

Subtypes of Metabolic Syndrome and of Other Risk Factors in Japanese Women With Erosive Esophagitis

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Abstract: Obesity and metabolic syndrome (MS) are strongly associated with erosive esophagitis (EE). The prevalence of MS and EE, and the distribution of adipose tissue have been known to differ markedly between men and women. Although the prevalence of EE in men with MS is known to be higher in visceral fat type MS (V-type MS) than in subcutaneous fat type MS (S-type MS), the association between EE and the types of MS in women with MS is unclear. This study was a cross-sectional study elucidating the association between EE and the types of MS in women with MS.

Subjects were 454 women with MS who underwent a regular health check-up. A distinction was made between V-type MS and S-type MS and the prevalence of EE and the association between EE and other data were elucidated.

Although there were some significant different factors in characteristics between V-type MS and S-type MS, there was no significant difference in the prevalence of EE between V-type MS and S-type MS. The presence of *Helicobacter pylori* (*H. pylori*) was significantly lower than in subjects with EE (13.7%) than in subjects without EE (41.9%). The frequency of hiatal hernia was significantly higher in subjects with EE (60.8%) than in subjects without EE (24.6%). Logistic regression analysis showed hiatal hernia (odds ratio: 4.673; 95% confidence interval: 2.448–8.920; $P < 0.001$), hemoglobin A1c (HbA1c) (2.325; 1.110–4.870; $P < 0.05$), and the presence of *H. pylori* (0.239; 0.101–0.567; $P < 0.005$) were significant predictors of the prevalence of EE.

V-type MS may not be such an important factor for the prevalence of EE in women with MS as in men with MS. The absence of *H. pylori*, hiatal hernia, and HbA1c may be more important for the prevalence of EE than the types of MS in women with MS.

(*Medicine* 93(28):e276)

Abbreviations: AFI = abdominal wall fat index, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body

Editor: Vijayaprasad Gopichandran.

Received: August 22, 2014; revised: October 26, 2014; accepted: October 27, 2014.

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The authors have no funding or conflicts of interest to disclose.

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ISSN: 0025-7974

DOI: 10.1097/MD.0000000000000276

mass index, CI = confidence interval, CT = computed tomography, CV = coefficient of variation, DBP = diastolic blood pressure, EE = erosive esophagitis, FPG = fasting plasma glucose, GERD = gastroesophageal reflux disease, GGT = γ -glutamyl transpeptidase, *H. pylori* = *Helicobacter pylori*, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, IGT = impaired glucose tolerance, LA = Los Angeles, LDL-C = low-density lipoprotein cholesterol, LES = lower esophageal sphincter, MS = metabolic syndrome, NGSP = National Glycohemoglobin Standardization Program, NS = not significant, OR = odds ratio, P = preperitoneal fat thickness, P = probability, S = subcutaneous fat thickness, SBP = systolic blood pressure, SD = standard deviation, S-type = subcutaneous fat type, T-CHO = total cholesterol, TG = triglyceride, UA = uric acid, V-type = visceral fat type, WC = waist circumference.

INTRODUCTION

The prevalence of gastroesophageal reflux disease (GERD), including erosive esophagitis (EE), has been increasing in both developed and developing countries, including Japan and Western countries.^{1–3} Various conditions, such as obesity, disturbance of the lower esophageal sphincter (LES), increase in gastric acid production, increase in intragastric pressure, and esophageal acid exposure, have been believed to play an important role in the development of GERD.^{4–9} The recent increase in numbers of obese individuals with lifestyle-related diseases associated with abnormalities in glucose metabolism and dyslipidemia, defined as metabolic syndrome (MS), has been alarming. Individuals with MS or visceral fat-dominant obesity are known to be likely to exhibit GERD or EE.^{4,10–13} Additionally, the prevalence of MS and EE was known to be higher in men than in women.^{14–16} Although there have been several studies on the association between MS and EE in the general population, there have been few reports on the association between types of MS and EE in the subjects with MS. The prevalence of EE in men with MS is reported to be different between visceral fat type MS (V-type MS) and subcutaneous fat type MS (S-type MS),¹⁷ but the association between EE and the types of MS in women with MS is unclear. Generally, subcutaneous and visceral fat-dominant MS types are not distinguished on medical check-ups, and individuals with both types of MS are treated in the same way. In this study, we divided women with MS into those with V-type MS and those with S-type MS by ultrasonography, and the association between EE and both types of MS was elucidated in Japanese women with MS.

METHODS

Study Subjects

Subjects were Japanese women with MS aged 30 to 85 years, who underwent a regular health check-up including physical examinations, blood-test screening, upper gastrointestinal endoscopy, and abdominal ultrasonography at our

hospital between April 2008 and March 2013. Most subjects were asymptomatic, healthy adults residing around Takamatsu city. Subjects who had a history of digestive tract surgery, who took medications such as H₂-receptor antagonist or proton pump inhibitors, or who were diagnosed with gastric or esophageal cancer at the time of upper gastrointestinal endoscopy were excluded from this study. Body weight and height of the subjects were determined, and body mass index (BMI) was calculated. Waist circumference (WC) was measured at the umbilical level. Venous blood samples were taken from all subjects at around 09:00 hours following a 12-hours overnight fast, and the levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ -glutamyl transpeptidase (GGT), total cholesterol (T-CHO), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), uric acid (UA), fasting plasma glucose (FPG), and hemoglobin A1c (HbA1c) (National Glycohemoglobin Standardization Program [NGSP]) were determined by common enzymatic methods using an auto analyzer (TBA-80FR; Toshiba Medical System, Tokyo, Japan). Assessment for *Helicobacter pylori* (*H. pylori*) infection was based on the detection of the *H. pylori*-specific antibody in serum. *H. pylori*-specific immunoglobulin G antibody titers were measured using the direct ELISA kit (E Plate "Eiken" *H. pylori* antibody; Eiken Kagaku, Tokyo, Japan). All subjects were informed that the clinical data obtained by medical check-up may be retrospectively analyzed, and informed consent was obtained. This study was approved by the Ethics Committees of the Kagawa Prefectural Cancer Detection Center.

Diagnosis of MS

The diagnostic criteria for MS adopted by the international diabetes federation and the adult treatment panel III criteria are used worldwide. We adopted the MS criteria proposed by the international diabetes federation¹⁸ to take account of ethnic specific values for WC. The MS criteria used in this study were as follows: WC must exceed 80 cm for women, and 2 or more of the following components must be present: (a) dyslipidemia: TG at least 150 mg/dL and/or HDL-C less than 50 mg/dL, or medicated for dyslipidemia; (b) hypertension: blood pressure at least 130/85 mm Hg or medicated for hypertension; and (c) impaired glucose tolerance: FPG at least 100 mg/dL or medicated for diabetes.

Upper Gastrointestinal Endoscopy

Standard endoscopic examination of the esophagus, stomach, and duodenum was performed by endoscopy specialists from the Gastroenterology Department of our hospital. All examiners had more than 10 years of experience in endoscopy, and were blinded to the results of the blood-test screening, physical, and physiological examinations. Upper gastrointestinal endoscopy was performed using a conventional single-channel endoscope (GIF-H260, -PQ260, or -XP260; Olympus, Tokyo, Japan). The severity of EE was graded from A to D according to the Los Angeles classification. We also considered a hiatal hernia to be present if the gastroesophageal junction extended at least 2 cm above the diaphragmatic hiatal impression during quit inspiration. Endoscopic findings from each subject were finally independently validated by a single endoscopy specialist.

Ultrasonography

Abdominal ultrasonography was performed in a morning fasting state. A Xario SSA-660A instrument with a 3.5 MHz

convex-array probe (Toshiba Medical System) was used for ultrasonography. We used the procedure reported by Suzuki et al,¹⁹ because there were significant correlations between the visceral fat area/the subcutaneous fat area ratio or visceral fat area on computed tomography (CT) and the pre-peritoneal fat thickness (P)/subcutaneous fat thickness (S) ratio or P observed on ultrasonography in their report.^{19,20} Scanning was performed at the optimal position, and the surface of the liver was kept almost parallel to the skin by breath-holding. The subcutaneous fat thickness was measured as the distance from the skin to the linea alba. The pre-peritoneal fat thickness was measured as the distance from the linea alba to the anterior surface of the liver (peritoneum). The maximal pre-peritoneal fat thickness was designated as P and subcutaneous fat thickness at the same time point as S. The abdominal wall fat index (AFI), defined as the P/S ratio, was calculated and AFI at least 1 and AFI less than 1 were considered as V-type MS and S-type MS, respectively. The intra-individual reproducibility of sonographic measurements [coefficient of variation (CV%)] was $8.8 \pm 3.1\%$ for S, $6.6 \pm 2.3\%$ for P, and $8.5 \pm 3.5\%$ for AFI. The criteria of fatty liver diagnosis by ultrasonography were as follows: the fatty liver must have liver–kidney echo contrast and liver brightness, as well as having deep attenuation and/or liver vessel blurring.²¹

Statistical Analysis

This study was a cross-sectional study elucidating the association between EE and the types of MS in women with MS. Data are expressed as means \pm standard deviation (SD). A probability (*P*) value of less than 0.05 was considered statistically significant. Comparison between 2 groups was performed using the χ^2 -test or Student's *t*-test for independent samples. *P*^a value was adjusted for confounding variables using analysis of covariance. Age, BMI, WC, and the factors that *P* value was less than 0.5 on univariate analysis were then subjected to a multivariate logistic regression analysis. The covariates used for the multivariate analysis were age, BMI, WC, HDL, LDL, HbA1c, alcohol consumption, *H. pylori*, and hiatal hernia. The odds ratios and 95% confidence interval were analyzed for each variable. All statistical analyses were performed using Med Calc Software (Broekstraat, Mariakerke, Belgium).

RESULTS

Subject Description

Figure 1 shows the flow diagram of the enrolment of subjects in this study. Of the 20,205 women who underwent

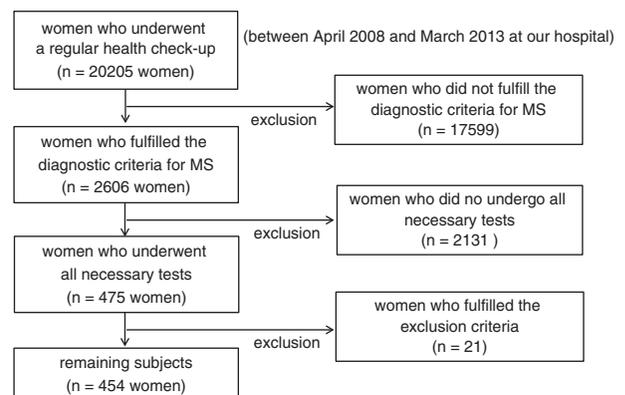


FIGURE 1. Flow diagram of the enrollment of subjects in this study. MS = metabolic syndrome.

a regular health check-up between April 2008 and March 2013 at our hospital, 2606 women fulfilled the diagnostic criteria for MS (data not shown). Of the 2606 subjects, 475 subjects underwent physical examinations, blood-test screening, upper gastrointestinal endoscopy, and abdominal ultrasonography. Of the 475 subjects, 21 fulfilled the exclusion criteria and were excluded, and the remaining 454 subjects were enrolled in this study. Subject characteristics are shown in Table 1; mean age was 58.3 ± 8.1 years, mean BMI was 26.0 ± 3.5 kg/m², and mean WC was 89.6 ± 7.1 cm of all subjects. Of the 454 subjects with MS, 50 (11.0%) and 404 (89.0%) had V-type MS or S-type MS, respectively. The frequency of the positive of *H. pylori* in all subjects was 38.8%. The frequency of hiatal hernia in all subjects was 28.6%. The frequency of EE in all subjects was 11.2%. In the EE group, the distribution of Los Angeles grades A, B, C, and D was 42, 9, 0, and 0 cases, respectively.

Comparison Between V-Type MS and S-Type MS in Women With MS

Comparison of clinical characteristics in women with MS between V-type MS and S-type MS is shown in Table 2, in

TABLE 1. Subjects Characteristics

Number	454
Age (years)	58.3 ± 8.1
BMI (kg/m ²)	26.0 ± 3.5
WC (cm)	89.6 ± 7.1
SBP (mm Hg)	130.9 ± 15.1
DBP (mm Hg)	77.8 ± 9.2
Hypertension, n (%)	375 (82.6%)
T-CHO (mg/dL)	210.5 ± 33.3
TG (mg/dL)	116.6 ± 60.6
HDL-C (mg/dL)	60.8 ± 14.3
LDL-C (mg/dL)	134.3 ± 30.2
Dyslipidemia, n (%)	307 (67.6%)
UA (mg/dL)	4.9 ± 1.1
FPG (mg/dL)	108.0 ± 17.2
HbA1c (NGSP) (%)	6.1 ± 0.7
IGT, n (%)	332 (73.1%)
ALT (IU/L)	27.7 ± 18.9
AST (IU/L)	24.4 ± 10.5
GGT (IU/L)	35.6 ± 36.4
Fatty liver, n (%)	236 (52.0%)
V-type MS, n (%)	50 (11.0%)
Alcohol consumption, n (%)	140 (30.8%)
Smoking habit, n (%)	18 (4.0%)
Presence of <i>Helicobacter pylori</i> , n (%)	176 (38.8%)
Hiatal hernia, n (%)	130 (28.6%)
EE (+/-), n (%)	51 (11.2%)
LA classification (grade A/B/C/D)	42/9/0/0

Data are means \pm standard deviation (SD).

ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, DBP = diastolic blood pressure, EE = erosive esophagitis, FPG = fasting plasma glucose, GGT = γ -glutamyl transpeptidase, HbA1c = hemoglobin A1c, HDL-C = high density lipoprotein cholesterol, IGT = impaired glucose tolerance, LA = Los Angeles, LDL-C = low density lipoprotein cholesterol, MS = metabolic syndrome, NGSP = National Glycohemoglobin Standardization Program, SBP = systolic blood pressure, T-CHO = total cholesterol, TG = triglyceride, UA = uric acid, V-type = visceral type, WC = waist circumference.

which the *P*^a value was adjusted for confounding variables, including age, BMI, WC, alcohol consumption, and smoking habit. HbA1c, TG, and UA were significantly higher in V-type MS than in S-type MS. ALT, AST, GGT, and the frequency of fatty liver were significantly higher in V-type MS than in S-type MS. The frequency of hiatal hernia was significantly higher in V-type MS than in S-type MS. In terms of the frequency of EE, V-type MS and S-type MS had 12.0% and 11.1%, respectively. There was no significant difference in the prevalence of EE between V-type MS and S-type MS.

Comparison Between With and Without EE in Women With MS

Comparison of clinical characteristics in women with MS between with and without EE is shown in Table 3. The frequency of the positive of *H. pylori* was significantly lower in subjects with EE than in subjects without EE. The frequency of hiatal hernia was significantly higher in subjects with EE than in subjects without EE.

Predictors of EE

Univariate and multivariate independent predictors of EE in women with MS are shown in Table 4. Of the 24 items related to the clinical background of subjects with and without EE, the presence of *H. pylori* and hiatal hernia were identified as significant factors by univariate analysis. Multiple logistic regression analysis was performed with age, BMI, WC, and 6 items that *P* value was less 0.5 by univariate analysis, such as HDL-C, LDL-C, HbA1c, alcohol consumption, presence of *H. pylori*, and hiatal hernia as covariates. Hiatal hernia, presence of *H. pylori*, and HbA1c were significant and independent predictors of the prevalence of EE. The odds ratios (95% confidence intervals, *P* value) for EE were as follows: hiatal hernia, 4.673 (2.448–8.920, *P* < 0.001), presence of *H. pylori*, 0.239 (0.101–0.567, *P* < 0.005), and HbA1c, 2.325 (1.110–4.870, *P* < 0.05).

DISCUSSION

This study aimed to investigate whether there is a difference in the prevalence of EE between V-type MS and S-type MS in Japanese women with MS. GERD and EE are particularly likely to be associated with obesity and MS.^{4,10–13} Additionally, the prevalence of GERD including EE and the distribution of adipose tissue are known to be different between men and women.^{10,11,14–16,22,23} Although there have been several studies on the association between MS and EE in the general population, there are few reports on the association between the types of MS and EE in the subjects with MS. The prevalence of EE in men with MS is reported to be higher in V-type MS than in S-type MS,¹⁷ but there is no report on the association between EE and the types of MS in women with MS. To our knowledge, this study is the first to show that there is no significant difference in the prevalence of EE between V-type MS and S-type MS and the absence of *H. pylori*, hiatal hernia, and HbA1c are significant predictors of the prevalence of EE in Japanese women with MS.

In the majority of reports on MS, V-type MS and S-type MS were regarded as MS, without making a distinction between the types. Generally, subcutaneous and visceral fat-dominant MS types are not distinguished on medical check-ups, and individuals with both types of MS are treated in the same way. MS is known to be associated with EE, and the visceral

TABLE 2. Comparison of Clinical Characteristics in Women With MS Between V-Type MS and S-Type MS

	V-type MS (n = 50)	S-type MS (n = 404)	P value (P ^a value)
Age (years)	54.9 ± 8.9	58.7 ± 8.0	<0.005
BMI (kg/m ²)	27.1 ± 4.0	25.8 ± 3.5	<0.05
WC (cm)	92.2 ± 7.6	89.3 ± 6.9	<0.01
SBP (mm Hg)	129.6 ± 14.1	131.1 ± 15.2	(NS)
DBP (mm Hg)	78.5 ± 8.5	77.7 ± 9.3	(NS)
Hypertension, n (%)	37 (74.0%)	338 (83.7%)	(NS)
T-CHO (mg/dL)	206.4 ± 33.2	211.0 ± 33.3	(NS)
TG (mg/dL)	139.3 ± 63.0	113.8 ± 59.8	(<0.05)
HDL-C (mg/dL)	56.7 ± 11.9	61.3 ± 14.5	(NS)
LDL-C (mg/dL)	132.1 ± 29.0	134.5 ± 30.3	(NS)
Dyslipidemia, n (%)	37 (74.0%)	270 (66.8%)	(NS)
UA (mg/dL)	5.3 ± 0.9	4.8 ± 1.1	(<0.05)
FPG (mg/dL)	113.0 ± 20.6	107.4 ± 16.6	(NS)
HbA1c (NGSP) (%)	6.3 ± 0.8	6.0 ± 0.6	(<0.005)
IGT, n (%)	42 (84.0%)	290 (71.8%)	(NS)
ALT (IU/L)	40.4 ± 20.6	26.1 ± 18.2	(<0.001)
AST (IU/L)	31.5 ± 13.8	23.5 ± 9.6	(<0.001)
GGT (IU/L)	50.3 ± 45.2	33.8 ± 34.8	(<0.005)
Fatty liver, n (%)	41 (82.0%)	195 (48.3%)	(<0.001)
AFI	1.15 ± 0.17	0.69 ± 0.14	(<0.001)
Alcohol consumption, n (%)	15 (30.0%)	125 (30.9%)	NS
Smoking habit, n (%)	3 (6.0%)	15 (3.7%)	NS
Presence of <i>Helicobacter pylori</i> , n (%)	20 (40.0%)	156 (38.6%)	(NS)
Hiatal hernia, n (%)	23 (46.0%)	107 (26.5%)	(<0.005)
EE (+/-), n (%)	6 (12.0%)	45 (11.1%)	(NS)

Data are means ± SD. P value is based on the χ^2 test or Student's *t*-test. P^a values within parentheses were adjusted for confounding variables.

AFI = abdominal wall fat index, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, DBP = diastolic blood pressure, EE = erosive esophagitis, FPG = fasting plasma glucose, GGT = γ -glutamyl transpeptidase, HbA1c = hemoglobin A1c, HDL-C = high density lipoprotein cholesterol, IGT = impaired glucose tolerance, LDL-C = low density lipoprotein cholesterol, MS = metabolic syndrome, NGSP = National Glycohemoglobin Standardization Program, NS = not significant, SBP = systolic blood pressure, S-type = subcutaneous type, T-CHO = total cholesterol, TG = triglyceride, UA = uric acid, V-type = visceral type, WC = waist circumference.

fat predominance was reported to be associated with EE in men with MS.¹⁷ However, we noticed that there might be no significant difference in the prevalence of EE in women with MS between V-type MS and S-type MS at medical check-up. Thus, to elucidate differences between the types of MS, we simply divided women with MS into those with V-type MS and those with S-type MS. Although a making a distinction between V-type MS and S-type MS by CT is the best method, radiation exposure of CT is known as very danger for young women, especially pregnancy women. Therefore, we selected the ultrasonography as a method for making a distinction between V-type MS and S-type MS in women with MS.

A recent study demonstrated that hyperglycemia was a significant risk factor of EE.²⁴ The hyperinsulinism may have promotion of visceral fat tissue and the hyperglycemia may increase the esophageal acid exposure due to the anti-reflux barrier mechanism through modulation of transient LES relaxation.²⁵ In fact, the present study showed that HbA1c was significantly higher in V-type MS than in S-type MS and was one of the significant predictors of the prevalence of EE in women with MS.

Although many studies have suggested that the risk for developing GERD symptoms or EE increases with increasing BMI,⁶ these associations have remained controversial.²⁶⁻²⁹ Obesity and abdominal visceral adipose tissue may increase intra-abdominal pressure. BMI and WC are significantly

associated with intragastric pressure, gastroesophageal pressure gradient, and separation of the gastroesophageal junction pressure components.^{30,31} Visceral adipose tissue is a source of inflammatory cytokines and is associated with systemic inflammation in obese individuals.^{32,33} Although visceral adipose tissue rather than BMI and WC played a key role in driving the association between MS and GERD in a previous study,^{34,35} there was no significant difference in women with MS in the prevalence of EE between V-type MS and S-type MS in present study. A recent study showed that visceral adipose tissue volume was strongly associated with EE in both sexes.³⁵ However, visceral adipose tissue volume was not associated with EE in the highest group of visceral adipose tissue volume in females.³⁵ There may not be such a significant difference in the visceral fat accumulation between V-type MS and S-type MS in women with MS as there is between individuals with and without MS. Therefore, there may be no significant difference in the prevalence of EE in women with MS between V-type MS and S-type MS in present study.

In some previous reports, *H. pylori* infection in patients with EE was significantly less than in patients without EE,¹³ and *H. pylori* serostatus has shown an inverse association with GERD.³⁶ This above mechanism may be cause of the generation of ammonia, decreased acid production of gastric atrophy, and a neuroimmunological influence.³⁶ In present study, the frequency of positive *H. pylori* infection in subjects with EE

TABLE 3. Comparison of Clinical Characteristics in Women With MS Between With and Without EE

	EE (+) (n = 51)	EE (-) (n = 403)	P value
Age (years)	59.1 ± 8.4	58.2 ± 8.1	NS
BMI (kg/m ²)	26.2 ± 4.4	26.0 ± 3.5	NS
WC (cm)	89.3 ± 7.1	89.7 ± 7.1	NS
SBP (mm Hg)	129.9 ± 16.1	131.0 ± 15.0	NS
DBP (mm Hg)	75.8 ± 9.3	78.0 ± 9.2	NS
Hypertension, n (%)	42 (82.4%)	333 (82.6%)	NS
T-CHO (mg/dL)	204.5 ± 32.7	211.3 ± 33.4	NS
TG (mg/dL)	107.6 ± 52.9	117.8 ± 61.4	NS
HDL-C (mg/dL)	61.6 ± 12.9	60.7 ± 14.5	NS
LDL-C (mg/dL)	128.3 ± 30.1	135.0 ± 30.1	NS
Dyslipidemia, n (%)	33 (64.7%)	274 (68.0%)	NS
UA (mg/dL)	4.8 ± 1.0	4.9 ± 1.1	NS
FPG (mg/dL)	111.5 ± 21.8	107.6 ± 16.5	NS
HbA1c (NGSP) (%)	6.2 ± 0.7	6.1 ± 0.7	NS
IGT, n (%)	38 (74.5%)	294 (73.0%)	NS
ALT (IU/L)	31.2 ± 29.3	27.2 ± 17.2	NS
AST (IU/L)	26.5 ± 15.7	24.2 ± 9.6	NS
GGT (IU/L)	32.3 ± 23.5	36.0 ± 37.7	NS
V-type MS, n (%)	6 (11.8%)	44 (10.9%)	NS
Fatty liver, n (%)	28 (54.9%)	208 (51.6%)	NS
Alcohol consumption, n (%)	19 (37.3%)	121 (30.0%)	NS
Smoking habits, n (%)	1 (2.0%)	17 (4.2%)	NS
Presence of <i>Helicobacter pylori</i> , n (%)	7 (13.7%)	169 (41.9%)	<0.001
Hiatal hernia, n (%)	31 (60.8%)	99 (24.6%)	<0.001

Data are means ± SD. P value is based on the χ^2 test or Student's *t* test.

ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, DBP = diastolic blood pressure, EE = erosive esophagitis, FPG = fasting plasma glucose, GGT = γ -glutamyl transpeptidase, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, IGT = impaired glucose tolerance, LDL-C = low-density lipoprotein cholesterol, MS = metabolic syndrome, NGSP = National Glycohemoglobin Standardization Program, NS = not significant, SBP = systolic blood pressure, T-CHO = total cholesterol, TG = triglyceride, UA = uric acid, V-type = visceral type, WC = waist circumference.

(13.7%) was significant lower than in subjects without EE (41.9%), and the absence of *H. pylori* was one of the significant predictors for EE. Thus, the result obtained from present study was similar to previous studies.

The prevalence of the hiatal hernia was significantly higher in subjects with EE than in subjects without EE, and the hiatal hernia was a significant predictor of an increased prevalence of EE. Additionally, the prevalences of the hiatal hernia, TG, ALT, and fatty liver were significantly higher in V-type MS than in S-type MS. Therefore, we surmise that subjects with V-type MS may be more likely to develop EE than subjects with S-type MS, similar to the development of non-alcoholic fatty liver disease in subjects with MS.³⁷ Dietary fat intake may reduce LES pressure,³⁸ and the presence of hiatal hernia and the increase in upper abdominal pressure because of the visceral adipose, may induce gastroesophageal reflux. However, present study showed that there was no significant difference in the prevalence of EE in women with MS between V-type MS and S-type MS. The discrepancy of the prevalence of EE between V-type MS and S-type MS in gender may be related to the estrogen-related sex hormones, which have protects on the mucosa in the upper gastrointestinal tract.^{39,40} Interestingly, our previous study showed that the prevalence of EE in V-type MS in men with MS was 28.3%.¹⁷ On the other hand, the present study showed that the prevalence of EE in V-type MS in women with MS was 12.0%. There was a significant difference in the prevalence of EE in V-type MS between men and women. Therefore, although V-type MS was one of the most significant

predictors of an increased prevalence of EE in men with MS, V-type MS may not be a predictor of the prevalence of EE in women with MS.

There were several limitations to the present study. First, we would not fully evaluate the cause-and-effect relationship between EE and women with MS because the present study was a cross-sectional study design. Second, levels of estrogen-related sex hormones and adipocytokines were not measured, and the physical activity and the state of menses were not investigated. Third, the numbers of the female subjects fulfilled the diagnostic criteria for MS and EE was very small in the present study. Fourth, most 2606 women who had MS (Figure 1) did not undergo upper gastrointestinal endoscopy in the present study, because the Japanese who undergo a medical check-up tend to select upper gastrointestinal series than upper gastrointestinal endoscopy for the assessment of upper gastrointestinal. However, there was no significant difference in the characteristics between women with MS who underwent upper gastrointestinal series and women with MS who underwent upper gastrointestinal endoscopy (data not shown). Fifth, there was a possibility of selection bias because most of the participants in the present study were healthy individuals who hoped to undergo a medical check-up in Ningen Dock.

In conclusion, the present study showed that there was no significant difference in women with MS in the prevalence of EE between V-type MS and S-type MS. In addition, the hiatal hernia and HbA1c were significant factors of an increased

TABLE 4. Results of Univariate and Multivariate: Independent Predictors of EE in Women With MS

	Univariate analysis			Multivariate analysis		
	EE (+) (n = 51)	EE (-) (n = 403)	P value	OR	95% CI	95% CI
Age (≥ 50 / <50 years)	46/5	349/54	NS	1.448	0.505–4.157	NS
BMI (≥ 25 / <25)	28/23	212/191	NS	1.831	0.856–3.916	NS
WC (≥ 90 / <90 cm)	20/31	179/224	NS	0.687	0.324–1.455	NS
SBP (≥ 130 / <130 mm Hg)	27/23	239/159	NS			
DBP (≥ 85 / <85 mm Hg)	9/42	90/313	NS			
Hypertension (+/–)	42/9	333/70	NS			
T-CHO (≥ 220 / <220 mg/dL)	16/35	149/254	NS			
TG (≥ 150 / <150 mg/dL)	10/41	93/310	NS			
HDL-C (<50 / ≥ 50 mg/dL)	10/41	105/298	NS	0.563	0.255–1.243	NS
LDL-C (≥ 140 / <140 mg/dL)	18/33	169/234	NS	0.792	0.412–1.520	NS
Dyslipidemia (+/–)	33/18	274/129	NS			
UA (≥ 7.0 / <7.0 mg/dL)	1/50	16/387	NS			
FPG (≥ 100 / <100 mg/dL)	38/13	292/111	NS			
HbA1c (NGSP) (≥ 6.5 / <6.5 %)	14/37	68/335	NS	2.325	1.110–4.870	<0.05
IGT (+/–)	38/13	294/109	NS			
ALT (≥ 31 / <31 IU/L)	14/37	114/289	NS			
AST (≥ 31 / <31 IU/L)	9/42	70/333	NS			
GGT (≥ 70 / <70 IU/L)	4/47	36/367	NS			
V-type MS/S-type MS	6/45	44/359	NS			
Fatty liver (+/–)	28/23	208/195	NS			
Alcohol consumption (+/–)	19/32	121/282	NS	1.149	0.595–2.220	NS
Smoking habit (+/–)	1/50	17/386	NS			
Presence of <i>Helicobacter pylori</i> (+/–)	7/44	169/234	<0.001	0.239	0.101–0.567	<0.005
Hiatal hernia (+/–)	3/1/20	99/304	<0.001	4.673	2.448–8.920	<0.001

ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, CI = confidence interval, DBP = diastolic blood pressure, EE = erosive esophagitis, FPG = fasting plasma glucose, GGT = γ -glutamyl transpeptidase, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, IGT = impaired glucose tolerance, LDL-C = low-density lipoprotein cholesterol, MS = metabolic syndrome, NGSP = National Glycohemoglobin Standardization Program, NS = not significant, OR = odds ratio, SBP = systolic blood pressure, S-type = subcutaneous type, T-CHO = total cholesterol, TG = triglyceride, UA = uric acid, V-type = visceral type, WC = waist circumference.

prevalence of EE, and the presence of *H. pylori* was a significant factor of a decreased prevalence of EE in women with MS. We suggest that the hiatal hernia, HbA1c and the absence of *H. pylori* may be more important factors for the prevalence of EE than the types of MS in Japanese women with MS.

ACKNOWLEDGMENT

The authors would like to thank all subjects in our study. This study received no grant support.

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