Prevalence and Lifestyle Characteristics of Hypertensive Patients with Metabolic Syndrome Followed at an Outpatient Clinic in Fukuoka, Japan

Yuko OHTA¹⁾, Takuya TSUCHIHASHI¹⁾, Kimika ARAKAWA¹⁾, Uran ONAKA¹⁾, and Michio UENO¹⁾

A new guideline on metabolic syndrome (MS) in Japanese was introduced in 2005. The purpose of this study was to evaluate the prevalence and lifestyle characteristics of Japanese hypertensive patients with MS. Subjects were 290 patients (mean age: 64±11 years) who had been followed at our hospital. The waist circumference (WC) and body mass index (BMI) were assessed. Subjects who had BMI 25 kg/m² were defined as having BMI obesity, while abdominal obesity was defined as a WC 85 cm in men and 90 cm in women, respectively. Since all patients had hypertension, the definition of MS was made when the patient had abdominal obesity plus either dyslipidemia or glucose intolerance, or both. Among the subjects, 230 patients underwent 24-h home urine collection to measure urinary salt and potassium excretions. Dietary habits were also assessed by use of a questionnaire. Mean values of BMI and WC were 24.2±3.4 kg/m² and 87.1±9.6 cm, respectively. Among the total subject group, 39% patients were classified as having BMI obesity, 49% as having abdominal obesity, and 27% as having MS. BMI was significantly correlated with WC both in men (r=0.86; p<0.01) and in women (r=0.79; p<0.01). More men than women belonged to the BMI obesity (46% vs. 33%, p<0.05), abdominal obesity (63% vs. 39%, p<0.01) and MS (39% vs. 18%, p<0.01) groups. There were no significant differences in blood pressure between patients with and without MS, while patients with MS needed a greater number of antihypertensive drugs than those without MS. Mean urinary salt and potassium excretions were 8.9±3.8 g/day and 1.9±0.7 g/day, respectively. Urinary salt excretion of <6 g (100 mmol of sodium)/day was achieved in 20% of the subjects. Urinary salt excretion in the patients with MS was significantly higher than that in the patients without (10.1 \pm 4.2 vs. 8.5 \pm 3.6 g/day; p<0.01). Only 16% of the patients with MS achieved salt restriction (<6 g/day). The patients with MS had a significantly greater the chance to eat out than the patients without MS. They were also less aware of the need to increase their vegetable consumption. The results suggested that MS is prevalent in Japanese hypertensive patients. Patients with MS showed higher urinary salt excretion and needed more antihypertensive drugs to manage their blood pressure. Dietary counseling focusing not only on sodium restriction but also on the need to increase fruit and vegetable consumption seems to be important. (Hypertens Res 2007; 30: 1077-1082)

Key Words: metabolic syndrome, hypertensive patients, abdominal obesity, urinary salt excretion

From the ¹⁾Division of Hypertension, Clinical Research Center, National Kyushu Medical Center, Fukuoka, Japan.

Address for Reprints: Yuko Ohta, M.D., Division of Hypertension, Clinical Research Center, National Kyushu Medical Center, Jigyohama 1–8–1, Chuo-ku, Fukuoka 810–8563, Japan. E-mail: yukoo@qmed.hosp.go.jp

Received December 28, 2006; Accepted in revised form June 29, 2007.

Introduction

In recent years, the prevalence of glucose intolerance, hypercholesterolemia, and obesity has greatly increased in Japan (1). The concept and the definition of metabolic syndrome (MS) have been established by the National Cholesterol Education Program's Adult Treatment Panel III (2) and by WHO (3). Following these guidelines, a guideline on MS in Japanese was introduced in 2005 (4). MS has been reported to be associated with an increased risk for type 2 diabetes mellitus, cardiovascular disease and other manifestations of atherosclerotic disease (5–10). Since lifestyle factors can make a major contribution to the development of MS, dietary modification and enhanced physical activity may delay or prevent the disease (2, 11–13).

Among the relevant lifestyle factors, dietary sodium intake plays a major role in the development of hypertension. Although the National Nutrition Survey in Japan showed a tendency for decreased sodium intake in recent years, it still remains high (14). In the present study, we evaluated the prevalence and lifestyle characteristics—including sodium intake—of Japanese hypertensive patients with MS.

Methods

Participants were recruited from among hypertensive outpatients who visited the National Kyushu Medical Center, Fukuoka, Japan. Subjects included 290 patients, 167 women and 123 men, with a mean age of 64±11 years. The waist circumference (WC) and body mass index (BMI) were assessed. WC was measured at the umbilical level in standing subjects after normal expiration. Subjects who had a BMI $\geq 25 \text{ kg/m}^2$ were defined as having BMI obesity, while abdominal obesity was defined as a WC \geq 85 cm in men and \geq 90 cm in women, respectively. Blood pressure (BP) was measured with a sphygmomanometer by the doctors while the patients were seated. The averaged BP determined by two consecutive measurements was used for analysis. Body fat was measured by bioelectric impedance analysis (InBody 3.0; Biospace Tokyo Japan Inc., Tokyo, Japan). Since all patients had hypertension (systolic blood pressure [SBP] ≥130 mmHg and/or diastolic blood pressure [DBP] ≥85 mmHg or current use of antihypertensive drugs), the definition of MS was made when the patient had abdominal obesity plus either dyslipidemia (serum triglyceride \geq 150 mg/dL and/or serum high-density lipoprotein [HDL] cholesterol <40 mg/dL or the current use of anti-lipemic agents) or glucose intolerance (fasting plasma glucose $\geq 110 \text{ mg/dL}$ or the current use of anti-diabetic agents), or both.

In the second part of the analysis, 24-h urine samples were collected using a partition cup, which collects a 1/50 portion of the 24-h urine. If the 24-h creatinine excretion was within $\pm 30\%$ of the estimated values, the urine collection was considered successful. Subjects included 230 patients who under-

went successful 24-h home urine collection. Urinary salt, potassium, and creatinine were measured. Dietary habits focusing on the chance to eat out (≥ 1 /week) and the awareness of the need to increase vegetable and fruit consumption were also assessed by use of a questionnaire.

The detailed procedure of the study was explained and informed consent was obtained from each subject. This study was conducted following the institutional guidelines.

Statistical Analysis

Values are presented as the mean±SD. The differences in the variables were compared by one-way ANOVA or generalized linear model (GLM) when applicable. A χ^2 test was also utilized when appropriate. *p* values less than 0.05 were considered significant.

Results

The patient characteristics are shown in Table 1. The mean age was 64±11 years, and 58% of the patients were women. The mean values of BMI and WC were 24.2 ± 3.4 kg/m² and 87.1 ± 9.6 cm, respectively. Among the total patient group, 39% were classified as having BMI obesity, 49% as having abdominal obesity, and 27% as having MS. More men than women belonged to the BMI obesity (46% vs. 33%, p < 0.05), abdominal obesity (63% vs. 39%, p < 0.01) and MS (39% vs. 18%, p < 0.01) groups. BMI was significantly correlated with WC both in men (r=0.86; p<0.01) and in women (r=0.79; p < 0.01). Table 2 compares the profiles of hypertensive patients with and without MS. As a matter of course, WC, serum triglyceride and plasma glucose were significantly higher and HDL cholesterol was significantly lower in both male and female patients with MS than those without MS. The values of total cholesterol and uric acid in men and BMI in women were significantly higher in the MS group. On the other hand, there were no significant differences in BP between patients with and without MS, while patients with MS needed a greater number of antihypertensive drugs than those without MS (men: 2.0 ± 1.3 vs. 1.6 ± 1.0 , p=0.10; women: 2.1 ± 1.0 vs. 1.6 ± 1.1 , p < 0.05). As shown in Fig. 1, angiotensin II receptor blockers and α -blockers were prescribed more frequently in the patients with MS. Table 3 shows the characteristics of the patients with and without MS who underwent successful 24-h home urine collection. The mean urinary salt and potassium excretions of all patients who underwent successful 24-h home urine collection were 8.9 ± 3.8 g/day and 1.9 ± 0.7 g/day, respectively. A urinary salt excretion of <6 g (100 mmol of sodium)/day was achieved in 20% of the subjects. The urinary salt excretion in the patients with MS was significantly higher than that in the patients without MS (10.1±4.2 vs. 8.5±3.6 g/day; p<0.01). Only 16% of the patients with MS achieved salt restriction (<6 g/ day). The patients with MS had a significantly greater chance to eat out than the patients without MS (Table 3). They were

	Total	Men	Women
Number of patients	290	123	167
Age (years)	64±11	63±12	65 ± 10
BMI (kg/m ²)	24.2 ± 3.4	24.4±3.3	24.0 ± 3.5
Waist circumference (cm)	87.1±9.6	87.9 ± 8.6	86.5±10.2
Serum total cholesterol (mg/dL)	205 ± 30	199±31	210±28**
Serum triglyceride (mg/dL)	135±89	145 ± 84	127±93
Serum HDL cholesterol (mg/dL)	59±16	54 ± 14	62±17**
Serum creatinine (mg/dL)	$0.8 {\pm} 0.4$	1.0 ± 0.4	0.7±0.3**
Serum uric acid (mg/dL)	5.9 ± 1.4	6.7±1.3	5.3±1.1**
Plasma glucose (mg/dL)	102±19	103 ± 16	101±21
Systolic blood pressure (mmHg)	135±16	134±13	136 ± 17
Diastolic blood pressure (mmHg)	71±11	71 ± 10	71±11
Number of antihypertensive drugs	1.7 ± 1.1	1.8 ± 1.1	1.7 ± 1.1
Prevalence of BMI obesity (%)	39	46	33*
Prevalence of AO (%)	49	63	39**
Prevalence of MS (%)	27	39	18**

Table 1. Characteristics of the Patients

Values are means \pm SD. *p<0.05, **p<0.01 vs. men. BMI, body mass index; HDL, high-density lipoprotein; AO, abdominal obesity; MS, metabolic syndrome.

	Men		Women	
	Non-MS	MS	Non-MS	MS
Number of patients	75	48	137	30
Age (years)	65±11	61±12**	64±10	67±8
Body mass index (kg/m ²)	23.1±3.1	26.6±2.3	23.3 ± 3.2	27.1±3.2**
Waist circumference (cm)	84.2±8.2	$93.6 \pm 5.6^{\dagger\dagger}$	83.8±9.0	$98.4 \pm 6.4^{\dagger\dagger}$
Serum total cholesterol (mg/dL)	194±31	$207\pm30^{\dagger}$	212±27	201 ± 31
Serum triglyceride (mg/dL)	106 ± 58	$205\pm84^{\dagger\dagger}$	116±67	$177 \pm 156^{\dagger\dagger}$
Serum HDL cholesterol (mg/dL)	58±14	$48\pm13^{\dagger\dagger}$	63 ± 17	$55 \pm 15^{\dagger}$
Serum creatinine (mg/dL)	1.0 ± 0.4	1.0 ± 0.3	0.7 ± 0.3	0.7 ± 0.3
Serum uric acid (mg/dL)	6.5±1.3	$7.1 \pm 1.3^{\dagger}$	5.3 ± 1.1	$5.3 \pm 1.0^{\dagger}$
Plasma glucose (mg/dL)	99±12	$110\pm19^{\dagger\dagger}$	96±14	$120 \pm 34^{\dagger\dagger}$
Systolic blood pressure (mmHg)	135±12	132±15	135 ± 17	138±16
Diastolic blood pressure (mmHg)	71±11	72±9	71±11	70 ± 11
Number of antihypertensive drugs	1.6 ± 1.0	2.0 ± 1.3	1.6 ± 1.1	$2.1\pm1.0^{\dagger}$

Values are means ±SD. *p<0.05, **p<0.01 vs. non-MS. †p<0.05, ††p<0.01 vs. non-MS adjusted for age and body mass index. MS, metabolic syndrome.

also less aware of the need to increase their vegetable consumption (Table 3). Similarly, the patients with MS tended to be less aware of the need to increase fruit consumption (Table 3).

Discussion

In our present group of hypertensive patients, we found that the prevalence of MS was 39% for men and 18% for women. Epidemiological studies have shown that MS occurs in a wide variety of ethnic groups (12, 15-18). Data extracted from the

third National Health and Nutrition Examination Survey (12) have shown that the age-adjusted prevalence of MS is 24% as defined by the NCEP-ATP III definition of MS. The prevalence of MS in the Hungarian population (16) and in Okayama Prefecture (18) have been reported as 15% and 31% for men, and 9% and 4% for women, respectively. The prevalence of MS in the present study was higher than any of these previously reported values. This finding was expected given that all our subjects were hypertensive. Our study used the new definition of MS for Japanese, which primarily requires a WC \geq 85 cm in men and \geq 90 cm in women in addition to

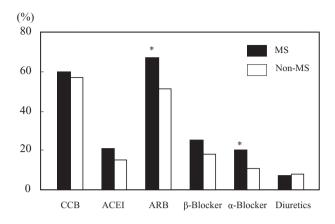


Fig. 1. Antihypertensive drugs used in the patients with and without MS. *p < 0.05 vs. non-MS. MS, metabolic syndrome; CCB, Ca antagonist; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

two or more of the following risk factors: hypertension, dyslipidemia, and glucose intolerance. These cutoff points of the WC are reported to correspond to a visceral fat area of 100 cm^2 at the umbilical level (19). Although the prevalence of MS varies by the definition used and the population studied, there is strong epidemiological evidence suggesting that the number of subjects with MS is increasing rapidly in many countries.

In the present study, the prevalence of abdominal obesity differed from that of BMI obesity; however, there was a significant association between abdominal obesity and BMI obesity. Based on the regression analysis, BMI of 25 kg/m² corresponded to a WC of 89.3 cm in men and 88.7 cm in women, respectively. These WC values were close to the criteria for abdominal obesity in the new guidelines on MS in Japanese.

Since multiple risk factors for cardiovascular disease exist in patients with MS, aggressive pharmacological as well as non-pharmacological intervention to achieve strict BP control should be required. In the present study, BP levels were comparable between the patients with and without MS, while the patients with MS required a greater number of antihypertensive drugs. Our results are consistent with previous studies in which obese patients required a greater number of antihypertensive drugs (20, 21). Among the lifestyle modifications recommended for hypertensive patients, sodium restriction seems to be the most important. One of the main findings of this study was that urinary salt excretion in the patients with MS was significantly higher than that in the patients without MS. The rate of achievement of urinary salt excretion < 6 g/day in the patients with MS was also low. We have previously reported that sodium intake in Japanese hypertensive patients remains fairly high, and that very few of our patients were able to achieve the sodium restriction recommended by the guidelines (22, 23). Recently, it has been reported that the

Table 3.	Characteristics	of the	Patients	with	and	without
MS Who	Underwent 24-h	Urine	Collection	n		

	Non-MS	MS
Number of patients	175	55
Sex (men/women)	66/109	37/18**
Age (years)	64±10	63±12
Body mass index (kg/m ²)	23.3 ± 2.9	26.8±2.5**
Body fat (%)	28 ± 7	29±6
Waist circumference (cm)	84.4 ± 8.3	95.0±6.3**
Systolic blood pressure (mmHg)	135±16	134 ± 14
Diastolic blood pressure (mmHg)	71±11	71 ± 10
Serum creatinine (mg/dL)	$0.8 {\pm} 0.4$	$0.9 {\pm} 0.4$
Urinary salt excretion (g/day)	8.5 ± 3.6	10.1±4.2**
Urinary potassium excretion (g/day)	$1.9 {\pm} 0.7$	$1.9 {\pm} 0.6$
Urinary creatinine excretion (mg/day)	944±274	$1,187 \pm 360$
Chance to eat out $(\geq 1/\text{week})$ (%)		
All	41.9	72.3††
Men	52.7	78.1^{+}
Women	35.5	60.0#
Awareness to increase vegetable consur-	mption (%)	
All	75.4	60.0^{\dagger}
Men	71.2	62.2
Women	78.0	55.6 [†]
Awareness to increase fruit consumption	on (%)	
All	73.1	52.7#
Men	59.1	43.2
Women	81.7	72.2

Values are means±SD. MS, metabolic syndrome. **p<0.01 *vs*. non-MS. $^{\#}p$ <0.01, $^{\dagger}p$ <0.05, $^{\dagger\dagger}p$ <0.01 *vs*. non-MS (adjusted for age).

prevalence of sodium-sensitive hypertension is significantly higher in patients with MS than in those without MS, and the patients with MS show higher homeostasis model assessment of insulin resistance (HOMA-IR) (24). These findings indicate the close association between sodium-sensitive hypertension and insulin resistance. Taken together, these results indicate that sodium restriction in the hypertensive patients with MS may have an additional therapeutic advantage to reduce the risk of cardiovascular complication. In addition, the present patients with MS had a significantly greater chance to eat out, and were also less aware of the need to increase vegetable and fruit consumption. However, the urinary potassium excretion in the patients with MS was equal to that in the patients without MS in the present study, in spite of the reduced awareness of the need to increase vegetable consumption in the former group. One possible explanation for this finding is that actual potassium intake tends to differ from the natural content of food because of the influence of cooking. Some previous studies have reported on the association between food intake and MS (11, 25-28). A whole array of dietary factors, such as high intakes of saturated fatty acids and low intakes of n-3 fatty acids, have been reported to contribute to the development of components of MS (26, 27). It has also been reported that the Dietary Approaches to Stop Hypertension (DASH) diet and the Mediterranean-style diet might be effective in reducing the prevalence of MS (11, 28). In addition, Riccardi and Rivellese introduced a diet with high amounts of vegetables, fruits, and legumes as well as reductions in saturated fat, salt, and alcohol as an optimal diet for MS (29). Thus, lifestyle modifications to target not only weight reduction, dietary sodium reduction, regular aerobic physical activity, and decreased alcohol consumption, but also increased fruit and vegetable consumption, may be help-ful in hypertensive patients with MS.

One of the limitations of this study is that all subjects were hypertensives, and thus we did not examine the prevalence and lifestyle characteristics of normotensive patients with MS. Another limitation is that the present investigation was conducted in a hospital in Fukuoka. Therefore, our observations may not reflect the prevalence and lifestyle characteristics of hypertensive patients with MS in the general population.

In conclusion, our findings suggest that MS is prevalent in Japanese hypertensive patients. We found that our patients with MS required more antihypertensive drugs to manage BP than our hypertensive patients without MS. Urinary salt excretion was also high in the hypertensive patients with MS. These results indicate that dietary counseling focusing not only on sodium restriction but also on the value of increasing fruit and vegetable consumption is important.

References

- Kubo M, Kiyohara Y, Kato I, *et al*: Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community: Hisayama study. *Stroke* 2003; 34: 2349–2354.
- 2. National Cholesterol Education Program (NCEP) Expert Panel: Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002; **106**: 3143–3421.
- Alberti KG, Zimmet PZ, for the WHO Consultation: Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998; 15: 539–553.
- Committee to Evaluate Diagnostic Standards for Metabolic Syndrome: Definition and the diagnostic standard for metabolic syndrome. *Nippon Naika Gakkai Zassi* 2005; 94: 794– 809 (in Japanese).
- Solymoss BC, Bourassa MG, Campeau L, *et al*: Effect of increasing metabolic syndrome score on atherosclerotic risk profile and coronary artery disease angiographic severity. *Am J Cardiol* 2004; **93**: 159–164.
- Lakka HM, Laaksonen DE, Lakka TA, *et al*: The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 2002; 288: 2709–2716.

- Laaksonen DE, Lakka HM, Niskanen LK, Kaplan GA, Salonen JT, Lakka TA: Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. *Am J Epidemiol* 2002; 156: 1070–1077.
- Isomaa B, Almgren P, Tuomi T, *et al*: Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001; 24: 683–689.
- Malik S, Wong ND, Franklin SS, *et al*: Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. *Circulation* 2004; **110**: 1245–1250.
- Takeuchi H, Saitoh S, Takagi S, *et al*: Metabolic syndrome and cardiac disease in Japanese men: applicability of the concept of metabolic syndrome defined by the National Cholesterol Education Program–Adult Treatment Panel III to Japanese Men—the Tanno and Sobetsu Study. *Hypertens Res* 2005; 28: 203–208.
- Azadbakht L, Mirmiran P, Esmaillzadeh A, Azizi T, Azizi F: Beneficial effect of a dietary approaches to stop hypertension eating plan on features of the metabolic syndrome. *Diabetes Care* 2005; 28: 2823–2831.
- Ford ES, Giles WH, Dietz WH: Prevalence of the metabolic syndrome among US adults: findings from the third national health and nutrition examination survey. *JAMA* 2002; 287: 356–359.
- Grundy SM, Cleeman JI, Daniels SR, *et al*: Diagnosis and management of the metabolic syndrome. An American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Executive summary. *Circulation* 2005; **112**: 2735–2740.
- Ministry of Health, Labour and Welfare, Japan: The National Nutrition Survey in Japan, 2002. Tokyo, Dai-ichi Shuppan Press, 2004, p 182.
- Nakanishi N, Shiraishi T, Wada M: Brachial-ankle pulse wave velocity and metabolic syndrome in a Japanese population: the Minoh study. *Hypertens Res* 2005; 28: 125–131.
- Császaf A, Kékes E, Abel T, Papp R, Kiss I, Balogh S: Prevalence of metabolic syndrome estimated by international diabetes federation criteria in a Hungarian population. *Blood Press* 2006; 15: 101–106.
- Aizawa Y, Kamimura N, Watanabe H, *et al*: Cardiovascular risk factors are really linked in the metabolic syndrome: this phenomenon suggests clustering rather than coincidence. *Int J Cardiol* 2006; **109**: 213–218.
- Miyatake N, Kawasaki Y, Nishikawa H, Takenami S, Numata T: Prevalence of metabolic syndrome in Okayama prefecture, Japan. *Intern Med* 2006; 45: 107–108.
- The Examination Committee of Criteria for 'Obesity Disease' in Japan, Society for the Study of Obesity: New criteria for 'obesity disease' in Japan. *Circ J* 2002; 66: 987–992.
- Saito I, Murata K, Hirose H, Tsujioka M, Kawabe H: Relation between blood pressure control, body mass index, and intensity of medical treatment. *Hypertens Res* 2003; 26: 711–715.
- Modan M, Almog S, Fuchs Z, Chetrit A, Lusky A, Halkin H: Obesity, glucose intolerance, hyperinsulinemia, and response to antihypertensive drugs. *Hypertension* 1991; 17: 565–573.

- 22. 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.
- Ohta Y, Tsuchihashi T, Onaka U, Eto K, Tominaga M, Ueno M: Long-term compliance of salt restriction in Japanese hypertensive patients. *Hypertens Res* 2005; 28: 953– 957.
- 24. Uzu T, Kimura G, Yamauchi A, *et al*: Enhanced sodium sensitivity and disturbed circadian rhythm of blood pressure in essential hypertension. *J Hypertens* 2006; **24**: 1627–1632.
- 25. Azadbakht L, Mirmiran P, Esmaillzadeh A, Azizi F: Dairy consumption is inversely associated with the prevalence of

the metabolic syndrome in Tehranian adults. *Am J Clin Nutr* 2005; **82**: 523–530.

- Vessby B: Dietary fat and insulin action in humans. Br J Nutr 2000; 83: S91–S96.
- 27. Connor WE: Importance of n-3 fatty acids in health and disease. *Am J Clin Nutr* 2000; **71**: S171–S175.
- Esposito K, Marfella R, Ciotola M, *et al*: Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA* 2004; **292**: 1440–1446.
- Riccardi G, Rivellese AA: Dietary treatment of the metabolic syndrome—the optimal diet. *Br J Nutr* 2000; 83: S143–S148.