Associations of Urinary and Dietary Sodium-To-Potassium Ratios with Albuminuria in Community-Dwelling Japanese Adults: A Cross-Sectional Study

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\textbf{Keywords}  
Chronic kidney disease · Microalbuminuria · Nutrients · Potassium · Salt intake

\textbf{Abstract}  
\textbf{Introduction:} The urinary sodium-to-potassium ratio is an indicator of dietary sodium intake and has been associated with reduced kidney function. However, less is known about its association with albuminuria, the other key component of chronic kidney disease, in the community-dwelling adult population. We examined the association of the spot urinary sodium-to-potassium ratio with albuminuria and compared spot urinary and dietary sodium-to-potassium ratios.  
\textbf{Methods:} We quantified the association of the urinary sodium-to-potassium ratio with albuminuria in 6,274 Japanese adults (aged 40–97 years; 50.9\% women) based on spot urine samples. We performed linear and logistic regression modeling to account for potential confounders. Elevated albuminuria was defined as a spot urinary albumin-to-creatinine ratio (ACR) \( \geq 30 \) mg/g. We secondarily evaluated the dietary sodium-to-potassium ratio based on a food-frequency questionnaire.  
\textbf{Results:} The median spot urinary and dietary sodium-to-potassium ratios were 2.70 (interquartile interval, 1.87–3.83) and 1.50 (1.21–1.84), respectively. The median ACR was 11.0 (6.0–24.0) mg/g. In a multivariable linear regression model, the spot urinary sodium-to-potassium ratio (per increment) was significantly associated with the natural logarithm of the ACR (regression coefficient, 0.023 [95\% confidence interval {95\% CI}, 0.007–0.038]). This result was consistent in a multivariable logistic regression model (adjusted odds ratio, 1.08 [95\% CI: 1.04–1.12]). The corresponding estimates for the dietary sodium-to-potassium ratio were 0.139 (95\% CI: 0.087–0.191) and 1.28 (95\% CI: 1.14–1.45), respectively.  
\textbf{Conclusions:} Both spot urinary and dietary sodium-to-potassium ratios were associated with elevated albuminuria in community-dwelling Japanese adults. Our findings further support the potential usefulness of the spot urinary sodium-to-potassium ratio as an indicator of sodium intake and suggest a link between sodium intake and kidney damage.

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Introduction

Dietary sodium and potassium intakes are key determinants of blood pressure (in positive and inverse directions, respectively) [1–6]. Indeed, sodium plays a critical role in extracellular volume regulation [7, 8], whereas potassium, the most abundant electrolyte in intracellular fluid, is crucial for normal cell function, including vascular resistance [9]. Notably, potassium modulates sodium excretion in the kidney [10, 11].

The urinary sodium-to-potassium ratio has recently attracted attention as an indicator of dietary sodium intake [12, 13], due to some potential advantages over the gold standard of repeated measurements for 24-h urinary sodium excretion [14, 15]. For example, although a single time point of 24-h urinary sodium excretion may still be susceptible to intrinsic or random variations, the 24-h urinary sodium-to-potassium ratio may be less susceptible because such variations in both the numerator and the denominator may be canceled out. Indeed, some studies preferred the sodium-to-potassium ratio to sodium excretion, even when they had data on 24-h urine samples [1]. In addition, the association of the 24-h urinary sodium-to-potassium ratio with blood pressure was actually stronger than that of either 24-h urinary sodium or potassium excretion alone [2, 4]. Another and potentially more important advantage is that even a spot urine sample may provide useful information on sodium intake if we use the sodium-to-potassium ratio. Indeed, the spot urinary sodium-to-potassium ratio predicts increased total body fat [16] and incident stroke [17].

A few studies have also explored the associations of the urinary sodium-to-potassium ratio with kidney measures. For example, the 24-h urinary sodium-to-potassium ratio estimated by using spot urine is robustly associated with reduced kidney function [18, 19]. However, conflicting results have been reported regarding the association of the 24-h urinary sodium-to-potassium ratio with albuminuria, the other key component of chronic kidney disease [20–22]. Because the study population and design differed in those previous studies, additional investigation is warranted.

Therefore, we examined the association of the spot urinary sodium-to-potassium ratio with albuminuria in a Japanese community-based cohort, the Uonuma cohort study [23]. Uniquely, this cohort allowed us to compare both spot urinary and dietary sodium-to-potassium ratios in terms of their associations with albuminuria. If they are found to show similar associations with albuminuria, it would further support the potential usefulness of the spot urinary sodium-to-potassium ratio as an indicator of dietary sodium intake and highlight the link between dietary sodium intake and kidney damage.

Methods

Study Population

At baseline (2012–2014), the Uonuma cohort study invited all residents aged 40 years or older in Minamiuonuma and Uonuma City, Niigata Prefecture, Japan (n = 61,765); 39,761 residents consented to complete a questionnaire. Of these, 6,425 residents consented to provide urine samples. For this specific study, we excluded those with missing information on the timing of the spot urine collection, spot urinary potassium, estimated glomerular filtration rate (eGFR), history of heart disease, and drinking habit (n = 73) and those who had an extremely high or low energy intake (> or <3 standard deviations from the mean) based on the questionnaire (n = 78), leaving 6,274 residents as the final study sample (Fig. 1). The participants with spot urine testing were more likely to be older and have hypertension compared with those without such testing; however, the prevalence of diabetes, stroke, and heart disease was almost the same in both groups (online suppl. Table 1; see www.karger.com/doi/10.1159/000526277 for all online suppl. material). The study protocol was approved by the Ethics Committee of Niigata University School of Medicine (2012-1403, 2013-1640, and 2017-0054).

Spot Urine Sample Measurements

A spot urine sample was collected as part of governmental health checkups in the morning or afternoon and was immediately transported to a certified clinical laboratory for analysis. Spot urinary sodium was measured by the indirect ion-selective electrode method. Spot urinary potassium was measured by the indirect ion-selective electrode method in 2019 using stored frozen specimens [24]. For a representative measure of albuminuria, we calculated the spot urinary albumin-to-creatinine ratio (ACR) [25]. Spot urinary albumin and creatinine concentrations were measured by the latex agglutination method and the enzymatic method, respectively, using fresh urine.

Dietary Assessment

The dietary assessment was based on the self-administered food-frequency questionnaire (FFQ) from the Japan Public Health Center-based Prospective Study for the Next Generation [26]. It contains 172 food and beverage items with nine frequency categories and three amounts for each meal and asks participants about the average consumption of the listed foods and beverages during the past year. Intakes of energy, sodium, potassium, and the remaining 50 nutrients and 29 food groups were calculated using the Standard Tables of Food Composition in Japan 2010 [27]. The Spearman’s rank correlation coefficients for energy-adjusted sodium and potassium with intake based on the FFQ and 12-day weighed food records were 0.34 and 0.48 in men and 0.38 and 0.54 in women, respectively [28].

Covariates

The baseline health checkup included blood tests and measurements of body weight, height, and systolic and diastolic blood pres-
smokes. Smoking status (current smoker or not), drinking habit (drinking every day or not), history of stroke, and history of heart disease were self-reported by each participant. Body mass index (BMI) was calculated as measured body weight (kilogram) divided by measured body height (meter) squared. Seated blood pressure was measured once on the upper arm. Serum creatinine was measured using the enzymatic method, and eGFR was based on an equation for Japanese adults: eGFR (mL/min/1.73 m²) = 194 × (serum creatinine [mg/dL])^{−1.094} × age (years)^{−0.287} × 0.739 [for women] [29]. Plasma glucose and glycated hemoglobin (HbA1c) were measured by the hexokinase method and high-performance liquid chromatography, respectively. Diabetes was defined as HbA1c ≥6.5%, fasting plasma glucose ≥126 mg/dL, casual plasma glucose ≥200 mg/dL, or the use of antidiabetic medication. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or the use of antihypertensive medication.

Statistical Analysis

Participant characteristics are summarized as mean ± standard deviation, median (interquartile interval [IQI]), or number (percentage) by the quartiles of the spot urinary sodium-to-potassium ratio and that of the dietary sodium-to-potassium ratio. We obtained the Spearman’s correlation coefficients between the spot urinary and dietary sodium-to-potassium ratios and their components (e.g., spot urinary or dietary sodium and potassium). When we calculated the Spearman’s correlation coefficients of dietary sodium and potassium separately (but not when we analyzed their ratio), we adjusted for energy intake using the residual method [30]. The Spearman’s correlation coefficients between spot urinary and dietary sodium-to-potassium ratios were calculated in key subgroups.

To estimate the associations of the urinary and dietary sodium-to-potassium ratios (independent variables) with the ACR (dependent variable), we performed linear regression modeling. We took the natural logarithm for the ACR (ln-ACR) due to its skewed distribution. We also modeled spot urinary and dietary sodium-to-potassium ratios with their spline terms (knots at the thresholds of quartiles) to visualize their potentially nonlinear associations with the ln-ACR. We also ran logistic regression models with elevated albuminuria (ACR ≥30 mg/g) [25] as a dependent variable. To assess the impact of potential confounders, we constructed the following three models: Model 1 was adjusted for sex and age (demographics); Model 2 was additionally accounted for the timing of urine collection (morning or not), smoking, and drinking (lifestyle); and Model 3 was further adjusted for BMI, diabetes, systolic blood pressure, use of antihypertensive medication, and eGFR (clinical factors). We repeated the analysis (model 3) with quartiles of the spot urinary sodium-to-potassium ratio as a dependent variable, except for age (with the oldest mean age in the highest quartile) and energy intake (online suppl. Table 2). The spot urinary and dietary sodium-to-potassium ratios were modestly correlated, with a Spearman’s correlation coefficient of 0.185 (Table 2). The correlation coefficients between the spot urinary and dietary sodium-to-potassium ratios ranged from ~0.15 to ~0.21 across subgroups (online suppl. Table 3). The spot urinary sodium-to-potassium ratio was more strongly correlated with spot urinary sodium (correlation coefficient, 0.678) than with spot urinary potassium (~0.232). Similarly, the dietary sodium-to-potassium ratio showed a stronger correlation with dietary sodium intake than with dietary potassium intake. The correlation coefficients between spot urinary sodium and spot urinary potassium and between dietary sodium and dietary potassium were about 0.5.

Results

The mean age of the study population was 68.3 ± 9.8 years, and 50.9% (n = 3,196) were women. The median spot urinary sodium-to-potassium ratio was 2.70 (IQR, 1.87–3.83), whereas the median dietary sodium-to-potassium ratio was 1.50 (IQR, 1.21–1.84). The median ACR was 11.0 (IQR, 6.0–24.0) mg/g. Participants in the highest quartile of the spot urinary sodium-to-potassium ratio were more likely to be younger, male, and on antihypertensive medication and to have lower energy intake and higher ACR, BMI, eGFR, and systolic and diastolic blood pressure compared with those in the other three quartiles (Table 1). Generally, similar patterns were observed across the quartiles of the dietary sodium-to-potassium ratio, except for age (with the oldest mean age in the highest quartile) and energy intake (online suppl. Table 2).

Spot urinary and dietary sodium-to-potassium ratios were modestly correlated, with a Spearman’s correlation coefficient of 0.185 (Table 2). The correlation coefficients between the spot urinary and dietary sodium-to-potassium ratios ranged from ~0.15 to ~0.21 across subgroups (online suppl. Table 3). The spot urinary sodium-to-potassium ratio was more strongly correlated with spot urinary sodium (correlation coefficient, 0.678) than with spot urinary potassium (~0.232). Similarly, the dietary sodium-to-potassium ratio showed a stronger correlation with dietary sodium intake than with dietary potassium intake. The correlation coefficients between spot urinary sodium and spot urinary potassium and between dietary sodium and dietary potassium were about 0.5.
| Table 1. Descriptive characteristics according to quartiles of the spot urinary sodium-to-potassium ratio |

| Quartiles of the spot urinary sodium-to-potassium ratio | <1.87 | 1.87–2.69 | 2.70–3.82 | >3.82 |
|---------------------------------------------------------|-------|----------|-----------|-------|
| Participants, n                                        | 1,569 | 1,567    | 1,569     | 1,569 |
| Spot urinary sodium-to-potassium ratio                 | 1.42  (1.13, 1.65) | 2.26  (2.07, 2.48) | 3.18  (2.93, 3.46) | 4.95  (4.31, 6.09) |
| Spot urinary sodium, mmol/g Cr                         | 89.9  (60.4, 127.6) | 146.7 (108.3, 198.9) | 193.3 (147.1, 252.8) | 262.7 (195.2, 342.2) |
| Spot urinary potassium, mmol/g Cr                      | 65.9  (47.5, 89.2) | 65.3  (48.1, 87.6) | 60.4  (46.0, 79.3) | 49.6  (36.6, 66.7) |
| ACR, mg/g                                               | 10 (6.23) | 10.2 (6.21) | 11 (6.25) | 13 (6.631) |
| Dietary sodium-to-potassium ratio                      | 1.38  (1.12, 1.70) | 1.46  (1.19, 1.77) | 1.53  (1.23, 1.88) | 1.63  (1.33, 1.98) |
| Dietary sodium intake, mg/day                          | 4,425.5 (3,499.6, 5,490.1) | 4,582.3 (3,659.4, 5,679.1) | 4,668.3 (3,660.9, 5,882.9) | 4,698.1 (3,739.4, 5,922.2) |
| Dietary potassium intake, mg/day                        | 3,255.7 (2,609.8, 3,923.0) | 3,225.4 (2,612.1, 3,846.5) | 3,118.6 (2,532.9, 3,707.1) | 2,945.6 (2,343.3, 3,626.7) |
| Male, n (%)                                            | 739 (47.1) | 745 (47.5) | 752 (47.9) | 842 (53.7) |
| Age, years                                              | 68.2±9.5 | 68.6±9.6 | 68.8±9.8 | 67.8±10.3 |
| Body mass index, kg/m²                                  | 22.4±3.0 | 22.6±2.9 | 22.7±3.1 | 22.9±3.2 |
| Systolic blood pressure, mm Hg                         | 126.1±17.0 | 129.0±17.9 | 130.8±18.1 | 133.8±18.2 |
| Diastolic blood pressure, mm Hg                        | 73.5±10.2 | 74.7±11.0 | 75.4±10.9 | 76.7±10.9 |
| eGFR, mL/min/1.73 m²                                   | 72.1±14.8 | 73.6±14.6 | 74.8±15.4 | 78.4±17.3 |
| Energy intake, kcal/day                                 | 1,986.1 (1,580.2, 2,484.7) | 1,925.2 (1,525.6, 2,432.1) | 1,927.7 (1,548.4, 2,482.5) | 1,848.1 (1,450.8, 2,366.8) |
| Use of any antihypertensive medication, n (%)          | 530 (33.8) | 535 (34.1) | 510 (32.5) | 594 (37.9) |
| Use of any antidiabetic medication, n (%)              | 88 (5.6) | 98 (6.3) | 95 (6.1) | 89 (5.7) |
| Diabetes, n (%)                                        | 143 (9.1) | 151 (9.6) | 171 (10.9) | 143 (9.1) |
| Hypertension, n (%)                                     | 725 (46.2) | 773 (49.3) | 797 (50.8) | 928 (59.2) |
| History of stroke, n (%)                               | 80 (5.1) | 66 (4.2) | 49 (3.1) | 71 (4.5) |
| History of heart disease, n (%)                        | 100 (6.4) | 74 (4.7) | 76 (4.8) | 71 (4.5) |
| Current smoking, n (%)                                 | 221 (14.1) | 211 (13.5) | 220 (14.0) | 242 (15.4) |
| Drink alcohol every day, n (%)                         | 497 (31.7) | 501 (32.0) | 486 (31.0) | 541 (34.5) |
| Spot urine collection in the morning, n (%)           | 1,275 (81.3) | 1,211 (77.3) | 1,149 (73.2) | 896 (57.1) |

Values are presented as the mean±standard deviation, median (interquartile interval), or number (percentage). ACR, urinary albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate. Dietary sodium and potassium intakes were adjusted by energy intake using the residual method.
The associations between the spot urinary or dietary sodium-to-potassium ratio with their spline terms and the ln-ACR are shown in online supplementary Figures 1 and 2. Given this observation, in subsequent analyses, we modeled both the spot urinary and dietary sodium-to-potassium ratios linearly. After adjustment for age and sex, the spot urinary sodium-to-potassium ratio was positively and significantly associated with the ln-ACR ($\beta = 0.049$ [95% confidence interval [95% CI], 0.033–0.065] per increment in the spot urinary sodium-to-potassium ratio) (Model 1 in Table 3). Further adjustment for the timing of urine collection (morning or not), smoking status, and drinking habits did not alter the result. Additional adjustment for clinical factors attenuated this association, but it remained statistically significant ($\beta = 0.023$ [95% CI: 0.007–0.038]) (Model 3 in Table 3).

Similarly, dietary sodium-to-potassium was significantly associated with the ln-ACR (e.g., $\beta = 0.144$ [95% CI: 0.090–0.198] per increment in the dietary sodium-to-potassium ratio) (Model 1 in Table 4). This association was materially unchanged after adjustment for lifestyle and clinical factors ($\beta = 0.139$ [95% CI: 0.087–0.191]) (Model 3 in Table 4). In terms of other predictors, age, current smoking, diabetes, systolic blood pressure, and use of antihypertensive medication were positively associated, and male sex was inversely associated with the ACR across these models (Model 3 in Tables 3, 4). Large-ly similar results were observed in logistic regression models (online suppl. Tables 4, 5). When we modeled the quartiles of the spot urinary or dietary sodium-to-potassium ratio, there was a general dose-response relationship between the dietary sodium-to-potassium ratio and the ACR (Fig. 2). The spot urinary sodium-to-potassium ratio demonstrated a slight J-shaped association with the ACR, but the second lowest quartile was not significantly different from the lowest quartile. The $p$ for trend was $<0.001$ for both spot urinary and dietary sodium-to-potassium ratios.

In subgroup analysis, we observed that the association of the spot urinary sodium-to-potassium ratio with albuminuria was more evident in women, older participants, and participants with diabetes, hypertension, or reduced kidney function than in their counterparts (Fig. 3). In contrast, the association of the dietary sodium-to-potassium ratio with albuminuria was largely consistent across subgroups, with only a significant interaction by kidney function (Fig. 4).

**Table 2.** Correlations of the spot urinary and dietary sodium-to-potassium ratios with each component

| Spot urinary sodium-to-potassium ratio | Spot urinary sodium, mmol/g Cr | Spot urinary potassium, mmol/g Cr | Dietary sodium-to-potassium ratio | Dietary sodium, mg/day | Dietary potassium, mg/day |
|---------------------------------------|--------------------------------|----------------------------------|----------------------------------|------------------------|--------------------------|
| 1                                     | 0.678                          | −0.232                           | 0.067                            | −0.122                 | −0.122                   |
| Spot urinary sodium, mmol/g Cr        | 1                              | −0.322                           | 0.122                            | 0.106                  | 0.106                    |
| Spot urinary potassium, mmol/g Cr     | 0.051                          | 1                                | −0.367                           | −0.367                 | −0.367                   |
| Dietary sodium-to-potassium ratio     | 0.550                          | −0.367                           | 1                                | 1                      | 1                        |
| Dietary sodium, mg/day                | 0.135                          | −0.367                           | 1                                | 1                      | 1                        |
| Dietary potassium, mg/day             | 0.144                          | −0.367                           | 1                                | 1                      | 1                        |

Values are Spearman’s correlation coefficients. *Dietary sodium and potassium intakes were adjusted by energy intake using the residual method.
### Table 3. Multivariable linear regression analysis between the spot urinary sodium-to-potassium ratio and the natural logarithm of the ACR

|                                | Model 1 regression coefficient (95% CI) | Model 2 regression coefficient (95% CI) | Model 3 regression coefficient (95% CI) |
|--------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Spot urinary sodium-to-potassium ratio, per increment | 0.049 (0.033, 0.065)                  | 0.048 (0.032, 0.064)                  | 0.023 (0.007, 0.038)                  |
| Male sex                       | −0.228 (−0.285, −0.171)                | −0.273 (−0.340, −0.206)                | −0.338 (−0.403, −0.274)                |
| Age, per year                  | 0.033 (0.030, 0.036)                   | 0.034 (0.031, 0.037)                   | 0.024 (0.021, 0.027)                   |
| Current smoking                | 0.168 (0.081, 0.255)                   | 0.238 (0.154, 0.321)                   |                                          |
| Drink alcohol every day        | 0.022 (−0.047, 0.092)                  | −0.055 (−0.122, 0.002)                 |                                          |
| Spot urine collection in the morning | −0.009 (−0.074, 0.056)                | −0.016 (−0.078, 0.046)                |                                          |
| Body mass index, per kg/m²     | 0.006 (−0.003, 0.015)                  |                                          |                                          |
| Diabetes                       | 0.414 (0.321, 0.507)                   |                                          |                                          |
| Systolic blood pressure, per mm Hg | 0.015 (0.013, 0.016)                  |                                          |                                          |
| Use of any antihypertensive medication | 0.353 (0.292, 0.415)                  |                                          |                                          |
| eGFR, per mL/min/1.73 m²       | −0.0002 (−0.002, 0.002)                |                                          |                                          |

ACR, urinary albumin-to-creatinine ratio; CI, confidential interval; eGFR, estimated glomerular filtration rate.

### Table 4. Multivariable linear regression analysis between the dietary sodium-to-potassium ratio and the natural logarithm of the ACR

|                                | Model 1 regression coefficient (95% CI) | Model 2 regression coefficient (95% CI) | Model 3 regression coefficient (95% CI) |
|--------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Dietary sodium-to-potassium ratio, per increment | 0.144 (0.090, 0.198)                  | 0.139 (0.084, 0.193)                  | 0.139 (0.087, 0.191)                  |
| Male sex                       | −0.250 (−0.308, −0.192)                | −0.285 (−0.353, −0.217)                | −0.357 (−0.422, −0.292)                |
| Age, per year                  | 0.032 (0.030, 0.035)                   | 0.034 (0.031, 0.037)                   | 0.023 (0.020, 0.026)                   |
| Current smoking                | 0.164 (0.077, 0.251)                   | 0.234 (0.151, 0.317)                   |                                          |
| Drink alcohol every day        | 0.009 (−0.061, 0.079)                  | −0.072 (−0.139, −0.004)                |                                          |
| Spot urine collection in the morning | −0.047 (−0.110, 0.016)                | −0.032 (−0.092, 0.029)                |                                          |
| Body mass index, per kg/m²     | 0.006 (−0.004, 0.015)                  |                                          |                                          |
| Diabetes                       | 0.413 (0.320, 0.506)                   |                                          |                                          |
| Systolic blood pressure, per mm Hg | 0.015 (0.013, 0.017)                  |                                          |                                          |
| Use of any antihypertensive medication | 0.357 (0.295, 0.418)                  |                                          |                                          |
| eGFR, per mL/min/1.73 m²       | −0.0001 (−0.002, 0.002)                |                                          |                                          |

ACR, urinary albumin-to-creatinine ratio; CI, confidential interval; eGFR, estimated glomerular filtration rate.
**Fig. 2.** Adjusted odds ratios (95% CIs) of the quartiles of the spot urinary sodium-to-potassium ratio (a) and dietary sodium-to-potassium ratio (b) for elevated albuminuria. Note. Adjusted odds ratios (95% CIs) were adjusted by male sex, age, current smoking, drinking habit, body mass index, spot urine collection in the morning, diabetes, systolic blood pressure, use of any antihypertensive medication, and eGFR. Y-axes show adjusted odds ratios transformed to the natural logarithm. CI, confidence interval; eGFR, estimated glomerular filtration rate; OR, odds ratio.

**Fig. 3.** Regression coefficients (95% CIs) of the spot urinary sodium-to-potassium ratio for the natural logarithm of the ACR by subgroup. Note. Regression coefficients (95% CI) were adjusted by male sex, age, current smoking, drinking habit, body mass index, spot urine collection in the morning, diabetes, systolic blood pressure, use of any antihypertensive medication, and eGFR. The variable defining a relevant subgroup was not included in that subgroup analysis model (e.g., age was not included in the model when we analyzed age subgroups). ACR, urinary albumin-to-creatinine ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate.

**Fig. 4.** Regression coefficients (95% CIs) of the dietary sodium-to-potassium ratio for the natural logarithm of the ACR by subgroup. Note. Regression coefficients (95% CI) were adjusted by male sex, age, current smoking, drinking habit, spot urine collection in the morning, body mass index, diabetes, systolic blood pressure, use of any antihypertensive medication, and eGFR. The variable defining a relevant subgroup was not included in that subgroup analysis model (e.g., age was not included in the model when we analyzed age subgroups). ACR, urinary albumin-to-creatinine ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate.
Discussion

In this cross-sectional study, the spot urinary sodium-to-potassium ratio was independently and positively associated with albuminuria. We found a similar positive association between the dietary sodium-to-potassium ratio and albuminuria. In our subgroup analysis, we observed interactions with the demographic and clinical factors tested for the association between the spot urinary sodium-to-potassium ratio and albuminuria, but this was not necessarily the case for the association between the dietary sodium-to-potassium ratio and albuminuria. Overall, the association with albuminuria was more evident and robust for the dietary sodium-to-potassium ratio than for the spot urinary sodium-to-potassium ratio.

Our findings are generally consistent with a Chinese study by Sun et al. [22] but not necessarily with two other studies [20, 21]. The inconsistent results may be due to different study populations and study designs. Nonetheless, there are a few unique aspects to our study. For example, to our knowledge, this is the largest study exploring the association of the urinary sodium-to-potassium ratio with albuminuria. It is also the first study to evaluate the urinary sodium-to-potassium ratio using spot urine samples instead of 24-h urine samples. This approach represents a potential advantage of urinary sodium-to-potassium ratio as an indicator of sodium intake, not requiring 24-h urine collection. In addition, we rigorously adjusted for potential confounders, including kidney function (e.g., eGFR). Moreover, we were able to uniquely compare spot urinary and dietary sodium-to-potassium ratios regarding their associations with the ACR in a single study population.

Because higher sodium intake has been linked to albuminuria [31] and the urinary sodium-to-potassium ratio is an indicator of sodium intake [32], our results may not be surprising. Nonetheless, plausible mechanisms linking the urinary sodium-to-potassium ratio to elevated albuminuria deserve some discussion. Sodium and potassium are mainly excreted by renal channels and transporters of tubule interstitial compartments [33, 34], which also regulate urinary albumin excretion [35, 36]. Indeed, experimental studies have shown that both high sodium intake and low potassium intake can induce tubulointerstitial damage and glomerulosclerosis [34, 37]. In addition, endothelial dysfunction and activation of the renin-angiotensin-aldosterone system and sympathetic nervous system can result from high sodium and low potassium intakes [34, 37, 38]. Notably, a small 12-week randomized crossover trial in the UK showed that higher potassium supplementation resulted in reduced albuminuria in individuals with high blood pressure [39].

We cannot fully explain why we observed interactions with the demographic and clinical factors tested for the spot urinary sodium-to-potassium ratio but not necessarily for the dietary sodium-to-potassium ratio. Interestingly, in our study, the association of the spot urinary sodium-to-potassium ratio with elevated albuminuria was generally stronger in higher risk subgroups, namely, older adults and persons with comorbidities, such as diabetes, hypertension, and reduced kidney function, than in their counterparts. This observation may indicate a shared pathophysiology behind the elevated sodium and/or decreased potassium excretion and the elevated albumin excretion in the kidneys. In addition, this interaction may be mediated by the medications used for these clinical conditions. Indeed, these clinical conditions, especially when elevated albuminuria is present, can be an indication for renin-angiotensin system inhibitors [25], which can reduce renal sodium reabsorption [40]. Nonetheless, since we did not see similar effect modifications for the dietary sodium-to-potassium ratio, future studies are needed to confirm our observation and, if confirmed, explore potential mechanisms.

In this study, the spot urinary sodium-to-potassium ratio was independently associated with albuminuria but less so compared with the dietary sodium-to-potassium ratio. Although we are unsure of the exact reasons behind this observation, this may be because the dietary sodium-to-potassium ratio reflects sodium intake better than the spot urinary sodium-to-potassium ratio. However, administration of a FFQ in clinical practice does not seem practical. Similarly, repeated 24-h urine collection, the current gold standard evaluation of sodium intake, islogistically cumbersome. In contrast, spot urine collection is widely performed. Thus, the selection of these different methods should be determined by a few factors, including the objective of the measurement, available resources, and the accuracy required. In this regard, it seems important to acknowledge that 24-h urinary sodium excretion [41] may be more strongly associated with cardiovascular outcomes than with estimated sodium excretion from spot urine [42].

Some limitations to this study should be noted. First, this study included only 16% of the Uonuma cohort study participants due to the limited availability of urine samples. However, the selection was not made according to any demographic or clinical conditions. Indeed, the characteristics were largely similar between
those who were included and those who were not. Second, we evaluated the spot urinary sodium-to-potassium ratio and albuminuria at a single time point, an approach that is prone to misclassification. Thus, it is likely that our estimates are conservative. Third, we did not have information on the types of antihypertensive medications, such as diuretics and renin-angiotensin system inhibitors, which could influence urinary electrolyte excretion and albuminuria. Fourth, the dietary sodium-to-potassium ratio was based on a self-reported FFQ, although it has been validated [28]. Fifth, although we strived to adjust for potential confounders, as in all observational studies, we cannot deny the possibility of residual confounding. Fifth, this cross-sectional study cannot determine temporality and causality. Finally, the study participants were enrolled from one area in Japan and the generalizability of our findings should thus be carefully assessed.

There are a few potential implications from this study. Our results seem to further support the spot urinary sodium-to-potassium ratio as an indicator of dietary sodium intake by showing a largely similar association with albuminuria. Simultaneously, we must acknowledge that the dietary sodium-to-potassium ratio overall demonstrated more robust associations with albuminuria than the spot urinary sodium-to-potassium ratio. Therefore, although time-consuming, whenever the situation allows, a FFQ would be an optimal means to evaluate dietary patterns, including sodium intake. However, this is unlikely to be practical in busy clinical settings.

Conclusion

Both spot urinary and dietary sodium-to-potassium ratios were positively associated with albuminuria in community-dwelling middle-aged and older Japanese adults. Our findings further support the potential usefulness of the spot urinary sodium-to-potassium ratio as an indicator of sodium intake and suggest a link between sodium intake and kidney damage.

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Statement of Ethics

The study protocol was reviewed and approved by the Ethics Committee of Niigata University (approval numbers 2012-1403, 2013-1640, and 2017-0054). Written informed consent was obtained from participants. The study adhered to the tenets of the Declaration of Helsinki.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Keiko Kabasawa, Ribeka Takachi, Kazutoshi Nakamura, Yumi Ito, Junta Tanaka, and Kunihiro Matsushita designed the study and created the concept of the study; Keiko Kabasawa, Yumi Ito, Junta Tanaka, and Ichie Narita conducted research; Keiko Kabasawa analyzed data; Keiko Kabasawa and Kunihiro Matsushita wrote the paper; Ribeka Takachi, Kazutoshi Nakamura, Norie Sawada, Shoichiro Tsugane, Yumi Ito, Junta Tanaka, Ichie Narita, and Kunihiro Matsushita provided a critical review, advice, and consultation throughout. All the authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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