JSH STATEMENT



Practical use and target value of urine sodium-to-potassium ratio in assessment of hypertension risk for Japanese: Consensus Statement by the Japanese Society of Hypertension Working Group on Urine Sodium-to-Potassium Ratio

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Abstract

Epidemiological studies have demonstrated that the urine sodium-to-potassium (Na/K) ratio is more positively associated with high blood pressure and cardiovascular disease risk than either urine sodium or potassium excretion alone. In this consensus statement, we recommend using the average Na/K ratio of casual urines randomly taken in various times on at least four days a week for a reliable individual estimate because of high day-to-day and intraday variability of casual urine Na/K ratio within individuals. Although a continuous positive association exists between the Na/K ratio and high blood pressure or cardiovascular disease risk, for clinical and public health decision making for Japanese, we recommend using an average urine Na/K ratio of 2 as an optimal target value because this aligns with recommendations for both sodium and potassium intake in the Dietary Reference Intakes for Japanese, 2020, considering a typical Japanese dietary pattern. We also suggest that an average urine Na/K ratio of 4 is a feasible target value to achieve a temporary goal of being below the mean values of the urine Na/K ratio across Japanese general populations. These recommendations apply mainly for apparently healthy individuals, but not for patients with specific conditions due to the lack of supporting data. Current evidence for the usefulness of measuring the urine Na/K ratio for the prevention or control of hypertension remains inconclusive and warrants further investigation.

Keyword Blood pressure · Hypertension · Sodium-to-potassium ratio · Target value · Urine

Introduction

High blood pressure (BP), known as hypertension, is the leading preventable risk factor for premature mortality from

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cardiovascular diseases (CVDs) and is ranked first as a cause of disability-adjusted life years [1]. The prevalence of hypertension remains high, and the highest absolute burden of hypertension is in the East Asian and Pacific regions, including Japan [2, 3]. Numerous factors can accelerate or contribute to the development of hypertension, although, among them, sodium (Na) and potassium (K) intakes are its major modifiable determinants [4]. High Na consumption is associated with excess fluid retention, diminished arterial compliance, impaired renin-angiotensin system function, and decreased glomerular filtration rate, which exacerbate the burden of hypertension [5-7]. By contrast, dietary K lowers BP by promoting the excretion of Na, suppressing Na absorption, reducing salt sensitivity, and promoting vasodilation [8–10]. As a result, low consumption of K-rich foods contributes to the development of hypertension.

The Japanese Society of Hypertension Working Group on Urine Sodium-to-Potassium Ratio belongs to the Salt Reduction and Nutrition Committee of the Japanese Society of Hypertension.

Graphical Abstract

Consensus Statement by JSH Working Group on Urine Na/K Ratio Practical use and target value of urine Na/K ratio for Japanese Proposed target value for apparently healthy individuals **Prognostic significance** Categories Average Na/K ratio - Continuous positive association High blood pressure <2 Optimal Cardiovascular disease risk Feasible <4 K - Optimal to meet dietary goals by DRIs, 2020 - Feasible to achieve means across Japan - Values not for patients with specific conditions Urine Na/K Ratio Measurement - Average of casual urines collected **Relevant factors** randomly in various times on at least 4 days a week Body mass index

Point of view

Void before bedtime

• Clinical relevance

1st morning void 2nd morning void 💋

We suggest using the average Na/K ratio of casual urines randomly collected in various times on at least four days a week for a reliable individual estimate. We also recommend an average urine Na/K ratio of 2 as an optimal target aligning with DRIs for Japanese, 2020 and of 4 as a feasible temporary target to stay below the mean values across Japanese healthy populations.

Casual urine samples

4 5

7 Days

Average Na/K ratio

- Future direction
 - Further research is required to determine whether measuring the urine Na/K ratio can aid lifestyle modification efforts, encouraging lower salt intake and higher consumption of K-containing foods, thereby reducing the risk of hypertension and CVD.
- Consideration for the Asian population
 A substantial burden of high salt intake has been
 observed, particularly among Asians, making the use of
 the urine Na/K ratio in clinical and public health settings
 especially promising for hypertension prevention in
 these populations.

Cumulative evidence has demonstrated that the urine sodium-to-potassium (Na/K) ratio is a superior metric to

either urine Na or K excretion alone in relation to BP, incident hypertension and CVD risk [11-16]. It is important to define the optimal measurement strategy and target value of the urine Na/K ratio for clinical and public health decision-making. Existing evidence from some multiethnic studies has suggested that a urine Na/K ratio falling within the range of 1-2 aligns with standard dietary guidelines [16–18]; however, a specific target value tailored to the Japanese population in accordance with the Dietary Reference Intakes (DRIs) for Japanese, 2020, has not been determined. Therefore, in this consensus statement, we summarize the evidence from epidemiological and interventional studies, and we also recommend optimal and feasible target values of the urine Na/K ratio for Japanese individuals to meet the daily intake recommendations for Na and K in the DRIs for Japanese, 2020, to align with typical Japanese dietary patterns. Furthermore, we consider the optimal measurement strategy, especially using casual urine samples, to determine the urine Na/K ratio.

✓ Renal function

Antihypertensive medication use

Socioeconomic factors Nocturnal urination

Evidence from epidemiological studies: associations with BP

Throughout this consensus statement, basically (with some exceptions), Na/K ratio was calculated from 24-h urine or casual urine samples by dividing the Na concentration by the K concentration, both in mmol/L.

Fig. 1 The relationship between average morning urine sodiumto-potassium (Na/K) ratio during 10 days and adjusted mean home systolic blood pressure [32]. Adjusted mean home systolic blood pressure was calculated from the analysis of covariance. Error bars represent a 95% confidence interval



Several cross-sectional studies have reported associations between the Na/K ratio and BP. The International Study on Salt and Blood Pressure (the INTERSALT Study) in 10,079 men and women, across 52 centers from 32 countries, aged 20-59 years reported a positive association between the 24h urine Na/K ratio and BP [19]. The National Health and Nutrition Examination Survey (NHANES) in 766 residents in the United States aged 20-69 years reported that systolic BP increased by 1.72 mmHg per 0.5 unit increase in the 24h urine Na/K ratio [20]. Other studies have also demonstrated a positive association between the urine Na/K ratio and BP [21-23]. The studies mentioned above were based on evaluations using 24-h urine collection [15, 19, 20, 22–29], and thus included several hundred to a few thousand participants, whereas only a few studies have involved evaluations of large populations.

In Japan, as in studies around the world, most studies regarding the Na/K ratio and BP have been cross-sectional [12, 13, 30-36]. However, a few studies have examined large populations using casual urine samples [12, 31–33]. The Nagahama Study involving 9,144 healthy Japanese individuals with a mean age of 54 years, excluding those with an estimated glomerular filtration rate <30 ml/min/ 1.73m², found that the casual urine Na/K ratio showed a clearer association with BP than 24-h dietary salt excretion estimated from casual urine (correlation coefficient between urine Na/K ratio and BP, r = 0.131; P < 0.001) [12]. Similarly, the Nagahama study showed an independent positive association between the casual urine Na/K ratio and BP, and revealed that both high-Na/high-K and low-Na/low-K had the same degree of effect on BP, even with the same value of the Na/K ratio [31]. The Tohoku Medical Megabank Project Cohort Study using an electronic device (HEU-001F, OMRON Healthcare Co., Ltd., Kyoto, Japan) for the assessment of urine Na/K molar ratio [37], which targeted 3,122 Japanese residents aged 20 years or older without antihypertensive treatment, demonstrated that mean urine Na/K ratio in the morning during 10 days was linearly associated with home systolic BP (r = 0.172; P < 0.001) (Fig. 1) [32]. In a more recent report among 62,367 participants aged 20 years or older from the Tohoku Medical Megabank Project Cohort Study, the authors calculated estimated 24-h urine Na/K ratio by dividing the estimated 24-h urine Na excretion by the estimated 24-h urine K excretion and found its positive association with office systolic BP (r = 0.103; p < 0.001) [33].

Several previous studies have reported that the urine Na/K ratio is more related to BP than either Na or K alone [11–13]. The International Study of Macro- and Micronutrients and Blood Pressure (the INTERMAP Study) among 4680 men and women aged 40-59 years (17 population samples in China, Japan, United Kingdom, and United States) reported that a 2-standard deviation (SD) higher 24-h urine Na/K ratio was associated with a higher systolic BP (3.52 mmHg) than 2-SD higher 24-h urine Na excretion (2.50 mmHg) [11]. The Nagahama study reported that the standardized coefficient of the casual urine Na/ K ratio to systolic BP was larger than that for Na or K alone (Na/K ratio: $\beta = 0.118$, Na/creatinine: $\beta = 0.092$, K/ creatinine: $\beta = -0.050$) [12]. The High-Risk and Population Strategy for Occupational Health Promotion Study (HIPOP-OHP) in 4,360 Japanese workers aged 19-55 years reported that, compared with that in the first quintile, systolic BP in the fifth quintile was higher by 3.1 mmHg for estimated 24-h urine Na excretion, was lower by 2.9 mmHg for estimated 24-h urine K excretion, and was higher by 3.5 mmHg for the estimated 24-h urine Na/K ratio [13].

Evidence from epidemiological studies: associations with CVD risk

Several studies have examined the association between the Na/K ratio and CVD risk. The Trials of Hypertension Prevention (TOHP) among adults aged 30-54 years who had prehypertension and were not taking antihypertensive medication reported that a high Na/K ratio evaluated by 24-h urine collection was associated with an elevated CVD risk [16]. Moreover, NHANES among 12,267 residents aged 20 years or older in the United States reported that the group with a high Na/K ratio calculated by the dietary survey had a higher risk of CVD and all-cause mortality than that of the group with a low Na/K ratio [38]. In Japan, the National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged 80 (NIPPON DATA80) in 8283 apparently healthy Japanese participants aged 30-79 years without hypertensive treatment revealed an association between a high dietary Na/K ratio and long-term elevated risk of CVD mortality [39], which was consistent with the results of previous studies in Western populations. A recent meta-analysis integrating data from six major prospective cohort studies which did not include the Japanese population, with a median follow-up of 8.8 years, found an association between 24-h urine Na/K ratio and CVD risk in a total of 10,709 participants with a mean age of 52 years [15].

Moreover, several previous studies reported that the urine Na/K ratio was more closely associated with CVD than urine Na or K excretion alone [15, 16]. The TOHP group reported the strongest trend in CVD risk between the quartiles of 24-h urine Na/K ratio, which was statistically significant (p for trend was 0.38 for urine Na excretion, 0.08 for urine K excretion, and 0.039 for urine Na/K ratio) [16]. A recent meta-analysis mentioned above showed that a 1000 mg increase in 24-h urine Na excretion elevated the CVD risk by 18%, while a 1000 mg increase in 24-h urine K excretion lowered the CVD risk by 18% [15]. Furthermore, an increase in 24-h urine Na/K ratio per unit elevated the CVD risk by 24% [15].

Superiority of the urine Na/K ratio than estimated salt intake

The urine Na/K ratio is an actual measurement value rather than an estimated value, and unlike the estimated salt intake, it does not require complex calculations, making it more feasible for use in the medical and public health fields. Additionally, as we mentioned above, several previous studies have demonstrated that the urine Na/K ratio is more strongly associated with BP or CVD risk than either urine Na or K excretion alone [11–13, 15, 16]. This is likely because the urine Na/K ratio simultaneously evaluates the impact of both urine Na and K excretions on BP or CVD risk. Therefore, the urine Na/K ratio has the potential to become a more practical indicator. However, there is insufficient evidence regarding the differentiation between the use of urine Na/K ratio and estimated salt intake or other nutrient indices. Future researches are needed to accumulate sufficient evidence to make a well-informed judgment on this matter.

Variability of the urine Na/K ratio

The urine Na/K ratio is highly variable within individuals. Factors associated with the urine Na/K ratio are shown in Table 1. Postprandial changes became reflected in the urine Na/K ratio within 2 h after a meal [12]. In an experimental feeding study of normotensive young volunteers (mean age, 23 years) [40], the casual urine Na/K ratio was tracked during changes from 3 g/day to 20 g/day of dietary salt intake, which produced the mean urine Na/K ratio of 1.1 and 6.6, respectively. In this study, the mean urine Na/K ratio reached a plateau roughly three days following the changes in dietary salt levels. These findings support to use urine Na/K ratio as an index of Na intake. In addition, independent of the postprandial change, urine Na/K ratio showed a diurnal variation, in other words, it was highest in urine collected during a sleeping period, especially in individuals with hypertension [41]. Salt sensitivity is a cause of increases in BP during sleep [42] via carryover of natriuresis to sleeping periods [43]. Hypertensive patients may excrete larger amounts of Na during sleep than normotensive individuals because they are more likely to be salt-sensitive and to have reduced renal function. Given this physiology, nocturnal urination frequency may also be considered in assessment of daily urine Na/K ratio. An inverse association reported between nocturnal urination frequency and daytime urine Na concentrations in a general population [44] supports the importance of considering urination frequency during sleep. The most long-term variability is seasonality, with the lowest Na/K ratio value during the hotter season [12]. This phenomenon may be explained by that the urine Na excretion lowers in the hotter season [45]. While, BP also exhibits seasonal variation mainly due to changes in external temperature [46]. The magnitude of the contributions of dietary factors (high Na and low K) to seasonal variation in BP levels remains unclear and should be further examined in future researches. Given the high variability of the urine Na/K ratio, multiple rather than single measurements are recommended to assess an individual's high Na and low K burdens [30].

Table 1 Effect size of factors associated with the urine Na/K ratio $\left[12,\,53\right]$

Factors	Effect size	Unit/reference
Men	0.13	vs. women
Men without a live-in wife	0.50	vs. men with wife and women
Body mass index	0.04	per 1 kg/m ²
Renal function (eGFR)	0.19	per 10 ml/min/1.73m ²
Antihypertensive drug use	0.20	yes
Fasting time	-0.04	per 1 h
Measurement season		
Middle	-0.09	vs. winter
Summer	-0.22	vs. winter
Education attainment		
>9 and ≤ 12 years	-0.17	vs. ≤9 years
>13 years	-0.36	vs. ≤9 years
Nocturnal urination	-0.09	per 1 void

Effect size was re-calculated using individual-level data of the followup investigation of the Nagahama study performed between 2013 and 2016. Participants with estimated glomerular filtration rate (eGFR) less than 30 ml/min/1.73m² were excluded from the analysis. Na/K, sodium-to-potassium

Relevant factors

In assessment of the urine Na/K ratio, consideration should be given to factors that affect the Na/K ratio even after multiple measurements (Table 1). Body mass index was positively correlated with the urine Na/K ratio [12, 41]. Although the precise mechanism for the positive association is unclear, the association between Na intake and obesity was reported to be independent of total energy intake [47, 48]. Renal function was another strong determinant of the urine Na/K ratio, and individuals with a lower estimated glomerular filtration rate had lower Na/K ratio [12]. A greater decline of Na excretion than K excretion with decreasing glomerular filtration rate may account for this association. Age was inversely associated with the urine Na/ K ratio independent of glomerular filtration rate, although this association may, in part, be because of more frequent nocturnal urination in older adults [12, 41]. The results of previous studies on the effect of antihypertensive drug use on urine Na/K ratio were inconsistent: one study reported individuals taking antihypertensive drugs had higher urine Na/K ratio compared with those not taking such drugs [12] while another study reported the opposite result [41]. Although the specific classes of antihypertensive drugs affecting the urine Na/K ratio was undetermined, drugs that inhibit renal Na re-absorption, such as diuretics, may affect the urine Na/K ratio. Sodium glucose cotransporter 2 inhibitors may also influence the urine Na/K ratio via increases in natriuresis [49], although the effect on natriuresis remains controversial [50]. By contrast, some studies have shown that the association between casual and 24-h urine Na/K ratio are robust to the use of angiotensin 2 receptor blockers, calcium channel blockers, and thiazide diuretics [51, 52].

In addition to these clinical factors, socioeconomic factors also have significant effects on urine Na/K ratios. Low educational attainment was associated with higher urine Na/ K ratio [53, 54]. Low household expenditures may also be associated with higher Na/K ratio [54] although conflicting results have also been reported [53]. Regarding the association with occupation, men younger than 65 years of age who worked in factories or in heavy labor were reported to have higher urine Na/K ratio [54]. The results of a study on the association of the Na/K ratio with family structure showed that men who did not have a live-in wife had extremely high Na/K ratio, while the values for women were independent of whether they had a live-in husband [53].

As for lifestyle factors, frequent intakes of vegetables, fruits, and dairy products (which contain high amount of K) were inversely associated with the urine Na/K ratio [53]. Individuals who self-report as having a salt restriction habit showed lower urine Na/K ratio [12]. These clinical, socio-economic, and lifestyle factors may be a clue for identifying at-risk individuals for whom urine Na/K ratio assessment may be helpful.

Proposed target value for the Japanese population

Although a continuous positive association exists between the Na/K ratio and high BP or CVD risk, it is useful to define the target value of the urine Na/K ratio for clinical and public health decision-making for Japanese. In a population of 1,145 Japanese men and women aged 40-59 years from the INTERMAP study using two 24-h urine collections and four 24-h dietary recalls [55], the receiver operating characteristic curves of the average Na/K ratio at a cutoff of approximately 2 predicted combined Na and K dietary intakes based on the recommendations by sex from the DRIs for Japanese, 2020, for Japanese healthy individuals. In this study, the range of average urine Na/K ratios to meet both Na and K dietary goals simultaneously shown in the cross-classified tables was 1.6-2.2 for men and 1.7-1.9 for women (Fig. 2). Similarly, in a total of 3122 Japanese participants aged 20 years or older without antihypertensive treatment from the Tohoku Medical Megabank Project Cohort Study, the mean of the casual urine Na/K ratio, which was calculated by converting the urine Na and K excretions based on the Na and K dietary intakes recommended in the DRIs for Japanese, 2020, for Japanese healthy individuals, was approximately 2 for both men and women [32]. By contrast, NIPPON DATA2010, a cohort study representative of the general population aged 20 years Fig. 2 Range (means ± standard deviations) and number of participants in each category of the 24-h urine Na/K ratio, cross classified by estimated salt and K intake by sex [55]. A) Men (N = 574) and **B**) women (N = 571). Color-shaded matrix guide of the range of the mean urine Na/K ratio: red, urine Na/ K ratio of ≥6; yellow, urine Na/ K ratio of 3-6; green, urine Na/ K ratio of 2-3; blue, urine Na/K ratio <2. The DRIs dietary goal of salt intake of <7.5 g/day (Na < 2.95 g/day [128.3 mmol/ day]) for men and <6.5 g/day (Na < 2.56 g/day [111.3 mmol/ day]) for women. The daily K intake goal is ≥ 3 g/day for men (77 mmol/day) and ≥ 2.6 g/day for women (67 mmol/day). DRI, Dietary Reference Intakes; N.A., not applicable; SD, standard deviation; Na, sodium; Na/K, sodium-to-potassium; K, potassium

(mean±SD)

)		Estimated K intake (g/day)			
		< 2	2-3	≥3	
ke (g/day)	≥12	7.2 – 9.2 (n= 8)	4.6 – 6.4 (n= 136)	3.5 – 5.1 (n= 135)	atio
salt intal	7.5 – 12	4.3 - 6.9 (n= 46)	3.4 - 4.6 (n= 156)	2.5 - 3.5 (n= 57)	y Na/K ra
estimated	5 - 7.5	3.4 - 5.0 (n= 14)	2.5 - 3.3 (n= 18)	1.6-2.2 (n=4)	Urinar
Ι	< 5	N.A.	N.A.	N.A.	

B)

A

		< 1.8	1.8 - 2.6	≥2.6	
ce (g/day)	≥10	6.2 - 7.4 (n= 8)	4.5 - 6.3 (n= 109)	3.1 - 4.9 (n= 208)	
salt intak	6.5 - 10	4.3 - 5.9 (n= 26)	3.4 - 4.4 (n= 104)	2.1 - 3.1 (n= 85)	
Estimated	5-6.5	3.5 - 4.5 (n= 8)	2.5 - 3.1 (n= 14)	1.7 – 1.9 (n= 5)	
	< 5	2.2 - 3.2 (n= 3)	2.4 (n= 1)	N.A.	

Estimated K intake (g/dav)

Urinary Na/K ratio (mean±SD)

or older across Japan, revealed that means of the Na/K ratio from single casual urine samples were approximately 4 in men and women across all age groups (Table 2 and Fig. 3). Other population-based cohort studies in Japan using 24-h urine or multiple casual urine samples also reported mean urine Na/K ratio of approximately 4 (for example, 4.3 for INTERMAP Japan study, 3.2 for Nagahama Study, and 4.4 for Tohoku Medical Megabank Project Cohort Study) [12, 30, 55]. Therefore, in the present consensus statement, given the prior epidemiological findings, we recommend a urine Na/K ratio of 2 as an optimal target value to align with goals for both Na and K intake recommendation in the DRIs for Japanese, 2020, which consider the typical dietary patterns of the Japanese healthy population. We also define a feasible target value of the urine Na/K ratio of 4 based on the mean values of urine Na/K ratio across the Japanese general population. However, because of the lack of evidence

regarding the target values of urine Na/K ratio in patients with specific conditions such as sever renal dysfunction and congestive heart failure, older adults requiring long-term nursing care, or individuals taking certain medications that affect Na and K metabolism, this recommendation apply mainly for apparently healthy individuals living independently in communities. Further studies are needed to

Table 2 Mean and median values of the casual urine Na/K ratio by sex and age groups, NIPPON DATA2010

	Men	Women
All	<i>n</i> = 1198	N = 1599
Mean (SD)	4.2 (2.5)	4.3 (2.4)
Median (25%tile, 75%tile)	3.8 (2.7, 5.2)	3.8 (2.6, 5.3)
20-39 years	n = 159	n = 292
Mean (SD)	4.4 (2.3)	4.3 (2.6)
Median (25%tile, 75%tile)	4.1 (2.8, 5.4)	3.7 (2.3, 5.5)
40-49 years	<i>n</i> = 125	<i>n</i> = 173
Mean (SD)	4.4 (3.1)	4.1 (2.3)
Median (25%tile, 75%tile)	3.8 (2.8, 5.5)	3.7 (2.4, 5.2)
50-59 years	n = 187	n = 276
Mean (SD)	4.4 (2.3)	4.4 (2.3)
Median (25%tile, 75%tile)	3.9 (2.8, 5.7)	3.8 (2.7, 5.4)
60-69 years	<i>n</i> = 365	n = 425
Mean (SD)	4.2 (2.4)	4.4 (2.5)
Median (25%tile, 75%tile)	3.7 (2.7, 5.3)	3.9 (2.8, 5.4)
70 years or older	<i>n</i> = 362	<i>n</i> = 433
Mean (SD)	4.0 (2.4)	4.0 (2.3)
Median (25%tile, 75%tile)	3.6 (2.5, 4.8)	3.7 (2.5, 5.2)

Na/K ratio was assessed based on the single measurement of casual urine samples

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



Fig. 3 Distributions of casual urine Na/K ratio in men and women, NIPPON DATA2010. Na/K ratio was assessed based on the single measurement of casual urine samples. No. (%) of participants with casual urine Na/K ratio of <2, 2 to 3.9, and \geq 4.0 were 156 (13.0), 503 (42.0), and 539 (45.0), respectively, for men and 216 (13.5), 645

determine appropriate target values of urine Na/K ratio for patients with the specific conditions.

Measurement strategy for the casual urine Na/K ratio

The Na/K ratio can be calculated using two methods: one based on dietary survey data and the other based on biological samples. However, accurately assessing Na intake from regular meals is challenging because Na sources often include seasonings such as soy sauce and miso. It is considered difficult to accurately estimate the amount of seasoning used in each case of home-cooked or ready-made meals or when eating out. In this context, biological samples refer to urine. Typically, approximately 90% of orally consumed Na is excreted through the kidneys in urine, making urine Na excretion the most accurate biomarker reflecting Na intake [56]. However, K is also excreted to some extent in feces, so urine excretion accounts for approximately 70-80% of K intake [56]. Among the evaluation methods using urine, the gold standard is measurement based on 24-h urine collection. However, this method is time-consuming and comes with various challenges, such as inconvenience when going out or insufficient urine collection during bowel movements. In addition, a single 24-h urine collection may not be sufficient to estimate usual Na and K intake because it does not account for day-by-day variations in food intake.

Given the simplicity and convenience of measuring the urine Na/K ratio using casual urine samples, we will address when and how many days the casual urine Na/K ratio should be measured to minimize systematic errors arising from daily and diurnal variations in the Na/K ratio in this consensus statement. In Japanese normotensive individuals



(40.3), and 738 (46.2), respectively, for women. NIPPON DATA2010, the National Integrated Project for Prospective Observation of Noncommunicable Disease and its Trends in the Aged 2010; Na/K, sodium-to-potassium; SD, standard deviation



Fig. 4 Correlation specification between numbers of repeated casual urine sampling and 7-day 24-h urine of sodium-to-potassium (Na/K) ratio in normotensive and hypertensive individuals [52, 57]. (a) Normotensive individuals and (b) hypertensive individuals

and hypertensive individuals taking antihypertensive medication, a high correlation (r = 0.80-0.88) and good agreement were observed between mean values of the urine Na/K ratio from casual urines sampled randomly in a day or casual urines sampled randomly in daytime for 4-7 days and the 24-h urine Na/K ratio for 7 days (Figs. 4, 5) [52, 57]. Interestingly, the correlation and agreement quality of the mean urine Na/K ratio from casual urines sampled randomly in a day for 4-7 days with the mean 24-h urine Na/K ratio for 7 days were similar to those of the mean 24-h urine Na/K ratio for 1-2 days with the mean 24-h urine Na/ K ratio for 7 days [52, 57]. In addition, the Tohoku Medical Megabank Project Cohort Study found that the average Na/ K ratio from multiple casual urine measurements, over a period of three or more days, was closely related to prevalent home hypertension (Fig. 6) [30]. Taken together, we strongly recommend the use of the average Na/K ratio of casual urines collected randomly in various times on at least four days a week for the reliable individual estimate of the dietary Na/K ratio [58]. Random samples of casual urines in various times on at least four days would be preferable for the control of both day-to-day and intraday variability of urine Na/K ratio within individuals (Fig. 7).

When measuring the casual urine Na/K ratio only once (for example, for a health check-up), it remains unknown which urine sample is most appropriate for accurate assessment of the urine Na/K ratio, namely the first morning voiding urine, second morning voiding urine, or another sample. In a prior study examining the diurnal variation in urine Na/K ratio [41], approximately similar levels were observed between casual urine sampled at around 9 a.m. and 24-h urine for Na and K concentrations and Na/K ratio, suggesting the second morning voiding urine sampled at around 9 a.m. may be one of the ideal choices if we have only one occasion for the measurement of urine Na/K ratio. However, this field warrants further investigation. Importantly, the casual urine Na/K ratio obtained, even from a single measurement, holds the potential to retrospectively review individual dietary habits, and thus the consensus statement does not negate the usefulness of a single measurement of the casual urine Na/K ratio.

Why we use the randomly sampled casual urines in assessment for urine Na/K ratio

The urine Na/K ratio exhibits diurnal variation [41], with several time points when the Na/K ratio of the casual urine is comparable to that measured using 24-h urine collections. On average, the second morning urine may be at the time point, though it was uncertain whether the comparability can be extrapolated into various individuals: for example, older adults with nocturia exhibited lower urine Na/K ratio in casual urine [44]. Furthermore, the amount of dietary intake of Na or K varies by days. Therefore, even in the estimation of Na and K intake using 24-h collected urine, using urine samples collected over a 7-day period was recognized as the most accurate method [59]. The way to balance the difficulties in the assessment of urine Na and K excretions and easy to use in the health practices is using the casual urines obtained at various times on different days [58]. This simple once-a-day method of measurement allows daily measurements and has been reported to provide a reliable estimate of urine Na/K ratio [52, 57]. Given these findings, the average Na/K ratio from casual urine samples randomly taken in various times on at least four different



Fig. 5 Plots of sodium-to-potassium (Na/K) ratios of casual urine vs. 24-h urine, and Bland–Altman plots in normotensive and hypertensive individuals [52, 57]. (a) Normotensive individuals (scattered plots);

(**b**) hypertensive individuals (scattered plots); (**c**) normotensive individuals (Bland–Altman plots); and (**d**) hypertensive individuals (Bland–Altman plots)

days is recommended as the most simple and reliable way for the estimation of urine Na/K ratio.

The consensus document of the World Hypertension League, International Society of Hypertension, and Resolve to Save Lives has criticized the traditional methods of estimating Na intake using a single casual urine sample [60]. We are also recognizing that the estimated daily salt intake from a casual spot urine is less reliable particularly at the individual level. Causes for the limited reliability may be (1) estimating salt intake from age, body height and weight, and spot urine Na and creatinine levels, and (2) using the single measurement value in the assessment. However, urine Na/K ratio could overcome these two issues, because urine Na/K ratio is a measured value but not an estimated value and easy to perform multi-day measurements. In Asians, excessive Na intake and insufficient K intake contribute more severely to CVD than in Europeans [61]. The implementation of this new index in the society is expected to make a significant contribution to CVD prevention, even if it has some limitations.



Fig. 6 Relationship between 1 day and 10 days average urine sodium-to-potassium (Na/K) ratio and home hypertension [30]. P values for linear trends were derived from multiple logistic regression analysis. Error bars represent a 95% confidence interval



Evidence from interventional studies

Recently, OMRON Healthcare Co., Ltd. developed a handy-sized device for monitoring the urine Na/K ratio (HEU-001F; OMRON Healthcare Co., Ltd., Kyoto, Japan) that can quickly and easily measure the urine Na/K ratio as a research equipment. The correlation between the urine Na/K ratio measured by the device and the ratio measured at the inspection center was high ($R^2 = 0.9676$) [37]. In fact, the device is gradually being widely used to conveniently assess the urine Na/K ratio in health check-ups or health promotion projects in Japan [34, 62].

Dietary interventions play a pivotal role in the prevention and management of high BP, with particular attention on the impact of high Na and low K intakes. Randomized controlled trials (RCTs) assessing the use of monitoring with the Na/K ratio or salt (Na) intake to motivate individuals to promote low salt (Na) and high K consumptions have garnered much interest. Iwahori et al. [37]. conducted an RCT of a 1-month dietary intervention involving selfmonitoring of the urine Na/K ratio using an electronic device (HEU-001F, OMRON Healthcare Co., Ltd., Kyoto, Japan) vs. standard care in voluntary Japanese participants (mean age, 55 years; 22% hypertensives) for the purpose of reducing Na and increasing K intakes, and lowering BP through self-monitoring. In this RCT, however, the effect of the self-monitoring device for the urine Na/K ratio did not reach the level of statistical significance on the pre-specified effect size (a target reduction of 1-unit difference of urine Na/K ratio between the intervention and control groups) under only self-management (no additional professional support). There were also no significant changes observed in Na and K excretions and BP. This RCT indicates the necessity for additional research to explore effective methods for enhancing the synergetic effects of dietary programs and self-monitoring practice, with the aim of achieving Na reduction and K increase [37].

Kogure et al. [34]. conducted a single-arm interventional study based on measurement of the urine Na/K ratio using an electronic device (HEU-001F, OMRON Healthcare Co., Ltd.) at a community health check-up among Japanese participants with a mean age of 65 years. The check-up included the provision of feedback on the results and information about the urine Na/K ratio, for the purpose of reducing Na, increasing K intakes, and lowering BP. Subsequently, significant decreases in the urine Na/K ratio and BP levels were found between the pre- and postimplementation phases. The findings suggest that assessing the urine Na/K ratio in community settings holds the potential to prevent and control hypertension through a population-based approach.

Additionally, some RCTs have used a self-monitoring device for urine salt (Na) excretion (KME-03; Kohno ME Laboratory, Kanagawa, Japan) to motivate individuals to decrease their urine Na/K ratio (by reducing salt (Na) intake and increasing K intake) and decrease their BP [63, 64]. Yasutake et al. [63]. found that the 24-h urine Na/K ratio and systolic BP significantly decreased in the selfmonitoring group compared with that in the control group in a 4-week RCT among Japanese women aged 18 to 25 years. Yasutake et al. [64]. also reported that selfmonitoring helped to reduce the 24-h urine Na/K ratio but not BP levels in a 4-week RCT among healthy Japanese volunteers with a mean age of 58 years (~30% hypertensive). Overall, the current evidence from RCTs on the utility of measuring the urine Na/K ratio or Na excretion, especially for the prevention or control of hypertension, remains inconclusive, and further investigation is warranted.

Perspective of Asia

High salt intake remains a global concern, with a substantial burden observed especially in Central and East Asia [65]. Additionally, the prevalence of hypertension has been rising globally, particularly in the Asia and Pacific region [66, 67]. Therefore, despite certain limitations, the application of the urine Na/K ratio in clinical and public health settings holds significant potential for the prevention and management of hypertension, especially in Asia.

Conclusions

This consensus statement is a first step towards a better understanding of the role of the urine Na/K ratio in the prevention and control of hypertension. Given the high variability of the urine Na/K ratio within individuals, the use of the average Na/K ratio of casual urines randomly taken in different times on at least four days a week is highly recommended for reliable individual estimates of the dietary Na/K ratio.

Continuous positive associations of the Na/K ratio with the risks of hypertension and CVD have been reported; however, it is important to establish a specific target value for the urine Na/K ratio for Japanese individuals in relation to decision making in the clinical and public health setting. We recommend an optimal target value for the average urine Na/K ratio of 2 to simultaneously meet the dietary goals for both Na and K intake recommendation by the DRIs for Japanese, 2020, considering the typical dietary patterns of the Japanese healthy population. We also recommend an average urine Na/K ratio of 4 as a feasible target value to achieve a temporary goal of being below the mean values of urine Na/K ratio across Japanese general populations. These recommendations apply mainly for apparently healthy individuals, but not for patients with specific conditions due to the lack of sufficient evidence. Thus, dietary habit modification, including reduced salt intake and higher consumption of K-containing foods, would strongly be recommended especially for individuals with an average urine Na/K ratio of 4 or higher.

The INTERSALT study [18] reported that the 24-h urine Na/K ratio could predict Na intake under the dietary goal of the World Health Organization [68, 69], with a sensitivity of >90% when the 24-h urine Na/K ratio was <1. Although achieving a urine Na/K ratio of 1 through stringent dietary intake, as recommended by international guidelines, may pose challenges in some populations and necessitate substantial nationwide dietary habit changes, it is crucial to advocate for the appropriate threshold taking into account the applicability of the proposed level for each specific population. In addition, a target value for the urine Na/K ratio is attractive for future public health or clinical interventions. In other words, further studies are needed to investigate whether the measurement of urine Na/K ratio by itself (or accompanied by an effective education program) may provide the support for lifestyle modification efforts and promote lower salt intake and higher intake of K-containing foods, resulting in a reduced risk of hypertension.

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