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Seasonal Variation in the Daily Urinary Sodium Excretion in Outpatients from the Morioka Region of Northern Japan

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Abstract

Objective Although the daily urinary sodium excretion (UNaV) is considered to provide the most reliable estimate of the daily sodium intake, it may be affected by salt loss due to sweating in summer. However, the seasonal variation in the daily UNaV associated with a normal lifestyle is unknown.

Methods This study was performed in 348 outpatients from the Morioka region during three seasons: summer (summer 1), winter, and the following summer (summer 2). The daily UNaV (g salt/day) was estimated by the second morning urine method three times during each season. Seasonal variation was defined as a significant trend across the three seasons together with a significant difference between winter and both summers.

Results In women, the daily UNaV was higher in winter (11.8±3.0 g salt/day) than in summer 1 (11.2±2.9 g salt/day) or summer 2 (11.0±2.9 g salt/day). In contrast, there was no marked seasonal variation in men. An analysis stratified by age (4 quartiles) identified seasonal variation in the older 2 quartiles of women (aged ≥ 68 years). In these women, the mean seasonal difference in the daily UNaV was 0.9 g of salt/day for both winter vs. summer 1 and winter vs. summer 2, while it was 0.1-0.8 g of salt/day in the other groups.

Conclusion Seasonal variation in the daily UNaV only occurred in older female patients and was relatively small. This is evidence for restricting salt intake throughout the year and should reassure patients who are anxious about salt loss due to sweating in summer.

Key words: salt intake, seasonal variation, second morning urine, sex difference, sweat, urinary sodium excretion

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Introduction

While sodium is an essential substance for life maintenance (1), excess sodium intake increases the blood pressure and causes cardiovascular diseases, such as stroke, ischemic heart disease, heart failure, and renal failure in both a blood pressure-dependent manner and independently of its influence on blood pressure (2, 3). The measurement of the daily urinary sodium excretion (UNaV) is considered to be the most reliable method for estimating the daily sodium intake (4, 5), since approximately 90% of dietary sodium intake is excreted in the urine through unremarkable sweating (6, 7).

However, in hot environments, especially with exercise, the daily UNaV is not suitable as an estimate of the daily sodium intake since sodium loss in sweat is remarkable. For example, it was reported that 4.8 g of salt is lost in 1 hour

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of playing soccer (8) and 6.9 g in 3 hours of playing badminton during summer (9). In addition, there is a lack of population-level information on sodium loss in sweat during normal daily life during summer, although patients in clinical practice often ask whether their dietary salt intake should be increased in summer because of salt loss due to sweating.

The kidneys play a crucial role in maintaining the sodium balance in the body via the regulation of the UNaV (10). The daily UNaV is considered to represent the excretion of excess sodium that remains after sodium lost by sweating is subtracted from the dietary sodium intake, while sodium loss from the feces has been reported to be very low (0.03 to 0.3 g salt /day) (11) and can be ignored clinically. Seasonal variations in the daily UNaV may provide useful information for advising patients about dietary salt intake in summer. We only found 1 prospective study (performed in 34 men and published 34 years ago) evaluating the daily UNaV in both summer and winter based on 24 hours urine collection, and it showed that the daily UNaV was significantly higher in winter than in summer (12).

Therefore, we performed the present study to investigate the daily UNaV during summer and winter in a large population of both male and female subjects. We also investigated the UNaV during the following summer to assess the seasonal reproducibility of the daily UNaV data in order to distinguish seasonal changes from changes occurring randomly over time. We used the second morning urine (SMU) method of Kawasaki et al. (13, 14) to measure the daily UNaV instead of 24 hours urine collection, as this method is convenient, and its reliability has been confirmed by our laboratory (15-18) and other laboratories (19-21).

Materials and Methods

Subjects

Outpatients with 1 or more of 3 cardiovascular risk factors (hypertension, diabetes, and dyslipidemia) were recruited at 3 hospitals and 22 clinics in the Morioka region during April and May 2013. Patients were eligible if they had attended the study center for more than 3 months and were aged from 20 to 79 years, but shift workers were excluded.

Approval for this study was granted by the ethics committee of Iwate Prefectural Central Hospital on behalf of all the study centers because only this hospital had an ethics committee. All subjects were given detailed information about the study protocol before enrollment, and their written consent was obtained. This study was performed in accordance with the Declaration of Helsinki.

Study outline

The study was started in June 2013 and completed in September 2014, with the period from June to September 2013 being designated as "summer 1", the period from December 2013 to March 2014 as "winter", and the period from June to September 2014 as "summer 2". The subjects were asked to visit their medical center three times during each period. After voiding urine on waking in the morning, they were asked to either walk, stand, or sit (but not lie down) until collection of the second voided urine specimen at the study center from 8:00-9:30, followed by the measurement of blood pressure and body weight. Breakfast and the morning doses of oral drugs were postponed until urine collection. A blood sample was obtained at the time of one urine collection while fasting in July or August 2013 (summer 1). Height was measured once at the start of the study. The daily UNaV data obtained on three occasions in each season were averaged for the analysis. Lifestyle modifications, including exercise and diet details, were maintained during the study period if the patients had undertaken the modification before the study entry. Subjects who completed the protocol in summer 1 were registered with the data center at Ogino Hospital as study participants. Fig. 1 shows the flow chart of the patient follow-up with extrusion criteria. Of the 260 men and 224 women initially registered by 3 hospitals and 16 clinics in the Morioka region, 178 men (68%) and 170 women (76%) completed the study protocol at 3 hospitals and 12 clinics.

Estimation of the daily UNaV

The daily UNaV was estimated by the SMU method (13). First, the sodium and creatinine concentrations in the urine specimen were measured by an ion-selective method and enzymatic colorimetry, respectively. The daily UNaV was then calculated as the sodium/creatinine ratio of the SMU specimen multiplied by the predicted 24-hour creatinine excretion, which was based on demographic factors (sex, age, height, and body weight). The correlation between the daily UNaV determined by 24 hours urine collection and the daily UNaV determined by the SMU method is relatively strong (0.74 [13] and 0.71 [19]). Subjects were instructed to sit, stand, or walk (but not lie down) until urine collection because we previously found that posture influences the estimation of UNaV (16). In this study, the daily UNaV was expressed as grams of salt (NaCl), with 1 g of salt being equivalent to 17.1 mmol or 393.4 mg of sodium.

Measurement of blood pressure

Blood pressure was measured in accordance with the guideline of the Japanese Society of Hypertension (22). Using an automated digital sphygmomanometer with a suitable cuff size for the arm girth of the patients, measurement was performed at least twice at 1- to 2-minute intervals with the subject in the seated position. The mean value of 2 measurements in which the systolic blood pressures differed by less than 5 mmHg was adopted as the clinic blood pressure.

Other measurements

Hemoglobin A1c was measured by ion-exchange high-performance liquid chromatography. Total cholesterol and triglycerides were determined by enzymatic colorimetry, and

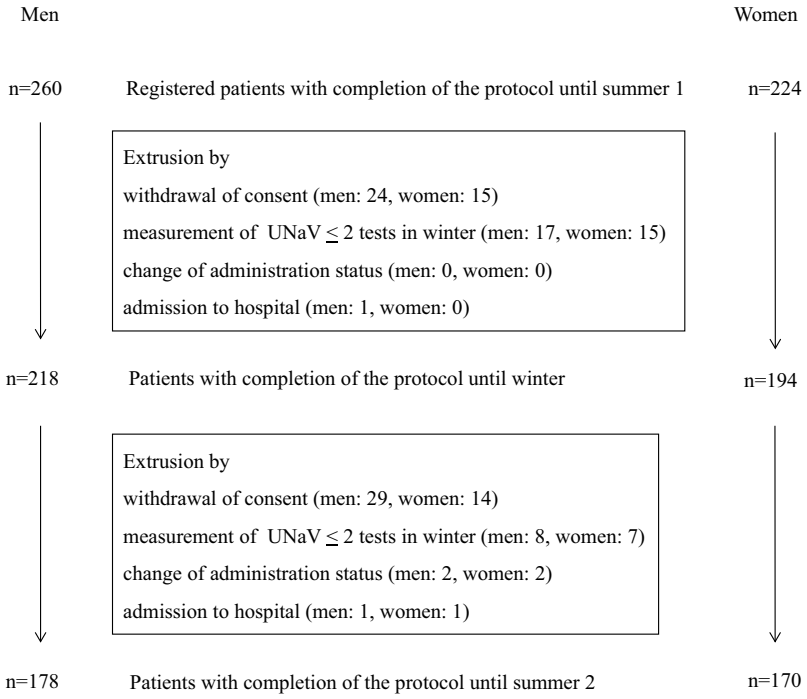

Figure 1. **Flow chart of the patient follow-up with the exclusion criteria.**

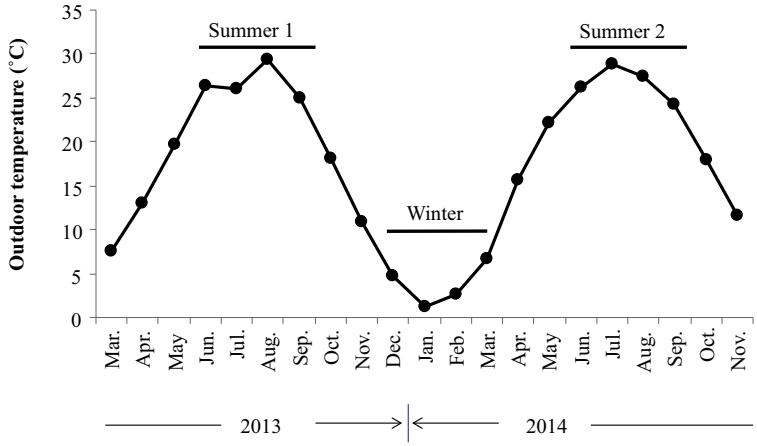

Figure 2. **Monthly averaged daily maximum outdoor temperature in Morioka. The lines indicate the periods of summer 1 (June to September 2014), winter (December 2013 to March 2014), and summer 2 (June to September 2014).**

high-density lipoprotein cholesterol was assessed by the homogeneous direct method. Low-density lipoprotein cholesterol was calculated using Friedwald's formula (23) when triglycerides were <10.36 mmol/L and by the homogeneous direct method when triglycerides were ≥10.36 mmol/L. Serum creatinine was measured by enzymatic colorimetry, and the estimated glomerular filtration rate was calculated by the formula in the Japanese Society of Nephrology Chronic Kidney Disease (CKD) Practice Guide (24).

Determination of the outdoor temperature

Data on the average daily maximum outdoor temperature in Morioka were obtained from the local meteorological observatory, and the monthly averaged daily maximum outdoor temperature in Morioka is shown in Fig. 2. The average temperatures were 26.7℃ during summer 1, 3.9℃ during the winter, and 26.7℃ during summer 2.

Statistical analyses and definition of seasonal variation

The results are expressed as the mean ± standard deviation (SD) for normally distributed variables and as the median (interquartile range [IQR]) for variables with skewed distribution. Differences in various parameters between men and women were analyzed by the Mann-Whitney U test or Pearson's chi-squared test, as appropriate. Differences in the daily UNaV among the three seasons (summer 1, winter, and summer 2) were analyzed by Friedman's test. When the probability (P) for trend was <0.05, comparison between the two seasons was performed using the Wilcoxon signed-rank

Table 1. Characteristics of the Subjects in Summer 1.

Variable	Men (n=178)	Women (n=170)
Age, years	67 (62-73)	67 (62-72)
Body weight, kg	67.0 (61.1-73.6)	56.4 (50.8-64.2)*
BMI, kg/m^2	24.8±3.4	24.8±3.9
Daily UNaV, g salt/day	12.5±3.4	11.2±2.9*
Systolic blood pressure, mmHg	132±10	132±14
Diastolic blood pressure, mmHg	76±8	76±8
Hemoglobin A_{1c}, %	6.1 (5.7-6.7)	6.0 (5.7-6.6)
Low density lipoprotein cholesterol, mmol/L	2.59±0.70	2.74±0.62
High density lipoprotein cholesterol, mmol/L	1.33 (1.14-1.54)	1.61 (1.35-1.90)*
Triglycerides, mmol/L	3.04 (2.05-4.81)	2.70 (2.03-3.46)*
Estimated glomerular filtration rate, mL/min/1.73 m^2	69±16	72±14
Antidiabetic drugs, number (%)	66 (37)	47 (28)
Lipid-lowering drugs, number (%)	87 (49)	109 (64)
Antihypertensive drugs number (%)	165 (93)	155 (88)
ARB or ACEI, number	145	120
Calcium channel blockers, number	106	113
Diuretics, number	49	34
Alpha/beta blockers or beta blockers, number	33	19

Data obtained in summer 1 are expressed as the mean ± SD, median (IQR), number (percentage), or number.
ARB: angiotensin II receptor blockers, ACEI: angiotensin I-converting enzyme inhibitors
BMI: body mass index, UNaV: urinary sodium excretion
*p<0.05 compared with men by the Mann-Whitney U test.

test. If a parameter showed a significant difference between winter and both summers (1 and 2), this was defined as seasonal variation. Men and women were classified into four quartiles based age, and seasonal variation in the daily UNaV was also analyzed in these quartiles. In all analyses, p<0.05 was considered to indicate statistical significance.

Results

The characteristics of the subjects in summer 1 are presented by gender in Table 1. The body weight, daily UNaV, and triglyceride levels were significantly higher in men than in women, whereas the high-density lipoprotein cholesterol levels were significantly higher in women. There were no significant differences in the types of antihypertensive medications between men and women. Diuretics were used by 49 men and 34 women. Forty-two men were taking thiazide diuretics or thiazide-like diuretics [hydrochlorothiazide (daily dose: 6.25-12.5 mg), indapamide (0.5-1 mg), trichlormethiazide (0.5-2 mg), and tripamide (15 mg), 5 men were using aldosterone antagonists [eplerenone (25-50 mg) and spironolactone (25 mg)], and 4 men were receiving loop diuretics [furosemide (20 mg), torasemide (4 mg) and azosemide (30 mg)], while 29 women were taking thiazide diuretics or thiazide-like diuretics [hydrochlorothiazide (daily dose: 6.25-12.5 mg), indapamide (0.5-1 mg), trichlormethiazide (0.5-1 mg), and tripamide (15 mg)], 2 women were using aldosterone antagonists [eplerenone (50 mg) and spironolactone (25 mg)], and 3 women were receiving loop diuretics [furosemide (20 mg) and azosemide (30 mg)].

Table 2 shows the relationship between the number of times the daily UNaV was estimated per season and its seasonal variation. In men, the daily UNaV did not show a significant trend across the three seasons, and there was no seasonal variation in the daily UNaV, irrespective of the number of times it was estimated per season. Conversely, seasonal variation in the daily UNaV was observed in women, irrespective of the number of times it was estimated per season, and the daily UNaV showed a significant trend across the three seasons, being significantly larger in winter than in either summer 1 or summer 2. The p value for trend decreased as the number of daily UNaV measurements increased. Therefore, further analyses were performed using the average value of three daily UNaV tests per season.

Table 3 shows the influence of the administrations of antidiabetic drugs, lipid-lowering drugs, and antihypertensive drugs on evaluating the seasonal variation in the daily UNaV. In men, there was no seasonal variation in the daily UNaV, irrespective of the administration of these drugs. In contrast, seasonal variation in the daily UNaV was noted in females, irrespective of the administration of these drugs, since the daily UNaV showed a significant trend across the three seasons after being divided into administration and non-administration groups and was significantly higher in winter than in either summer.

We stratified the men and women into four quartiles each based on age (Table 4). No seasonal variation in the daily UNaV was found in any of the male quartiles. However, seasonal variations in the daily UNaV were noted in female quartiles 3 (age 68-72 years) and 4 (age 73-79 years), since the daily UNaV showed a significant trend across the three seasons in these quartiles and was significantly higher in

Table 2. Influence of the Number of Estimates of Daily UNaV Per Season on Evaluation of Seasonal Variation.

No. of estimates of daily UNaV per season	Daily UNaV, g salt/day			p value for trend
	Summer 1	Winter	Summer 2	
Men (n=178)				
First test only	12.7±4.1	12.7±3.9	12.4±3.4	0.66
Average of first and second tests	12.5±3.6	12.7±3.5	12.3±3.3	0.60
Average of first, second, and third tests	12.5±3.4	12.7±3.4	12.4±3.2	0.63
Women (n=170)				
First test only	11.4±3.6*	12.0±3.6	11.5±3.6*	0.03
Average of first and second tests	11.2±3.1*	11.9±3.2	11.1±2.9*	0.01
Average of first, second, and third tests	11.2±2.9*	11.8±3.0	11.0±2.9*	0.00

UNaV: urinary sodium excretion

When the p value for trend across the 3 seasons was <0.05 by Friedman's test, comparison of two seasons was done by Wilcoxon's signed-rank test.

*p<0.05 vs. winter by Wilcoxon's signed-rank test.

Table 3. Influences of the Administrations of Antidiabetic Drugs, Lipid-lowering Drugs and Antihypertensive Drugs on Evaluating the Seasonal Variation of Daily UNaV.

Sex	Administration status	Daily UNaV, g salt/day			p value for trend
		Summer 1	Winter	Summer 2	
Men	Antidiabetic drugs				
	Yes (n=66)	12.9±3.3	13.2±3.5	12.5±3.2	0.22
	No (n=112)	12.3±3.5	12.4±3.3	12.3±3.3	0.87
	Lipid-lowering drugs				
	Yes (n=87)	12.3±3.5	12.2±2.9	11.8±3.0	0.61
	No (n=91)	12.8±3.3	13.2±3.8	12.9±3.4	0.56
	Antihypertensive drugs				
	Yes (n=165)	12.6±3.5	12.7±3.5	12.3±3.3	0.71
	No (n=13)	11.8±2.1	12.2±2.4	12.8±2.5	0.23
Women	Antidiabetic drugs				
	Yes (n=47)	12.1±2.5*	13.1±2.7	11.7±2.4*	0.00
	No (n=123)	10.8±3.0*	11.3±3.0	10.7±3.1*	0.01
	Lipid-lowering drugs				
	Yes (n=109)	11.2±3.0*	11.6±3.1	10.9±3.1*	0.00
	No (n=61)	11.2±2.9*	12.2±2.7	11.2±2.5*	0.02
	Antihypertensive drugs				
	Yes (n=155)	11.3±2.9*	11.9±3.0	11.0±2.9*	0.00
	No (n=15)	10.1±2.8*	11.3±3.4	10.4±3.3*	0.02

UNaV: urinary sodium excretion

UNaV in each season was obtained from average of first, second, and third tests.

When the p value for trend across the 3 seasons was <0.05 by Friedman's test, comparison of two seasons was done by Wilcoxon's signed-rank test.

*p<0.05 vs. winter by Wilcoxon's signed-rank test.

winter than in either summer. Seasonal variation in the daily UNaV was also noted in female quartiles 1 (p=0.08) and 2 (p=0.10), but it was not significant.

Table 5 compares the seasonal difference in the daily UNaV (winter vs. summer 1 and winter vs. summer 2) in men and women before and after stratification of each sex into a younger group (≤67 years) and an older group (≥68 years). Compared with men, women showed a significantly greater seasonal difference in the daily UNaV between winter and both summers. There was also a significantly greater seasonal difference in the daily UNaV between winter and both summers in the older female group than in the older male group, but there was no such sex difference between the younger male and female groups. In the older female group, the mean seasonal difference in the daily UNaV was 0.9 g of salt/day for both winter vs. summer 1 and winter vs. summer 2. In other groups, the mean seasonal difference in the daily UNaV ranged from 0.1 to 0.8 g of salt/day for

Table 4. Seasonal Variation of Daily UNaV in Men and Women Classified Into 4 Age Quartiles.

Sex	Quartile	Range (Age, years)	Daily UNaV, g salt/day			p value for trend
			Summer 1	Winter	Summer 2	
Men						
	Quartile 1 (n=45)	38-61	13.4±3.9	13.4±3.6	12.8±3.7	0.32
	Quartile 2 (n=43)	62-66	13.1±3.6	12.9±3.2	12.8±3.5	0.91
	Quartile 3 (n=44)	67-72	12.3±3.3	12.9±4.1	12.3±3.3	0.38
	Quartile 4 (n=46)	73-79	11.4±2.6	11.5±2.4	11.7±2.2	0.35
Women						
	Quartile 1 (n=41)	33-61	10.6±3.0	11.4±2.7	10.7±3.1	0.08
	Quartile 2 (n=48)	62-67	11.4±3.4	11.4±3.3	10.6±2.6	0.10
	Quartile 3 (n=42)	68-72	11.3±2.6*	12.3±2.8	11.1±2.7*	0.00
	Quartile 4 (n=39)	73-79	11.4±2.7*	12.2±3.2	11.6±3.3*	0.01

UNaV: urinary sodium excretion

Age was divided into 4 quartiles based on the age as of July 1st, 2013.

UNaV in each season was obtained from average of first, second, and third tests.

When the p value for trend was <0.05 across the 3 seasons by Friedman's test, comparison of two seasons was done by Wilcoxon's signed-rank test.

*p<0.05 vs. winter by Wilcoxon's signed-rank test.

Table 5. Comparisons of the Seasonal Differeces in Daily UNaV in Men and Women Before and After Stratification of Each Sex Into a Younger Group and an Older Group.

Patients	Seasonal difference in daily UNaV, g salt/day	
	men	women
Winter vs. summer 1		
Younger group (< 67 years)	0.1±3.5	0.4±2.8
Older group (> 68 years)	0.2±2.1	0.9±2.5*
Total	0.1±3.0	0.6±2.7*
Winter vs. summer 2		
Younger group (< 67 years)	0.5±3.0	0.8±2.8
Older group (> 68 years)	0.1±2.7	0.9±2.8*
Total	0.3±2.8	0.9±2.8*

UNaV: urinary sodium excretion

The male numbers of younger and older groups were 99 and 79, respectively.

See Table 4 in female numbers.

Seasonal difference in daily UNaV was calculated from subtraction of summer 1 or summer 2 from winter.

*p<0.05 vs. men by the Mann-Whitney U test.

winter vs. summer 1 or winter vs. summer 2.

Discussion

In this study, we detected seasonal variations in the daily UNaV in women, with UNaV being higher during winter than summer, but there was no such seasonal variation in men. We also found significantly greater seasonal differences in the daily UNaV (winter vs. summer 1 and winter vs. summer 2) in women than in men. To our knowledge, this is the first report of a gender-related difference in the seasonal variation in the daily UNaV.

When evaluating the seasonal variation in the daily UNaV in this study, we paid attention to the number of estimates of the daily UNaV made per season and estimated the daily UNaV for two summer seasons. The first important point of our study concerns the number of estimates of the daily UNaV made per season. There is substantial day-to-day variation in the dietary salt intake (25, 26), which means that the daily salt intake should be estimated multiple times, so we assessed the daily UNaV three times per season because the majority of subjects attended the clinic once a month. Uechi et al. (27) recently reported that the daily UNaV was estimated more accurately with three spot urine samples than with only one or two samples, using the UNaV from two 24-hour urine collections as a reference. Although we detected a seasonal variation in the daily UNaV in women with even one test per season, multiple estimates of the daily UNaV per season were needed to overcome confounding factors for seasonal variation, as the

trend in the p values across the three monitored seasons suggested that statistical reliability was improved by increasing the number of tests. Of note, however: there was no marked seasonal variation in the daily UNaV in men, even when three tests were performed per season, and the lack of a p value trend across the three monitored seasons suggested that seasonal variation would not have been detected by further increasing the number of tests.

The second important point of our study was that we estimated the daily UNaV in summer, winter, and the following summer to distinguish seasonal variation from changes occurring randomly over time. For example, a doctor might advise a patient to reduce their salt intake, leading to a decrease in the daily UNaV over time, and this change might be mistaken for seasonal variation in the daily UNaV (higher in summer than winter) if data from the following summer data were lacking. Therefore, we defined seasonal variation as both a significant trend across the three seasons and the presence of a significant difference between winter and both summers. Using this conservative definition, we identified seasonal variations in the daily UNaV (higher in winter than summer) in women but not in men.

It is generally accepted that chronic administration of drugs may not affect overall the daily UNaV, but may affect the circadian pattern of sodium excretion (28). The administrations of antidiabetic drugs, lipid-lowering drugs, and antihypertensive drugs may influence the estimation of the daily UNaV by the SMU method by altering the sodium/creatinine ratio resulting from the change in the circadian pattern of sodium excretion. However, it is unlikely that the administrations of these drugs influenced the seasonal variations in the daily UNaV because the statistical significance of the seasonal variations in the daily UNaV was unchanged, irrespective of the administration of the respective drugs in both sexes (Table 3). We previously reported no marked differences in the estimation of the daily UNaV between the 24 hours urinary collection method and the SMU method in patients taking various antihypertensive drugs (16, 18) containing calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers and thiazide diuretics, which have a natriuretic effect (29-31) that can influence the estimation of the daily UNaV. We have no data on whether or not the chronic administration of loop diuretics, which have the strongest natriuretic effect, interferes with the accuracy of the SMU method. However, only four men and two women used loop diuretics in our study population, suggesting that the results were unlikely to have been affected by these medications. Although sodium-glucose co-transporter 2 inhibitors, which are anti-diabetic drugs, are known to have a natriuretic effect (32), these drugs were not used in the present study. These results also support the notion that the administrations of these drugs did not modify the seasonal variation the daily UNaV.

We identified seasonal variations in the daily UNaV in female quartiles 3 and 4 (older women aged ≥68 years), and these older women showed a significantly greater seasonal difference in the daily UNaV (higher in winter vs. summer 1 and summer 2) than older men, suggesting that the older female group made the main contribution to the gender difference in the seasonal variation in the daily UNaV. However, even among older women, the mean seasonal difference in the daily UNaV was 0.9 g of salt/day, which was small compared with the actual daily UNaV (11-12 g of salt/day). This suggests that people increase their sodium intake in the summer to compensate for salt loss due to sweating. Indeed, a dietary survey performed across 4 seasons in 459 Japanese subjects (including 208 men) identified significant seasonal variations in the daily salt intake, with intake being higher in summer than in winter among both men and women (33). Alternatively, this suggests that sodium intake is similar in summer and winter if salt loss from sweating is assumed to be minimal. In either case, our findings support the restriction of salt intake throughout the year, even if patients are anxious about salt loss due to sweating in summer. These findings are also compatible with the guidelines for the prevention of heat-related disorders in daily life released by the Japanese Society of Biometeorology, which recommends drinking water in normal daily life and only supplementing water with approximately 0.2% salt if exercise or manual labor is likely to cause salt loss through excessive sweating (34).

Several limitations associated with the present study warrant mention. First, our study included outpatients in a regional area (Morioka) of Japan and the results cannot be generalized to populations of other countries and geographic areas different in climate or lifestyles. Many participants (n= 129) dropped out by withdrawing their consent or due to having received less than 3 measurements of UNaV in a season, suggesting that the present analyses were performed in select patients with good compliance. Although our study population was apparently healthy, we cannot exclude the possibility of some patients having chronic disease such as malnutrition, hepatic disease, or cancer, as these diseases were not included as exclusion criteria at entry. We must therefore emphasize the conditions under which the present data were obtained. Second, smoking and alcohol drinking may influence the seasonal variation in the daily UNaV. Although we did not collect information about these habits in the present study, a nutrition survey in Iwate Prefecture (in which Morioka is located) indicated that 34% of men and 6% of women were current smokers, and 52% of men and 14% of women were drinkers who consumed alcohol daily (35). It is likely that the sex differences in these habits may influence the gender differences in the seasonal variation in the daily UNaV. We also did not assess the lifestyle of our subjects, including factors such as the indoor environment (air conditioning) and degree of daily physical activity, so these factors will also need to be evaluated by future studies. Third, we used the SMU method to estimate the daily UNaV instead of 24-hour urine collection. Kawasaki et al. (13, 14) developed the SMU method based on the as-

sumption that 24-hour creatinine excretion can be predicted from demographic factors and that the sodium/creatinine ratio of a 24-hour urine specimen is proportional to that of the second morning urine specimen. Accordingly, the 24-hour sodium excretion is calculated as the sodium/creatinine ratio in the second morning urine specimen multiplied by the predicted 24-hour creatinine excretion. Although the influence of posture was not discussed in the original report (13), posture is known to affect the urinary sodium/creatinine ratio (36-38) and might influence the estimation of the daily salt intake by this method. We previously demonstrated that sitting or standing until collection of the second morning urine specimen improves the estimation of daily salt intake (16), so this modified SMU method was used in the present study. While the exact effect of regulating the posture during this test remains unclear, the correlation between the SMU method and the 24-hour UNaV method was reported to be high (r=0.85) in hospitalized patients receiving a constant salt intake (17, 18). Finally, it is known that hemoglobin A1c (39), low-density lipoprotein cholesterol (40), high-density lipoprotein cholesterol (40), and triglyceride (40) levels vary with the seasons, being higher in winter than in summer. We measured these parameters only in the summer in the present study, and it is assumed that higher levels of these parameters would have been obtained in winter had we assessed them then.

In conclusion, we detected seasonal variations in the daily UNaV in older women but not in younger women or in men of any age. However, the mean seasonal difference in the daily UNaV ranged from 0.1 to a maximum of 0.9 g of salt/day in all groups, which was small in comparison with the daily UNaV (11-13 g of salt/day). These findings support the restriction of salt intake throughout the year, even in patients who are anxious about salt loss due to sweating in summer.

The authors state that they have no Conflict of Interest (COI).

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