Hypertension Research (2019) 42:1590–1598
https://doi.org/10.1038/s41440-019-0263-1

ARTICLE

Urinary sodium-to-potassium ratio and intake of sodium and potassium among men and women from multiethnic general populations: the INTERSALT Study

Toshiyuki Iwahori[1,2,3] · Katsuyuki Miura[1,4] · Hirotsugu Ueshima[1,4] · Sachiko Tanaka-Mizuno[5] · Queenie Chan[6] · Hisatomi Arima[7] · Alan R. Dyer[8] · Paul Elliott[6] · Jeremiah Stamler[8] · for the INTERSALT Research Group

Received: 23 October 2018 / Revised: 18 February 2019 / Accepted: 24 March 2019 / Published online: 17 April 2019

Abstract

The Na/K ratio may be more strongly related to blood pressure and cardiovascular disease than sodium or potassium. The casual urine Na/K ratio can provide prompt on-site feedback, and with repeated measurements, may provide useful individual estimates of the 24-h ratio. The World Health Organization has published guidelines for sodium and potassium intake, but no generally accepted guideline prevails for the Na/K ratio. We used standardized data on 24 h and casual urinary electrolyte excretion obtained from the INTERSALT Study for 10,065 individuals aged 20–59 years from 32 countries (52 populations). Associations between the casual urinary Na/K ratio and the 24-h sodium and potassium excretion of individuals were assessed by correlation and stratification analyses. The mean 24-h sodium and potassium excretions were 156.0 mmol/24 h and 55.2 mmol/24 h, respectively; the mean 24-h urinary Na/K molar ratio was 3.24. Pearson's correlation coefficients (r) for the casual urinary Na/K ratio with 24-h sodium and potassium excretions were 0.42 and −0.34, respectively, and these were 0.57 and −0.48 for the 24-h ratio. The urinary Na/K ratio predicted a 24-h urine Na excretion of <85 mmol/day (the WHO recommended guidelines) with a sensitivity of 99.7% and 94.0%, specificity of 39.5% and 48.0%, and positive predictive value of 96.3% and 61.1% at the cutoff point of 1 in 24 h and casual urine Na/K ratios, respectively. A urinary Na/K molar ratio <1 may be a useful indicator for adherence to the WHO recommended levels of sodium and, to a lesser extent, the potassium intake across different populations; however, cutoff points for Na/K ratio may be tuned for localization.

Keywords Sodium-to-potassium ratio · sodium · potassium · casual urine · 24-h urine excretion

Introduction

The World Health Organization (WHO) has recommended that individuals reduce sodium (Na) and increase potassium (K) intake to lower blood pressure (BP) and improve cardiovascular health [1, 2]; however, large gaps remain between actual and recommended levels [3–6]. The commonly used formulas to estimate 24-h urine (gold standard for estimating dietary intake) for Na and K from casual urine contain both random and systematic errors [7–9]. These formulas are for population estimates rather than individual estimates; repeated measurements may minimize the random error introduced from the enormous intra-individual variability, although systematic error contained in these formulas cannot be reduced.

Emerging evidence suggests that the urinary Na/K ratio, as a measure of relative intake, may be more strongly related to BP and cardiovascular disease (CVD) risk than Na and K considered separately [6, 10–16]. Previous findings have indicated that casual urine Na/K ratio estimates of the 24-h urine Na/K ratio contain less systematic error [17–19]. Repeated measurements of the casual urine

Supplementary information The online version of this article (https://doi.org/10.1038/s41440-019-0263-1) contains supplementary material, which is available to authorized users.

✉ Toshiyuki Iwahori
iwahori@belle.shiga-med.ac.jp

Extended author information available on the last page of the article

Na/K ratio may minimize both systematic and random errors [18–20]; this method may be useful for estimation in individuals. Measurement of the casual urine Na/K ratio also has the potential for providing prompt feedback to individuals using a self-monitoring device [21]. However, it has not yet been established what levels of the urinary Na/K ratio correspond to particular levels of Na or K excretion in diverse demographic groups, i.e., cutoff values set in guidelines. Setting a goal for the Na/K ratio may be helpful to support efforts to reduce Na and increase K for individuals, and reduce the gaps between the actual and recommended target levels of Na and K intake in individuals and populations.

The present study used highly standardized data from 24 h and casual urine from the International Cooperative Study on Salt, Other Factors, and Blood Pressure (INTERSALT) [22, 23] to address two main aims. The first aim was to analyze the associations of casual and 24-h urinary Na/K ratios with 24-h urinary Na and K excretion. The second aim was to investigate the sensitivities, specificities and positive predictive values at different levels of the Na/K ratio that appear to meet the WHO guidelines for Na and K intake (Na: <85 mmol/day, K: >90 mmol/day) [1, 2], based on Na and K measured in a single 24-h urine collection. Our overall goal was to contribute to achieving a guideline for the Na/K ratio that may then be used to monitor Na and K intake.

Methods

Population samples and participants

A total of 10,079 men and women aged 20–59 years from 52 population samples of 32 countries participated in INTERSALT [6, 10, 22–24]. The data for 14 persons were excluded due to missing data on either casual urine Na or K excretion; hence, the data for 10,065 participants were analyzed here. Field work took place between 1985 and 1987. Each study center was asked to recruit 200 men and women, stratified by age and sex, from samples selected randomly or by sampling from whole population groups. Institutional ethics committee approval was obtained for each collaborating center, and all participants gave informed consent.

Urinary measurements and data set

INTERSALT collected standardized data on casual urinary Na and K concentrations, and also on timed 24-h urinary Na and K excretions. To avoid under- and over-collection, start and end times of the 24-h urine collection were supervised by clinic staff [22, 23]. Each participant was asked to empty his or her bladder completely when starting (specimen not included as part of 24-h urine collection, saved as casual urine) and ending the collection (specimen included as part of 24-h urine collection). Twenty-four-hour urine collections were rejected if the participant reported that "more than a few drops" were missing from the collection, if the 24-h urinary volumes were <250 ml, or if the timing of the collection fell outside the 20- to 28-h range [22, 23]. Aliquots of the casual and 24-h urinary specimens were sent frozen to a central laboratory (Leuven, Belgium) for urinary biochemistry, including Na (mmol) and K (mmol), by emission flame photometry [22].

Statistical analyses

The Na/K ratio and Na and K intake were estimated based on urinary excretions (corrected to 24 h). The associations between the casual urinary Na/K ratio and 24-h urinary excretions of Na and K in individuals were analyzed by correlation analysis. The associations between the 24-h urinary Na/K ratio and excretions of Na and K of individuals were also analyzed; urinary Na/K ratios of casual and 24-h urine stratified in one unit (mmol/mmol) intervals were compared with 24-h urinary Na excretion and K excretion, and the positive predictive values for satisfying the recommended cutoff levels of Na and K intake in WHO guidelines (urinary Na excretion <85 mmol/day [~2 g/day of Na, 5 g/day of NaCl], and urinary K excretion ≥90 mmol/day [~3.51 g/day of K]) [1, 2].

The receiver operating characteristic (ROC) curves explored the relationship between the urinary Na/K ratio of either casual or 24-h urine and either 24-h urine Na excretion <85 mmol/day or 24-h urine K excretion ≥90 mmol/day. Furthermore, the relationships between either the casual urine Na or K concentration and either 24-h urine Na excretion <85 mmol/day or 24-h urine K excretion ≥90 mmol/day, and those between either the casual urine Na/creatinine ratio or K/creatinine ratio and either 24-h urine Na excretion <85 mmol/day or 24-h urine K excretion ≥90 mmol/day were also explored.

Results

Descriptive statistics and associations among urinary variables

The mean 24-h urinary Na excretion was 156.0 mmol/24 h, and the mean 24-h urinary K excretion was 55.2 mmol/24 h. The mean 24-h urinary Na/K ratio was 3.24 (Table 1 and Supplementary Table 1). The mean casual urinary Na/K ratio was 2.85 (Table 1 and Supplementary Table 1).

Table 1 Characteristics of individual study participants, overall ($N = 10{,}079$) and by demographic stratum

Population sample		24-h urine sodium, mmol/24 h		24-h urine potassium, mmol/24 h		24-h urine Na/K ratio		Casual urine Na/K ratio		
	N	Mean	SD	Mean	SD	Mean	SD	*N*	Mean	SD
Overall	10,079	156.0	78.6	55.2	25.3	3.24	1.90	10,065	2.85	2.15
Men	5045	172.1	84.2	60.4	27.5	3.29	1.92	5039	2.87	2.11
Women	5034	139.9	68.8	49.9	21.7	3.20	1.89	5026	2.83	2.18
Ages 20–29	2507	150.5	77.1	52.7	25.9	3.29	1.91	2504	2.97	2.35
Ages 30–39	2539	156.7	77.8	55.3	24.6	3.26	1.96	2535	2.83	2.05
Ages 40–49	2529	160.5	81.1	57.1	25.5	3.21	1.88	2524	2.85	2.09
Ages 50–59	2504	156.4	77.8	55.6	25.1	3.21	1.87	2502	2.76	2.08
White	5860	164.1	66.8	61.9	22.7	2.84	1.20	5853	2.51	1.56
Black	980	115.0	67.9	35.7	17.6	3.57	2.16	980	2.89	2.10
Native American[a]	561	48.0	78.6	65.7	39.1	1.13	1.79	561	1.10	2.13
Asian-Indian[b]	406	181.3	71.7	47.4	18.8	4.17	1.84	406	3.95	2.47
East Asian[c]	1578	191.6	74.9	39.4	15.9	5.26	2.16	1578	4.61	2.79
Other ethnicities (Others)	694	137.4	93.5	57.8	29.9	2.76	1.92	687	2.48	1.93

Details of the definition of ethnic groups are defined in reference 22. Proportion of study participants in specific ethnic groups by populations and the data for sodium, potassium, Na/K ratio and urine volume are previously published in reference 16 and in [34]

SD standard deviation, Na/K ratio sodium-to-potassium ratio

[a]Native American individuals are recruited from native tribes in Northern and Southern American continent

[b]Asian-Indian individuals are recruited from India

[c]East Asian individuals are defined as Chinese, Japanese and Korean individuals

Pearson's correlation coefficients for the Na/K ratio of casual urine with Na and K excretions of 24-h urine were 0.42 and −0.34 in individuals, and 0.68 and −0.76 in populations, respectively (Fig. 1 and Supplementary Figs. 1–3). Pearson's correlation coefficients for the Na/K ratio of 24-h urine with Na and K excretions of 24-h urine were 0.57 and −0.48 in individuals, and 0.72 and −0.67 in populations, respectively.

Urinary Na/K ratio compared with the recommended level in WHO Na guideline (85 mmol/day: ~2 g/day of Na, 5 g/day of NaCl)

The Na/K ratios of casual urine and 24-h urine stratified into 1-unit intervals were positively associated with the 24-h urinary Na excretion (Fig. 2). The ROC curves explored the relationship between 24-h urine Na/K ratio and 24-h urine Na excretion <85 mmol/day, and those between casual urine variables (Na concentration, Na/K and Na/creatinine ratio) and 24-h urine Na excretion< 85 mmol/day (Fig. 3). The area under the ROC curve for the relationship between 24-h urine Na/K ratio and 24-h urine Na excretion< 85 mmol/day was the highest (0.838 [95% CI: 0.826–0.850]) compared with the corresponding area under the ROC curve for 24-h urine Na excretion and casual urine values of Na concentration, and Na/K and Na/creatinine ratios; however, those for the relationship between casual urine Na/K ratio and 24-h urine Na excretion< 85 mmol/day (0.785 [95% CI: 0.771–0.798]) were lower than those for the relationship between 24-h urine Na/Creatinine ratio and 24-h urine Na excretion <85 mmol/day (0.819 [95% CI: 0.807–0.832]), and those for the relationship between 24-h urine Na concentration and 24-h urine Na excretion <85 mmol/day (0.799 [95% CI: 0.787–0.812]).

The 24-h urinary Na/K ratio predicted 24-h urine Na excretion <85 mmol/day (the WHO recommended guideline) with a sensitivity of 99.7% and 85.7%, specificity of 39.5% and 67.0%, and positive predictive value of 96.3% and 47.8% at the cutoff points 1 and 2 of 24-h urine Na/K ratio, respectively (Fig. 3, Table 2 and Supplementary Tables 2 and 3). The casual urinary Na/K ratio predicted 24-h urine Na excretion <85 mmol/day (the WHO recommended guideline) with a sensitivity of 94.0% and 66.3%, specificity of 48.0% and 73.0%, and positive predictive value 61.1% and 29.7% at the cutoff points 1 and 2 of casual urine Na/K ratio, respectively.

The area under the ROC curve for the relationship between 24-h urine Na/K ratio and 24-h urine Na excretion <85 mmol/day was similar among age, gender, and anti-hypertensive medication subgroups; however, the area under the ROC curve was larger among Native American

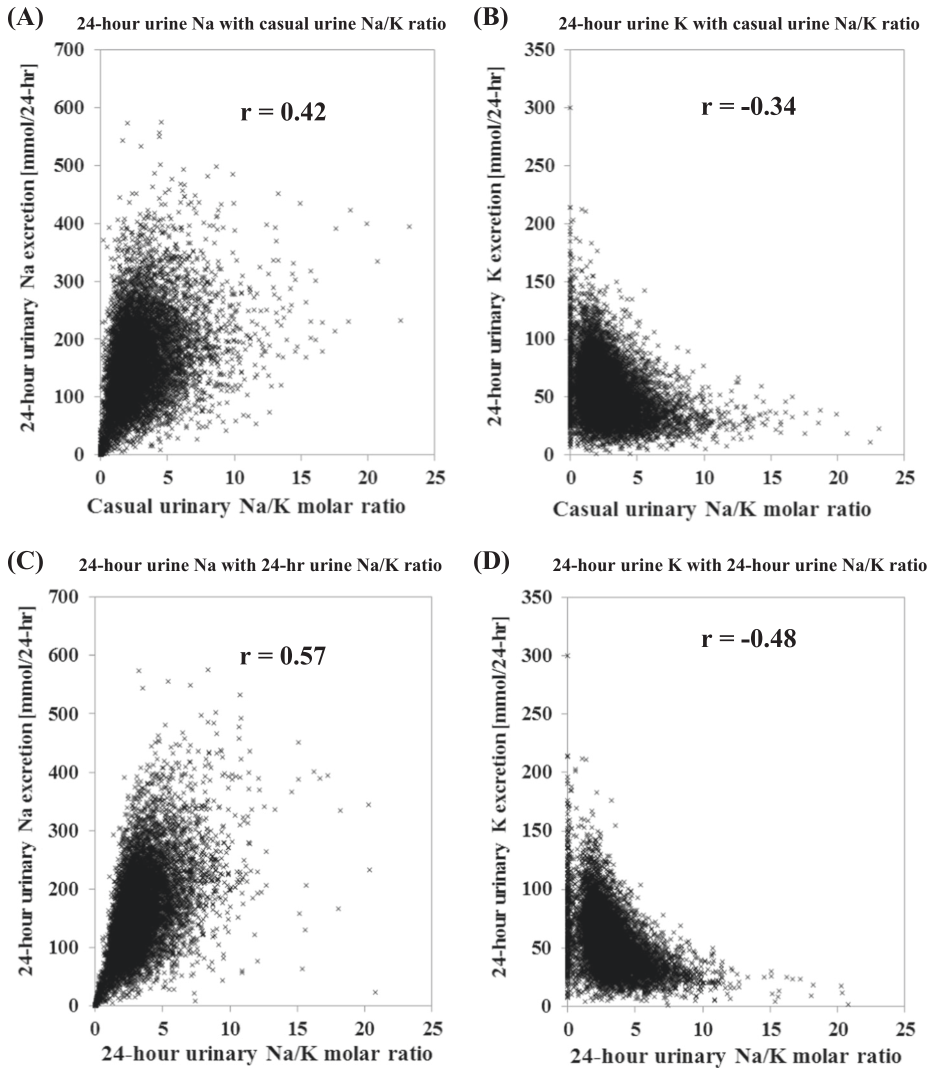

Fig. 1 Plots of casual urinary Na/K ratio versus 24-h Na and K excretion (**a**, **b**) and 24-h urinary Na/K ratio versus 24-h Na and K excretion in individuals (**c**, **d**)

Indians and individuals from other ethnic groups compared with White, Black and Asian individuals (Supplementary Fig. 4). Similar findings were observed for the area under the ROC curve for the relationship between casual urine Na/K ratio and 24-h urine Na excretion <85 mmol/day (Supplementary Fig. 5).

Urinary Na/K ratio compared with the recommended level in WHO K guideline (90 mmol/day: ~3.51 g/day of K)

Na/K ratios of casual urine and 24-h urine stratified into 1-unit intervals were inversely associated with the 24-h urinary K excretion (Supplementary Tables 2 and 3). The ROC curves explored the relationship between 24-h urine Na/K ratio and 24-h urine K excretion ≥90 mmol/day, and those between casual urine variables (K concentration, Na/K and K/creatinine ratio) and 24-h urine K excretion ≥90 mmol/day. The area under the ROC curve calculated for predicting 24-h urine K excretion ≥90 mmol/day was lower than those for 24-h Na excretion <85 mmol/day among these urinary variables (Fig. 3). The area under the ROC curve for the relationship between 24-h urine Na/K ratio and 24-h K excretion ≥ 90 mmol/day was the highest (0.795 [95% CI: 0.783–0.808]) compared with the corresponding area under the ROC curve for 24-h urine K excretion and casual urine values of K concentration, and the Na/K and K/creatinine ratios (Fig. 3).

The 24-h urinary Na/K ratio predicted 24-h urine K excretion ≥90 mmol/day (the WHO recommended guideline) with a sensitivity of 94.7% and 80.6%, specificity of 21.3% and 58.4%, and positive predictive value of 28.6% and 22.9% at the cutoff points 1 and 2 of the 24-h urine Na/K ratio, respectively (Fig. 3, Supplementary Tables 2 and 3). The casual urinary Na/K ratio predicted 24-h urine Na excretion <85 mmol/day (the WHO recommended guideline) with a sensitivity of 88.9% and 62.8%,

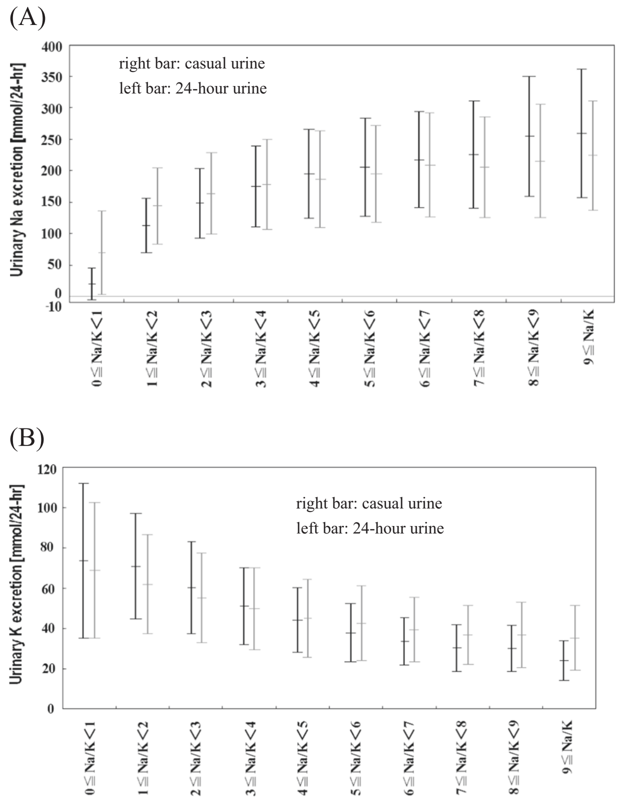

Fig. 2 Associations of casual urinary Na/K ratio and 24-h urinary Na/K ratio stratified into 1-unit intervals with 24-h urinary **a** Na and **b** K excretion. Bars indicate mean values and mean ± standard deviation of either 24-h urinary Na or K excretion within each stratified value of casual urinary Na/K ratio (right bar) and 24-h urinary Na/K ratio (left bar)

specificity of 30.4% and 69.2%, and positive predictive value of 21.3% and 15.5% at the cutoff points 1 and 2 of casual urine Na/K ratio, respectively (Fig. 3, Supplementary Tables 2 and 3).

Prevalence of low casual and 24-h urine Na/K ratio among ethnic subgroups

In ethnic subgroups, 71.8% of Native Americans showed a casual urinary Na/K ratio of <1, and 69.1% of Native Americans showed a 24-h urinary Na/K ratio of <1 (Supplementary Tables 4 and 5). However, few individuals in other subgroups showed casual and 24-h urinary Na/K ratios of <1 (Supplementary Tables 4 and 5).

Discussion

The main findings from the INTERSALT Study data here are that the urinary Na/K ratio predicted 24-h urine Na excretion <85 mmol/day (~2 g/day of Na, 5 g/day of NaCl) with a sensitivity of over 90% for urinary Na/K ratio <1 and over 60% for urinary Na/K ratio <2 in both 24 h and casual urine. The positive predictive value of a urinary Na/K ratio of <1 for predicting the recommended level of Na intake (< 85 mmol/day) reached over 61% of people with casual urine and over 96% with 24-h urine, and, to a lesser extent, the K intake set down in WHO guidelines [1, 2]. Thus, the urinary Na/K ratio could serve as a surrogate marker for monitoring Na and K intake in populations and individuals.

The dietary and urinary Na/K ratios mainly reflect dietary habits and have several benefits compared to the measurement and use of Na and K separately [25]. The first is that studies suggest stronger associations for Na/K ratio with BP and CVD compared to Na and K considered separately [6, 10–16]. It was estimated from INTERSALT that reducing the urinary Na/K ratio from 3.09 to 1.00 could potentially lower BP by 3.36 mmHg in populations, an effect that was greater than the estimated effects of reducing Na alone and increasing K alone [10]. Cook et al. reported that the Na/K ratio is a metric superior to either Na or K alone in the evaluation of CVD risk [12]. Accuracy of measurement of Na and K at the individual level is important to mitigate against paradoxical findings in association studies, e.g., in relation to CVD [26, 27].

Casual rather than 24-h urine collections offer a lower participant burden and may be valuable for monitoring of Na and K intake and adherence to WHO guidelines. Higher correlations and better agreements are observed for the casual Na/K ratio than for casual Na or K alone when compared with 24-h urine values, especially with the use of repeated casual urine collections [17–19]. The use of formulas to estimate 24-h urinary Na excretion from a single casual urine sample depends on other parameters, such as body weight and creatinine, and may be biased [7–9], whereas the Na/K ratio is independent of both creatinine excretion and body weight. Since the measurement of urinary creatinine is not as handy as those for measuring electrolytes, repeated casual urine Na/K ratios might be a useful and practical means of obtaining individual values of urinary Na/K ratio [18, 19]. In this regard, a self-monitoring device for urinary Na/K ratio measurement that provides prompt on-site feedback has been evaluated with a view to support an individual approach for Na reduction and K increase [21].

Currently, there is no formal recommended cutoff value for the urinary Na/K ratio. Since the positive predictive value for predicting NaCl intake of <85 mmol/day based on a single casual urine Na/K ratio of <1 reached 61% in this study, using repeated measurements of the casual urine Na/K ratio may reduce random and systematic errors and provide a more reliable estimation of adherence to WHO guidelines. The correlation and agreement quality of the mean Na/K ratio of 4–7 repeated

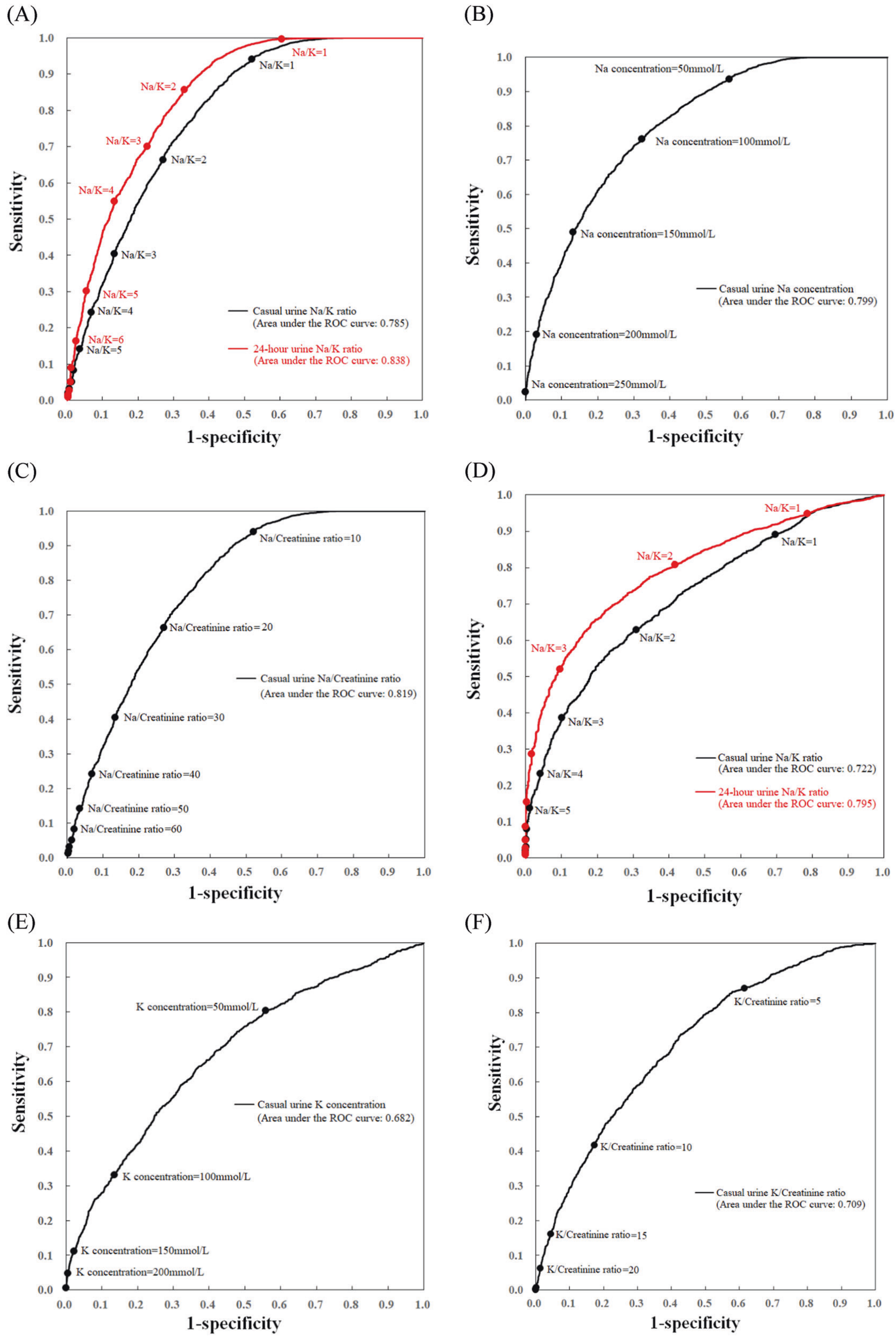

Fig. 3 The receiver operating characteristic (ROC) curve analysis for predicting 24-h urine Na excretion <85 mmol/day by **a** urinary Na/K ratio, **b** casual urine Na concentration and **c** casual urine Na/creatinine ratio. The ROC curve analysis for predicting 24-h K excretion ≥90 mmol/day by **d** urinary Na/K ratio, **e** casual urine K concentration and **f** casual urine K/creatinine ratio

Table 2 The positive predictive values at a given value of casual and 24-h urine Na/K ratio to detect 24-h urine Na excretion< 85 mmol/day (the WHO recommended guideline) and characteristics in 10,079 individuals

Casual urinary Na/K molar ratio	24-h urine sodium, mmol/24 h					
	N	Mean	SD	≤85 mmol/day (NaCl ≤ 5 g/day)	≤103 mmol/day (NaCl ≤6 g/day)	≤171 mmol/day (NaCl ≤10 g/day)
0 ≤ Na/K ratio < 1	1288	70.2	66.6	61.1%	69.4%	92.5%
0 ≤ Na/K ratio < 2	4028	120.6	71.7	29.7%	39.4%	78.3%
0 ≤ Na/K ratio < 3	6429	136.8	72.4	22.1%	31.3%	71.1%
0 ≤ Na/K ratio < 4	7909	144.6	74.1	19.3%	27.9%	66.9%
0 ≤ Na/K ratio < 5	8808	148.9	75.5	18.0%	26.3%	64.9%
0 ≤ Na/K ratio < 6	9339	151.5	76.3	17.2%	25.3%	63.5%
0 ≤ Na/K ratio < 7	9607	153.1	77.1	16.9%	24.8%	62.8%
0 ≤ Na/K ratio < 8	9780	154.1	77.5	16.7%	24.5%	62.3%
0 ≤ Na/K ratio < 9	9887	154.7	77.9	16.5%	24.4%	62.0%
Overall	10,065	156.0	78.5	16.3%	24.0%	61.3%
24-h urinary Na/K molar ratio	**24-h urine sodium, mmol/24 h**					
	N	Mean	SD	≤85 mmol/day (NaCl ≤ 5 g/day)	≤103 mmol/day (NaCl ≤ 6 g/day)	≤171 mmol/day (NaCl ≤ 10 g/day)
0 ≤ Na/K ratio < 1	675	20.1	25.9	96.3%	98.8%	100.0%
0 ≤ Na/K ratio < 2	2301	85.8	57.8	47.8%	59.7%	93.0%
0 ≤ Na/K ratio < 3	5219	121.0	64.5	27.2%	38.1%	79.3%
0 ≤ Na/K ratio < 4	7438	137.1	69.0	20.9%	30.1%	71.1%
0 ≤ Na/K ratio < 5	8660	145.4	72.2	18.5%	27.0%	66.6%
0 ≤ Na/K ratio < 6	9297	149.6	74.2	17.5%	25.6%	64.5%
0 ≤ Na/K ratio < 7	9629	151.9	75.3	16.9%	24.9%	63.3%
0 ≤ Na/K ratio < 8	9834	153.5	76.3	16.6%	24.5%	62.4%
0 ≤ Na/K ratio < 9	9946	154.6	77.3	16.5%	24.2%	61.9%
Overall	10,079	156.0	78.6	16.3%	24.0%	61.2%

SD standard deviation, *NaCl* sodium chloride

measurements of casual urine with 7-day 24-h urine Na/K ratio were similar to those of 1–2 day 24-h urine Na/K ratio with 7-day 24-h urine Na/K ratio in our previous studies [18, 19]. Furthermore, systematic error introduced from the diurnal variation of urinary Na/K ratio was minimized by repeated casual urine sampling from diverse time slots [18–20]. Thus, it is reasonable to infer that increasing the number of repeated casual urine Na/K ratio measurements will approximate to the 24-h urine Na/K ratio value; repeated measurement of casual urine Na/K ratio may deliver higher positive predictive value for predicting NaCl intake of <85 mmol/day, which may reach ~96% (close to the value shown in this study for 1-day 24-h urine Na/K ratio). Our findings suggest that a mean urinary Na/K ratio of <1 obtained from repeated casual urine collection during our daily life may adhere to the recommended level of Na intake (<85 mmol/day); a urinary Na/K ratio of <2 may be suboptimal.

A limitation of the present study is that casual urinary and 24-h urinary data were collected only once in the majority of individuals, limiting the ability to correct for measurement errors due to high day-to-day variability in urinary Na and K excretion. The urinary Na and K excretions were used to evaluate the estimated individual Na and K intake in this study. Na and K intake might be underestimated, especially for K, since reported data indicate that 80–95% and 63–77% of dietary intakes are reflected in urinary Na and K, respectively [28–33]. The INTERSALT data were derived from general population samples aged 20–59 years. It is unknown whether our findings are applicable to individuals outside these age ranges or to individuals with high physical activity or various diseases, e.g., diabetes, chronic kidney diseases, or atherosclerotic diseases. In INTERSALT, casual urine was obtained during daytime hours. The urinary Na/K ratio is known to show diurnal variation and is lower in the daytime hours compared to the 24-h urine value [20]. Thus, underestimation of the casual urine Na/K ratio versus the 24-h urine Na/K ratio reported here may be explained by diurnal variation in the urinary Na/K ratio [20]. However, lowering the Na/K ratio to 1 would require very strict sodium restriction in populations with low potassium intake. Setting a cutoff value of

Na/K ratio for practical implementation may need to be balanced for local dietary habits among ethnicities and populations, as seen for Na dietary guidelines set worldwide. Further studies may be required to evaluate associations between Na/K ratio levels and CVD outcomes by longitudinal studies, and assure appropriate cutoff levels to support clinical practice for localization.

WHO reports suggest that achieving guidelines for both Na and K intakes would yield an Na/K ratio of ~1.00 [1, 2]. Few people (12.8% in casual urine, 6.7% in 24-h urine; mostly in remote populations) had urinary Na/K ratio of <1 in INTERSALT, although even these proportions may be overestimated due to measurement error and the regression dilution problem [24].

In conclusion, our findings suggest that a urine Na/K ratio of <1 could serve as a surrogate marker for reaching WHO goals for reduced Na intake and, to a lesser extent, increased K intake. Population-wide efforts are needed to reduce Na and increase K intake to achieve these goals. Repeated measurements of the Na/K ratio in casual urine may provide a ready and low participant burden means to monitor adherence to WHO guidelines at both the individual and population levels.

Acknowledgments We thank all INTERSALT staff at local, national, and international centers for their invaluable efforts. This work was supported by JSPS KAKENHI Grant Number JP 18K17377. TI participated in the data analysis and contributed to the drafting of the manuscript. All authors participated in the critical revision of the manuscript. All authors approved the final version of the manuscript for submission.

Funding This work was supported by JSPS KAKENHI Grant Number JP 18K17377. The International Cooperative Study on Salt, Other Factors, and Blood Pressure (INTERSALT) was supported by the Council on Epidemiology and Prevention of the World Heart Federation (Geneva, Switzerland); the World Health Organization (Geneva, Switzerland); the International Society of Hypertension (Ware, United Kingdom); the Wellcome Trust (London, United Kingdom); the National Heart, Lung, and Blood Institute, National Institutes of Health (Bethesda, MD); the Heart and Stroke Foundation of Canada (Ottawa, ON); the British Heart Foundation (London, Great Britain); the Japan Heart Foundation (Tokyo, Japan); Netherlands Heart Foundation (Den Haag, Netherlands); the Chicago Health Research Foundation (Chicago, IL); the Belgian National Research Foundation (Brussels, Belgium); Parastatal Insurance Company (Brussels, Belgium); and by many national agencies supporting local studies. Dr. Paul Elliott is supported by the National Institute for Health Research (NIHR) Imperial College Healthcare NHS Trust (ICHNT) and Imperial College Biomedical Research Centre (BRC), the Medical Research Council (MRC)- Public Health England (PHE) Centre for Environment and Health (grant number MRC G0801056), the NIHR Health Protection Research Unit in Health Impact of Environmental Hazards (HPRU-2012-10141), and the UK MEDical BIOinformatics partnership (UK MED-BIO), which is supported by the MRC (MR/L01632X/1). Dr. Elliott also holds a foundation grant from MRC as part of the Dementia Research Institute at Imperial College London.

Compliance with ethical standards

Conflict of interest TI was an employee of OMRON Healthcare Co., Ltd, which manufactures a device for monitoring the Na/K ratio in urine samples until March, 2018; however, he did not receive any research fund from OMRON Healthcare Co., Ltd. KM had received a research fund from OMRON Healthcare Co. Ltd. HU had served as a consultant of OMRON Healthcare Co., Ltd. The remaining authors declare that they have no conflict of interest.

References

1. WHO Guideline Sodium intake for adults and children. Geneva: World Health Organization (WHO); 2012.
2. WHO Guideline Potassium intake for adults and children. Geneva: World Health Organization (WHO); 2012.
3. Brown IJ, Tzoulaki I, Candeias V, Elliott P. Salt intakes around the world: implications for public health. Int J Epidemiol. 2009;38:791–813.
4. Stamler J, Elliott P, Dennis B, Dyer AR, Kesteloot H, Liu K, INTERMAP Research Group. et al. INTERMAP: background, aims, design, methods, and descriptive statistics (nondietary). J Hum Hypertens. 2003;17:591–608.
5. Drewnowski A, Rehm CD, Maillot M, Mendoza A, Monsivais P. The feasibility of meeting the WHO guidelines for sodium and potassium: a cross-national comparison study. BMJ Open. 2015;5:e006625.
6. INTERSALT Co-operative Research Group INTERSALT: an international study of electrolyte excretion and blood pressure. Results for 24-hr urinary sodium and potassium excretion. BMJ. 1988;297:319–28.
7. Mente A, O'Donnell MJ, Dagenais G, Wielgosz A, Lear SA, McQueen MJ, et al. Validation and comparison of three formulae to estimate sodium and potassium excretion from a single morning fasting urine compared to 24-h measures in 11 countries. J Hypertens. 2014;32:1005–14.
8. Polonia J, Lobo MF, Martins L, Pinto F, Nazare J. Estimation of populational 24-h urinary sodium and potassium excretion from spot urine samples: evaluation of four formulas in a large national representative population. J Hypertens. 2017;35:477–86.
9. Huang L, Crino M, Wu JH, Woodward M, Barzi F, Land MA, et al. Mean population salt intake estimated from 24-h urine samples and spot urine samples: a systematic review and meta-analysis. Int J Epidemiol. 2016;45:239–50.
10. Stamler J, Rose G, Stamler R, Elliott P, Dyer A, Marmot M. INTERSALT study findings. Public health and medical care implications. Hypertension. 1989;14:570–7.
11. Tzoulaki I, Patel CJ, Okamura T, Chan Q, Brown IJ, Miura K, et al. A nutrient-wide association study on blood pressure. Circulation. 2012;126:2456–64.
12. Cook NR, Obarzanek E, Cutler JA, Buring JE, Rexrode KM, Kumanyika SK, Trials of Hypertension Prevention Collaborative Research Group. et al. Joint effects of sodium and potassium intake on subsequent cardiovascular disease: the Trials of Hypertension Prevention follow-up study. Arch Intern Med. 2009;169:32–40.
13. Yang Q, Liu T, Kuklina EV, Flanders WD, Hong Y, Gillespie C, et al. Sodium and potassium intake and mortality among US adults: prospective data from the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2011;171:1183–91.

14. Khaw KT, Barrett-Connor E. The association between blood pressure, age, and dietary sodium and potassium: a population study. Circulation. 1988;77:53–61.
15. Cook NR, Appel LJ, Whelton PK. Sodium intake and all-cause mortality over 20 years in the trials of hypertension prevention. J Am Coll Cardiol. 2016;68:1609–17.
16. Thi Minh Nguyen T, Miura K, Tanaka-Mizuno S, Tanaka T, Nakamura Y, Fujiyoshi A, et al. members of the HIPOP-OHP Research Group. Association of blood pressure with estimates of 24-h urinary sodium and potassium excretion from repeated single-spot urine samples. Hypertens Res. 2019;42:411–8. https://doi.org/10.1038/s41440-018-0152-z.
17. Iwahori T, Miura K, Ueshima H, Chan Q, Dyer AR, Elliott P, Stamler J, INTERSALT Research Group Estimating 24-hour urinary sodium/potassium ratio from casual ("spot") urinary sodium/potassium ratio: The INTERSALT Study. Int J Epidemiol. 2017;46:1564–72.
18. Iwahori T, Ueshima H, Miyagawa N, Ohgami N, Yamashita H, Ohkubo T, et al. Six random samples of casual urine on different days are sufficient to estimate daily sodium/potassium ratio as compared to 7-day 24-hr urine collections. Hypertens Res. 2014;37:765–71.
19. Iwahori T, Ueshima H, Torii S, Saito Y, Fujiyoshi A, Ohkubo T, et al. Four to seven random casual urine specimens are sufficient to estimate 24-hr urinary sodium/potassium ratio in individuals with high blood pressure. J Hum Hypertens. 2016;30:328–34.
20. Iwahori T, Ueshima H, Torii S, Saito Y, Kondo K, Tanaka-Mizuno S, et al. Diurnal variation of urinary sodium-to-potassium ratio in free-living Japanese individuals. Hypertens Res. 2017;40:658–64.
21. Iwahori T, Ueshima H, Ohgami N, Yamashita H, Miyagawa N, Kondo K, et al. Effectiveness of a self-monitoring device for urinary sodium/potassium ratio on dietary improvement in free-living adults: a randomized controlled trial. J Epidemiol. 2018;28:41–47.
22. The INTERSALT Co-operative Research Group INTERSALT Study an international co-operative study on the relation of blood pressure to electrolyte excretion in populations. I. Design and methods. J Hypertens. 1986;4:781–7.
23. Elliott P, Stamler R. Manual of operations for "INTERSALT", an international cooperative study on the relation of sodium and potassium to blood pressure. Control Clin Trials. 1988;9(2 Suppl):1S–117S.
24. Elliott P, Stamler J, Nichols R, Dyer AR, Stamler R, Kesteloot H, et al. Intersalt revisited: further analyses of 24-hr sodium excretion and blood pressure within and across populations. Intersalt Cooperative Research Group. BMJ. 1996;312:1249–53.
25. Iwahori T, Miura K, Ueshima H. Time to consider use of the sodium-to-potassium ratio for practical sodium reduction and potassium increase. Nutrients. 2017;9:E700.
26. Cogswell ME, Mugavero K, Bowman BA, Frieden TR. Dietary sodium and cardiovascular disease risk - measurement matters. N Engl J Med. 2016;375:580–6.
27. Cobb LK, Anderson CA, Elliott P, Hu FB, Liu K, Neaton JD, American Heart Association Council on Lifestyle and Metabolic Health. et al. Methodological issues in cohort studies that relate sodium intake to cardiovascular disease outcomes: a science advisory from the American Heart Association. Circulation. 2014;129:1173–86.
28. Pietinen PI, Findley TW, Clausen JD, Finnerty FA, Altschul AM. Studies in community nutrition: estimation of sodium output. Prev Med. 1976;5:400–7.
29. Hunter D. Biochemical indicators of dietary intake. In: Willet W., editor. Nutritional epidemiology. 2nd ed. New York, NY, USA: Oxford University Press; 1998. p. 174–243.
30. Voors AW, Dalferes ER Jr., Frank GC, Aristimuno GG, Berenson GS. Relation between ingested potassium and sodium balance in young Blacks and whites. Am J Clin Nutr. 1983;37:583–94.
31. Clark AJ, Mossholder S. Sodium and potassium intake measurements: dietary methodology problems. Am J Clin Nutr. 1986;43:470–6.
32. Holbrook JT, Patterson KY, Bodner JE, Douglas LW, Veillon C, Kelsay JL, et al. Sodium and potassium intake and balance in adults consuming self-selected diets. Am J Clin Nutr. 1984;40:786–93.
33. Rakova N, Juttner K, Dahlmann A, Schröder A, Linz P, Kopp C, et al. Long-term space flight simulation reveals infradian rhythmicity in human Na(+) balance. Cell Metab. 2013;17:125–31.
34. The INTERSALT Co-operative Research Group. Appendix tables. Centre-specific results by age and sex. J Hum Hypertens. 1989;3:331–407.

Affiliations

Toshiyuki Iwahori[1,2,3] · Katsuyuki Miura[1,4] · Hirotsugu Ueshima[1,4] · Sachiko Tanaka-Mizuno[5] · Queenie Chan[6] · Hisatomi Arima[7] · Alan R. Dyer[8] · Paul Elliott[6] · Jeremiah Stamler[8] for the INTERSALT Research Group

[1] Department of Public Health, Shiga University of Medical Science, Shiga, Japan

[2] Graduate School of Science, Technology and Innovation, Kobe University, Hyogo, Japan

[3] Research and Development Department, Omron Healthcare Co., Ltd, Kyoto, Japan

[4] Center for Epidemiologic Research in Asia, Shiga University of Medical Science, Shiga, Japan

[5] Department of Medical Statistics, Shiga University of Medical Science, Shiga, Japan

[6] MRC-PHE Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK

[7] Department of Preventive Medicine and Public Health, Fukuoka University, Fukuoka, Japan

[8] Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA