alteration in hypertensive patients is not uniform, and concentric hypertrophy among various LV geometric patterns is shown to be most closely related to poor cardiovascular prognosis.[13]

Thus, we hypothesized that the presence of reverse white-coat effect may promote LV hypertrophy, especially concentric hypertrophy, in treated hypertension. To assess the hypothesis, the present study investigated the influence of reverse white-coat effect on LV mass and geometry in treated hypertensive patients.

Methods

Subjects

From consecutive patients with essential hypertension who were chronically treated and underwent a 24-h ambulatory BP monitoring at an outpatient clinic of our hospital between May 2000 and December 2003, 272 subjects (142 men and 130 women; mean age, 65 years) in whom satisfactory echocardiographic data were simultaneously obtained were enrolled in the present study. Patients with secondary hypertension, stroke, ischaemic heart disease including myocardial infarction, congestive heart failure, renal failure (serum creatinine $\geqslant 160\,\mu$mol/l) or poorly controlled (haemoglobin A1c $\geqslant 8.0\%$) or insulin-treated diabetes mellitus were excluded from this study. Individuals with a remarkable white-coat effect (described below) were also excluded. Diabetes mellitus was diagnosed according to the American Diabetes Association criteria, such as a fasting plasma glucose of $\geqslant 7.0$ mmol/l and/or a plasma glucose level at 2 h after a 75-g oral glucose load of $\geqslant 11.1$ mmol/l, or when medication was taken for treatment of hyperglycaemia. A diagnosis of hyperlipidemia required a serum total cholesterol level of $\geqslant 5.69$ mmol/l and/or a serum triglyceride level of $\geqslant 1.69$ mmol/l or the use of lipid-lowering drugs, according to the Japan Atherosclerosis Society guidelines.[14]

All patients had taken antihypertensive drugs for at least 1 year (average, 12 years). One hundred and ninety-five patients (72%) were treated with Ca channel blockers, 140 (51%) with renin angiotensin system inhibitors (i.e., angiotensin II receptor blockers and angiotensin converting enzyme inhibitors), 82 (30%) with β-blockers, 53 (19%) with diuretics and 29 (11%) with other classes of agents. All subjects gave their informed consent to participate in the present study. All procedures of the present study were carried out in accordance with institutional and national ethical guidelines for human studies.

Measurement of BP

In each visit, office BP was measured twice by a physician in a hospital outpatient clinic with the patient in a sitting position after over 20 min of rest, using an appropriate-size cuff on the left arm and mercury sphygmomanometer. The first and fifth Korotkoff sounds were used to identify systolic and diastolic values, respectively, and measurements were taken to the nearest 2 mm Hg. Office BP was determined by averaging six measurements taken on three separate occasions during a 3-month period.

In the same study period, all subjects underwent 24-h ambulatory BP monitoring. BP was measured every 30 min during the day and night by the oscillometric method using an automatic monitoring device (TM-2421, A&D Co Ltd, Tokyo, Japan).[15] The accuracy and performance of this device have been demonstrated previously.[16] The patients were instructed to carry on with their normal daily activities during measurements and note their activity and location in a diary. According to the diary, daytime and night time were determined as the waking and sleeping periods of the patient, respectively, and mean values of daytime, night time and 24-h BP (systolic and diastolic) were calculated. Nocturnal BP dipping was determined as $100 \times$ (daytime BP$-$night time BP)/daytime BP.

In the present study, all subjects were classified into two groups by the difference between office and daytime ambulatory systolic BP levels; that is, subjects without reverse white-coat effect (Group 1: office systolic BP$\geqslant$daytime systolic BP, and office systolic BP$-$daytime systolic BP<20 mm Hg) and with reverse white-coat effect (Group 2: office systolic BP$<$daytime systolic BP). Subjects with a remarkable white-coat effect (office systolic BP$-$daytime systolic BP $\geqslant 20$ mm Hg) were excluded from the study.

Echocardiography

A comprehensive 2-dimensional and M-mode echocardiography was performed using a cardiac ultrasound unit (Sonos 5500, Philips Medical Systems, Andover, MA, USA) as described previously.[17] Echocardiographic parameters were measured by the consensus of two experienced investigators who were blinded to the clinical data including office and ambulatory BP of the subjects. Interventricular septal thickness (IVSTd), posterior wall thickness (PWTd), LV diameter at end-diastole (LVDd), and LV diameter at end-systole (LVDs) were measured according to the American Society of Echocardiography recommendations.[18,19] Fractional shortening was calculated as $100 \times$ (LVDd$-$LVDs)/LVDd. Relative wall thickness (RWT) was calculated as (IVSTd + PWTd)/LVDd. LV mass was estimated using the formula validated by Devereux and Reichek[20]: LV mass (g) $= 1.04 \times \{$(IVSTd + PWTd + LVDd)$^3-$LVDd$^3\}-13.6$. LV mass was normalized for body surface area and expressed as the LV mass index (LVMI). LVH was defined as a LVMI of $\geqslant 125$ g/m^2 in men and 110 g/m^2 in women.[21] The intra-observer and inter-observer coefficients of variation of LVMI were 6.7 and 9.8%, respectively.

The geometry of LV was stratified into four different patterns according to the values of LVMI (< or ⩾125/110 g/m^2, men/women) and RWT (< or ⩾0.44). Patients with increased LVMI and increased RWT were considered to have concentric hypertrophy, and those with increased LVMI and normal RWT were considered to have eccentric hypertrophy. Those with normal LVMI and increased or normal RWT were considered to have concentric remodelling or normal geometry, respectively.

Biochemical measurement

Blood samples were obtained in the morning after an overnight fast. Total cholesterol, triglycerides, fasting plasma glucose, haemoglobin A1c and serum creatinine levels were determined by standard laboratory measurements. Creatinine clearance was calculated from the Cockcroft-Gault formula.[22]

Statistical analysis

Statistical analysis was performed using StatView Version 5 Software (Abacus Concepts Inc., Berkeley, CA, USA). Values are expressed as the mean ± s.d. Simple correlations between variables were assessed using univariate linear regression analyses and Pearson's correlation coefficient. An unpaired Student's *t*-test was used for comparison between the two groups. The significance of differences among the three groups was evaluated by an unpaired ANOVA with subsequent Fisher's multiple comparison test. A multiple logistic regression analysis was performed to identify independent determinants of LV mass increase and concentric hypertrophy. A value of $P<0.05$ was accepted as statistically significant.

Results

Simple correlations of office and ambulatory BP levels with two indices of LV structural changes, LVMI and RWT, in all subjects are shown in Table 1. Office systolic or diastolic BP had no correlation with either LVMI or RWT. In contrast, LVMI and RWT were positively correlated with daytime and 24-h systolic BPs, and LVMI was also correlated with night time systolic BP. In addition, these two indices were significantly correlated with the difference between office BP and daytime BP. As shown in Figure 1, LVMI had a close negative correlation with office–daytime systolic BP difference ($r=-0.377$, $P<0.001$). RWT were also inversely correlated with office–daytime systolic BP difference ($r=-0.170$, $P=0.005$). These results suggested that reverse white-coat effect was significantly associated with increases in LVMI and RWT.

Clinical characteristics of the two subject groups classified according to the difference between office and daytime ambulatory systolic BP levels are summarized in Table 2. One hundred and twenty-three (45%) patients were identified as having reverse white-coat effect (Group 2), and the other 149 (55%) patients belonged to Group 1. The proportion of men and the rate of habitual drinkers

Table 1 Correlation of office and ambulatory blood pressure with left ventricular structure in all subjects

	LVMI		*RWT*	
	r	P	r	P
Office systolic BP	0.039	0.526	0.014	0.816
Office diastolic BP	−0.124	0.053	−0.040	0.508
Daytime systolic BP	0.290	<0.001	0.173	0.004
Daytime diastolic BP	0.020	0.742	0.100	0.099
Night time systolic BP	0.318	<0.001	0.113	0.062
Night time diastolic BP	0.099	0.104	0.078	0.198
24-h systolic BP	0.325	<0.001	0.158	0.009
24-h diastolic BP	0.051	0.398	0.096	0.113
(Office − daytime) systolic BP	−0.377	<0.001	−0.170	0.005
(Office − daytime) diastolic BP	−0.211	<0.001	−0.147	0.015

Abbreviations: BP, blood pressure; LVMI, left ventricular mass index; RWT, relative wall thickness.

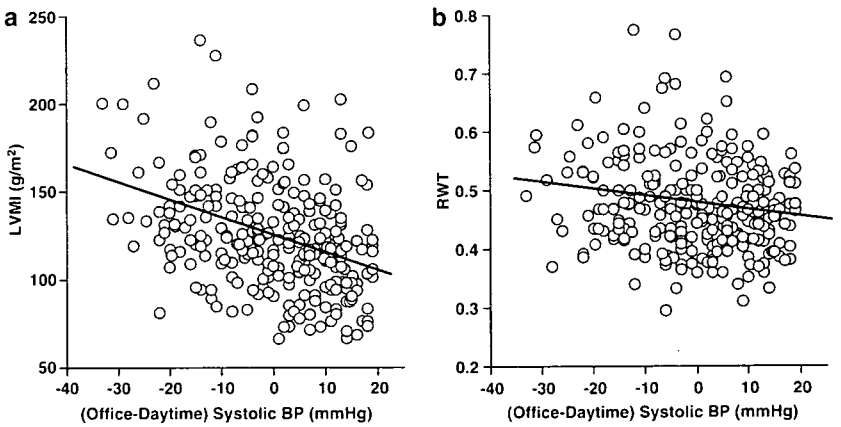

Figure 1 Correlation of the difference between office and daytime systolic BP levels with LVMI (**a**, $r=-0.377$, $P<0.001$) and RWT (**b**, $r=-0.170$, $P=0.005$) in all subjects.

Table 2 Clinical characteristics of two study groups

	Group 1 (n = 149)	*Group 2 (n = 123)*	P
Age (years)	65.8±9.1	65.1±11.0	0.593
Sex (male) (%)	41.6	65.0	<0.001
Body mass index (kg/m^2)	24.2±2.9	24.7±4.0	0.182
Duration of hypertension (years)	17.6±10.8	17.8±11.0	0.850
Diabetes mellitus (%)	19.5	23.6	0.412
Hyperlipidemia (%)	64.9	66.1	0.831
Current smoking (%)	15.6	21.1	0.235
Habitual drinking (%)	50.7	63.6	0.033
Creatinine clearance (ml/min)	81.5±24.8	85.1±32.8	0.297
Fasting plasma glucose (mmol/l)	5.7±1.2	5.8±1.1	0.486
Hemoglobin A1c (%)	5.6±0.8	5.7±0.7	0.257
Total cholesterol (mmol/l)	5.3±0.8	5.2±0.7	0.576
Triglycerides (mmol/l)	1.4±0.7	1.5±0.8	0.126
Antihypertensive treatment			
Period of medication (years)	12.4±9.3	11.7±9.1	0.497
Ca channel blockers (%)	71.8	71.5	0.961
RAS inhibitors (%)	49.7	53.7	0.514
β-Blockers (%)	28.2	32.5	0.440
Diuretics (%)	16.8	22.8	0.216
Others (%)	9.4	12.2	0.458
Total number of classes	1.8±0.9	1.9±0.9	0.141
Office systolic BP (mm Hg)	145.6±12.7	133.8±11.6	<0.001
Office diastolic BP (mm Hg)	83.4±9.9	78.8±10.0	<0.001
Daytime systolic BP (mm Hg)	136.5±12.6	145.1±11.9	<0.001
Daytime diastolic BP (mm Hg)	80.1±9.3	84.8±11.5	<0.001
Night time systolic BP (mm Hg)	126.8±14.9	134.1±15.8	<0.001
Night time diastolic BP (mm Hg)	73.1±9.5	76.9±11.1	0.002
24-h systolic BP (mm Hg)	134.0±12.3	141.6±12.2	<0.001
24-h diastolic BP (mm Hg)	78.2±9.0	82.3±10.5	<0.001
Nocturnal systolic BP dipping (%)	7.1±8.0	7.6±8.0	0.572
Nocturnal diastolic BP dipping (%)	8.5±8.4	9.0±8.5	0.671

Abbreviations: BP, blood pressure; RAS, renin angiotensin system.
RAS inhibitors represent angiotensin II receptor blockers and angiotensin converting enzyme inhibitors. Values are mean±s.d. or percentage.

were significantly higher in Group 2 than in Group 1. Age, body mass index, hypertension duration, the prevalence of diabetes mellitus and hyperlipidemia, the rate of current smokers, renal function and glucose and lipid parameters did not differ between the two groups. In addition, there were no inter-group differences in the period of medication, the use of any class of antihypertensive agent and the total number of classes of antihypertensive drugs.

Office and ambulatory BP levels had clear differences between the two groups. That is, Group 2 had significantly lower office systolic and diastolic BPs than Group 1, but daytime, night time, and average 24-h ambulatory BPs in Group 2 were significantly elevated compared with those in Group 1. The degree of nocturnal BP dipping, an index of circadian BP variation, did not differ between the two groups.

The comparison of echocardiographic parameters between the two groups is shown in Table 3. Group 2 had a significantly greater LVMI than Group 1, resulting from more increased LV wall thickness and internal dimension. RWT was also significantly increased in Group 2 compared with Group 1. In addition, the prevalence of LVH, defined as an increased LVMI by sex, was significantly higher in Group 2. There was no difference in fractional shortening between the two groups.

Table 3 Comparison of ecchocardiographic parameters between the two groups

	Group 1 (n = 149)	*Group 2 (n = 123)*	P
IVSTd (mm)	10.3±1.5	11.4±1.9	<0.001
PWTd (mm)	10.3±1.4	11.1±1.5	<0.001
LVDd (mm)	44.8±4.5	46.8±4.2	<0.001
LVDs (mm)	26.5±4.9	27.7±4.6	0.037
Fractional shortening (%)	41.1±7.4	41.0±6.8	0.920
LVMI (g/m^2)	115.3±28.3	136.4±30.8	<0.001
RWT	0.46±0.07	0.49±0.09	0.010
Prevalence of LVH (%)	41.6	65.9	<0.001

Abbreviations: IVSTd, interventricular septal thickness at end-diastole; LVDd, left ventricular diameter at end-diastole; LVDs, left ventricular diameter at end-systole; LVMI, left ventricular mass index; LVH, left ventricular hypertrophy; PWTd, posterior wall thickness at end-diastole; RWT, relative wall thickness.
LVH is defined as LVMI of ⩾125 g/m^2 in men and 110 g/m^2 in women.
Values are mean±s.d. or percentage.

To assess the impact of reverse white-coat effect on LVH, Group 2 was divided into two sub-groups by the extent of its phenomenon. As shown in Figure 2, both LVMI and prevalence of LVH were

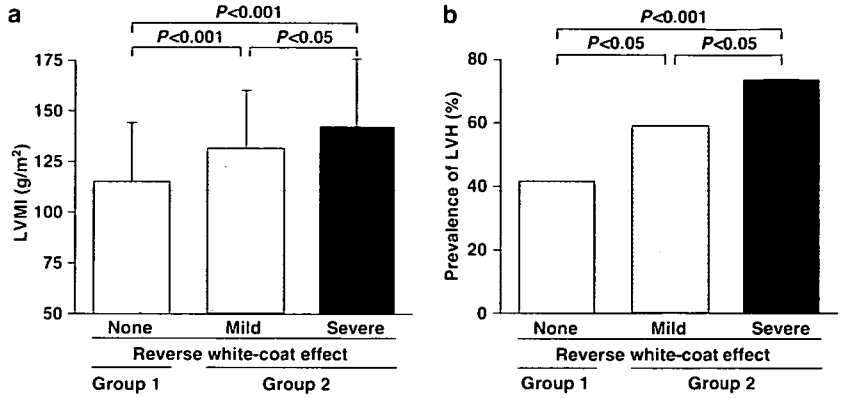

Figure 2 Comparison of LVMI (**a**) and prevalence of LVH (**b**) among the three groups classified by the extent of reverse white-coat effect. None, office systolic BP ≥ daytime systolic BP (i.e., Group 1, $n = 149$); Mild, office systolic BP < daytime systolic BP, but daytime systolic BP−office systolic BP < 10 mm Hg ($n = 63$); Severe, daytime systolic BP−office systolic BP ≥ 10 mm Hg ($n = 60$). LVH is defined as LVMI of ≥125 g/m² in men and 110 g/m² in women. Values are given as the mean ± s.d. (**a**) or percentage (**b**).

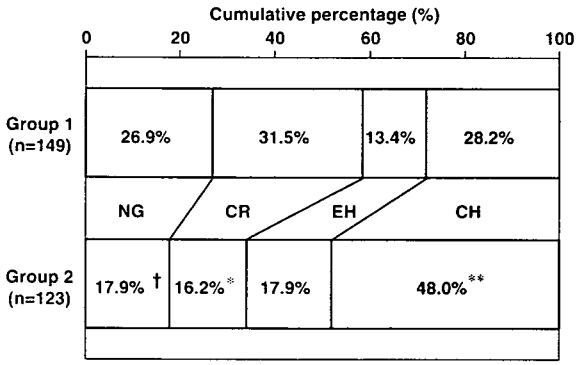

Figure 3 Comparison of LV geometric patterns between the two groups. NG, normal geometry (normal LVMI and RWT); CR, concentric remodelling (normal LVMI and increased RWT); EH, eccentric hypertrophy (increased LVMI and normal RWT); CH, concentric hypertrophy (increased LVMI and RWT). †$P<0.05$, *$P<0.01$, and **$P<0.001$ vs Group 1.

significantly greater in subjects with mild reverse white-coat effect (office systolic BP < daytime systolic BP, but daytime systolic BP−office systolic BP < 10 mm Hg) than in those without reverse white-coat effect (i.e., Group 1), and these values were further increased significantly in the sub-group with severe reverse white-coat effect (daytime systolic BP−office systolic BP ≥ 10 mm Hg).

Figure 3 shows the comparison of LV geometric patterns between the two groups. Group 2 had a significantly higher rate of concentric hypertrophy compared with Group 1 (48 vs 28%, $P<0.001$). In contrast, the rates of patients with normal geometry and concentric remodelling were significantly lower in Group 2 than in Group 1.

To confirm whether the influence of reverse white-coat phenomenon on LV mass increase and specific geometric change was independent of various clinical parameters, we investigated possible predictive factors using a multiple logistic regression analysis in all subjects (Table 4). Although average 24-h systolic BP was the strongest predictor for both LVH and concentric hypertrophy, the presence of reverse white-coat effect (i.e., Group 2) was found to be a significant determinant for these LV structural changes, independent of age, sex, body mass index, hypertension duration, the use of any class of antihypertensive agent and 24-h systolic and diastolic BP levels (for LVH: odds ratio 2.42 vs Group 1, $P=0.005$; for concentric hypertrophy: odds ratio 1.89, $P=0.039$). The significant predictive value of reverse white-coat effect remained even when daytime systolic and diastolic BPs, instead of 24-h BPs, were adopted as independent predictors (data not shown).

Discussion

This study has demonstrated that the presence of reverse white-coat effect is one of the independent predictors for LVH, especially for LV concentric hypertrophy, in patients with treated essential hypertension. The new findings suggest that reverse white-coat phenomenon, independent of average ambulatory blood pressure levels, may have an unfavourable influence on left ventricular geometry in essential hypertension.

The present subjects with reverse white-coat effect (Group 2) had a controlled office BP in spite of elevated ambulatory BP, indicating that the group took on an aspect of masked hypertension. There have been a few studies reporting the possible association between masked hypertension and cardiac and carotid arterial structural changes in the general population. Liu *et al.*[23] found that LV mass and carotid wall thickness in patients with masked hypertension were significantly greater than those in true normotensive subjects and similar to those in patients with sustained hypertension. The data from the PAMELA Study also showed that LVMI was

Table 4 Independent predictors for left ventricular mass increase and concentric hypertrophy by multiple logistic regression analysis

	LVH		*Concentric hypertrophy*	
	OR (95% CI)	P	*OR (95% CI)*	P
Age (10 years)	0.88 (0.58–1.34)	0.544	0.70 (0.46–1.05)	0.087
Sex (male)	0.60 (0.30–1.16)	0.128	0.82 (0.42–1.60)	0.557
Body mass index (1 kg/m^2)	1.10 (1.00–1.23)	0.046	1.10 (1.00–1.22)	0.053
Hypertension duration (1 year)	1.02 (0.99–1.05)	0.123	1.03 (1.00–1.06)	0.028
Diabetes mellitus (yes)	1.04 (0.48–2.22)	0.929	1.02 (0.49–2.13)	0.959
Hyperlipidemia (yes)	1.49 (0.82–2.71)	0.186	1.35 (0.73–2.47)	0.339
Current smoking (yes)	0.99 (0.46–2.13)	0.978	1.25 (0.60–2.58)	0.553
Habitual drinking (yes)	1.09 (0.58–2.06)	0.783	1.22 (0.64–2.32)	0.541
Creatinine clearance (10 ml/min)	0.91 (0.77–1.06)	0.231	0.87 (0.74–1.02)	0.095
Ca channel blocker (yes)	1.36 (0.67–2.77)	0.402	1.09 (0.53–2.24)	0.808
RAS inhibitor (yes)	1.15 (0.60–2.21)	0.678	1.57 (0.82–2.99)	0.170
β-Blocker (yes)	1.89 (0.99–3.59)	0.052	1.36 (0.73–2.55)	0.337
Diuretic (yes)	1.04 (0.49–2.22)	0.921	0.72 (0.34–1.56)	0.407
24-h systolic BP (10 mm Hg)	2.35 (1.66–3.33)	<0.001	1.97 (1.45–2.68)	<0.001
24-h diastolic BP (10 mm Hg)	0.60 (0.40–0.90)	0.014	0.67 (0.45–0.98)	0.041
Reverse white-coat effect				
Absence (Group 1)	1 (reference)		1 (reference)	
Presence (Group 2)	2.42 (1.31–4.48)	0.005	1.89 (1.03–3.44)	0.039

Abbreviations: BP, blood pressure; CI, confidence interval; LVH, left ventricular hypertrophy; OR, odds ratio; RAS, renin angiotensin system. RAS inhibitor represents angiotensin II receptor blocker or angiotensin converting enzyme inhibitor. LVH is defined as LVMI of $\geq$125 g/m^2 in men and 110 g/m^2 in women. Concentric hypertrophy is defined as LVH combined with increased RWT ($\geq$0.44).

increased in untreated subjects with masked hypertension and sustained hypertension than in those with true normotension.[24] In addition, our recent study showed that masked hypertension was associated with advanced target organ damage in treated hypertensive patients, comparable to that in cases of sustained hypertension.[25] Furthermore, prospective studies have revealed that a high ambulatory or home BP is a powerful predictor for cardiovascular morbidity and mortality in the general population and treated hypertensive patients even when their office BP is normal or well controlled.[10,11,26–28] As for the association between LV geometry and cardiovascular prognosis, it was reported that hypertensive patients with concentric hypertrophy among four LV geometric patterns had the highest incidence of cardiovascular events and death.[13] Taken together, it is likely that advanced target organ changes including LV concentric hypertrophy in patients with masked hypertension or reverse white-coat condition are linked to poor cardiovascular prognosis in such patients.

A higher level of ambulatory BP is a major determinant of target organ damage in hypertensive patients.[1,2] In the present study, however, the presence of reverse white-coat effect was a significant predictor for LVH and concentric hypertrophy, independent of average 24-h ambulatory BP levels. Other factors than a higher ambulatory BP could contribute to target organ damage in reverse white-coat hypertension. Our study has not provided the specific mechanism by which reverse white-coat effect could promote LV concentric hypertrophy in patients with treated hypertension. Therefore, further investigations are required to clarify how reverse white-coat or masked hypertension has a specific unfavourable effect on the hypertensive target organ.

There were some limitations in our study. The present findings were derived from cross-sectional data on the basis of one-time examination of ambulatory BP monitoring and echocardiography. Our subjects were divided into subgroups based on office–daytime difference only in systolic BP, not considering diastolic BP difference. In addition, cardiac magnetic resonance imaging might be more adequate than echocardiography in evaluating LV mass exactly.

All patients in the present study had received antihypertensive medication. As another limitation of this study, therefore, we must consider the possibility that different classes of antihypertensive drugs may have differently affected the development of LVH, partly independently of their BP-lowering effects. Renin angiotensin system inhibitors, particularly, are known to have BP fall-independent protective effects on hypertensive target organ. However, the percentage of patients treated with angiotensin II receptor antagonists or angiotensin converting enzyme inhibitors did not differ between the two study groups. Our multivariate analysis also showed that the association of reverse white-coat effect with LVH and concentric hypertrophy was independent of the use of any class of antihypertensive agent.

In conclusion, the present study indicates that reverse white-coat effect is a significant determinant of LVH, especially concentric hypertrophy, in patients with treated essential hypertension, independent of average ambulatory BP levels and

various other clinical risk factors. Our findings suggest that the presence of this phenomenon may be an independent risk for the adverse LV geometric change in treated hypertensive patients and ambulatory BP monitoring seems to be necessary to unmask this latent risk that is not detectable by routine BP measuring in the office.

What is known about this topic

- Ambulatory blood pressure is an important determinant of target organ damage and a predictor for cardiovascular morbidity and mortality in hypertensive patients.
- The converse phenomenon of white-coat hypertension called 'reverse white-coat hypertension' or 'masked hypertension' is associated with poor cardiovascular prognosis.
- Left ventricular hypertrophy, especially concentric hypertrophy, is a significant risk factor for cardiovascular complications and death.

What this study adds

- Reverse white-coat effect was an independent predictor for left ventricular hypertrophy, especially for concentric hypertrophy, in treated hypertensive patients.
- The presence of reverse white-coat phenomenon, independent of average ambulatory blood pressure levels, may have an unfavourable influence on left ventricular geometry.

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References

1 Pickering TG, Harshfield GA, Devereux RB, Laragh JH. What is the role of ambulatory blood pressure monitoring in the management of hypertensive patients? *Hypertension* 1985; **7**: 171–177.
2 Schillaci G, Verdecchia P, Sacchi N, Bruni B, Benemio G, Pede S *et al.* Clinical relevance of office underestimation of usual blood pressure in treated hypertension. *Am J Hypertens* 2000; **13**: 523–528.
3 Cuspidi C, Meani S, Fusi V, Valerio C, Catini E, Magrini F *et al.* Isolated ambulatory hypertension and changes in target organ damage in treated hypertensive patients. *J Hum Hypertens* 2005; **19**: 471–477.
4 Perloff D, Sokolow M, Cowan R. The prognostic value of ambulatory blood pressures. *JAMA* 1983; **249**: 2792–2798.
5 Staessen JA, Thijs L, Fagard R, O'Brien ET, Clement D, de Leeuw PW *et al.* Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. *JAMA* 1999; **282**: 539–546.
6 Verdecchia P, Reboldi G, Porcellati C, Schillaci G, Pede S, Bentivoglio M *et al.* Risk of cardiovascular disease in relation to achieved office and ambulatory blood pressure control in treated hypertensive subjects. *J Am Coll Cardiol* 2002; **39**: 878–885.
7 Pickering TG, Davidson K, Gerin W, Schwartz JE. Masked hypertension. *Hypertension* 2002; **40**: 795–796.
8 Wing LMH, Brown MA, Beilin LJ, Ryan P, Reid CM. 'Reverse white-coat hypertension' in older hypertensives. *J Hypertens* 2002; **20**: 639–644.
9 Bombelli M, Sega R, Facchetti R, Corrao G, Friz HP, Vertemati AM *et al.* Prevalence and clinical significance of a greater ambulatory versus office blood pressure ('reversed white coat' condition) in a general population. *J Hypertens* 2005; **23**: 513–520.
10 Clement DL, De Buyzere ML, De Bacquer DA, de Leeuw PW, Duprez DA, Fagard RH *et al.* Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. *N Engl J Med* 2003; **348**: 2407–2415.
11 Bobrie G, Chatellier G, Genes N, Clerson P, Vaur L, Vaisse B *et al.* Cardiovascular prognosis of 'masked hypertension' detected by blood pressure self-measurement in elderly treated hypertensive patients. *JAMA* 2004; **291**: 1342–1349.
12 Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med* 1990; **322**: 1561–1566.
13 Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. *Ann Intern Med* 1991; **114**: 345–352.
14 Hata Y, Mabuchi H, Saito Y, Itakura H, Egusa G, Ito H *et al.* Report of the Japan Atherosclerosis Society (JAS) Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese adults. *J Atheroscler Thromb* 2002; **9**: 1–27.
15 Kawano Y, Matsuoka H, Takishita S, Omae T. Effects of magnesium supplementation in hypertensive patients: assessment by office, home, and ambulatory blood pressures. *Hypertension* 1998; **32**: 260–265.
16 Imai Y, Sasaki S, Minami N, Munakata M, Hashimito T, Sakuma H *et al.* The accuracy and performance of the A&D TM 2421, a new ambulatory blood pressure monitoring device based on the cuff-oscillometric and the Korotkoff sound technique. *Am J Hypertens* 1992; **5**: 719–726.
17 Horio T, Miyazato J, Kamide K, Takiuchi S, Kawano Y. Influence of low high-density lipoprotein cholesterol on left ventricular hypertrophand diastolic function in essential hypertension. *Am J Hypertens* 2003; **16**: 938–944.
18 Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978; **58**: 1072–1083.
19 Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H *et al.* Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr* 1989; **2**: 358–367.
20 Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. *Circulation* 1977; **55**: 613–618.

21 Cifkova R, Erdine S, Fagard R, Farsang C, Heagerty AM, Kiowski W *et al.* Practice guidelines for primary care physicians: 2003 ESH/ESC hypertension guidelines. *J Hypertens* 2003; **21**: 1779–1786.
22 Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; **16**: 31–41.
23 Liu JE, Roman MJ, Pini R, Schwartz JE, Pickering TG, Devereux RB. Cardiac and arterial target organ damage in adults with elevated ambulatory and normal office blood pressure. *Ann Intern Med* 1999; **131**: 564–572.
24 Sega R, Trocino G, Lanzarotti A, Carugo S, Cesana G, Schiavina R *et al.* Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension: data from the general population (Pressione Arteriose Monitorate E Loro Associazioni [PAMELA] Study). *Circulation* 2001; **104**: 1385–1392.
25 Tomiyama M, Horio T, Yoshii M, Takiuchi S, Kamide K, Nakamura S *et al.* Masked hypertension and target organ damage in treated hypertensive patients. *Am J Hypertens* 2006; **19**: 880–886.
26 Björklund K, Lind L, Zethelius B, Andrén B, Lithell H. Isolated ambulatory hypertension predicts cardiovascular morbidity in elderly men. *Circulation* 2003; **107**: 1297–1302.
27 Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, Hashimoto J *et al.* Prognosis of 'masked' hypertension and 'white-coat' hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. *J Am Coll Cardiol* 2005; **46**: 508–515.
28 Pierdomenico SD, Lapenna D, Bucci A, Di Tommaso R, Di Mascio R, Manente BM *et al.* Cardiovascular outcome in treated hypertensive patients with responder, masked, false resistant, and true resistant hypertension. *Am J Hypertens* 2005; **18**: 1422–1428.

Report

Report of the Working Group for Dietary Salt Reduction of the Japanese Society of Hypertension: (1) Rationale for Salt Restriction and Salt-Restriction Target Level for the Management of Hypertension

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Salt excess is well known to be involved in the pathophysiology of hypertension, and thus restriction of salt intake is widely recommended for management of the disease. Excessive salt intake induces blood pressure (BP)–dependent as well as –independent progression of cardiovascular disease. Although the human body is considered to be adapted to very low salt intake (0.5–3 g/day), restriction to such a low level of salt intake is extremely difficult to accomplish in developed countries. Significant BP reduction has been reported in large-scale clinical studies in which salt intake was decreased to less than 6 g/day, and the results of a meta-analysis have shown that systolic BP was reduced about 1 mmHg with every decrease in salt intake of 1 g/day in hypertensive subjects. Current guidelines for the treatment of hypertension, including Japanese guidelines, recommend dietary salt reduction to 6 g/day or less in hypertensive patients. However, it appears to be fairly difficult to attain this target of salt intake, especially in Japan. There is thus a need for feasible and effective measures to attain this salt restriction target. (*Hypertens Res* 2007; 30: 879–886)

***Key Words*: dietary salt, hypertension, cardiovascular disease, guidelines, large-scale clinical study**

Introduction

Salt excess is well known to be involved in the pathophysiology of hypertension, and thus restriction of salt intake is widely recommended for management of the disease. Treatment guidelines for hypertension in Western countries recommend salt restriction to 6 g/day (sodium [Na] 100 mmol/day) or less for hypertensives (*1*, *2*). Because salt intake is higher in Japan than in Western countries, the 2000 version of the Guidelines for the Management of Hypertension (JSH 2000) from the Japanese Society of Hypertension (JSH) set the target of salt intake at 7 g/day or less (*3*). However, the target was revised to less than 6 g/day in the new Japanese guidelines (2004 version: JSH 2004) (*4*). To promote salt restriction for the management of hypertension, the JSH organized the Working Group for Dietary Salt Reduction in 2005. In this report, we summarize the rationale for restricting salt intake for the management of hypertension. The Japanese version of the working group report has been published previously (*5*).

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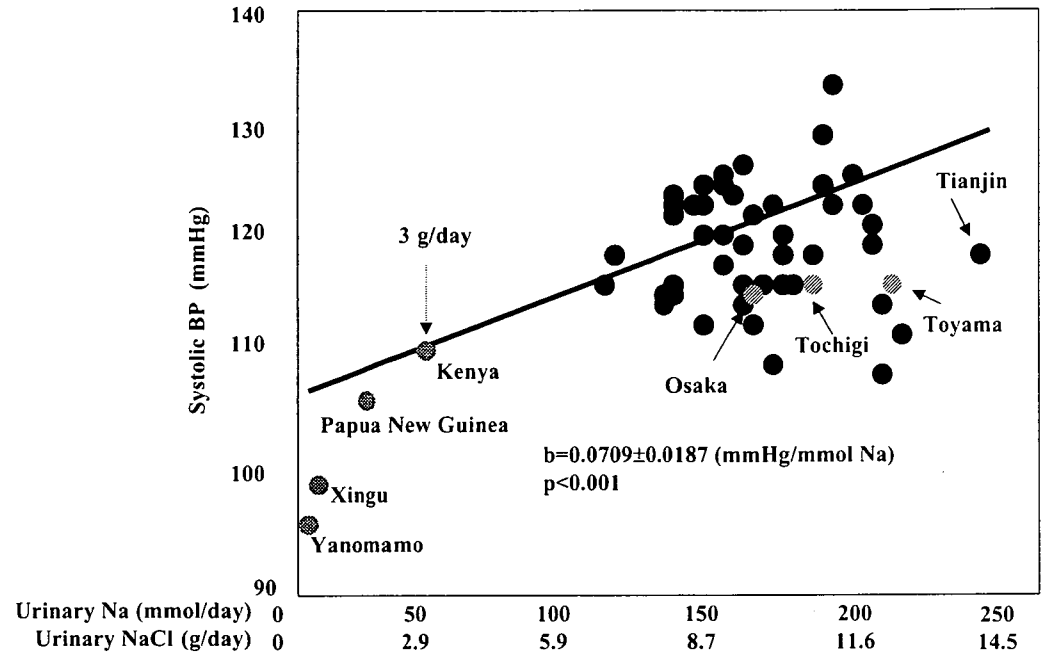

Fig. 1. *Relationship between salt intake and systolic blood pressure (BP) (from Intersalt Cooperative Research Group (8) with modification).*

Historical Background and Current Status of Salt Intake

Many land-dwelling animal species have difficulty gaining free access to salt and an innate salt appetite. In humans, low availability of salt has been a problem for millennia, and the period in which they could consume a large amount of salt has been very short in the history of mankind. It is estimated that humans in the Stone Age consumed salt at only 0.5–3 g/day (*6*), and the human body is considered to be adapted to such low salt intake. Physiologic studies have also suggested that the minimum salt requirement for human survival is about 0.5 g/day (*7*).

The amount of salt intake in humans shows wide regional and individual variations. The international cooperative Intersalt study, which investigated salt intake and blood pressure (BP) in various parts of the world, reported that salt intake ranged from less than 0.1 g/day in Yanomano, South America to about 15 g/day in Tianjin, China (*8*) (Fig. 1). Generally, salt intake is low in undeveloped regions and high in developed countries.

In Japan, the salt intake was traditionally high, especially in the Tohoku District (about 25 g/day in the 1950s) (*3*). Although the amount of salt consumption in Japanese has considerably decreased, the intake remains high, at about 11 g/day (*9*) (Fig. 2). Therefore, even today, most Japanese are consuming about 10 times the required amount of salt. In hypertensive patients treated on an outpatient basis, the mean salt intake estimated from the urinary Na excretion has also been reported to be high, at about 11 g/day (*10*) or 10 g/day (*11*). Salt intake is slightly higher in males than in females (*9*, *11*). Since this gender difference disappears when the values are corrected for body weight, it is considered to be ascribable to gender-related differences in physique (*11*).

Effects of Excessive Salt Intake

Hypertension

Many epidemiological, experimental, and clinical studies have clearly indicated that excessive salt intake is related to increases in BP and the progression of hypertension (*12*). For example, the Intersalt study found that salt intake was significantly correlated with BP; BP was extremely low particularly in groups with very low (less than 3 g/day) salt intake (*8*, *13*) (Fig. 1, Table 1). Moreover, little age-associated increase in BP was noted in these groups. Therefore, salt intake of less than 3 g/day is considered to be ideal for the prevention or treatment of hypertension.

Experimentally, the intake of excessive salt has been shown to induce or exacerbate hypertension in many models, including Dahl salt-sensitive rats and deoxycorticosterone acetate (DOCA)–salt hypertensive rats. Although the mechanism by which salt increases BP has not been completely elucidated, the kidney is considered to play an important role. The central

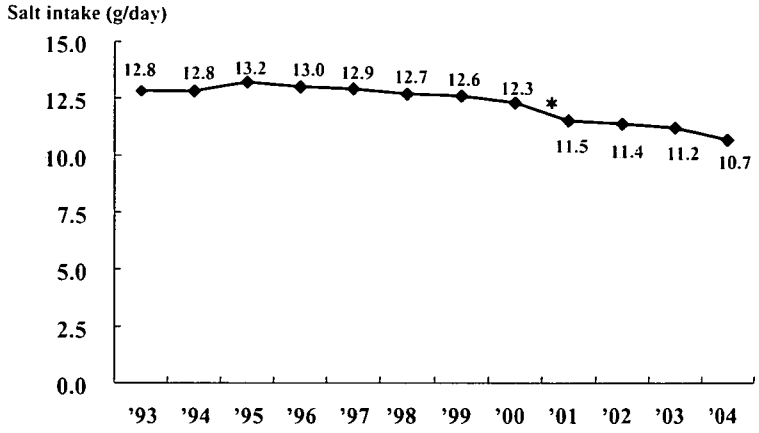

Fig. 2. *Trend of daily salt intake in Japan (based on data of Lifestyle-Related Disease Control Section, General Affairs Division, Health Bureau, Ministry of Health, Labor and Welfare (9)). *Calculated on the basis of the 4th edition of the Standard Tables of Food Composition in Japan until 2000 and 5th edition after 2001.*

Table 1. Comparison of Low Salt Intake Groups with Other Groups—Intersalt Study*

	Yanomamo	Xingu	Papua New Guinea	Kenya	Others (n=48)
Lifestyle					
Salt intake (g/day)	<0.06	0.35	1.6	3.0	9.4
Na/K ratio	<0.01	0.08	0.48	1.8	3.4
BMI (kg/m^2)	21.2	23.4	21.7	20.8	25.2
Regular drinkers (%)	0	0	8.7	30.7	53.0
Bood pressure					
Systolic BP (mmHg)	95.4	98.9	107.7	109.9	118.7
Diastolic BP (mmHg)	61.4	61.7	62.9	67.9	74.0
Hypertensives (%)	0	1.0	0.8	5.0	17.4
Age-associated increases in BP (mmHg/10 years)	−1.1	+0.6	−1.4	+2.4	+5.0

*From Stamler *et al.* (*13*) with permission. Na/K ratio, sodium/potassium ratio; BMI, body mass index; BP, blood pressure.

nervous system, various neurohumoral factors, and vasoactive substances may also be involved (*12*).

Many clinical reports have suggested that BP is increased by excessive salt intake. However, the increase in BP due to excessive salt intake varies widely among individuals, and many people remain normotensive even on a high-salt diet. In fact, hypertensives can be classified into salt-sensitive and non–salt-sensitive groups, because the responses of BP to a high-salt or low-salt diet are not uniform (*14*, *15*). Many factors, including genetic interference, renal function, and neurohumoral elements, are involved in the salt sensitivity of BP.

Cardiovascular Diseases

Salt excess is related to the occurrence and progression of cardiovascular diseases through its BP-increasing effects, but it has also been shown that salt exerts adverse effects on the cardiovascular system by different mechanisms in addition to rise in BP (*16*) (Table 2). Excessive salt intake causes left ventricular hypertrophy and thickening of the vascular wall independently of its effects on BP. According to a report from Finland, mortality from ischemic heart disease, stroke and all causes increased significantly with increases in salt intake even after correction for BP or other factors (*17*) (Table 3). Furthermore, salt intake has been shown to be an independent risk factor of stroke and heart failure (*18*, *19*). Dietary salt may also relate to impairment of platelet aggregation and renal function (*15*), so that salt excess is considered to confer a greater risk of cardiovascular diseases than would be expected by a mere increase in BP.

Other Disorders

Excessive salt intake is also related to several other disorders (*16*) (Table 2). An increase in salt intake elevates the urinary calcium (Ca) excretion and the incidence of urolithiasis. This loss of Ca through the kidney also decreases Ca in the bone and increases the risk of osteoporosis. Moreover, a relation-

Table 2. Adverse Effects of Salt Independent of BP

Cardiovascular system
Left ventricular hypertrophy
Thickening/hardening of vascular wall
Platelet aggregation
Cardiovascular disorders
Stroke
Ischemic heart disease, Heart failure
Impairment of renal function
Other disorders
Urolithiasis
Osteoporosis
Stomach cancer
Asthma

ship between salt intake and stomach cancer has been suggested by epidemiological studies. A high-salt environment has recently been reported to promote the propagation of *Helicobacter pyroli*. A relationship between salt intake and asthma has also been suspected. Thus, excessive salt intake is considered to exert various adverse effects.

Antihypertensive Effect of Salt Restriction

There is much evidence based on clinical studies that restriction of salt intake reduces BP in hypertensives. In Japan, Ito *et al.* reported the results of moderate restriction of salt intake in a small number of subjects. Blood pressure decreased slightly but not significantly when salt intake was reduced from 13 g/day to 7 g/day but significantly when it was rigorously restricted to 3 g/day (*20*). All large-scale clinical studies to date have been performed in Europe or America. Significant decreases in BP were observed in the Trials of Hypertension Prevention (TOHP)-Phase I (TOHP-I) (*21*), the Trial of Nonpharmacologic Interventions in the Elderly (TONE) (*22*), a report from He *et al.* (*23*), and the Dietary Approaches to Stop Hypertension (DASH)-Sodium trial (*24*), in all of which salt intake was reduced to less than 6 g/day (Table 4). But the decreases were not significant in the TOHP-II study (*25*), in which restriction of salt intake was milder. In the Hypertension Prevention Trial (HPT), salt intake was reduced to less than 6 g/day, but no significant decrease in BP was observed, probably because salt intake was also decreased in the control group (*26*). In the TONE, evaluations were also performed at various levels of salt restriction achieved, and salt intake to 5.64 g/day or less was effective for the maintenance of a normal BP after discontinuation of antihypertensive medication (*22*). On the basis of these results, many guidelines for the management of hypertension in Western countries recommend less than 6 g/day as a target for salt restriction (*1*, *2*).

According to a meta-analysis of randomized studies on the effect of moderate salt restriction, BP decreased by a mean of 5.0/2.7 mmHg in hypertensive subjects (*27*) (Fig. 3). The

Table 3. Hazard Ratios and 95% CI of Deaths Due to Ischemic Heart Disease, Stroke, and All Causes Associated with Increases in the Urinary Na Excretion (100 mmol/day) after Adjustment*

Cause of death	Hazard ratio (95% CI)
Ischemic heart disease	1.56 (1.15–2.12)
Stroke	1.36 (1.05–1.76)
All causes	1.22 (1.02–1.47)

*From Tumilehto *et al.* (*17*) with modification. CI, confidence interval; BP, blood pressure.

median urinary Na excretion was 161 mmol/day (conversion to salt: 9.5 g/day) on an unrestricted diet and 87 mmol/day (5.1 g/day) on a low-salt diet, with a median decrease in the urinary Na excretion of 78 mmol/day (4.6 g/day). In normotensive subjects, the mean decrease in BP was 2.0/1.0 mmHg, and the decrease in the urinary Na excretion was 74 mmol/day (4.4 g/day). A recent analysis showed a clear quantitative relationship between the degree of decrease in salt intake and BP in a salt intake range of 3–12 g/day (*27*). In hypertensives, the systolic BP is considered to decrease by about 1 mmHg with each decrease in salt intake of 1 g/day. If a person who has consumed salt at 12 g/day restricts salt intake to 6 g/day, a considerable decrease in BP is expected with a consequent decrease in the dose of antihypertensive medication and prevention of cardiovascular diseases.

There have been no large-scale clinical studies about the effects of salt reduction on BP in Japan. However, many short-term clinical studies have shown that the restriction of salt intake effectively lowers BP in hypertensive Japanese (*20*, *28–31*). The average reduction in mean BP with a low-salt diet in those studies was 5–10 mmHg, which was comparable to the results of a meta-analysis. It has been shown that there is a racial difference in the salt sensitivity of BP, with the sensitivity in blacks being greater than that in whites (*32*). Although there are no studies directly comparing the salt sensitivity among Japanese and other races, the salt sensitivity of BP in Japanese may be intermediate between those of blacks and whites.

However, the responses of BP to a decrease in salt intake show marked individual variation. The depressor effect of reduction in salt intake has been shown to be large in the elderly, patients with renal dysfunction, those with severe hypertension, and those with low-renin hypertension (*28*, *32*). However, because hypertension arises through the intricate interplay of many factors, it is not easy to predict the salt sensitivity of BP in individual patients, and evidence is not sufficient to warrant individualized recommendations of salt restriction.

Decreases in BP due to salt restriction are observed 24 h a day (*29*). Also, it has been reported that many salt-sensitive hypertensives are non-dippers, who show only small nocturnal decreases in BP, on a high-salt diet, but become dippers

Table 4. Antihypertensive Effects of Reductions in Salt Intake in Large-Scale Clinical Studies

Study (year of publication)	Subjects	Observation period	Group	Number of subjects	Intake or urinary excretion of salt (g/day)			Systolic BP (mmHg)			Diastolic BP (mmHg)		
					Before	After	Difference	Before	After	Difference	Before	After	Difference
HPT (1990) (*26*)	Healthy adults	6 months	Control	196	7.66	6.97	−0.69	123.9	121.8	−1.7±0.9	83.0	80.0	−0.4±0.7
			Salt reduction	196	7.55	5.89	−1.66	124.0	120.2	p=0.126	82.6	79.2	p=0.664
		3 years	Control	196	7.66	7.66	0	123.9	121.0	0.1±1.0	83.0	80.0	0.2±0.8
			Salt reduction	196	7.55	6.81	−0.74	124.0	121.2	p=0.885	82.6	79.8	p=0.8
TOHP-I (1992) (*21*)	Healthy adults*	6 months	Control**	417	9.20			125.1	121.9	−1.69	83.9	80.6	−0.85
			Salt reduction**	327	9.09	6.50	−2.59	124.8	119.9	p<0.01	83.7	79.6	p<0.05
TOHP-II (1997) (*25*)	Healthy adults	36 months	Control	596	11.95	11.33	−0.62	127.3	127.0	−0.4±0.4	85.8	83.4	−0.1±0.3
			Salt reduction	594	11.98	8.99	−2.99	127.7	127.0	p=0.24	86.1	83.2	p=0.68
TONE (1998) (*22*)	Healthy adults***	30 months	Control	147	8.53	8.51	−0.02		24.4%†	RR 0.69			
			Salt reduction	144	8.53	6.19	−2.34		37.8%†	p<0.001			
He *et al.* (2000) (*23*)	Healthy adults (from TOHP-I)	7 years	Control	70	8.69	7.5	−1.19	122.6	120.2	p=0.01	84.2	78.6	p=0.08
			Salt reduction	58	8.71	5.56	−3.15	122.7	117.0		83.8	76.6	
DASH-Sodium†† (2001) (*24*)	Healthy adults (including hypertensives)†††	30 days	DASH diet/Salt reduction	204	8.47	6.29	−2.18	128.1	126.8	p<0.001	83.1	82.5	n.s.
			Control/Salt reduction	208	8.29	6.24	−2.05	135.0	132.9	p<0.05	86.0	84.9	p<0.01

*Diastolic BP: 80–89 mmHg. **Frequency of hypertensives: 11.3% in the control group, 8.6% in the salt reduction group (RR 0.84, 95% CI 0.62–1.13). ***BP < 145/85 mmHg at ages 60–80 years. †Percentage of subjects not having reached the endpoint (diagnosis of hypertension, beginning of antihypertensive medication, cardiovascular event). ††Only the results of moderate salt reduction. †††BP > 120/80 mmHg, including mildly hypertensive (140–159/90–99 mmHg). BP, blood pressure; RR, relative risk; CI, confidence interval.

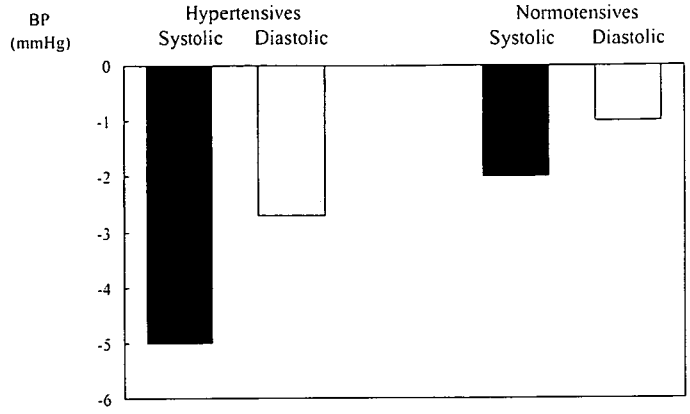

Fig. 3. *Effects of moderate salt reduction on BP according to a meta-analysis of randomized clinical trials (based on data of He et al. (27)).*

Table 5. Salt Reduction Accomplishment Rate in the TONE Study*

Salt reduction level	<5.6 g/day	>7.1 g/day
Control group	15.3%	67.7%
Salt reduction group	51.2%	29.7%
Weight control group	6.1%	79.6%
Salt reduction+weight control group	23.8%	49.0%

*From Espeland *et al.* (*36*) with modification.

with salt restriction (*31*).

Dietary intakes of potassium and sodium interact in the regulation of BP (*33*). Increasing potassium intake decreases BP mainly *via* natriuresis, and increasing sodium intake stimulates potassium excretion. A high potassium diet accomplished by means of fruit and vegetable intake is now widely recommended in the management of hypertension (*1*, *2*, *4*). The DASH-Sodium study has shown that a DASH (high potassium) diet and sodium restriction additively lower BP, but the effect of sodium restriction was greater under a normal diet than under the DASH diet (*24*). Thus a low sodium, high potassium diet is suitable for hypertensive subjects, but the BP-lowering effect of salt reduction appears to be attenuated by increasing potassium intake.

Restriction of salt intake also enhances the effects of some antihypertensive agents. This effect is particularly evident in inhibitors of the renin-angiotensin system. Sympatholytic agents are also expected to have similar effects.

An improvement of cardiovascular disease outcome can be expected with long-term restriction of sodium intake. The follow-up study of the TOHP-I and -II has shown that risk of a cardiovascular event is 30% lower among participants in the intervention (sodium restriction) group compared to those in the control group after adjustment for confounding factors (*34*). Therefore, sodium restriction not only lowers BP but may also reduce long-term risk of cardiovascular events.

Attainment and Maintenance of the Salt-Reduction

Lifestyle modifications, including salt restriction, are extremely important for the management of hypertension, but the difficulty of attaining and maintaining such changes is a problem (*35*). There have been few reports on the attainment rate of salt reduction in hypertensives, but in the TONE, a trial with elderly hypertensive subjects, the target of less than 5.6 g/day was attained by about half of the patients in the salt reduction guidance group and about 1/4 of the patients in the salt reduction plus weight control group (*36*) (Table 5). In Japan, in a trial in which physicians provided salt reduction guidance to hypertensives with a target of less than 6 g/day, mean salt intake decreased from 11.2 to 9.9 g/day, but the target was attained in only 12% of subjects (*10*, *35*). Also, while salt intake was lower in hypertensives intending to reduce salt intake than in those not intending, it was 9.4 and 10.6 g/day, respectively, with a minor difference (*11*). According to a report of the International Population Study on Macronutrients and Blood Pressure (INTERMAP), in Japanese subjects, among those practicing salt reduction, only 41.6% attained a target of less than 10 g/day, and the average salt intake estimated from the urinary Na excretion was 10.5 g/day (*37*). Therefore, attainment of the target of less than 6 g/day appears to be fairly difficult.

Limitations of long-term compliance to salt restriction and its effects have also been demonstrated. In the Treatment of Mild Hypertension Study (TOMHS), which provided 4-year lifestyle guidance to mildly hypertensive subjects, salt intake decreased by 2–3 g/day during the first year, but the decrease regressed to less than 1 g/day after 4 years (*38*). Moreover, a meta-analysis of long-term randomized interventional studies of 6 months or longer duration in normotensive and hyperten-

sive subjects showed that the mean decrease in salt intake was 2.1 g/day, and the mean decrease in BP was only 1.1/0.6 mmHg (*39*).

Salt-Reduction Target for the Management of Hypertension

Dietary salt appears to be related to hypertension, and excessive salt intake exerts adverse effects on the cardiovascular system independently of BP. While the antihypertensive effect of salt restriction is dependent on the degree of salt reduction, significant depressor effects have been confirmed at restriction levels of 6 g/day or less in large-scale clinical trials. Therefore, for the management of hypertension, the target of salt reduction should ideally be less than 6 g/day as in Western guidelines. In Japan, the target of salt reduction was set at 7 g/day or less in JSH 2000 (*3*) because of the traditionally high salt intake, but salt intake of Japanese has since decreased by about 1 g/day, so that it was considered reasonable to reset the target to less than 6 g/day in the subsequent JSH 2004 guidelines (*4*).

Presently, it appears to be difficult to attain the target of less than 6 g/day, but promotion of nationwide educational activities about the importance of the prevention and treatment of hypertension by salt restriction and its considerable preventive effect against cardiovascular and other diseases is considered to be a socially, economically, and medically important task. The establishment of feasible and effective measures by multi-faceted approaches is desirable for the attainment of the target of salt reduction.

Conclusions

Excessive salt intake is closely related to the occurrence and progression of hypertension, and it also exerts adverse effects on the cardiovascular system independently of BP. The depressor effect of salt restriction is dose-dependent, and despite marked individual variation, BP has been shown to decrease about 1 mmHg on average with each decrease in salt intake of 1 g/day. Salt reduction is important for the prevention and treatment of hypertension, and there is reasonable evidence in support of the current salt-restriction target of less than 6 g/day (Na < 100 mmol/day). Salt reduction is particularly important in Japan, a country with high salt intake, but attaining the new target has proven difficult in Japanese hypertensives. There is thus a need to establish new effective measures for attaining the target.

References

1. Chobanian AV, Bakris GL, Black HR, *et al*: The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC-7 report. *JAMA* 2003; **289**: 2560–2572.
2. Guidelines Committee: 2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003; **21**: 1011–1053.
3. Japanese Society of Hypertension Guidelines Subcommittee for the Management of Hypertension: Guidelines for the Management of Hypertension for General Practitioners. *Hypertens Res* 2001; **24**: 613–634.
4. Japanese Society of Hypertension: Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2004). *Hypertens Res* 2006; **29** (Suppl): S1–S105.
5. Kawano Y, Ando K, Matsuura H, Tsuchihashi T, Fujita T, Ueshima H: Rationale of salt restriction and its target for the management of hypertension, in Report of the Working Group for Dietary Salt Reduction of the Japanese Society of Hypertension. Tokyo, Japanese Society of Hypertension, 2006, pp 1–12 (in Japanese).
6. Eaton SB, Eaton SB 3rd, Konner MJ, *et al*: An evolutionary perspective enhances understanding of human nutritional requirement. *J Nutr* 1996; **126**: 1732–1740.
7. Dahl LK: Salt intake and salt need. *N Engl J Med* 1958; **258**: 1205–1208.
8. Intersalt Cooperative Research Group: Intersalt: an international study of electrolyte excretion and blood pressure: results for 24 hour urinary sodium and potassium excretion. *BMJ* 1988; **297**: 319–328.
9. Lifestyle-Related Disease Control Section, General Affairs Division, Health Bureau, Ministry of Health, Labor and Welfare: An outline of the results of the 2004 National Health and Nutrition Survey (in Japanese). http://www.mhlw.go.jp/houdou/2006/05/h0508-1a.html
10. Kawano Y, Minami J, and Takishita S: Evaluation of the effects of mineral intake in hypertensive patients by blood pressure monitoring: combination of K, Ca, and Mg supplementation and Na restriction. *Ther Res* 1998; **19**: 1517–1520 (in Japanese).
11. Ohta Y, Tsuchihashi T, Ueno M, *et al*: Relationship between the awareness of salt restriction and the actual salt intake in hypertensive patients. *Hypertens Res* 2004; **27**: 243–246.
12. Fujita T (ed): Salt and Hypertension. Tokyo, Nihon Igaku Shuppan, 2002 (in Japanese).
13. Stamler J, Rose G, Elliott P, *et al*: Findings of the international cooperative INTERSALT study. *Hypertension* 1991; **17** (Suppl 1): I-9–I-15.
14. Kawasaki T, Delea CS, Bartter FC, *et al*: The effect of high-sodium and low-sodium intakes on blood pressure and other related variables in human subjects with idiopathic hypertension. *Am J Med* 1978; **64**: 193–198.
15. Fujita T, Ando K, Ogata E: Systemic and regional hemodynamics in patients with salt-sensitive hypertension. *Hypertension* 1990; **16**: 235–244.
16. de Wardener HE, MacGregor GA: Harmful effects of dietary salt in addition to hypertension. *J Hum Hypertens* 2002; **16**: 213–223.
17. Tumilehto J, Jousilahti P, Rastenyte D, *et al*: Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study. *Lancet* 2001; **357**: 848–851.
18. Nagata C, Takatsuka N, Shimizu N, *et al*: Salt intake and risk of death from stroke in Japanese men and women.

Stroke 2004; **35**: 1543–1547.
19. He J, Ogden LG, Bazzano LA, *et al*: Dietary sodium intake and incidence of congestive heart failure in overweight US men and women: First National Health and Nutrition Examination Survey Epidemic Follow-up study. *Arch Intern Med* 2002; **162**: 1619–1624.
20. Ito K, Kuroda K, Tsuchiya M, *et al*: Gradient salt reduction and its antihypertensive effect in patients with essential hypertension. *Magnesium* 1982; **1**: 224–231.
21. The Trials of Hypertension Prevention Collaborative Research Group: The effects of nonpharmacologic interventions on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. *JAMA* 1992; **267**: 1213–1220.
22. Whelton PK, Appel AJ, Espeland MA, *et al*: Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). *JAMA* 1998; **279**: 839–846.
23. He J, Whelton PK, Appel LJ, *et al*: Long-term effects of weight loss and dietary sodium reduction on incidence of hypertension. *Hypertension* 2000; **35**: 544–549.
24. Sacks FM, Svetkey LP, Vollmer WM, *et al*: Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med* 2001; **344**: 3–10.
25. The Trials of Hypertension Prevention Collaborative Research Group: Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure: the Trials of Hypertension Prevention, phase II. *Arch Intern Med* 1997; **157**: 657–667.
26. Hypertension Prevention Trial Research Group: The Hypertension Prevention Trial: three-year effects of dietary changes on blood pressure. *Arch Intern Med* 1990; **150**: 153–162.
27. He FJ, MacGregor GA: Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. *J Hum Hypertens* 2002; **16**: 761–770.
28. Oshima T, Matsuura H, Kido K, *et al*: Factors determining sodium chloride sensitivity of patients with essential hypertension: evaluation by multivariate analysis. *J Hypertens* 1989; **7**: 223–227.
29. Kawano Y, Abe H, Kojima S, *et al*: Different effects of alcohol and salt on 24-hour blood pressure and heart rate in hypertensive patients. *Hypertens Res* 1996; **19**: 255–261.
30. Ando K, Takahashi K, Shimosawa T, *et al*: Effect of aging on salt sensitivity of blood pressure in patients with essential hypertension. *Clin Exp Nephrol* 1999; **1**: 18–22.
31. Uzu T, Ishikawa K, Fujii K, *et al*: Sodium restriction shifts circadian rhythm of blood pressure from nondipper to dipper in essential hypertension. *Circulation* 1997; **96**: 1859–1862.
32. Luft FC, Miller JZ, Grimm CE, *et al*: Salt sensitivity and resistance of blood pressure: age and race as factors in physiological responses. *Hypertension* 1991; **17**: I-102–I-108.
33. Adrogue HJ, Madias NE: Sodium and potassium in the pathogenesis of hypertension. *N Engl J Med* 2007; **356**: 1966–1978.
34. Cook NR, Cutler JA, Obarzanek E, *et al*: Long term effects of dietary sodium restriction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ* 2007; **334**: 885–888.
35. Kawano Y, Omae T: Lifestyle modifications in the management of hypertension: effects and limitations. *CVD Prevention* 1998; **1**: 336–346.
36. Espeland MA, Whelton PK, Kostis JB, *et al*: Predictors and mediators of successful long-term withdrawal from antihypertensive medications. TONE Collaborative Research Group. Trial of Nonpharmacologic Intervention in the Elderly. *Arch Fam Med* 1999; **8**: 228–236.
37. Tsunematsu N, Ueshima H, Okuda N, *et al*: The actual amount of reductions in salt intake among those on a restricted salt diet: from the INTERMAP Japan. *J Jpn Soc Prev Cardiovasc Dis* 2004; **39**: 149–155.
38. Neaton JD, Grimm RH Jr, Prineas RJ, *et al*: Treatment of Mild Hypertension Study: final results. *JAMA* 1993; **270**: 713–724.
39. Hooper L, Bartlett C, Smith GD, *et al*: Systematic review of long term effects of advice to reduce dietary salt in adults. *BMJ* 2002; **325**: 628–632.

Report

Report of the Working Group for Dietary Salt Reduction of the Japanese Society of Hypertension: (2) Assessment of Salt Intake in the Management of Hypertension

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Restriction of dietary salt is widely recommended in the management of hypertension, but assessment of individual salt intake has drawn little attention. The understanding of salt intake is important as a guide for optimizing salt-restriction strategies. However, precise evaluation of salt intake is difficult. More reliable methods are more difficult to perform, whereas easier methods are less reliable. Thus, the method to assess salt intake should be determined as the situation demands. The Working Group for Dietary Salt Reduction of the Japanese Society of Hypertension recommends the assessment of individual salt intake using one of the following methods in the management of hypertension. 1) The measurement of the sodium (Na) excretion from 24-h urine sampling or nutritionist's analysis of the dietary contents, which are reliable but difficult to perform, are suitable for facilities specializing in the treatment of hypertension. 2) Estimation of the Na excretion from the Na/creatinine (Cr) ratio in spot urine is less reliable but practical and is suitable for general medical facilities. 3) Estimation using an electronic salt sensor equipped with a calculation formula is also less reliable but is simple enough that patients can use it themselves. The patients are considered to be compliant with the salt-restriction regimen if salt intake measured by whichever method is less than 6 g (100 mmol)/day. (*Hypertens Res* 2007; 30: 887–893)

***Key Words*: salt intake, food weighing, food questionnaire, urinary sodium excretion, hypertension**

Introduction

Excessive salt or sodium (Na) intake causes hypertension, and restriction of salt intake is widely recommended for the management of hypertension. In the 2004 version of the Japanese Society of Hypertension (JSH) Guidelines for the Management of Hypertension (JSH 2004), the target of salt restriction was tightened from 7 g/day or less to less than 6 g/day (*1*). On the other hand, while the salt intake in Japan is decreasing, it is still high, being about 11 g/day (*2*). Also, salt intake shows considerable individual variation and daily fluctuation in the same individual.

An understanding of individual salt intake is considered to be important for successful salt reduction, because it leads to appropriate guidance and judgement of whether the target of salt restriction has been attained. However, there are several problems with the assessment of salt intake, and its imple-

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Table 1. Evaluation Methods of Salt Intake

Evaluation method	Reliability	Convenience
Evaluations based on dietary contents		
Weighing method	◎	×
Questionnaire method	○	△
Measurement before intake	◎	×
Evaluation using test paper or salt sensor	×	◎
Evaluations based on the measurement of urinary Na excretion		
24-h pooled urine	◎	×
Nighttime or early morning urine	○	△
The second urine sample after waking	○	△
Spot urine	△ (○*)	○
Evaluation using test paper or salt sensor	× (△**)	◎

◎, excellent; ○, good; △, fair; ×, poor. *When a formula for the estimation of the daily creatinine (Cr) excretion is used. **When a salt sensor installed with the formula is used.

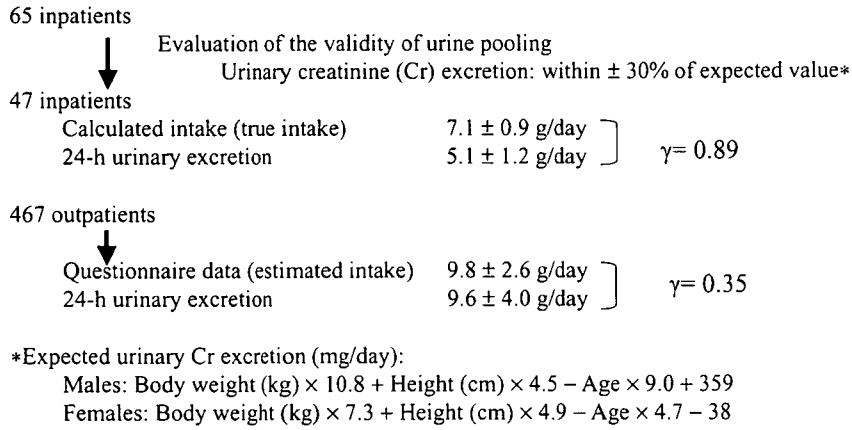

Fig. 1. *Calculated dietary salt intake and 24-h urinary excretion in inpatients and estimated salt intake based on a questionnaire and 24-h urinary excretion in outpatients (from data of Fukumoto et al. (9))*

mentation is often difficult. Most of the current guidelines for the management of hypertension do not mention the methodological aspect of assessing salt intake. While the guidelines of the World Health Organization and International Society of Hypertension (WHO/ISH) state that counseling by a skilled nutritionist and monitoring of the urinary Na level are necessary in most cases, they do not mention specific methods for these purposes (*3*).

This report describes variations and characteristics of salt intake–assessment methods and proposes the guidelines for the assessment of salt intake for the management of hypertension as part of the activities of the Working Group for Dietary Salt Reduction of the JSH. The Japanese version of the working group report has been published previously (*4*).

Methods to Assess Salt Intake

There are several methods for the assessment of salt intake. In general, however, the choice of method involves a compromise between accuracy and ease-of-use, with relatively precise methods being difficult to perform, and simpler methods being less reliable (Table 1). Also, because salt intake is not fixed in each person, its assessment is naturally subject to limitations in accuracy (*5*). Sodium, which is important in the occurrence and progression of hypertension, is primarily ingested as salt (NaCl). Since 1 g of salt is equivalent to 17 mmol (17 mEq) of Na, 6 g of salt is about 100 mmol (100 mEq) of Na. In terms of relative weight, a given amount of Na in salt would weigh 2.5 times more than the equivalent amount as pure Na (for example, 400 mg of Na is equal to 1 g of salt).

Assessment Based on Dietary Contents

Weighing Method

This method, by which salt intake is estimated by weighing

Table 2. Formula for the Estimation of the 24-h Sodium (Na) Excretion from Nighttime Urine Data and Estimated Cr Excretion (*18*)

24-h Na excretion (mmol/day)	
Male	$0.634 \times (Na_n/Cr_n) \times Pr.UCr_{24} + 104.7$
Female	$0.682 \times (Na_n/Cr_n) \times Pr.UCr_{24} + 62.6$
	Na_n: Na concentration in nighttime urine (mEq/L)
	Cr_n: Cr concentration in nighttime urine (g/L)
	$Pr.UCr_{24}$: estimated 24-h urinary Cr excretion (g/day)
	Male $0.027 \times$ LBM
	Female $0.022 \times$ LBM
	LBM = Body weight (kg) − Body fat mass (kg)

Cr, creatinine; LBM, lean body mass.

Table 3. Formula for the Estimation of the 24-h Na Excretion from Data in the Second Urine Sample after Waking and Estimated Cr Excretion (*19*)

24-h Na excretion (mmol/day) = $16.3 \times \sqrt{(Na_{SMU}/Cr_{SMU}) \times Pr.UCr_{24}}$
Na_{SMU}: Na concentration in 2nd urine sample after waking (mEq/L)
Cr_{SMU}: Cr concentration in 2nd urine sample after waking (mg/L)
$Pr.UCr_{24}$: estimated 24-h urinary Cr excretion (mg/day)
Male Body weight (kg) × 15.1 + Height (cm) × 7.4 − Age × 12.4 − 80
Female Body weight (kg) × 8.6 + Height (cm) × 5.1 − Age × 4.7 − 75

Cr, creatinine.

the food ingested by each subject, is highly reliable (*6*). Concerning Na, the values estimated from the food weight based on the Standard Tables of Food Composition in Japan (*7*) have been shown to be close to, and strongly correlated with, the actual values measured in the ingested food. However, this method is complicated and requires calculation by a nutritionist. Also, a 1-day survey is considered to be insufficient for accurate assessment of salt intake, which changes from day to day.

Questionnaire Method

By this method, dietary salt intake is estimated from data obtained by a questionnaire or interview performed over one to several days. While it is easier than the weighing method, this method still requires calculation by a nutritionist. Although there has been a report suggesting that its reliability is comparable to that of the weighing method (*8*), its accuracy is considered to be slightly inferior. Also, while the mean salt intake estimated by interview has been reported to agree with the value based on the 24-h urinary Na excretion, its correlation to actual salt intake was not high, and actual salt intake may be underestimated by this method (*9*) (Fig. 1).

Measurement before Intake

In the measurement-before-intake method, daily salt intake is determined by measuring or estimating the salt content of food to be eaten before ingestion. If performed precisely, this method is highly reliable. Hospital meals and test meals for clinical research are examined by this method. Since the salt intake is revealed before ingestion of the meal, this method is useful for the practice of salt reduction. However, it is inconvenient to measure the salt content before each meal. Moreover, accurate determination requires calculation by a nutritionist, although rough calculation can be performed by untrained individuals.

Measurement of the Urinary Na Excretion

Measurement by 24-h Urine

In this method, urine is collected for 24 h, and salt intake is assessed by determining the urinary Na excretion. This method is considered to be reliable and is used in many clinical and epidemiological studies, including the international cooperative Intersalt study (*10*). However, it is relatively difficult to perform because of the necessity of 24-h urine sampling, and inadequate urine pooling leads to underestimation of salt intake. The nuisance of 24-h urine collection is slightly mitigated by the use of a portable urine sampler (Urinmate®), which allows fractionated partial urine sampling (*11*). For accurate assessment of salt intake, even the 24-h urine sampling method is insufficient if performed over only 1 day, and thus measurement over several days is considered necessary (*11*, *12*). In addition, while most of the ingested Na is excreted in urine, part of it is contained in feces or sweat. Salt intake determined from the Na excretion in 24-h urine has been shown to be 0.5–3 g/day lower than the true intake, and

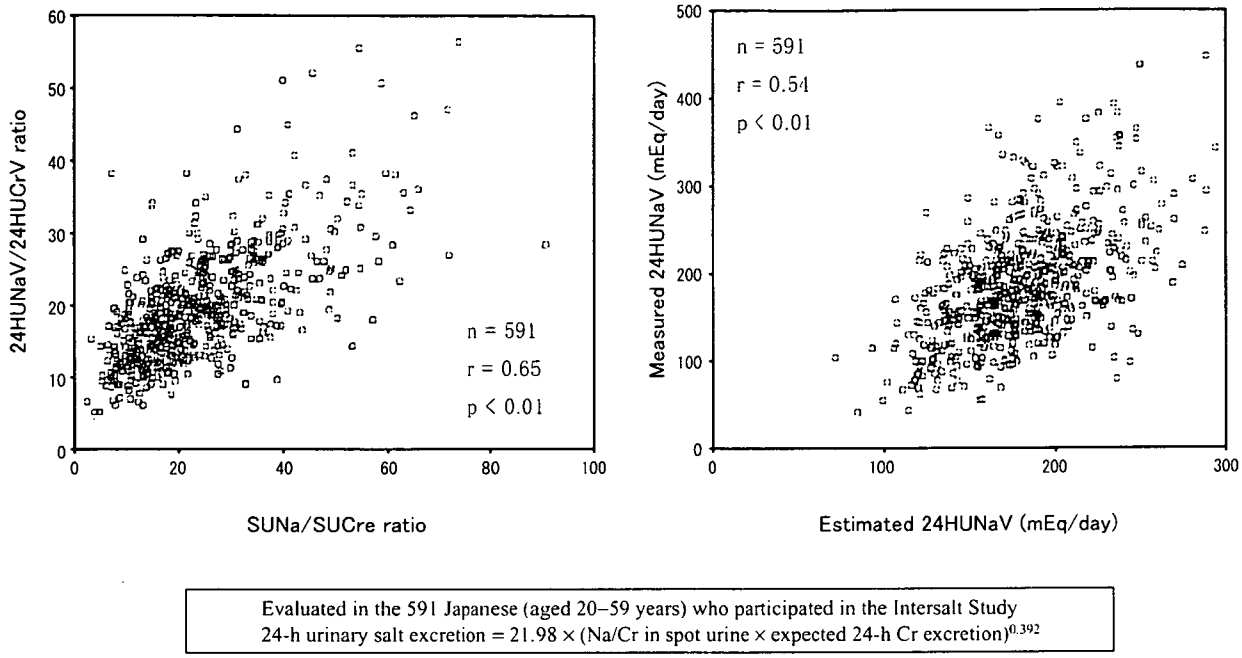

Fig. 2. *Evaluation of salt intake by spot urine. The left plot shows the relationship between the sodium (Na)/Cr ratio in spot urine (SUNa/SUCr ratio) and Na/Cr ratio in 24-h urine (24HUNaV/24HUCrV ratio). The right plot shows the relationship between the estimated 24-h urinary Na excretion by the calculation formula based on spot urine data (Estimated 24HUNaV) and measured 24-h urinary Na excretion (Measured 24HUNaV) (from Tanaka et al. (21) with modification).*

Table 4. Formula for the Estimation of the 24-h Na Excretion from Spot Urine Data and Estimated Cr Excretion (*21*)

24-h Na excretion (mmol/day) = $21.98 \times \{(Na_S/Cr_S) \times Pr.UCr_{24}\}^{0.392}$
Na_S: Na concentration in spot urine (mEq/L)
Cr_S: Cr concentration in spot urine (mg/L)
$Pr.UCr_{24}$: estimated 24-h urinary Cr excretion (mg/day)
$Pr.UCr_{24} = -2.04 \times$ Age $+ 14.89 \times$ Body weight (kg) $+ 16.14 \times$ Height (cm) $- 2244.45$

Cr, creatinine.

it is underestimated even with complete urine collection (*9*, *12*, *13*) (Fig. 1).

Measurement by Nighttime and Overnight Urine

Sampling of nighttime or early morning (overnight) urine, which consists of nighttime urine, is often employed, because it is easier than 24-h urine sampling and still provides a relatively long-term sample. In addition, Na excretion in nighttime urine is well correlated with that in 24-h urine (*14*, *15*). However, Na excretion exhibits diurnal fluctuation, being about 20% lower during the nighttime than the daytime (*16*, *17*). Therefore, simple estimation of salt intake from the Na excretion in nighttime urine is considered to result in greater underestimation than that in 24-h collected urine. However, the 24-h Na excretion estimated by the following calculation using Na excretions in nighttime urine has been reported to be in relatively close agreement with the value determined in 24-h sampled urine (*18*) (Table 2). In this method, 24-h Na excretion was estimated by applying Na and creatinine (Cr) excretions in nighttime urine and estimated 24-h urinary Cr excretion, calculated using the lean body mass from the height, body weight, and body fat mass.

Measurement by the Second Urine Sample after Waking

In another previously reported method to estimate the daily urinary Na excretion, the Na and Cr concentrations in the second urine sample after waking, and the 24-h urinary Cr excretion estimated from height, body weight, and age, are applied to a calculation formula (*19*) (Table 3). The Na excretion estimated by this method is closely correlated with the value determined in 24-h pooled urine. However, its clinical use may be limited by the condition that the urine must be col-

Table 5. Guidelines for the Evaluation of Salt Intake

Evaluation method	Recommendability	Major application target
Measurement of the Na excretion in 24-h pooled urine, or Weighing or questionnaire survey by a nutritionist	Although highly reliable and recommendable, these methods are complicated. Recommended if the patients' cooperation and the facility's ability are secured	Special facilities for hypertension treatment
Estimation as Na/Cr ratio based on measurement of Na and Cr in spot urine samples*	Although the reliability is relatively low, the method is simple and recommended as a practical evaluation procedure	Medical facilities in general
Estimation in early morning urine (nighttime urine) using an electronic salt sensor installed with calculation formula**	Although the reliability is relatively low, the method is recommendable. It is convenient and can be performed by the patients themselves	Patients themselves

*Early morning urine (nighttime urine) may also be used; the reliability is increased by the use of the calculation formula incorporating the estimated 24-h Cr excretion (Tables 2–4). **Methods using test paper or a simple salt sensor are convenient but unreliable, and quantitative evaluation is difficult. Cr, creatinine.

lected as the second urine sample after waking and before breakfast.

Measurement by Spot Urine

Evaluation of salt intake using a spot urine sample collected at any time would be easy to perform. The Na excretion per amount of Cr in spot urine correlates relatively well with the Na excretion per amount of Cr in 24-h urine sampling (*20, 21*) (Fig. 2), but the correlation between the Na excretion in spot urine and that in 24-h pooled urine is not very high (*15, 20*). However, the estimated Na excretion calculated using a formula incorporating the estimated 24-h urinary Cr excretion (Table 4) is reportedly close to the actually measured 24-h urinary Na excretion (*21*) (Fig. 2). The method to estimate the daily Na intake from the Na excretion per gram of Cr calculated from the Na and Cr concentrations in spot urine is not very reliable but is simple and considered to be clinically useful.

Assessment Using Test Paper or a Salt Sensor

This method, by which salt intake is estimated by measuring the salt concentration in spot urine or overnight urine using test paper or an electronic salt sensor, is the simplest (*22, 23*). The test paper or salt sensor usually detects chloride (Cl) rather than Na, and the results of examination of overnight urine using a test paper have been shown to be correlated with salt intake estimated by a nutritional survey (*23*). However, these should be regarded as unreliable and semi-quantitative methods. Recently, a urinary salt sensor, which estimates salt intake by analyzing data in overnight urine using a preinstalled calculation formula, has become available and is expected to increase the reliability (*24*).

The salt concentration in food can be determined using test paper or a salt sensor. In one previous report, however, the salt concentration of miso soup was found to be unrelated to the urinary salt level (*23*). The estimation of daily salt intake from the salt concentration of a single food item is thus considered to be difficult.

Assessment of Salt Intake for the Management of Hypertension

As mentioned above, there are several problems with the assessment of salt intake. Even measurement of the dietary salt content and the 24-h urine sampling method, which are considered to be highly reliable, are not sufficiently accurate and are difficult to perform (Table 1). Although the examination of the Na/Cr ratio in spot urine and the test paper method are easier to perform, they are less reliable. Calculation using a formula and the data of nighttime or spot urine is more reliable but more complicated. Also, it should be noted that salt intake determined from the urinary Na excretion or by the questionnaire method tends to be underestimated.

Despite these problems, the assessment of salt intake in individual patients is useful for motivating patients to reduce their salt intake, as well as for guiding their progress and evaluating the results. Such assessment is strongly recommended for the management of hypertension, because it provides patients with concrete numerical values of their salt intake. The use of more reliable methods is desirable, if possible, but even less reliable methods are of clinical value.

The Working Group for Dietary Salt Reduction of the JSH proposes the guidelines shown in Table 5 for the assessment of salt intake for the management of hypertension. In the management of hypertensive patients, salt intake should be evaluated individually using one of the following methods whenever possible.

1) The measurement of the Na excretion in 24-h pooled urine or a nutritionist's analysis of the dietary contents: These