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Title: Frequency of alcohol drinking modifies the association between salt intake and albuminuria: A 1-year observational study

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Abstract and key words

Abstract: Albuminuria is an important risk factor for end-stage kidney disease and cardiovascular mortality. This 1-year observational study aimed to assess the effect modification of alcohol drinking on the association between salt intake and albuminuria. Overall, 448 employees at a pharmaceutical company in Japan who underwent annual health checkups in both 2017 and 2018 were evaluated. The main exposure of interest was drinking frequency at their first checkups categorized as rarely, occasionally, and daily. To assess the association between the changes in salt intake and albuminuria, the differences in salt intake estimated from single-spot urine specimens and the urinary albumin-to-creatinine ratio (UACR) between 2017 and 2018 were calculated for each subject. A multivariable-adjusted linear regression model showed a significant association between Δsalt intake and ΔLog UACR (per 1 g/day of Δsalt intake, adjusted ß 0.16 [95% confidence interval 0.14, 0.19]) and an effect modification between drinking frequency and Δsalt intake (P for interaction = 0.088). The association between Δsalt intake and ΔLog UACR was enhanced by drinking frequency in a dose-dependent manner (per 1 g/day of Δsalt intake, adjusted ß 0.13 [0.06, 0.19], 0.16 [0.12, 0.20], and 0.20 [0.13, 0.27] in rare, occasional, and daily drinkers, respectively). In conclusion, the results of the present study indicated that salt-induced albuminuria was enhanced in

subjects with higher drinking frequency, suggesting that salt restriction may have a stronger renoprotective effect in subjects with higher drinking frequency.

Keywords: alcohol drinking, albuminuria, salt intake

Introduction

Albuminuria, one of the essential characteristics of chronic kidney disease (CKD),[1, 2] is a strong prognostic factor for cardiometabolic diseases, including hypertension,[3] diabetes,[4] and cardiovascular diseases (CVDs);[5, 6] end-stage kidney disease (ESKD);[7, 8] and mortality.[9, 10] Even urinary albumin levels within the upper limit of normal are associated with CKD[11] and cardiometabolic diseases.[12, 13] Because reduction in urinary albumin is associated with a lower risk of ESKD[14, 15] and cardiovascular mortality,[16] urinary albumin is a valid surrogate endpoint for CKD in addition to glomerular filtration rate (GFR).[17] Thus, albuminuria is one of the pivotal therapeutic targets for preventing the incidence of ESKD[18] and CVDs.[19]

Among dietary factors, including salt, protein,[20] fat,[21] and sugar,[22] salt plays a pivotal role in the incidence of albuminuria.[23, 24] Interestingly, previous cross-sectional studies suggested that the association between salt intake and albuminuria was enhanced in those with hypertension[25] and obesity,[26] suggesting that salt restriction may be more renoprotective in these subjects. Aside from hypertensive and obese subjects, drinkers may be potential candidates to benefit from salt restriction, as indicated by an enhanced association between salt intake and stroke mortality in drinkers.[27] Although alcohol drinking was identified as a risk factor for albuminuria in a large prospective cohort

study (i.e., the Australian Diabetes, Obesity, and Lifestyle (AusDiab) study),[28] few studies have assessed the effect modification of alcohol drinking on the association between salt intake and albuminuria.

The aim of the present 1-year observational study was to evaluate the clinical impact of drinking frequency on the association between salt intake and albuminuria in 448 employees of a pharmaceutical company in Japan. The present study provides deep insight into the mechanism of the deleterious effect of alcohol drinking on the kidney and stresses the clinical value of salt restriction in drinkers.

Methods

Study Design and Participants

This 1-year observational study included 507 employees at a pharmaceutical company who underwent annual health checkups in both 2017 and 2018 and gave informed consent to participate in the present study. We excluded 55 (10.8%) employees who had a positive answer to the question “Do you take antihypertensive medications now?”, regardless of blood pressure levels; 3 (0.6%) employees with self-reported kidney disease, who answered “I have been diagnosed with kidney disease”; and 1 (0.2%) female who was pregnant in either 2017 or 2018. The present study finally included 448 (88.4%) employees without current use of antihypertensive drugs or a history of kidney disease. Because of the prospective nature of the present study, the sample size was dependent on the number of employees of the company.

The study protocol was approved by the ethics committees of SHIONOGI & CO., LTD., Health and Counseling Center, Osaka University and Osaka University Hospital.

Measurements

Baseline demographic, physical, and laboratory data in 2017 included age; sex; drinking frequency; smoking status; current treatment for hypertension, dyslipidemia,

and diabetes; history of kidney disease; body mass index (= body weight [kg]/height [m]^2); systolic and diastolic blood pressure (SBP and DBP); hemoglobin A1c; serum concentration of total cholesterol, triglycerides, and creatinine; and urine concentration of albumin, sodium, and creatinine. Urinary levels of albumin, sodium, and creatinine were measured using single-spot urine specimens. Albuminuria was assessed using the urinary albumin-to-creatinine ratio (UACR), which was calculated as follows: UACR (mg/gCr) = (urinary albumin [mg/dL]/urinary creatinine [mg/dL]) × 1000. Tanaka's equation[29] was used to estimate the 24-hour sodium excretion: estimated 24-hour sodium excretion [mEq/day] = 21.98 × (urinary sodium [mEq/L]/[urinary creatinine [mg/dL] × 10] × 14.89 × body weight [kg] + 16.14 × height [cm] – 2.04 × age [year] − 2244.45)$^{0.392}$. Salt intake (g/day) was calculated by multiplying the 24-hour sodium excretion (mEq/day) by 0.0585. Estimated GFR (eGFR) was calculated using a three-variable equation modified for Japanese patients: eGFR (mL/min/1.73 m^2) = 194 × age (year)$^{-0.287}$ × serum creatinine (mg/dL)$^{-1.094}$ × 0.739 (if female).[30]

Drinking frequency, smoking status, and current treatment for dyslipidemia and diabetes were assessed using self-reported standard questionnaires. Drinking frequency was determined by the question "How often do you drink alcoholic beverages?" with responses of rarely, occasionally, or daily. Smoking status was classified into non-

smokers, past smokers, and current smokers, according to the question “Do you smoke?” with possible answers “I do not smoke,” “I quit smoking,” or “I smoke”. Current treatments for dyslipidemia and diabetes were assessed based on positive answers to the question, “Do you take a lipid-lowering drug now?” and “Do you take an antidiabetic drug now?”

The outcome measures of the present study were the differences in UACR between 2017 and 2018. We calculated ΔUACR and ΔLog UACR as follows:

ΔUACR [mg/gCr] = UACR in 2018 − UACR in 2017

ΔLog UACR [log mg/gCr] = Log UACR in 2018 − Log UACR in 2017

To evaluate the association between the changes in salt intake and albuminuria, we calculated the difference in salt intake between 2017 and 2018 as follows:

ΔSalt intake (g/day) = salt intake in 2018 − salt intake in 2017

In addition, the participants were divided into tertile groups according to Δsalt intake. Drinking frequency was also ascertained in 2018 to assess how the baseline drinking frequency reflected the drinking frequency during the follow-up period.

Statistical Analysis

The baseline characteristics, Δsalt intake, and ΔUACR of the participants were compared according to drinking frequency (rare, occasional, and daily) and tertiles of

Δsalt intake (first, second, and third) using ANOVA, the Kruskal-Wallis test, or the chi-square test, as appropriate. Reproducibility of the baseline drinking frequency 1 year after the baseline visit was evaluated using weighted Cohen's kappa statistics. Kappa statistics of <0.40, 0.41–0.60, 0.61–0.80, and 0.81–1.00 indicated fair, moderate, substantial, and almost perfect reproducibility, respectively.[31]

The association between Δsalt intake and ΔLog UACR was evaluated using simple linear regression models and multivariable linear regression models adjusted for the conventional risk factors for albuminuria at the baseline checkup, including age, sex, smoking status, drinking frequency, current treatment for dyslipidemia and diabetes, body mass index, systolic blood pressure, total cholesterol, triglycerides, hemoglobin A1c, eGFR, UACR, and salt intake. Effect modification between Δsalt intake and the baseline drinking frequency was evaluated by incorporating their interaction term into the multivariable-adjusted model. P for interaction <0.10 was regarded as statistically significant. To clarify the interaction between Δsalt intake and drinking frequency, the association of Δsalt intake (a continuous variable [per 1 g/day] or a categorical variable of first [T1], second [T2], and third [T3] tertiles) and ΔLog UACR was assessed in 3 subgroups stratified according to drinking frequency using multivariable-adjusted linear regression models.

Continuous variables are expressed as the mean ± standard deviation or median (interquartile range), as appropriate, and categorical variables as number (proportion). Statistical significance was set at $P < 0.05$, unless otherwise specified. All statistical analyses were performed using Stata, version 16.1 (Stata Corp, www.stata.com).

Results

The baseline characteristics of the 448 participants stratified by the 3 categories of drinking frequency are shown in Table 1. Rare drinkers had lower body mass index, whereas daily drinkers were likely to be older and have higher levels of blood pressure and UACR. Compared with rare drinkers, the prevalence of current smokers was higher among those who drank more frequently. With respect to the reproducibility of the drinking frequency in 2017 and 2018, the weighted kappa statistic was 0.88, suggesting that the baseline drinking frequency in 2017 reflected the drinking frequency in 2018. Regarding the 1-year changes in salt intake and albuminuria, Δsalt intake and ΔUACR were 0.1 ± 2.0 g/day and 1 (-9, 14) mg/gCr, respectively. Drinking frequency was not associated with either Δsalt intake or ΔUACR.

Differences in the baseline characteristics according to the tertiles of Δsalt intake are listed in Table 2. Those in the first tertile were more likely to have higher eGFR. Compared with those in the first tertile, those in the second and third tertiles had lower levels of baseline UACR and salt intake.

Unadjusted linear regression models showed a significant association between Δsalt intake and ΔLog UACR (Table 3). After adjusting for clinically relevant factors, Δsalt intake was still significantly associated with ΔLog UACR (per 1 g/day of Δsalt

intake, adjusted ß 0.16 [95% confidence interval 0.14, 0.19], P <0.001), indicating that a 1 g/day increase in salt intake resulted in an $e^{0.16} = 1.17$ times increase in UACR.

Because of a significant interaction between drinking frequency and Δsalt intake in an adjusted model including ΔLog UACR as a dependent variable (P for interaction = 0.088 in Table 3), we evaluated the association between Δsalt intake and ΔLog UACR according to the category of drinking frequency separately. The significant association between Δsalt intake and ΔLog UACR increased in drinkers with higher frequency (per 1 g/day of Δsalt intake, adjusted β 0.13 [0.06, 0.19], P <0.001 in rare drinkers; 0.16 [0.12, 0.20], P <0.001 in occasional drinkers; 0.20 [0.13, 0.27], P <0.001 in daily drinkers) (Table 3).

To clarify any dose-dependent association between Δsalt intake and ΔLog UACR, we calculated the multivariable-adjusted ß of tertiles (T1, T2, and T3) of Δsalt intake in each category of drinking frequency (Figure 1). With reference to the first tertile of Δsalt intake, the adjusted ß for the third tertile was 0.51 [0.21, 0.80] (P = 0.001) in rare drinkers, 0.60 [0.39, 0.80] (P <0.001) in occasional drinkers, and 0.88 [0.57, 1.19] (P <0.001) in daily drinkers, indicating that compared with the UACR of the individuals in the first tertile of Δsalt intake, the UACR of the individuals in the third tertile of Δsalt intake increased by factors of $e^{0.51} = 1.66$, $e^{0.60} = 1.81$, and $e^{0.88}$ =

2.40 in rare, occasional, and daily drinkers, respectively. These results suggested that compared with rare drinkers, the association between Δsalt intake and ΔLog UACR was enhanced by approximately 1.5 times in daily drinkers (multivariable-adjusted ß of Δsalt intake [per Δ1 g/day], 0.20/0.13 = 1.5 in Table 3; multivariable-adjusted ß of T3 vs. T1, 2.40/1.66 = 1.4 in Figure 1).

Discussion

Few studies have assessed the effect modification of alcohol drinking on the association between salt intake and albuminuria. The present study showed that drinking frequency enhanced the association between salt intake and albuminuria, suggesting that salt restriction may be more effective in reducing albuminuria in drinkers than non-drinkers. One of the advantages of the present study was its longitudinal study design, in contrast to the previous cross-sectional studies suggesting the enhanced association between salt intake and albuminuria in subjects with hypertension[25] and obesity.[26] The results of the present study provided clinically useful evidence to identify the subjects vulnerable to salt-induced albuminuria, which is one of the risk factors for cardiometabolic disease,[3, 4] ESKD,[7, 8] and cardiovascular mortality.[9, 10]

The AusDiab study, a prospective study with a 5-year follow-up, reported that alcohol drinking was a modifiable risk factor for albuminuria,[28] but evidence on the clinical impact of alcohol drinking on the association between salt intake and albuminuria remains limited. The effect modification of alcohol drinking on the association between salt intake and albuminuria in the present study may be explained by the deleterious effect of alcohol drinking on the kidney.[28, 32] One of the potential mechanisms by which alcohol drinking enhanced the association between salt intake

and albuminuria may be salt sensitivity. In our previous study that used the same cohort as the present study, drinking frequency modified the association of salt intake and blood pressure, suggesting that alcohol drinking enhanced salt sensitivity.[33] An Italian trial reported that urinary albumin levels significantly increased after salt loading in salt-sensitive subjects but not in salt-resistant subjects.[34] The results of these studies might suggest that subjects with alcohol-induced salt sensitivity were more vulnerable to albuminuria. A similar modification between alcohol drinking and salt intake was reported in a large Japanese cohort study that showed an enhanced association between salt intake and stroke mortality in heavy drinkers.[27] Alcohol drinking may be one of the key predictors of salt-induced noncommunicable diseases.

One of the major pathophysiologies of salt sensitivity is the impairment of NO-dependent vascular relaxation by decreasing NO in the vascular endothelium due to the suppression of endothelial nitric oxide synthase (eNOS).[35] Alcohol suppresses the expression of eNOS[36] and impairs endothelial function,[37] leading to salt sensitivity.[33] An interesting association between salt sensitivity and salt-induced albuminuria was reported in an Italian trial. The change in albuminuria after salt loading (low-sodium diet of 20 mEq/day to high-sodium diet of 250 mEq/day) was significantly larger in 12 subjects with salt sensitivity than in 10 subjects without salt sensitivity, suggesting that

salt sensitivity enhanced the association between salt intake and albuminuria.[34] Collectively, these results indicate that alcohol-enhanced salt sensitivity possibly augments salt-induced albuminuria. Further studies are essential to clarify the association between alcohol consumption and albuminuria.

The present study has several limitations. First, only a single spot urine specimen was measured in 2017 and 2018 in the present study; therefore, the estimation of salt intake in each subject was less accurate than those based on multiple measurements of 24-hour urine specimens. To evaluate Δsalt intake and ΔUACR more precisely, multiple measurements of 24-hour urine specimens are necessary. Second, the association between salt intake and albuminuria was not strictly measured in each subject using an interventional method of salt loading.[34] Because the present study assessed the association between changes in salt intake and albuminuria in a certain group of subjects, not in each subject, the results of the present study might be biased. The effect modification of drinking frequency on the association between salt intake and albuminuria should be assessed in detail using the interventional method of salt loading. Third, the generalizability of the results of the present study should be verified in different cohorts. In this study, the mean estimated salt intake at the baseline visit was 8.4 g/day, which was lower than that identified in previous studies.[38, 39] A Japanese

study of 2,073 healthy adults reported an average salt intake of 10.6 g/day estimated using spot urine specimens.[40] Fourth, self-reported drinking frequency might be biased. Several studies have shown that alcohol consumption was likely to be underreported.[41, 42] Given that daily drinkers who underreported their drinking frequency were misclassified as occasional or rare drinkers, the association between Δsalt intake and ΔUACR in occasional and rare drinkers was potentially enhanced, and therefore, the interaction between drinking frequency and Δsalt intake was attenuated, leading to no significant P value for the interaction. If we could control this underreporting bias, the association between Δsalt intake and ΔUACR in daily drinkers would be stronger than that in rare drinkers, leading to a smaller P value for the interaction between drinking frequency and Δsalt intake compared with the P value for the interaction observed in the present study. Fifth, lifestyle modification during the follow-up period might affect the effect of drinking frequency on salt-induced albuminuria, leading to biased results in the present study. If some daily drinkers switched to occasional or rare drinkers during the observational period, therefore attenuating the association between Δsalt intake and ΔUACR, the difference in the association between Δsalt intake and ΔUACR among rare, occasional, and daily drinkers at the baseline checkup would be reduced, resulting in a weaker interaction between drinking frequency and Δsalt intake. Similar to the

fourth limitation described above, if we could control for lifestyle modification during the follow-up period, the interaction between drinking frequency and Δsalt intake would be stronger. Sixth, regression to the mean phenomenon might affect the results of the present study. Because baseline salt intake and Δsalt intake were comparable among rare, occasional, and daily drinkers (Table 1), regression to the mean phenomenon had little influence on the difference in Δsalt intake among the 3 groups. Although there was a statistically significant difference in baseline UACR among the 3 groups, the difference in ΔUACR among the 3 groups was not significantly different, suggesting that regression to the mean phenomenon due to the difference in baseline UACR among the 3 groups did not affect ΔUACR. Accordingly, regression to the mean phenomenon in Δsalt intake and ΔUACR did not seem to result in a critical bias in the present study.

In conclusion, the findings of the present study showed that a higher frequency of alcohol drinking enhanced the effect of salt intake on albuminuria. These results indicate that drinkers would obtain a higher benefit from salt restriction in regard to reducing albuminuria. Well-designed randomized controlled trials are needed to validate our findings.

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Conflict of Interest: TM and YI are employed as occupational physicians by Shionogi & Co., Ltd.; YM is an employee of Shionogi & Co., Ltd. and acts as a managing director of Shionogi Health Insurance Association; and the other authors declare no conflict of interest.

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Table 1. Clinical characteristics of 448 participants stratified by drinking frequency

Clinical characteristics	Drinking frequency at baseline visit			P
	Rare	Occasional	Daily	
Number	91	235	122	
Baseline characteristics				
Age (year)*	44 (38, 51)	43 (39, 49)	50 (41, 54)	<0.001
Male (n [%])	57 (62.6)	166 (70.6)	92 (75.4)	0.129
Smoking status (n [%])*				
Non-smoker	81 (89.0)	183 (77.9)	68 (55.7)	<0.001
Past smoker	7 (7.7)	33 (14.0)	38 (31.1)	
Current smoker	3 (3.3)	19 (8.1)	16 (13.1)	
Current treatment for				
Dyslipidemia (n [%])	2 (2.2)	6 (2.6)	3 (2.5)	0.983
Diabetes mellitus (n [%])	0 (0.0)	2 (0.9)	0 (0.0)	0.402
Body mass index (kg/m^2)*	21.5 ± 2.5	22.4 ± 2.9	22.2 ± 2.7	0.033
Systolic blood pressure (mmHg)*	116 ± 11	117 ± 11	121 ± 12	0.008
Diastolic blood pressure (mmHg)*	73 ± 9	74 ± 9	78 ± 10	<0.001
Total cholesterol (mg/dL)	202 ± 30	203 ± 31	204 ± 35	0.893
Triglyceride (mg/dL)	69 (48, 94)	69 (53, 100)	70 (50, 104)	0.484
Hemoglobin A1c (%)	5.3 ± 0.2	5.3 ± 0.3	5.3 ± 0.3	0.124
eGFR (mL/min/1.73 m^2)	79 ± 12	79 ± 11	77 ± 11	0.365
UACR (mg/gCr)*	29 (19, 49)	25 (18, 49)	36 (24, 64)	0.001
Salt intake (g/day)	8.1 ± 1.7	8.3 ± 1.9	8.6 ± 1.7	0.106
Drinking frequency 1 year after the baseline visit†				
Rare (n [%])	83 (91.2)	6 (2.6)	1 (0.8)	
Occasional	8 (8.8)	220 (93.6)	14 (11.5)	
Daily	0 (0.0)	9 (3.8)	107 (87.7)	
Changes in salt intake and albuminuria over a 1-year period				
ΔSalt intake (g/day)	0.1 ± 1.8	0.0 ± 2.1	-0.4 ± 2.0	0.206
ΔUACR (mg/gCr)	-1 (-12, 14)	2 (-6, 14)	-1 (-16, 12)	0.104

Data are presented as mean ± standard deviation, median (25%, 75%), or n (%)

*P <0.05

†The weighted kappa statistics was 0.88 for reproducibility of drinking frequency at the baseline visit and 1 year after the baseline visit.

Abbreviations: eGFR, estimated glomerular filtration rate; UACR, urinary albumin-to-creatinine ratio

Table 2. Clinical characteristics of 448 participants stratified by tertiles of changes in salt intake (Δsalt intake)

Clinical characteristics	ΔSalt intake (g/day)			P
	First tertile	Second tertile	Third tertile	
	-1.9 (-2.8, -1.4)	-0.1 (-0.5, +0.3)	+1.9 (+1.4, +2.8)	
Number	150	149	149	
Baseline characteristics				
Age (year)	46 (39, 52)	46 (40, 52)	44 (38, 50)	0.067
Male (n [%])	112 (74.7)	103 (69.1)	100 (67.1)	0.334
Drinking frequency (n [%])				
Rare	27 (18.0)	29 (19.5)	35 (23.5)	0.324
Occasional	74 (49.3)	80 (53.7)	81 (54.4)	
Daily	49 (32.7)	40 (26.8)	33 (22.1)	
Smoking status (n [%])				
Non-smoker	106 (70.7)	109 (73.2)	117 (78.5)	0.555
Past smoker	31 (20.7)	27 (18.1)	20 (13.4)	
Current smoker	13 (8.7)	13 (8.7)	12 (8.1)	
Current treatment for				
Dyslipidemia (n [%])	2 (1.3)	6 (4.0)	3 (2.0)	0.294
Diabetes mellitus (n [%])	1 (0.7)	0 (0.0)	1 (0.7)	0.606
Body mass index (kg/m^2)	22.2 ± 2.7	21.9 ± 2.8	22.3 ± 2.8	0.445
Systolic blood pressure (mmHg)	119 ± 12	117 ± 11	118 ± 11	0.192
Diastolic blood pressure (mmHg)	76 ± 10	74 ± 9	74 ± 9	0.286
Total cholesterol (mg/dL)	201 ± 32	205 ± 33	203 ± 29	0.472
Triglyceride (mg/dL)	74 (54, 101)	65 (49, 93)	70 (52, 102)	0.105
Hemoglobin A1c (%)	5.3 ± 0.3	5.3 ± 0.3	5.3 ± 0.3	0.643
eGFR (mL/min/1.73 m^2)*	81 ± 11	77 ± 12	77 ± 11	0.002
UACR (mg/gCr)*	39 (22, 73)	29 (21, 49)	22 (15, 39)	0.001
Salt intake (g/day)*	9.5 ± 1.6	8.2 ± 1.5	7.4 ± 1.5	<0.001

Data are presented as mean ± standard deviation, median (25%, 75%), or n (%)

*P <0.05

Abbreviations: eGFR, estimated glomerular filtration rate; UACR, urinary albumin-to-creatinine ratio

Table 3. Changes in salt intake (Δsalt intake [per 1 g/day]) and changes in urinary albumin-to-creatinine ratio (ΔLog UACR [log mg/gCr])

	N	Unadjusted model		Adjusted model*		P for interaction†
		ß (95% CI)	P	ß (95% CI)	P	
Overall	448	0.18 (0.15, 0.20)	<0.001	0.16 (0.14, 0.19)	<0.001	0.088
Drinking frequency						
Rare	91	0.13 (0.07, 0.20)	<0.001	0.13 (0.06, 0.19)	<0.001	
Occasional	235	0.18 (0.14, 0.21)	<0.001	0.16 (0.12, 0.20)	<0.001	
Daily	122	0.20 (0.14, 0.26)	<0.001	0.20 (0.13, 0.27)	<0.001	

*Adjusted for age (year), sex, smoking status (non-, past, vs current smoking), drinking frequency (rare, occasional, vs daily), current treatment for dyslipidemia and diabetes, body mass index (kg/m^2), systolic blood pressure (mmHg), total cholesterol (mg/dL), triglyceride (log mg/dL), hemoglobin A1c (%), estimated glomerular filtration rate (mL/min/1.73 m^2), UACR (log mg/gCr) and salt intake (g/day) at the baseline visit

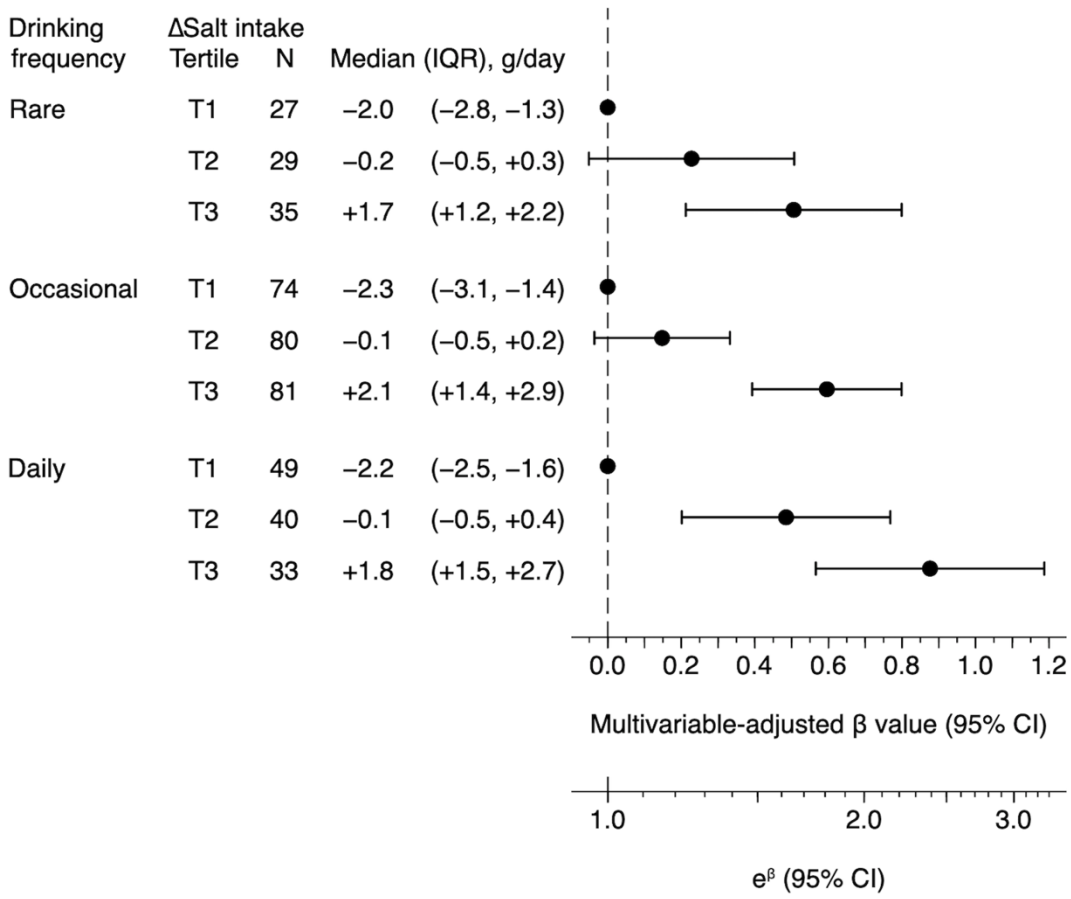
†P for interaction between Δsalt intake and drinking frequency in the adjusted model

Abbreviations: CI, confidence interval; UACR, urinary albumin-to-creatinine ratio

Figure legends

Figure 1. Drinking frequency modifies the association between changes in salt intake (Δsalt intake) and the urinary albumin-to-creatinine ratio (ΔLog UACR). Adjusted ß values were calculated using a linear regression model adjusted for age (year), sex, smoking status (non-smoking, past smoking, vs current smoking), current treatment for dyslipidemia and diabetes, body mass index (kg/m^2), systolic blood pressure (mmHg), total cholesterol (mg/dL), triglycerides (log mg/dL), hemoglobin A1c (%), estimated glomerular filtration rate (mL/min/1.73 m^2), UACR (log mg/gCr) and salt intake (g/day) at the baseline visit. Abbreviations: CI, confidence interval; IQR, interquartile range

Figure 1


Drinking frequency
ΔSalt intake Tertile
N
Median (IQR), g/day
Rare
T1 27 −2.0 (−2.8, −1.3)
T2 29 −0.2 (−0.5, +0.3)
T3 35 +1.7 (+1.2, +2.2)
Occasional
T1 74 −2.3 (−3.1, −1.4)
T2 80 −0.1 (−0.5, +0.2)
T3 81 +2.1 (+1.4, +2.9)
Daily
T1 49 −2.2 (−2.5, −1.6)
T2 40 −0.1 (−0.5, +0.4)
T3 33 +1.8 (+1.5, +2.7)
0.0 0.2 0.4 0.6 0.8 1.0 1.2
Multivariable-adjusted β value (95% CI)
1.0 2.0 3.0
eβ (95% CI)