

The Effects of the Habitual Consumption of Miso Soup on the Blood Pressure and Heart Rate of Japanese Adults: A Cross-sectional Study of a Health Examination

Koji Ito¹, Kenji Miyata², Masahiro Mohri³, Hideki Origuchi³ and Hideo Yamamoto³

Abstract

Objective It is recommended that middle-aged and elderly individuals reduce their salt intake because of the high prevalence of hypertension. The consumption of miso soup is associated with salt intake, and the reduced consumption of miso soup has been recommended. Recent studies have demonstrated that the consumption of miso soup can attenuate an autonomic imbalance in animal models. However, it is unclear whether these results are applicable to humans. This study examined the cross-sectional association between the frequency of miso soup consumption and the blood pressure and heart rate of human subjects.

Methods A total of 527 subjects of 50 to 81 years of age who participated in our hospital health examination were enrolled in the present study and divided into four groups based on the frequency of their miso soup consumption ([bowl(s) of miso soup/week] Group 1, <1; Group2, <4; Group3, <7; Group4, ≥7). The blood pressure levels and heart rates of the subjects in each group were compared. Furthermore, a multivariable analysis was performed to determine whether miso soup consumption was an independent factor affecting the incidence of hypertension or the heart rate.

Results The frequency of miso soup consumption was not associated with blood pressure. The heart rate was, however, lower in the participants who reported a high frequency of miso soup consumption. A multivariable analysis revealed that the participants who reported a high frequency of miso soup consumption were more likely to have a lower heart rate, but that the consumption of miso soup was not associated with the incidence of hypertension.

Conclusion These results indicate that miso soup consumption might decrease the heart rate, but not have a significant effect on the blood pressure of in middle-aged and elderly Japanese individuals.

Key words: salt, miso, blood pressure, heart rate, autonomic function

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Introduction

High salt diets are well known to be associated with increased blood pressure, particularly in patients with hypertension. This condition is termed salt-sensitive hypertension (1). Salt-induced sympathoexcitation has recently been reported to play an important role in its development (2, 3). A reduced salt intake is therefore highly recommended for

the prevention and treatment of hypertension. Miso (traditional Japanese soybean paste) is currently one of major sources of daily salt intake in the general Japanese population (4), and it has been recommended that individuals reduce their consumption of miso. On the other hand, miso has been reported to attenuate salt-induced hypertension in a model of salt-sensitive hypertension (5). We also reported that the habitual consumption of miso soup prevented salt-induced sympathoexcitation by reducing the autonomic im-

¹Department of Medical Informatics, Japan Community Health care Organization, Kyushu Hospital, Japan, ²Department of Health Examination, Japan Community Health care Organization, Kyushu Hospital, Japan and ³Department of Cardiology, Japan Community Health care Organization, Kyushu Hospital, Japan

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Correspondence to Dr. Koji Ito, ito-koji@kyusyu.jcho.go.jp

balance in mice (6, 7).

Miso, which is made from several fermented cereals, including soy beans, and soy protein, is reported to inhibit angiotensin converting enzyme (ACE) activity (8). The angiotensin system has a strong impact on blood pressure, including salt-sensitive hypertension. Numerous studies have demonstrated that the blockade of ACE activity reduced blood pressure and sympathetic activity (9-11). Miso is therefore thought to be able to decrease blood pressure and sympathetic activity via the inhibition of ACE activity.

Based on the results of previous studies, we expected that the habitual consumption of miso soup might have preferable effects on blood pressure or the heart rate by reducing the autonomic imbalance in humans. To test this hypothesis, we examined the cross-sectional association between the frequency of miso soup consumption and blood pressure or heart rate using data obtained from the health examinations of 527 middle-aged and elderly Japanese individuals. The frequency of miso soup consumption was examined using a self-reported questionnaire, and the study participants were classified into four groups ([bowl(s) of miso soup/week] Group 1, <1; Group2, <4; Group3, <7; Group4, ≥7). The blood pressure of the participants was measured using a sphygmomanometer, and the heart rate was evaluated based on an electrocardiogram that was obtained during a health examination in our hospital from October 2015 to March 2016. The blood pressure levels and heart rates of the subjects in each group were compared. In addition, a multivariable analysis was used to determine whether or not miso soup consumption independently associated with the incidence of hypertension or the heart rate. Age, gender, body mass index (BMI), smoking habit, the ratio of the patients with anti-hypertensive treatment, hemoglobin A1C (HbA1C), and estimated glomerular filtration ratio (eGFR) were evaluated as *a priori* identified covariates.

Materials and Methods

The study participants

This study was performed in accordance with the Declaration of Helsinki, Japanese privacy protection laws and the ethical guidelines for epidemiological studies established by the Ministry of Education, Science and Culture and the Ministry of Health, Labour and Welfare. This study also received approval from the Committee on Ethics of Clinical Research, Japan Community Healthcare Organization Kyushu Hospital (No. 389).

A cross-sectional study was performed of the middle-aged and elderly participants (50-81 years of age) who underwent a health examination at our hospital from October 2015 to March 2016. All of the participants gave their consent for the use of the self-reported questionnaire. The study participants completed the self-reported questionnaire regarding their medical history, the medicines that they were taking and their smoking history (smoking score: non-smoking, 0;

past smoking, 1; current smoking, 2). In addition, we also examined their frequency of miso soup consumption, the type of miso that they consumed (red, white, or combined), the main raw material of the miso (wheat, rice, soybean, or combined), and whether they used low-sodium miso. The patients were then divided into four groups according to the frequency of miso soup consumption (Group 1, <1 bowl of miso soup/week; Group 2, <4 bowls/week; Group 3, <7 bowls/week; Group 4, ≥7 bowls/week).

The measurement of the characteristics of the study participants

Trained staff measured the height and weight of the subjects. The BMI was calculated as follows: BMI=weight (kg)/height² (m²). Serum was collected to examine the subjects' HbA1C, eGFR, and total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL) and HbA1C levels and the eGFR.

The measurement of blood pressure and heart rate

The subjects' blood pressure was measured by skilled staff members using an automated-sphygmomanometer; their heart rate was evaluated using a 12-lead electrocardiogram. Hypertension was defined based on the presence of high blood pressure (a systolic blood pressure of >140 mmHg or a diastolic blood pressure of >90 mmHg) or a medical history of anti-hypertensive treatment. The definition of a higher heart rate was based on a value that was above the average heart rate of whole study population. The subjects were also divided into 3 groups based on their heart rate (lower quartile, interquartile range [IQR], upper quartile).

Statistical analysis

The differences in variables across Groups 1-4 were examined using an analysis variance (ANOVA) and compared using Tukey's multiple comparison test (continuous variables) and the chi-squared test (categorical variables). A multivariable analysis was performed to determine whether or not the frequency of miso soup consumption was an independent factor that affected the incidence of hypertension or the heart rate (the incidence of a higher relative heart rate). Age, gender, BMI, the ratio of patients with anti-hypertensive medication, smoking habit, eGFR, and HbA1C were evaluated as *a priori* identified covariates in the multivariable analysis.

All of the values were expressed as the mean ± SD. Two-tailed p values of <0.05 were considered to indicate statistical significance. All of the statistical analyses were performed using the EZR software program (Saitama Medical Center, Jichi Medical University) (12), which is a graphical user interface for the R software program (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is modified version of R commander that is designed to add the statistical functions that are frequently used in biostatistics.

Table 1. The Characteristics of the Study Participants.

Characteristics	total n=527		G1 n=105		G2 n=188		G3 n=177		G4 n=57		p value
	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD	
Age (y)	60.4	6.9	59.4	6.8	59.6	6.6	60.6	6.3	64.1	8.1	<0.01*
BMI (kg/m ²)	23.0	3.2	23.2	3.4	22.8	3.0	23.1	3.3	22.9	3.2	0.588
eGFR (mL/min/1.73m ²)	70.1	12.9	71.4	12.7	70.2	12.0	70.3	13.9	66.8	12.2	0.191
HbA1C (%)	5.88	0.59	5.90	0.54	5.80	0.49	5.93	0.72	5.92	0.51	0.176
TC (mg/dL)	211.4	34.4	213.6	40.6	210.4	34.9	210.5	31.4	213.3	29.1	0.834
TG (mg/dL)	111.5	69.2	110.8	60.4	110.8	73.7	112.9	74.1	110.6	52.9	0.990
LDL (mg/dL)	122.7	30.3	123.7	34.8	122.3	30.2	121.9	29.1	124.6	25.4	0.926
HDL (mg/dL)	61.5	16.2	61.7	16.5	61.4	17.2	61.8	15.5	60.7	15.0	0.973
smoking score	0.58	0.77	0.62	0.82	0.52	0.75	0.65	0.78	0.50	0.71	0.311
Male [n (%)]	304 (57.7)		70 (66.7)		97 (51.6)		104 (58.8)		33 (57.9)		0.095
anti-HT medication [n (%)]	138 (26.2)		26 (24.8)		44 (23.4)		48 (27.1)		20 (35.1)		0.375
anti-DM medication [n (%)]	40 (7.6)		9 (5.1)		11 (5.6)		16 (9.0)		4 (7.0)		0.746
anti-DL medication [n (%)]	73 (13.8)		15 (14.3)		25 (13.3)		23 (13.0)		10 (17.5)		0.802

G1: Group 1 (< 1 bowl / week of miso soup), G2: Group 2 (< 4 bowls / week of miso soup),

G3: Group 3 (< 7 bowls / week of miso soup), G4: Group 4 (≥ 7 bowls / week of miso soup)

BMI: body mass index, eGFR: estimated glomerular filtration ratio, HbA1C: hemoglobin A1C, TC: total cholesterol

TG: triglycerides, LDL: low-density lipoprotein cholesterol, HDL: high-density lipoprotein cholesterol

HT: hypertension, DM: diabetes mellitus, DL: dyslipidemia

smoking score: non-smoking, 0; past smoking, 1; current smoking, 2

Results

The participant characteristics

Table 1 summarizes the characteristics of the 527 participants in the study population. The mean (SD) age of the study participants was 60.4 (6.9) years. More than half of the study participants (57.7%) were men and 26.2% were using anti-hypertensive medications. The percentages of patients in Groups 1 (<1 bowl of miso soup/week) 2 (<4 bowls/week), 3 (<7 bowls/week) and 4 (≥7 bowls/week) were 19.9%, 35.7%, 33.6% and 10.8%, respectively. The mean (SD) systolic blood pressure was 130.1 (17.9) mmHg, the mean diastolic blood pressure was 80.3 (11.6) mmHg, and the mean heart rate was 63.6 (9.6) bpm. As a result, a relatively higher heart rate was defined as >63 bpm. After determining the median heart rate (62.5 bpm, IQR 57.0-68.0) the participants were divided into 3 groups according to the quartile of their heart rate (lower quartile, <57 bpm, IQR; 57-68 bpm, upper quartile: >68 bpm).

The association between miso soup consumption and the a priori identified covariates

Table 1 (G1-G4) shows the characteristics of study participants classified according to the frequency at which they consumed miso soup. The mean (SD) age of the study participants in Groups 1-4 was 59.4 (6.8), 59.6 (6.6), 60.6 (6.3) and 64.1 (8.1), respectively. The subjects in Group 4 were older than those in the other groups. The percentage of male participants in Groups 1-4, was 66.7%, 51.6%, 58.8% and 57.9%, respectively. With regard to the other variables, the

BMI values, gender, smoking habits (score), the TC, TG, LDL, HDL and HbA1C levels, the eGFR and the ratio of patients taking anti-hypertensive medications were similar among the four groups. Furthermore, there were no differences among the groups with regard to the ratio of the patients taking medications to treat diabetes mellitus and dyslipidemia. We found no differences among the groups regarding the type of miso that the subjects consumed (red, white, or combined), the main raw material of miso (wheat, rice, soybean, or combined), and the use of low-sodium miso (Table 2).

The association between miso soup consumption and blood pressure

There were no significant differences in the blood pressure of the subjects in the four groups. [(systolic blood pressure/diastolic blood pressure), Group 1, 130.5±17.4 mmHg; Group 2, 131.2±18.4 mmHg; Group 3, 129.9±17.8 mmHg; Group 4, 126.7±17.9 mmHg; p=0.395] (Figure). A multivariable analysis after adjusting for the *a priori* identified covariates [including age, gender, BMI, smoking habit (score), the eGFR and the HbA1C level] failed to show a relationship between the frequency of miso soup consumption and the incidence of hypertension (odds ratio 1.070, 95%CI 0.867-1.320, Table 3a). The difference in the type of miso and the main raw material of miso had no impact on the subjects' blood pressure (Table 4a).

The association between miso soup consumption and the heart rate

Although the blood pressure of the subjects' was unaffected, the heart rate of the participants who reported a high

Table 2. The Type, Main Raw Material, and Salinity of the Miso That the Subjects Consumed.

	total	type of miso [n(%)]			
		red miso	white miso	combined	unknown
G 1	105	16 (15.2)	80 (76.2)	4 (3.8)	5
G 2	188	35 (18.6)	137 (72.9)	16 (8.5)	0
G 3	177	31 (17.5)	128 (72.3)	17 (9.6)	1
G 4	57	8 (14.0)	41 (71.9)	7 (12.3)	1

	total	main raw material of miso [n(%)]				
		wheat	rice	soybean	combined	unknown
G 1	105	38 (36.2)	21 (20.0)	7 (6.7)	14 (13.3)	25
G 2	188	63 (33.5)	44 (23.4)	19 (10.2)	33 (17.6)	29
G 3	177	51 (28.8)	42 (23.7)	19 (10.7)	41 (23.2)	24
G 4	57	13 (22.8)	10 (17.5)	5 (8.8)	22 (38.6)	7

	total	solinity of miso [n]			
		unknown	regular salt	low salt	chi-squared
G 1	105	42	44	19	p=0.825
G 2	188	75	82	31	
G 3	177	60	86	27	
G 4	57	25	23	9	

G1: Group 1 (< 1 bowl / week of miso soup), G2: Group 2 (< 4 bowls / week of miso soup), G3: Group 3 (< 7 bowls / week of miso soup), G4: Group 4 (≥ 7 bowls / week of miso soup)

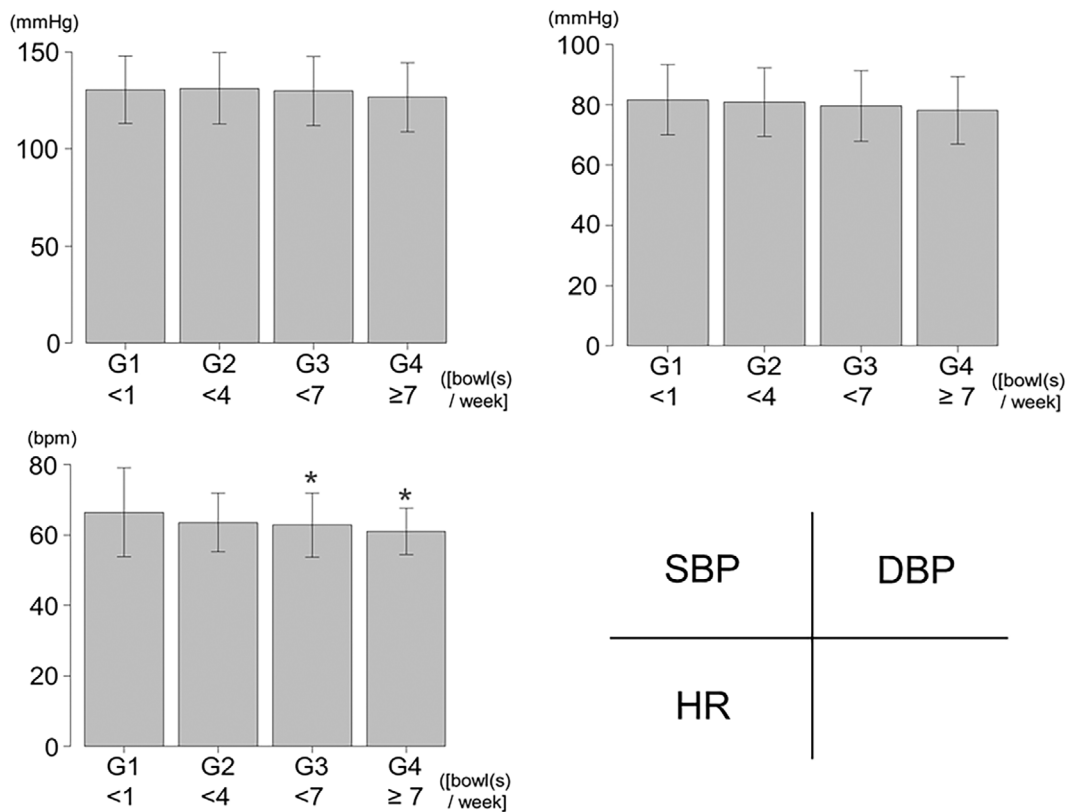


Figure. The blood pressure levels and heart rates of each group. G1: Group 1 (<1 bowl of miso soup/ week), G2: Group 2 (<4 bowls of miso soup/week), G3: Group 3 (<7 bowls of miso soup/week), G4: Group 4 (>7 bowls of miso soup/week). *p<0.05 versus G1.

Table 3. The Effects of Miso Consumption on the Incidence of Hypertension and the Heart Rate.

a				b				c			
HT Ds				High HR (>65 min)				Distribution of participants in each HR range (%)			
	odds ratio	95% C.I.	p value	(unadjusted)	odds ratio	95% C.I.	p value		Low miso (G 1)	High miso (G 2-4)	Chi-squared
(unadjusted)				(unadjusted)				HR < 57 /min (lower quartile)			
frequency of miso soup intake	1.090	0.908 - 1.320	0.342	frequency of miso soup intake	0.796	0.659 - 0.961	0.018*		19.8	22.7	< 0.01*
(adjusted model 1)				(adjusted model 1)				57 ≤ HR ≤ 68 (IQR)			
frequency of miso soup intake	1.070	0.877 - 1.300	0.520	frequency of miso soup intake	0.792	0.606 - 0.964	0.019*		38.7	50.7	
Age	1.040	1.010 - 1.070	< 0.01*	age	0.986	0.960 - 1.010	0.293		41.5	26.5	
Male	1.410	0.912 - 2.190	0.122	male	0.860	0.572 - 1.290	0.468				
BMI	1.290	1.210 - 1.380	< 0.01*	BMI	1.090	1.030 - 1.160	< 0.01*				
smoking score	0.736	0.559 - 0.969	0.029*	smoking score	0.881	0.686 - 1.130	0.320				
(adjusted model 2)				(adjusted model 2)				HR > 68 / min (upper quartile)			
frequency of miso soup intake	1.070	0.867 - 1.320	0.529	frequency of miso soup intake	0.795	0.652 - 0.968	0.022*				
age	1.040	1.010 - 1.070	0.022*	age	0.991	0.963 - 1.020	0.539				
male	1.370	0.872 - 2.140	0.173	male	0.928	0.611 - 1.410	0.726				
BMI	1.270	1.180 - 1.360	< 0.01*	BMI	1.100	1.030 - 1.170	0.033*				
smoking score	0.743	0.562 - 0.982	0.037*	smoking score	0.853	0.661 - 1.100	0.221				
eGFR	0.992	0.975 - 1.010	0.307	Anti-HT medication	1.280	0.832 - 1.980	0.260				
HbA1C	1.460	1.010 - 2.110	0.044*	eGFR	1.020	1.000 - 1.030	0.025*				
				HbA1C	1.190	0.863 - 1.630	0.294				

BMI: body mass index, eGFR: estimated glomerular filtration ratio, HbA1C: hemoglobin A1C, HT: hypertension
 smoking score: non-smoking, 0; past smoking, 1; current smoking, 2

Table 4. The Blood Pressure and Heart Rate Stratified according to the Type of Miso and the Raw Material of the Miso That the Subjects Consumed.

a					b					
Systolic blood pressure					Systolic blood pressure					
	red miso	white miso	combined	p value		wheat	rice	soybean	combined	p value
G 1	129.1 (21.1)	130.4 (17.4)	129.3 (4.3)	0.957	G 1	127.3 (17.4)	133.4 (18.3)	139.8 (4.3)	139.6 (24.4)	0.130
G 2	133.5 (14.8)	130.3 (19.3)	132.9 (18.5)	0.604	G 2	133.6 (15.0)	128.1 (17.9)	134.9 (22.0)	129.3 (16.1)	0.399
G 3	132.7 (15.2)	129.3 (18.8)	130.6 (15.1)	0.625	G 3	132.1 (19.7)	132.9 (16.6)	120.9 (14.7)	126.0 (15.9)	0.132
G 4	126.0 (18.6)	127.6 (17.5)	117.4 (17.1)	0.379	G 4	128.2 (22.4)	130.3 (10.2)	140.0 (8.9)	119.7 (19.3)	0.350

Diastolic blood pressure					Diastolic blood pressure					
	red miso	white miso	combined	p value		wheat	rice	soybean	combined	p value
G 1	79.6 (14.4)	81.6 (10.9)	81.5 (4.0)	0.817	G 1	79.1 (11.1)	83.4 (11.6)	90.4 (6.0)	85.0 (14.4)	0.209
G 2	80.9 (9.7)	80.7 (11.7)	81.6 (13.5)	0.960	G 2	82.3 (10.9)	79.3 (11.6)	81.6 (11.9)	79.6 (11.3)	0.507
G 3	79.7 (9.5)	79.3 (12.5)	81.8 (10.7)	0.722	G 3	80.8 (12.1)	81.8 (11.8)	77.1 (9.4)	76.2 (10.4)	0.135
G 4	75.0 (10.8)	79.2 (11.7)	74.1 (9.7)	0.405	G 4	79.0 (13.7)	83.3 (6.7)	85.0 (6.9)	73.9 (11.6)	0.285

Heart rate					Heart rate					
	red miso	white miso	combined	p value		wheat	rice	soybean	combined	p value
G 1	67.4 (8.4)	66.4 (13.8)	66.5 (13.7)	0.957	G 1	68.2 (13.6)	61.8 (10.4)	67.8 (12.9)	68.0 (18.3)	0.592
G 2	63.9 (7.4)	63.4 (8.6)	64.5 (9.2)	0.863	G 2	64.3 (7.9)	63.7 (9.2)	58.3 (4.5)	65.0 (8.3)	0.070
G 3	62.6 (9.7)	62.6 (9.1)	64.2 (8.6)	0.801	G 3	61.6 (6.5)	61.6 (9.1)	63.5 (6.6)	61.9 (9.8)	0.742
G 4	62.5 (4.8)	60.8 (7.1)	62.0 (6.0)	0.722	G 4	61.1 (6.7)	61.7 (7.2)	56.0 (8.9)	60.5 (5.9)	0.409

frequency of miso soup consumption was lower than that of the participants who reported a lower frequency of miso soup consumption (Figure). Furthermore, a multivariable analysis after adjusting for *a priori* identified covariates [including age, gender, BMI, smoking habit (score), and the ratio of the patients with anti-hypertensive treatment, the eGFR, and the HbA1C level] showed that the subjects who reported a high frequency of miso soup consumption were more likely to have a lower heart rate (odds ratio 0.795, 95%CI 0.652-0.968, Table 3b and c). The difference in the type of miso and the main raw material of the miso had no impact on the heart rate (Table 4b).

Discussion

The present study demonstrated a negative relationship between the frequency of miso soup consumption and the heart rate of middle-aged and elderly Japanese subjects. The subjects who reported a high frequency of miso soup consumption had a lower heart rate. In addition, after adjusting for *a priori* identified covariates, a multivariable analysis revealed that the frequency of miso soup consumption was independently associated with the heart rate. These results indicate that the habitual consumption of miso soup may be independently associated with the heart rate of middle-aged and elderly Japanese individuals.

The heart rate is a useful marker of the autonomic balance (13). An increased heart rate indicates high sympathetic activity and/or low parasympathetic activity, the so-called sympathetic nerve predominant state. In this study, we found that the participants who reported a high frequency of miso soup consumption had a lower heart rate, and that the high frequency of miso soup consumption was independently associated with a lower (below the average) relative heart rate. We previously demonstrated that miso soup attenuated the sympathetic nerve predominant state in mice through the direct and specific effects of miso on the autonomic function, blood pressure and heart rate (6, 7). We therefore thought that the habitual consumption of miso soup could alter the autonomic balance, resulting in a decrease in the heart rate. The present study was, however, designed as a cross-sectional study. We should therefore avoid claiming the existence of a causal relationship. Further studies will be needed to clarify the relationship between the habitual consumption of miso soup and the heart rate.

Generally, 1 bowl of miso soup contains 1 gram of salt and an increase in dietary salt intake is well known to contribute to the elevation of blood pressure (14). Thus, the moderate consumption of miso soup was recognized as being important in the prevention and treatment of hypertension. Reducing the consumption of miso soup was also reported to be an effective approach for decreasing the dietary salt intake in the general Japanese population (4). These results suggest the possibility that the habitual consumption of miso soup can lead to increased blood pressure. However, we did not observe a positive correlation between miso soup consumption and blood pressure elevation (or increases in the incidence of hypertension) in the present study. These results are consistent with those of a previous epidemiological study that revealed that miso soup consumption was not related to blood pressure (4). These results indicate that miso might not be involved in salt-induced blood pressure elevation. Miso was reported to have the potential to inhibit ACE activity (8). In addition, several studies have demonstrated that miso soup consumption attenuated salt-induced hypertension (5, 15). Although the findings obtained from these studies support the results of our study, further studies will be needed to clarify the detailed mechanisms underlying the absence of a relationship between miso soup consumption and blood pressure.

We successfully demonstrated the effects of the habitual consumption of miso soup on the heart rate. The heart rate that is observed with miso soup consumption might result from the alteration of the autonomic balance because miso has been reported to improve autonomic balance in mice (6, 7). The autonomic balance has an impact on blood pressure, and reduced sympathetic activity is expected to result in decreased blood pressure and a decreased incidence of hypertension. However, we were not able to demonstrate a decrease in blood pressure according to the frequency of miso soup consumption. The participants in the present study were undergoing a health examination. Most of the

participants did not have hypertension. Thus, it might have been difficult to observe the effects of the alteration of the autonomic balance on the blood pressure in the participants of the present study.

The present study is associated with several other limitations. First, the data regarding the frequency of miso soup consumption were self-reported, and there were some concerns with regard to the accuracy of the data. Second, the actual daily sodium intake (miso soup sodium concentration) was not evaluated in the present study. In the present study, the participants were undergoing a health examination, and the items that were investigated were limited. Thus, we could not evaluate items that reflected the daily sodium intake, such as urinary sodium excretion. Although we confirmed that there were no differences among the groups regarding the use of low-sodium miso, it would be necessary to evaluate the actual salt intake to strengthen the results of this study. Third, with the exception of the subjects' miso soup consumption habits, we did not examine the eating habits of the subjects in the present study. Thus, it is possible that there was another cause of the decreased heart rate. Fourth, all of the participants in the present study underwent a health examination. As a result, there may have been a selection bias. Fifth, it is possible that additional covariates (other than the *a priori* identified covariates) existed, such as socioeconomic status. Finally, the present study had a relative small sample size. Although further studies will be needed to clarify the direct effects of the habitual consumption of miso soup on the blood pressure and heart rate (including the autonomic balance), this is the first study to demonstrate that the heart rate of middle-aged and elderly Japanese individuals who had a habit of consuming miso soup was lower than the heart rate of those who did not.

In conclusion, miso soup consumption might decrease the heart rate but not have significant effect on blood pressure in middle-aged and elderly Japanese individuals.

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

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