Urinary sodium and potassium excretion and risk of hypertension in Chinese: report from a community-based cohort study in Taiwan

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Background **Dietary sodium intake is associated with blood pressure and hypertension risk. However, most of the studies have been conducted in whites and it is not clear whether the effects exist in Asian populations.**

Objective **The purpose of the present study was to investigate the role of 24-h urinary sodium excretion and hypertension risk among ethnic Chinese.**

Design **A prospective cohort design on community.**

Setting and participants **One thousand five hundred and twenty middle-aged and elderly participants who were free from hypertension at baseline and had available urine electrolyte data.**

Main outcome measures **Hypertension incidence.**

Results **During a median 7.93 years of follow-up (interquartile range = 4.07–9.04 years), we documented 669 cases of incident hypertension. The multivariate risk was 1.26 (95% confidence interval = 1.01–1.57; $P = 0.043$) for individuals in the highest quartile of urinary sodium excretion as compared with those in the second quartile. A significant J-shape relationship between urinary sodium excretion and the risk of hypertension was observed, with the test for linear relation being rejected ($P = 0.046$). Participants who were in the highest quartile of urinary sodium excretion and higher baseline blood pressure had a 2.43-fold increased risk of hypertension (95% confidence interval = 1.72–3.22) compared with those in the lowest quartiles of urinary sodium and lower blood pressure.**

Conclusion **Urinary sodium excretion was associated with the risk of hypertension among ethnic Chinese. Urinary sodium excretion, as a marker of dietary sodium intake, can be useful for a comprehensive evaluation of hypertension risk in Asian populations. *J Hypertens* 26:1750–1756 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Keywords: cohort, hypertension, urinary sodium

Abbreviations: HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol

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Introduction

Hypertension appreciably increases the cardiovascular risk and has a great public burden worldwide. High hypertension incidence rates are found among middle-to-elderly-aged adults, and the risk factors for hypertension incidence include age, sex, obesity, metabolic syndrome, and lifestyle factors [1,2]. Among lifestyle factors, dietary sodium and potassium intakes are associated with blood pressure (BP) and hypertension risk in many ecological and cross-sectional studies [3,4]. For example, a cross-sectional European study showed a linear trend between sodium intake and BP levels [5]. However, the ecological and cross-sectional studies were confounded by various modifying factors and were susceptible to bias [6]. Furthermore, geographical and ethnic variations on sodium intake were found [3,4,7]. Information about the role of urinary sodium and potassium excretion in hypertension risk has been relatively rare from the ethnic Chinese community, which actually has the highest sodium intake [3]. Therefore, prospective cohort data from community participants may provide a valid answer for the relationship between urinary sodium excretion and hypertension risk.

Methods

Study design and population

Details of the present cohort study have been published previously [2,8,9]. Briefly, the Chin-Shan Community Cardiovascular Cohort Study (CCCC) began in 1990 by recruiting 1703 men and 1899 women of Chinese

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ethnicity aged 35 years and older from the Chin-Shan township, 30 km north of metropolitan Taipei, Taiwan. Information about anthropometry, lifestyle, and medical conditions was assessed by interview questionnaires in 2-year cycles for the initial 6 years, and the validity and reproducibility of the collected data and measurements have been reported in detail elsewhere [9]. In brief, all study participants were individually interviewed with a structured questionnaire in the baseline survey. Trained medical students canvassed door-to-door with the assistance of community leaders to extend invitations for the baseline survey to collect information on sociodemographic characteristics, lifestyle behaviors, regular exercise, and a personal and family history of diseases and hospitalizations. With the consent of participants, physicians and students conducted physical examinations and laboratory tests for those participants invited to the clinic. BMI was calculated as weight (kg)/height (m^2). From 1992, the waist circumference was measured by using a measuring tape positioned at the midway between the lowest rib and the iliac crest. The measurement was made at minimal respiration status, with the tape snug but without compressing the skin. BP was measured twice in the right arm by a mercury sphygmomanometer with the participant seated comfortably and arms supported and positioned at the level of the heart. The average of the BP measurements was used as described previously [2,10].

Participants with a baseline diagnosis of hypertension (BP $\geq$140/90 mmHg or with an antihypertensive medication history, $n = 1096$) or incomplete urine collection data at baseline ($n = 986$) were excluded from this investigation. After these exclusions, the final analytic sample included 1520 participants with complete urine data. Because the recruitment strategy was volunteer based and the participants were from just one community, our participants were not representative of the general population. The National Taiwan University Hospital Committee Review Board approved the study protocol. Incident hypertension cases were ascertained through biennial BP measurements and medication history was obtained from questionnaires, and was defined as sitting systolic BP of at least 140 mmHg, diastolic BP of at least 90 mmHg, or antihypertensive treatment.

Measurement of urine sodium and potassium excretion

The 24-h urine collection was considered the most reliable method to evaluate sodium and potassium intake amounts [11,12]; however, other modifications, such as causal urine specimens [13] and second morning voiding urine collection [12], were more feasible methods and have been validated in epidemiological studies. We used the second morning voiding urine amount as follows. We dispersed a plastic container to all participants and instructed them to collect the overnight urine and record their sleep time. Participants were asked to collect their overnight urine after voiding all urine before sleep. The sleep time was recorded and the 24-h urine amount was calculated from the sleep time and morning voiding urine. We did not ask the participants to change their dietary patterns during the collection so that the urine sodium and potassium excretion amount could be considered as a marker for usual intake. Electrolytes in the urine were measured by selective electrodes of the Dimension autoanalyzer (Du Pont, Wilmington, Delaware, USA) [14,15].

Biochemical markers

The procedure for blood collection has been reported elsewhere [16,17]. Briefly, all venous blood samples drawn after a 12-h overnight fast were immediately refrigerated and transported within 6 h to the National Taiwan University Hospital. Serum samples were then stored at -70°C before batch assay for levels of total cholesterol, triglyceride, and high-density lipoprotein cholesterol (HDL-C) were performed. Standard enzymatic tests for serum cholesterol and triglyceride were used (Merck 14354 and 14366, Merck Chemical, Darmstadt, Germany, respectively). HDL-C levels were measured in supernatants after the precipitation of specimens with magnesium chloride phosphotungstate reagents (Merck 14993). The low-density lipoprotein cholesterol (LDL-C) concentration was calculated as the total cholesterol concentration minus the concentration of cholesterol in the supernatant obtained with the precipitation method (Merck 14992) [18]. Plasma uric acid concentrations were assayed with commercial kits (Merck Chemical, Darmstadt, Germany) and placed in an Eppendorf 5060 autoanalyzer (Eppendorf Corp, Hamburg, Germany) [19]. The diagnosis of diabetes was done by fasting glucose levels of at least 126 mg/dl or by the use of oral hypoglycemic medications or insulin.

Statistical analysis

Participants were categorized on the basis of quartiles of 24-h urinary sodium excretion, continuous variables were presented by mean and standard deviation, and analysis of variance was used to test the difference across the quartiles. Correlations between urinary sodium and potassium excretion and other cardiovascular risk factors were estimated by Spearman's partial correlation coefficients adjusted for age and sex. Incidence rates of hypertension were calculated by dividing the number of cases by the person-years of follow-up for each quartile of urinary sodium and potassium excretion. The relative risk (RR) of hypertension was calculated by dividing the incidence rate of urinary sodium excretion in each quartile by the rate in the second quartile. We chose the second quartile as the reference group because the median sodium excretion value in the second quartile was nearly identical to the recommended upper limit (100 mmol per day) in the general population [20]. We used the Cox proportional-hazards models to adjust for

potential confounding variables, including age groups (35–44, 45–54, 55–64, 65–74, ≥75 years of age), sex, BMI (<18, 18–20.9, 21–22.9, 23–24.9, or ≥25 kg/m^2), alcohol intake (nondrinker/current), smoking (yes/no), regular exercise (yes/no), marital status (single, married, or divorced), educational level (<9 years, ≥9 years), occupation (no work, manual work, or professional), and regular physical activity (yes/no). We further adjusted for continuous systolic BP and diabetes (yes/no) to examine whether the effects were reduced by baseline BP and diabetes status. In addition, we examined the nonlinear relationship between urinary sodium excretion and the risk of hypertension nonparametrically with restricted cubic splines [21]. Tests for nonlinearity included the likelihood ratio test, comparing the model with only the linear term with the model with the linear and the cubic spline terms. Furthermore, we examined whether the association between urinary sodium excretion and hypertension was mediated through several confounding factors, including sex, age, BMI, and systolic BP. The likelihood ratio tests were used to compare the model with the interaction terms and the model without the interaction terms. We also tested the goodness of fit for the model by using the Hosmer and Lemeshow test [22], and the goodness-of-fit test was acceptable ($P = 0.85$). Finally, we conducted joint analyses to evaluate potential additive effects by baseline BMI and systolic BP using median values as the cutoffs. All statistical tests were two-tailed with a type I error of 0.05, and $P < 0.05$ was considered statistically significant. Analyses were performed using the SAS software version 9.1 (SAS Institute, Cary, North Carolina, USA).

Results

Participants in the highest quartile of urinary sodium excretion had a higher education level and diabetes rate and were more likely to have a higher BMI, systolic and diastolic BP, and total cholesterol and LDL-C levels than the participants in the other quartiles (Table 1). Similar distributions of sex, age, triglyceride, HDL-C, fasting glucose, and uric acid levels were found across various quartiles of urinary sodium excretion, and there was no difference in the lifestyle and socioeconomic status across the urinary sodium excretion quartiles.

The correlations between urinary sodium and other risk factors ranged from 0.011 for triglycerides to 0.099 for BMI, and those between urinary potassium and other risk factors were higher, ranging from 0.035 for systolic BP to 0.133 for BMI (Table 2). The urinary sodium excretion

Table 1 Distribution of various baseline demographic, lifestyle, and socioeconomic factors in the study population in the CCCC cohort, specified by urinary sodium excretion quartiles

	Q1	Q2	Q3	Q4	*P*
Sodium (mmol/24 h)	<84	84–122	122–178	≥178	
Median (mmol/24 h)	63	103	147	231	
Number	380	380	380	380	
Sex (%)					0.61
Men	50.0	47.9	48.7	45.3	
Women	50.0	52.1	51.3	54.7	
Current smoker (%)	36.1	36.1	35.0	33.7	0.89
Alcohol drinking (%)	32.6	30.3	29.7	25.0	0.13
Marital status (%)					0.52
Single	3.2	2.1	1.9	2.9	
Living with spouse	87.9	89.5	92.3	90.0	
Divorced or separated	9.0	8.4	5.8	7.1	
Education level (%)					0.030
<9 years	92.9	94.5	96.3	91.3	
≥9 years	7.1	5.5	3.7	8.7	
Job status (%)					0.26
No job	47.9	43.2	46.3	42.9	
Blue collar	34.5	39.7	36.3	34.5	
White collar	17.6	17.1	17.4	22.6	
Regular exercise habit (%)	14.0	15.3	14.0	14.2	0.95
Family history of CHD (%)	12.1	14.0	9.7	9.7	0.19
Diabetes (%)	10.6	9.8	10.3	15.1	0.08
Age (year)	51.5 ± 12.0	52.9 ± 11.9	52.4 ± 11.4	51.3 ± 10.6	0.18
BMI (kg/m^2)	22.7 ± 3.1	22.8 ± 3.0	23.3 ± 3.0	23.6 ± 3.6	0.0001
Systolic BP (mmHg)	115.1 ± 11.3	114.5 ± 11.3	115.5 ± 10.9	117.0 ± 10.8	0.017
Diastolic BP (mmHg)	72.4 ± 7.8	72.3 ± 8.2	72.7 ± 7.8	74.0 ± 7.6	0.011
Cholesterol (mg/dl)	188.9 ± 42.2	197.7 ± 44.6	196.2 ± 43.3	201.6 ± 46.2	0.001
Triglyceride (mg/dl)	117.1 ± 91.1	119.3 ± 96.2	112.7 ± 84.6	118.4 ± 83.9	0.75
HDL-C (mg/dl)	47.2 ± 12.2	48.9 ± 12.3	48.6 ± 12.1	48.6 ± 12.9	0.26
LDL-C (mg/dl)	129.7 ± 39.3	137.2 ± 44.5	135.2 ± 41.3	140.2 ± 44.9	0.007
Fasting glucose (mg/dl)	107.3 ± 25.3	106.9 ± 26.6	108.9 ± 34.1	111.1 ± 29.3	0.19
Uric acid (mg/dl)	5.63 ± 1.68	5.50 ± 1.79	5.44 ± 1.54	5.47 ± 1.57	0.41
Urine sodium (mmol/24 h)	60 ± 17	103 ± 11	148 ± 16	248 ± 72	<0.0001
Urine sodium (g/24 h)	1.39 ± 0.40	2.36 ± 0.26	3.40 ± 0.37	5.70 ± 1.66	<0.0001

The values are mean ± SD. BP, blood pressure; CCCC, Chin-Shan Community Cardiovascular Cohort; CHD, coronary heart disease; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

Table 2 Age-adjusted and sex-adjusted Spearman partial correlation coefficients between various measurements and urinary electrolyte excretion among the study participants in the CCCC Study cohort

	BMI	Systolic BP	Diastolic BP	Cholesterol	Triglyceride	HDL-C	LDL-C	Glucose	Uric acid
Urinary sodium	0.099***	0.067**	0.075***	0.070**	0.011	0.034	0.059*	0.052*	−0.018
Urinary potassium	0.133***	0.035	0.052*	0.078**	0.049	−0.020	0.082**	0.108***	0.084***
Urinary sodium : potassium ratio	−0.018	0.022	0.026	0.012	−0.021	0.055*	−0.005	−0.010	−0.108***

BP, blood pressure; CCCC, Chin-Shan Community Cardiovascular Cohort; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol. * $P<0.05$. ** $P<0.01$. *** $P<0.001$.

was significantly correlated with BP (0.067–0.075) and cholesterol (0.059–0.070), and the urinary potassium excretion was significantly correlated with glucose (0.108) and uric acid (0.084).

During a median 7.93 years of follow-up (interquartile range = 4.07–9.04 years) among 1520 participants with available urinary sodium excretion data, we documented 669 cases of incident hypertension. Except for the first quartile, the incidence rates of hypertension increased with increasing quartiles of urinary sodium excretion (Table 3). In age and sex-adjusted analyses, the RR comparing individuals in the fourth quartile with those in the second quartile of urinary sodium excretion was 1.48 [95% confidence interval (CI) = 1.19–1.83; $P=0.004$], and the RR for individuals in the first quartile was 1.31 (95% CI = 1.05–1.64; $P=0.018$). The magnitude of risk of hypertension remained significant even after controlling for BMI, lifestyle, socioeconomic status, baseline diabetes status, and systolic BP; for individuals in the highest quartile, the multivariate RR was 1.26 (95% CI = 1.01–1.57; $P=0.043$) as compared with those in the second quartile. However, the risk for the participants in the first quartile became borderline significant (RR = 1.24; 95% CI = 0.99–1.56; $P=0.07$). A significant J-shape relationship between urinary sodium excretion and the risk of hypertension was observed (Fig. 1), with the test for a linear relation being rejected ($P=0.046$). In contrast, the incidence rates were similar across the quartiles for urinary potassium and sodium as compared with potassium ratio values, and the RRs were not significant (Table 2).

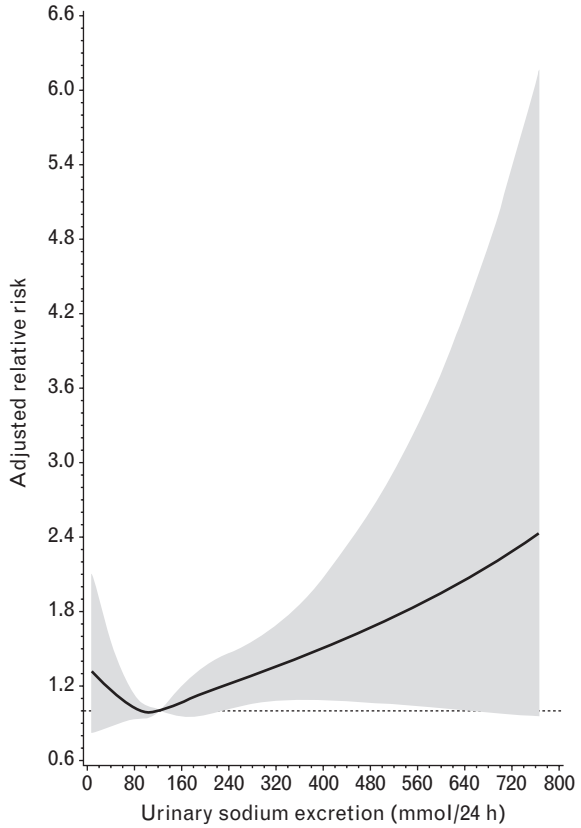
In joint analyses of BMI as well as systolic BP and urinary sodium excretion, participants with a higher BMI and systolic BP had a consistently higher risk than those with lower values, independent of quartiles of urinary sodium excretion (Fig. 2). The association between urinary

Table 3 Relative risks (and 95% confidence intervals) of hypertension incidence during a median 7.9 years of follow-up according to quartiles of urinary sodium and potassium excretion in the CCCC Study

	Q1				Q3			Q4		
Urinary sodium[a]	RR	95% CI	*P*	Q2	RR	95% CI	*P*	RR	95% CI	*P*
Model 1	1.31	1.05–1.64	0.018	1	1.16	0.92–1.44	0.21	1.48	1.19–1.83	0.0004
Model 2	1.32	1.05–1.65	0.016	1	1.10	0.88–1.37	0.42	1.41	1.14–1.76	0.002
Model 3	1.28	1.02–1.61	0.033	1	1.11	0.88–1.39	0.39	1.41	1.13–1.76	0.002
Model 4	1.24	0.99–1.56	0.07	1	1.11	0.89–1.39	0.37	1.26	1.01–1.57	0.043
		Q2			Q3			Q4		
Urinary potassium[b]	Q1	RR	95% CI	*P*	RR	95% CI	*P*	RR	95% CI	*P*
Model 1	1	1.16	0.93–1.44	0.19	1.10	0.88–1.37	0.40	1.17	0.94–1.46	0.16
Model 2	1	1.09	0.88–1.36	0.44	1.04	0.83–1.30	0.72	1.07	0.86–1.34	0.55
Model 3	1	1.10	0.88–1.37	0.40	1.06	0.85–1.33	0.60	1.09	0.87–1.37	0.44
Model 4	1	0.97	0.77–1.21	0.75	1.01	0.80–1.26	0.95	0.98	0.78–1.23	0.88
		Q2			Q3			Q4		
Sodium vs. potassium[c]	Q1	RR	95% CI	*P*	RR	95% CI	*P*	RR	95% CI	*P*
Model 1	1	0.96	0.77–1.19	0.71	1.01	0.81–1.26	0.92	1.07	0.87–1.33	0.52
Model 2	1	1.00	0.80–1.25	0.99	1.03	0.83–1.28	0.79	1.10	0.89–1.37	0.38
Model 3	1	0.99	0.79–1.23	0.90	1.04	0.83–1.30	0.72	1.10	0.89–1.37	0.38
Model 4	1	0.96	0.76–1.19	0.69	0.99	0.79–1.24	0.94	1.09	0.88–1.36	0.44

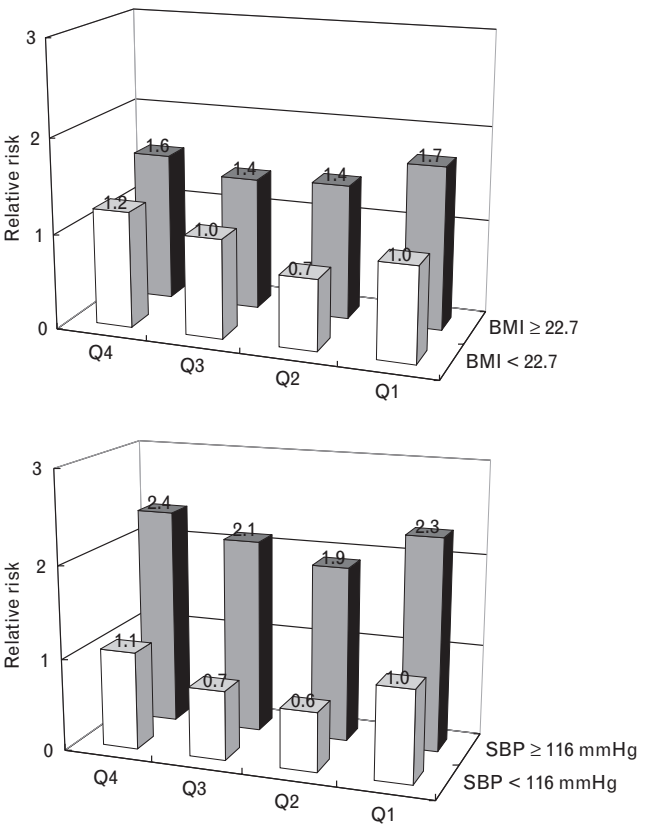
Incidence rates presented as per 1000 person-years. Model 1: adjusted for age groups (35–44, 45–54, 55–64, 65–74, ≥75 years of age) and sex. Model 2: Model 1 and BMI (<18, 18–20.9, 21–22.9, 23–24.9, or ≥25 kg/m^2). Model 3: Model 2 and smoking (yes/no or abstinence), current alcohol drinking (regular/no), marital status (single, married and living with spouse, or divorced and separated), education level (less than 9 years, at least 9 years), occupation (no work, labor, official or business), and regular exercise habit (yes/no). Model 4: Model 3 and baseline systolic blood pressure (continuous variable) and diabetes status (yes/no). CCCC, Chin-Shan Community Cardiovascular Cohort; CI, confidence interval; RR, relative risk. [a] Q1: cases: 165; person-years: 2432; rates (/1000): 67.8. Q2: cases: 144; person-years: 2558; rates (/1000): 56.3. Q1: cases: 167; person-years: 2581; rates (/1000): 64.7. Q1: cases: 193; person-years: 2453; rates (/1000): 78.7. [b] Q1: cases: 151; person-years: 2455; rates (/1000): 61.5. Q2: cases: 177; person-years: 2498; rates (/1000): 70.9. Q3: cases: 169; person-years: 2585; rates (/1000): 65.4. Q4: cases: 172; person-years: 2487; rates (/1000): 69.2. [c] Q1: cases: 160; person-years: 2482; rates (/1000): 64.5. Q2: cases: 163; person-years: 2565; rates (/1000): 63.5. Q3: cases: 168; person-years: 2482; rates (/1000): 67.7. Q4: cases: 178; person-years: 2494; rates (/1000): 71.4.

Fig. 1



Relationship between urinary sodium excretion and risk of hypertension. The multivariate adjusted relative risk is plotted as a function of the baseline urinary sodium excretion value with the 95% confidence bands shown as the shaded areas.

Fig. 2



Multivariate adjusted relative risk of hypertension incidence during a median 7.9 years of follow-up according to quartiles of urinary sodium excretion and BMI as well as blood pressure status. Cutoff points for the quartiles of urinary sodium excretion were less than 84 mmol, 84–122 mmol, 122–178 mmol and at least 178 mmol and cutoff points as the median values of BMI (22.7 kg/m^2) and systolic blood pressure (116 mmHg). SBP, systolic blood pressure.

sodium excretion and hypertension risk appears to be stronger among those with a higher systolic BP than those with a lower BP, and the interaction between urinary sodium excretion and BMI and BP was significant (both *P*-values for interaction <0.001). Participants who were in the highest quartile of urinary sodium excretion and higher baseline BP had a 2.43-fold increased risk of hypertension (95% CI = 1.72–3.22) compared with those in the lowest quartiles of urinary sodium excretion and lower BP.

Discussion

In the present prospective cohort study, 24-h urinary sodium excretion amounts were significantly associated with the risk of developing hypertension over a median of 7.9 years of follow-up. The J-shape relationship was independent of BMI, diabetes, physical activity, and other conventional risk factors and not explained by baseline BP levels. We did not find the urinary potassium excretion as a protective factor for hypertension risk.

Intrapopulation and interpopulation studies on sodium intake and the risk of hypertension have proven that there is a significant individual variation in daily sodium intake [23]. For example, the ecological Intersalt study showed that populations with a daily sodium intake of less than 1.3 g had low BP [3]. In contrast, a high-sodium diet was prevalent in both developed and developing countries. Among these Intersalt populations, northern Chinese have the highest sodium intake, up to 242 mmol/24 h, which is higher than median levels of the highest quartiles in our study population.

Increasing sodium intake is linked to arterial resistance, fluid intake and associated with platelet activation [23]. Excessive sodium also induces harmful effects, such as renal function impairment and aggravates the hypertension burdens [24]. Furthermore, increased sodium sensitivity is associated with less renin–angiotensin system activation and increased insulin resistance and therefore induces increased vasoconstriction and high BP [25]. A hypothesis of a threshold relationship between sodium intake and hypertension has been proposed [26]; individuals who ingest less than the amount for an increasing BP

effect of sodium do not develop hypertension; the lower limit is probably near 50 mmol/day sodium, and taking more than 100 mmol/day is enough to induce hypertension. However, our study supports that high urinary sodium excretion is related to hypertension risk. Furthermore, we found a J-shape relationship between BP and hypertension incidence; sodium intake in the lowest quartile (63 mmol/day) had a higher risk of hypertension, and those in the highest quartile (231 mmol/day) had a much higher risk. The median sodium excretion value in the second quartile was similar to the recommended upper limit (100 mmol/day) [20], and the median value of the third quartile was almost identical to the average intake in the United States (150 mmol/day) [27].

Although there is overwhelming evidence supporting dietary sodium as a major cause of raised BP [23,28], the findings with respect to an extremely low sodium risk have been inconclusive. Extremely low salt intake has been associated with increased cardiovascular risk, especially in vulnerable populations such as the elderly [29], although moderate sodium reduction is recommended [23,30]. Severe sodium restriction has been associated with elevated plasma catecholamine levels, which increases neurohormonal stress, and is related to a higher cardiovascular risk [31]. Participants in the lowest quartile of sodium intake from the National Health and Nutrition Examination Survey (NHANES) were likely to have a higher myocardial infarction and cardiovascular mortality [32,33]. According to the NHANES data, participants in the lowest quartile of sodium intake were more likely to have a lower body weight and to smoke more [34]. Putative dangers in strict sodium reduction have been proposed: (i) extremely low salt intake induces less cardiovascular reserve and the inability to reconstitute losses in stressful conditions and (ii) the activation of renin–angiotensin and sympathetic activity would make susceptible individuals at a higher risk for vascular damage [29,30]. Our study also showed similar patterns and our findings supported the hypothesis that a very low sodium intake was associated with increased hypertension risk. Further studies are warranted to clarify the underlying mechanism.

The dietary guidelines for sodium restriction to 100 mmol/day are well supported [23,30] because the threshold of a daily 100 mmol sodium intake is supported from short-term intervention trial data [30]. In fact, a moderate sodium reduction to a level of 100 mmol/day is reasonably easy to achieve and feasible [23]. Clinical trial data in Dietary Approaches to Stop Hypertension (DASH)-salt trial demonstrated that sodium reduction could lower BP significantly [27]. The levels of sodium intake were approximately 150 mmol, 100 mmol, and 50 mmol per day in three strata, which induced step-wise BP significantly [27]. Overall, reducing sodium intake by 50 mmol per day decreased BP by an average of 4–6 mmHg [35,36], with great variation between individuals. The large-scale well controlled Trials of Hypertension Prevention (TOHP-I) involving 2182 adults with diastolic BP from 80 to 89 mmHg for 18 months treatment on lifestyle interventions such as sodium restriction and weight reduction clearly demonstrated that a significantly substantial BP reduction was associated with decreased urinary sodium excretion [37]. Extended 10–15 years of observations on the 77% of the cohort participants found a 30% reduction in cardiovascular events among the intervention group [38]. Our study supports that the optimal daily sodium intake was around 100 mmol, consistent with the DASH-salt findings [27].

Our prospective study did not show the protective roles of urinary potassium excretion in the risk of hypertension incidence, although cross-sectional studies in various countries have shown an inverse relationship between dietary potassium and BP [39]. Our negative results resulted from urinary excretion as a poor surrogate for dietary potassium intake. In addition, our normotensive participants in the baseline may not be affected by a mildly increased potassium intake.

To our knowledge, this is the first extensive investigation of urinary sodium and potassium excretion and the risk of developing hypertension among ethnic Chinese. Because of the prospective cohort design, the baseline measurements of our cohort members were unlikely to be affected by disease status. Furthermore, the use of a community-based population could reduce the possibility of a selection bias. We also included important covariates including socioeconomic status, lifestyle factors, and clinical risk factors. Adjustment for these variables did not diminish the role of urinary sodium excretion in predicting hypertension incidence.

The study has several potential limitations. First, we only collected a single overnight urine sample, which may not be an adequate measurement of usual sodium intake. A single measurement of 24-h sodium excretion is a valid estimate of dietary sodium intake [13], and data from the overnight urine samples in the study were consistent with other population-based observational data. Furthermore, the participants did not change their dietary habits during the collection period so that the urine sample might be representative of a usual intake. Second, we did not validate the sodium intake through other methods such as a food frequency questionnaire and 24-h dietary recall methods. Furthermore, we did not estimate the processed foods with sodium intake and evaluate the different contents of foods. Methods for sodium intake from a 24-h dietary recall or a food frequency questionnaire are inaccurate measures of usual intake for the general population [40]. Accordingly, we used the secondary morning voiding urine amount as the surrogate for calculating 24-h urine sodium and potassium excretion [12]. We still did not

exclude measurement errors in quantifying the sodium intake. We believe the misclassification was undifferential and the true biological relationship between dietary sodium intake and BP may be more significant.

In summary, urinary sodium excretion is associated with the risk of hypertension among ethnic Chinese. Because of only a mild correlation between urinary sodium excretion and traditional vascular risk factors, urinary sodium excretion, as a marker of dietary sodium intake, can be useful for a comprehensive evaluation of hypertension risk in the Asian populations.

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There are no conflicts of interest.

References

1 Wang TJ, Gona P, Larson MG, Levy D, Benjamin EJ, Tofler GH, *et al.* Multiple biomarkers and the risk of incident hypertension. *Hypertension* 2007; **49**:432–438.
2 Chien KL, Hsu HC, Sung FC, Su TC, Chen MF, Lee YT. Incidence of hypertension and risk of cardiovascular events among ethnic Chinese: report from a community-based cohort study in Taiwan. *J Hypertens* 2007; **25**:1355–1361.
3 Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 h urinary sodium and potassium excretion. Intersalt Cooperative Research Group. *BMJ* 1988; **297**:319–328.
4 Zhou BF, Stamler J, Dennis B, Moag-Stahlberg A, Okuda N, Robertson C, *et al.* Nutrient intakes of middle-aged men and women in China, Japan, United Kingdom, and United States in the late 1990s: the INTERMAP study. *J Hum Hypertens* 2003; **17**:623–630.
5 Khaw KT, Bingham S, Welch A, Luben R, O'Brien E, Wareham N, Day N. Blood pressure and urinary sodium in men and women: the Norfolk Cohort of the European Prospective Investigation into Cancer (EPIC-Norfolk). *Am J Clin Nutr* 2004; **80**:1397–1403.
6 Rothman KJ, Greenland S. *Modern epidemiology*. Philadelphia: Lippincott-Raven Publishers; 1998.
7 The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC investigators. *Am J Epidemiol* 1989; **129**:687–702.
8 Chien KL, Hsu HC, Su TC, Chen MF, Lee YT, Hu FB. Apolipoprotein B and nonhigh-density lipoprotein cholesterol and risk of coronary heart disease in Chinese. *J Lipid Res* 2007; **48**:2499–2505.
9 Lee YT, Lin RS, Sung FC, Yang C, Chien K, Chen W, *et al.* Chin-Shan Community Cardiovascular Cohort in Taiwan: baseline data and five-year follow-up morbidity and mortality. *J Clin Epidemiol* 2000; **53**:838–846.
10 Chien KL, Yang CY, Lee YT. Major gene effects in systolic and diastolic blood pressure in the families receiving health examination in Taiwan. *J Hypertens* 2003; **21**:1–7.
11 INTERSALT Study an international co-operative study on the relation of blood pressure to electrolyte excretion in populations. I. Design and methods. The INTERSALT Co-operative Research Group. *J Hypertens* 1986; **4**:781–787.
12 Kawasaki T, Itoh K, Uezono K, Sasaki H. A simple method for estimating 24 h urinary sodium and potassium excretion from second morning voiding urine specimen in adults. *Clin Exp Pharmacol Physiol* 1993; **20**:7–14.
13 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.
14 Keller H, Niederer R, Richter W. Ion-selective electrodes for determination of urine electrolytes (author's transl). *Biomed Tech (Berl)* 1980; **25**:42–47.
15 Kirschbaum B, Sica D, Anderson FP. Urine electrolytes and the urine anion and osmolar gaps. *J Lab Clin Med* 1999; **133**:597–604.
16 Chien KL, Lee YT, Sung FC, Hsu HC, Su TC, Lin RS. Hyperinsulinemia and related atherosclerotic risk factors in the population at cardiovascular risk: a community-based study. *Clin Chem* 1999; **45 (6 Pt 1)**:838–846.
17 Chien KL, Sung FC, Hsu HC, Su TC, Chang WD, Lee YT. Relative importance of atherosclerotic risk factors for coronary heart disease in Taiwan. *Eur J Cardiovasc Prev Rehabil* 2005; **12**:95–101.
18 Wieland H, Seidel D. A simple specific method for precipitation of low density lipoproteins. *J Lipid Res* 1983; **24**:904–909.
19 Fossati P, Prencipe L, Berti G. Use of 3,5-dichloro-2-hydroxybenzenesulfonic acid/4-aminophenazone chromogenic system in direct enzymic assay of uric acid in serum and urine. *Clin Chem* 1980; **26**:227–231.
20 Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; **289**:2560–2572.
21 Durrleman S, Simon R. Flexible regression models with cubic splines. *Stat Med* 1989; **8**:551–561.
22 Hosmer DW Jr, Lemeshow S. The multiple logistic regression model. Applied logistic regression. 1st ed. New York: John Wiley & Sons; 1989. pp. 25–37.
23 Dickinson BD, Havas S. Reducing the population burden of cardiovascular disease by reducing sodium intake: a report of the Council on Science and Public Health. *Arch Intern Med* 2007; **167**:1460–1468.
24 Brenner BM, Chertow GM. Congenital oligonephropathy and the etiology of adult hypertension and progressive renal injury. *Am J Kidney Dis* 1994; **23**:171–175.
25 Morimoto A, Uzu T, Fujii T, Nishimura M, Kuroda S, Nakamura S, *et al.* Sodium sensitivity and cardiovascular events in patients with essential hypertension. *Lancet* 1997; **350**:1734–1737.
26 Kaplan NM. Salt and blood pressure. In: Izzo Jr J, HRF B, editors. *Hypertension primer: the essentials of high blood pressure*, 2nd ed Baltimore: American Heart Association; 1999. pp. 247–252.
27 Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, *et al.* Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med* 2001; **344**:3–10.
28 He FJ, MacGregor GA. Salt, blood pressure and cardiovascular disease. *Curr Opin Cardiol* 2007; **22**:298–305.
29 Kumanyika SK, Cutler JA. Dietary sodium reduction: is there cause for concern? *J Am Coll Nutr* 1997; **16**:192–203.
30 Kaplan NM. The dietary guideline for sodium: should we shake it up? *Am J Clin Nutr* 2000; **71**:1020–1026.
31 Alderman MH. Presidential Address: 21st Scientific Meeting of the International Society of Hypertension: dietary sodium and cardiovascular disease: the 'J'-shaped relation. *J Hypertens* 2007; **25**:903–907.
32 Alderman MH, Cohen H, Madhavan S. Dietary sodium intake and mortality: the National Health and Nutrition Examination Survey (NHANES I). *Lancet* 1998; **351**:781–785.
33 Alderman MH, Madhavan S, Cohen H, Sealey JE, Laragh JH. Low urinary sodium is associated with greater risk of myocardial infarction among treated hypertensive men. *Hypertension* 1995; **25**:1144–1152.
34 Poulter NR. Dietary sodium intake and mortality: NHANES. The Faculty 31st International Society and Federation of Cardiology 10-day Teaching Seminar in Cardiovascular Disease, Epidemiology and Prevention. National Health and Nutrition Examination Survey. *Lancet* 1998; **352**:987–988.
35 Robertson JI. Dietary salt and hypertension: a scientific issue or a matter of faith? *J Eval Clin Pract* 2003; **9**:1–22.
36 He FJ, MacGregor GA. How far should salt intake be reduced? *Hypertension* 2003; **42**:1093–1099.
37 The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels. Results of the Trials of Hypertension Prevention, Phase I. *JAMA* 1992; **267**:1213–1220.
38 Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK, *et al.* Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ* 2007; **334**:885.
39 Wehelton P. Potassium and blood pressure. In: Izzo Jr J, HR B, editors. *Hypertension primer: the essentials of high blood pressure*, 2nd ed. Baltimore: American Heart Association; 1999. pp. 250–252.
40 Beevers DG. The epidemiology of salt and hypertension. *Clin Auton Res* 2002; **12**:353–357.