.127	1.37 (0.97–1.94)	0.072
Quartile 4	0.99 (0.78–1.25)	0.939	0.76 (0.53–1.10)	0.147	1.06 (0.78–1.46)	0.702

Age, sex, daily calories intake, heavy alcohol drinking, regular exercise, and college graduation adjusted.
CI = confidence interval.

quartile in gender-stratified subgroups according to antihypertensive medication status (Table 4). Here, in subjects without antihypertensive medication, odd ratios showed significant graded associations with the presence of metabolic syndrome from the second quartile of 24hUNaE compared with the lowest quartile in all subjects. Compared with subjects in the lowest 24hUNaE quartile, the odd ratios for metabolic syndrome among those in the highest quartile was 1.66

TABLE 5. Weighted Clinical Characteristics of Korean Adults

	Total	Men	Women	*P*
Unweighted/weighted, N	17,541/33,200,054	7985/17,433,178	9556/15,766,877	
Age, y	45.2 (44.7–45.7)	43.9 (43.4–44.4)	46.6 (46.1–47.2)	<0.001
College graduation, %	31.4 (30.1–32.8)	35.8 (34.2–37.5)	26.6 (25.2–28.0)	<0.001
Heavy alcohol drinking, %	8.0 (7.5–8.6)	13.2 (12.3–14.1)	2.3 (2.0–2.8)	<0.001
Regular exercise, %	15.9 (15.1–16.8)	16.5 (15.5–17.7)	15.3 (14.3–16.3)	0.046
Total calories intake, cal/d	2044 (2022–2065)	2416 (2385–2448)	1677 (1657–1697)	<0.001
BMI, kg/m^2	23.7 (23.6–23.8)	24.1 (24.0–24.1)	23.3 (23.2–23.4)	<0.001
WC, cm	81.3 (81.0–81.5)	84.1 (83.8–84.4)	78.1 (77.8–78.5)	<0.001
Systolic BP, mm Hg	119.0 (118.5–119.4)	121.3 (120.8–121.8)	116.4 (115.9–116.9)	<0.001
Diastolic BP, mm Hg	77.6 (77.3–77.8)	80.4 (80.1–80.8)	74.4 (74.1–74.7)	<0.001
Hypertension, %	28.0 (27.1–29.0)	31.1 (29.8–32.4)	24.6 (23.4–25.8)	<0.001
Antihypertensive medication, %	14.6 (13.9–15.4)	13.0 (12.2–13.9)	16.4 (15.4–17.4)	<0.001
FPG, mg/dL	96.8 (96.4–97.2)	98.5 (97.9–99.1)	94.9 (94.4–95.4)	<0.001
Diabetes, %	8.3 (7.7–8.8)	8.9 (8.2–9.7)	7.5 (6.9–8.2)	0.003
Serum TC, mg/dL	187.8 (187.0–188.6)	186.8 (185.7–187.9)	188.9 (188.0–189.9)	0.003
Serum TG, mg/dL	136.1 (133.8–138.4)	157.7 (153.8–161.6)	112.2 (110.3–114.1)	<0.001
Serum HDL-C, mg/dL	52.6 (52.3–52.9)	49.8 (49.4–50.2)	55.7 (55.4–56.1)	<0.001
eGFR, mL/min per 1.73 m^2	95.3 (94.9–95.6)	92.9 (92.5–93.4)	97.9 (97.3–98.4)	<0.001
eGFR < 60 mL/min per 1.73 m^2, %	2.5 (2.3–2.8)	2.7 (2.4–3.2)	2.3 (2.0–2.7)	0.109
Component of metabolic syndrome				
High WC, %	24.8 (23.8–25.8)	25.4 (24.1–26.8)	24.1 (23.0–25.3)	0.104
High blood pressure, %	36.2 (35.1–37.3)	42.0 (40.5–43.5)	29.8 (28.6–31.0)	<0.001
High FPG, %	26.3 (25.3–27.3)	30.0 (28.7–31.4)	22.2 (21.1–23.3)	<0.001
High TG, %	29.2 (28.3–30.0)	36.9 (35.5–38.2)	20.7 (19.7–21.7)	<0.001
Low HDL-C, %	26.0 (25.1–26.8)	19.1 (18.0–20.2)	33.5 (32.4–34.7)	<0.001
Metabolic syndrome, %	22.2 (21.4–23.0)	24.3 (23.1–25.4)	19.9 (18.9–20.9)	<0.001
24hUNaE, mg/d	4331 (4268–4394)	3964 (3885–4044)	4736 (4654–4817)	<0.001

Data are expressed as means with 95% CI.
24hUNaE = 24-h urinary sodium excretion, BMI = body mass index, BP = blood pressure, CI = confidence interval, eGFR = estimation of glomerular filtration rate, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride, WC = waist circumference.

TABLE 6. Adjusted Weighted Prevalence of Metabolic Syndrome Component of Korean Adult Men and Women by Estimated 24-h Urine Na Excretion

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P_{trend}
Men					
Abdominal obesity, %	22.1 ± 1.2	25.9 ± 1.3	27.7 ± 1.4	$28.1 \pm 1.4^{\dagger}$	0.002
High BP, %	40.9 ± 1.3	41.3 ± 1.3	44.9 ± 1.5	$45.4 \pm 1.3^{\dagger}$	0.036
High FPG, %	29.9 ± 1.2	31.6 ± 1.3	29.1 ± 1.3	32.7 ± 1.3	0.221
High TG, %	35.4 ± 1.4	37.1 ± 1.4	38.5 ± 1.5	37.5 ± 1.5	0.470
Low HDL-C, %	17.9 ± 1.0	18.8 ± 1.1	20.7 ± 1.3	20.1 ± 1.4	0.297
Metabolic syndrome, %	22.4 ± 1.0	24.7 ± 1.1	26.8 ± 1.3	$26.6 \pm 1.3^{\dagger}$	0.025
Metabolic syndrome, %*	21.6 ± 1.0	24.2 ± 1.1	26.2 ± 1.3	$26.1 \pm 1.3^{\dagger}$	0.016
Women					
Abdominal obesity, %	19.4 ± 0.9	24.2 ± 1.1	25.2 ± 1.1	$29.8 \pm 1.2^{\dagger,\ddagger,\S}$	<0.001
High BP, %	27.6 ± 0.7	28.3 ± 0.8	31.7 ± 0.9	$35.1 \pm 1.0^{\dagger,\ddagger,\S}$	<0.001
High FPG, %	22.1 ± 0.9	20.7 ± 1.0	23.7 ± 1.1	22.9 ± 1.1	0.245
High TG, %	17.6 ± 0.9	19.0 ± 1.0	22.4 ± 1.0	$25.0 \pm 1.2^{\dagger,\ddagger}$	<0.001
Low HDL-C, %	33.3 ± 1.1	33.9 ± 1.1	33.6 ± 1.1	34.5 ± 1.2	0.909
Metabolic syndrome, %	18.1 ± 0.8	18.5 ± 0.9	21.2 ± 1.0	$23.7 \pm 1.0^{\dagger,\ddagger}$	<0.001
Metabolic syndrome, %*	17.3 ± 0.8	17.9 ± 0.9	20.7 ± 1.0	$23.3 \pm 1.0^{\dagger,\ddagger}$	<0.001

Mean ± standard error of the mean. Age, antihypertensive medication, daily calories intake, heavy alcohol drinking, regular exercise, and college graduation adjusted. Abdominal obesity, waist circumference, ≥90 cm in men and was ≥80 cm in women.

BP = blood pressure, eGFR = estimation of glomerular filtration rate, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein-cholesterol, TG = triglycerides.

*Metabolic syndrome (%), after exclusion of eGFR < 60 mL/min per 1.73 m^2.

$\dagger P < 0.05$, quartile 4 vs quartile 1.

$\ddagger P < 0.05$, quartile 4 vs quartile 2.

$\S P < 0.05$, quartile 4 vs quartile 3.

(95% CI = 1.34–2.06) in men and 1.94 (1.49–2.53) in women after adjustment for confounding factors. No significant association was observed in all subjects or in gender-stratified subgroups with antihypertensive medications.

DISCUSSION

In this nationwide survey, 22.2% of Korean adults had metabolic syndrome, and we observed that the mean 24hUNaE, estimated by spot urine sodium excretion, was higher in subjects with metabolic syndrome compared with those without, even though mean 24hUNaE was high (4331 mg/d) in Korean adults, which is more than double the recommended level. Even after adjusting for age, daily calorie intake, heavy alcohol drinking, regular exercise, college graduation, and antihypertensive medication, there was a significant independent association of high sodium intake with the presence of metabolic syndrome in men and women. In subjects not taking any antihypertensive medication, the weighted odds ratio for metabolic syndrome in the highest 24hUNaE quartile, with the lowest quartile as the reference, was 1.56 (95% CI = 1.33–1.84) in the total population, 1.66 (1.34–2.06) in men, and 1.94 (1.49–2.53) in women. Although the degree of renal function affects the 24hUNaE,[17] restricting analyses to subjects without decreased eGFR (<60 mL/min per 1.73 m^2) did not alter our findings.

To date, few studies have examined the association between sodium intake and metabolic syndrome. In a study of normotensive subjects in Brazil (<130/85 mm Hg, n = 781), there was no difference in 24hUNaE between subjects with and without metabolic syndrome (men: 96 ± 48 and 97 ± 49 mEq/12 h,

P = 0.75; women: 83 ± 51 and 93 ± 45, P = 0.22, respectively), and weight-adjusted urinary sodium values were lower in subjects with than in those without metabolic syndrome (1.27 ± 0.64 and 1.42 ± 0.88 mEq/kg, respectively, P = 0.06).[18] A previous Korean study using the KNHANES III database (2005) found that sodium intake, estimated from food composition tables, did not differ between subjects with and those without metabolic syndrome (5722.4 ± 3301.0 mg/d vs 5658.3 ± 3294.3 mg/d, respectively, P = 0.629).[19] That study examined the association between dietary patterns, including sodium intake and BP, relying on 24-h dietary recall, which is not suitable for estimating population sodium intake in epidemiological studies because of changes in or under-reporting of energy or sodium intake and difficulty in quantifying the dietary sodium in dietary assessments.[20] In contrast, whereas Hoffmann and Cubeddu reported that sodium intake was more closely associated with metabolic syndrome in Venezuelan men than in women (n = 251), Rhee et al reported that a significant association was only seen in Korean women (n = 272). These 2 studies used 24-h urine collection, which seems to be the most accurate method, but had small sample sizes and nonhomogenous study populations.[21,22] These differences in outcomes may be due to differences in study populations, differences in mean levels of sodium intake or salt sensitivity between populations, cultural groups, or genders, diagnostic criteria for metabolic syndrome (e.g., WC criterion for abdominal obesity), the method of salt-intake measurement, differences in adjustment of confounding factors, or statistical methods.

A previous study by Huh et al, which included 3545 men and 3617 postmenopausal women ages 45 years older and used KNHANES 2008 to 2010 data, found that the highest 24hUNaE

tertile was significantly associated with WC, hypertriglyceridemia, and hypertension in postmenopausal women but with only WC in men.[23] The prevalence of metabolic syndrome was higher in subjects in the third tertile compared with the first quartile in women but not in men ($P < 0.001$ vs 0.259, respectively). Compared with that study, which did not adjust for the effects of confounding factors including age, gender, daily calorie intakes, and socio-demographic factors, our study included an extensive population not limited with regard to menopausal status and age and represented a weighted comparison adjusted for confounding factors using population-based data from a representative population. Using this approach, we showed similar associations between 24hUNaE and the prevalence of metabolic syndrome in gender-stratified analyses.

In most epidemiologic data, sodium intake is higher in men than women, but this difference was reversed after adjustment for daily calorie intake because sodium intake is determined, to a large extent, by calorie intake.[24,25] Further studies about factors associated with high sodium intake in the daily diet are needed to clarify this difference in Koreans.

The mechanism of the connection between increased 24hUNaE and insulin resistance, the core component of metabolic syndrome, is not fully defined. Although a direct mechanism between abdominal obesity and high salt intake is not conclusive, a high-calorie diet could be a possible explanation.[26] In agreement with a previous report,[27] high 24hUNaE was associated with daily total calorie intake in the present study. However, after adjustment for daily calorie intake, the association between abdominal obesity and 24hUNaE remained statistically significance. Albuminuria is a common feature of insulin resistance and metabolic syndrome, and a marker of CVDs. We previously reported that the prevalence of albuminuria increased with 24hUNaE quartile, and the highest 24hUNaE quartile was significantly associated with the presence of albuminuria in the multiple logistic regression analysis adjusted for age, gender, diabetes, obesity, and hypertension.[10] High sodium intake has various effects on each component of metabolic syndrome and thus on metabolic syndrome overall. Recently, it was suggested that insulin increases salt sensitivity; furthermore, high salt intake was associated with increased glucocorticoid production, and it may induce insulin resistance and metabolic syndrome.[28,29] In addition, high salt intake increased intracellular Ca^{2+} leak which increased vascular tone in vascular smooth muscle cells and caused defective glucose homeostasis in β cells, via some mechanisms including the type 2 ryanodine receptor.[30,31] Further studies will be needed to clarify the underlying mechanism of high-salt diet-induced insulin resistance and metabolic syndrome.

There is solid evidence that high sodium intake increases BP, and interventions to reduce the sodium intake have been shown to reduce BP.[32,33] Our study showed that high BP could play a role in the association between sodium intake and metabolic syndrome. In this study, subjects taking antihypertensive medication showed lower 24hUNaE than did those without medication in both men and women; indeed, the results for the former group were comparable to results for those without hypertension. This finding raises the question of whether subjects receiving treatment for high BP restrict their sodium intake or whether the antihypertensive medications decrease sodium excretion. However, the latter possibility is inconsistent with the finding that sympathetic activation in subjects with hypertension increases renal sodium retention via stimulation of α_{1b}-adrenoreceptors and activation of juxtaglomerular cells by β_1-adrenoreceptors; additionally, antihypertensive medications, diuretics, and aldosterone blockers increase sodium excretion.[34,35] A more reasonable explanation for this finding is that individuals taking antihypertensive medications, where more extensive lifestyle modifications are often applied, restrict their sodium intake as recommended. Thus, this result is similar to findings that hypertensive patients taking medications showed lower daily salt intake compared to those without mediations under ambulatory conditions.[36] Thus, varying degrees of therapeutic lifestyle modification may be a confounding factor for the relationship between sodium intake and high BP in subjects with metabolic syndrome. Future studies may explain the observed differential association of decreased sodium intake with high BP by antihypertensive medication status.

There are several limitations to our study. We were not able to evaluate causality due to the cross-sectional design. Additionally, data on specific drug histories or other dietary components that might affect urinary sodium excretion were not available. Low dietary intake of potassium potentiates the effects of increased salt intake on BP.[6] Another limitation was that urinary sodium excretion was not determined by 24-h collection, but by estimation from spot urine specimens. Single measurements of spot urinary sodium excretion do not allow precise quantification of an individual's sodium intake or validation of the variability of an individual's day-to-day dietary patterns. Although 24-h urine collection was used as the gold standard in validation studies, collecting 24-h urine was not feasible in this large-scale survey because it is labor intensive, and low response rates and under-collection create the potential for bias. In this study, a low-cost method with easy sampling and a large sample size was used to provide a valid population estimate of the level of sodium intake using spot urine sampling. In this study, low cost with readily sampling and a large sample size could account for valid estimate of population level of sodium intake using spot urine sampling. Lastly, the genetic variations with sensitivity of BP to dietary salt were not considered in this study. However, knowing specific genetic variants associated with salt sensitivity or hypertension, like the G-protein-coupled receptor kinases,[37] calcium/calmodulin-dependent kinase IV,[38] or platelet antigen 1,[39] could understand susceptibility for hypertension and improve cardiovascular health in subjects with high sodium intake and metabolic syndrome. Despite these limitations, with the strength of a nationwide representative sample size, we found a clear association of the estimated 24hUNaE with the presence of metabolic syndrome. Thus, we suggest that sodium intake is involved in the development of metabolic syndrome.

In conclusion, subjects with metabolic syndrome had higher estimated 24hUNaE compared with those without it. 24hUNaE levels were increasing along the number of metabolic syndrome component, known as CVD risk factors. The relationship remained significant after adjustment for age, daily calorie intake, heavy alcohol drinking, regular exercise, college graduation, and antihypertensive medication, as well as excluding subjects with decreased renal function in men and women. This nationwide study of the relationship between 24hUNaE and metabolic syndrome may help to develop a comprehensive public health strategy to lower the prevalence of metabolic syndrome in Koreans.

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