BMC Public Health

RESEARCH ARTICLE Open Access

Elevated depressive symptoms in metabolic syndrome in a general population of Japanese men: a cross-sectional study

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Abstract

Background: Uncertainty still surrounds the association between metabolic syndrome (MetS) and depression. We aimed to evaluate the association between MetS and elevated depressive symptoms in a general Japanese population.

Methods: This is a cross-sectional survey of 3,113 community-dwelling individuals aged 40 years or over. MetS was defined according to the joint interim statement. MetS was diagnosed when a subject had three or more of the following components: 1) central obesity (waist circumference ≥90 cm for men, ≥80 cm in for women); 2) elevated blood pressure (≥130/85 mmHg or current use of antihypertensive medication); 3) hypertriglyceridemia (≥1.7 mmol/L); 4) low HDL cholesterol (< 1.0 mmol/L for men, < 1.3 mmol/L for women); and 5) elevated fasting plasma glucose (≥5.55 mmol/L or current use of antidiabetic medication). Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D). The age- and multivariable-adjusted odds ratio (OR) and 95% confidence interval (CI) were estimated using a logistic regression model.

Results: Elevated depressive symptoms were observed in 4.3% of male and 6.3% of female participants. In men, the age-adjusted prevalence of elevated depressive symptoms was significantly higher in subjects with MetS than in those without (7.1% versus 3.6%, p = 0.04). The prevalence of elevated depressive symptoms rose progressively as the number of MetS components increased (3.5%, 3.6%, 5.8%, and 9.2% in male subjects with 0–1, 2, 3, and ≥4 components, respectively; p = 0.02 for trend). This association remained significant even after adjustment for age, marital status, history of cardiovascular disease, smoking habit, alcohol intake, and regular exercise. In women, on the other hand, there was no clear association between MetS and depressive symptoms.

Conclusions: MetS was associated with elevated depressive symptoms in a general population of Japanese men.

Keywords: Depressive symptoms, Metabolic syndrome, Population-based, Japanese

Background

Depression is an important cause of long-term disability and dependency and is responsible for 11.8% of years-lived-with-disability [1,2]. Effective prevention of the burdens associated with depression will require a strategy based on better knowledge of its risk factors. Recently, a systematic review of observational studies demonstrated a link between metabolic syndrome (MetS) and depressive symptoms [3]. However, current knowledge of the association between MetS and depressive symptoms was derived mainly from studies conducted in Western populations; so it is unclear to what extent these findings apply to Asian populations. The present cross-sectional study evaluates the association of MetS with depressive symptoms in a general population of Japanese.

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Methods

Study population and design

The Hisayama Study is a prospective cohort study of cerebro-cardiovascular diseases in a suburban community, the town of Hisayama, adjacent to of the city of Fukuoka, Japan [4-6]. Based on data from the national census, the age and occupational distributions in Hisayama have been almost identical to those in Japan as a whole since the 1960s [4]. As a part of this study, all 4330 residents of the town of Hisayama aged 40 years or older were invited to participate in a cross-sectional examination in 2007 and 2008. Among them, 3,376 residents consented to participate (participation rate 78.0%). After the exclusion of 263 subjects with missing data on depression or MetS, a total of 3,113 subjects were included in the present analysis.

Metabolic syndrome

Information on current use of antihypertensive and antidiabetic medications was collected using a self-administered questionnaire and confirmed using the consumer drug information by trained staff. Blood pressure was measured three times after the subject had rested for at least 5 minutes prior to each measurement using a semi-automatic device (BP-203 RVIIIB; Omron Healthcare) based on the cuff-oscillometric principle with the subject in the sitting position. The mean of the three measurements was used for the analysis. Waist circumference was measured at the umbilical level in a standing position by a trained staff member. Blood samples were collected from an antecubital vein after an overnight fast for the determination of serum lipids and plasma glucose levels. Serum total cholesterol, triglyceride, and high-density lipoprotein (HDL) cholesterol concentrations were determined enzymatically. Fasting blood glucose levels were measured by the glucose oxidase method. MetS was defined based on the joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity [7]. MetS was diagnosed when a subject had three or more of the following components: 1) central obesity (waist circumference ≥90 cm for men, ≥80 cm for women); 2) elevated blood pressure (≥130/85 mmHg or current use of antihypertensive medication); 3) hypertriglyceridemia (≥1.7 mmol/L); 4) low HDL cholesterol (< 1.0 mmol/L for men, < 1.3 mmol/L for women); and 5) elevated fasting plasma glucose (≥5.55 mmol/L or current use of antidiabetic medication).

Other covariates

Each participant completed a self-administered questionnaire covering marital status, medical history, smoking habit, alcohol intake, and exercise. The questionnaire was checked by trained interviewers. Marital status was classified as either having a spouse on a family register or not (e.g. single, divorced). A history of cardiovascular disease was defined as prior stroke (ICD10 codes I60, I61, I63 and I64) or coronary heart disease (I20 – I25) with or without coronary revascularization (coronary intervention or bypass surgery). A smoking habit was defined as current habitual smoking of 1 or more cigarettes per day. Alcohol intake was defined as current habitual drinking of at least once per month. Subjects who engaged in sports or other forms of exercise ≥3 times a week during their leisure time made up a regular exercise group.

Elevated depressive symptoms

Depressive symptoms were assessed using the Japanese, 20-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) [8,9], the reliability of which has been validated [10]. Elevated depressive symptoms were defined as a CES-D score of ≥16 or current use of antidepressant medication defined based on the self-administered questionnaire and the consumer drug information.

Statistical analyses

In the present analysis, the key risk factor was MetS and its components, and the outcome was elevated depressive symptoms. All analyses were conducted separately for men and women. The prevalence of elevated depressive symptoms in each subgroup defined by MetS or its components was standardized for age distribution of the total study subjects by the direct method using 10-year age groupings. The association between components of Mets and elevated depressive symptoms was evaluated using an age-adjusted logistic regression model. The association of Mets and the number of its components with elevated depressive symptoms was evaluated using age- and multivariable-adjusted logistic regression models. The multivariable-adjusted models included age, marital status, history of cardiovascular disease, smoking habit, alcohol intake, and regular exercise as covariates. The differences in the association of MetS and the number of its components with elevated depressive symptoms between men and women were evaluated by adding interaction term(s) to the logistic regression models. $P < 0.05$ was considered statistically significant in all analyses. The SAS software package, version 9.2 (SAS Institute) was used for statistical analysis.

Ethical considerations

The study protocol was approved by Kyushu University Institutional Review Board for Clinical Research, and the procedures followed were in accordance with national

guidelines. All participants provided written informed consent.

Results

The baseline characteristics of subjects with and without MetS are shown by sex in Table 1. Subjects with MetS had higher values for waist circumference, systolic and diastolic blood pressures, serum total cholesterol, triglycerides and fasting plasma glucose; they also had lower levels of HDL cholesterol in both men and women. The frequencies of antihypertensive and antidiabetic medications were also higher in MetS subjects of both sexes. Women with MetS were older and less likely to be alcohol drinkers.

Elevated depressive symptoms were observed in 58 (4.3%) men and 111 (6.3%) women. Table 2 shows the age-adjusted prevalence and odds ratio [OR] for elevated depressive symptoms according to the presence of MetS components in men and women. The age-adjusted prevalence of elevated depressive symptoms was higher in men with low HDL cholesterol (age-adjusted OR 2.55 [95% CI 1.11-5.86]) and men with elevated fasting plasma glucose (1.90 [95% CI 1.06-3.42]). These associations remained significant even after controlling for age, marital status, history of cardiovascular disease, smoking habit, alcohol intake, and regular exercise (low HDL cholesterol: multivariable-adjusted OR 2.44 [95% CI 1.04-5.69], elevated fasting plasma glucose: 1.93 [95% CI 1.07-3.49]). In women, on the other hand, there were no clear associations between MetS components and depressive symptoms (all $p > 0.05$).

Table 3 shows the association of MetS with depressive symptoms in men and women. The age-adjusted prevalence of elevated depressive symptoms was significantly higher in men with MetS than in those without it (7.1% versus 3.6%; age-adjusted OR 1.78 [95% CI 1.03-3.08]). This association remained significant even after controlling for age, marital status, history of cardiovascular disease, smoking habit, alcohol intake, and regular exercise (multivariable-adjusted OR 1.82 [95% CI 1.05-3.15]). In women, on the other hand, there were no significant associations between MetS and depressive symptoms ($p = 0.10$; $p = 0.006$ for homogeneity between men and women).

The age-adjusted prevalence and adjusted OR for elevated depressive symptoms according to the number of MetS components are shown by sex in Table 4. In men, the age-adjusted prevalence rose with the number of MetS components: it was 3.5%, 3.6%, 5.8%, and 9.2% for subjects with 0–1, 2, 3, and ≥4 components, respectively ($p = 0.02$ for trend). A significant association was observed even after controlling for the aforementioned confounding factors ($p = 0.01$ for trend). When the number of MetS was used as a continuous variable, an increase in 1 component was associated with a 35% (95% CI 8-67%) increase in elevated depressive symptoms. In contrast to men, women showed no clear associations between the number of MetS components and

Table 1 Characteristics of men and women with and without metabolic syndrome

	Men			Women		
	MetS (–) (n = 965)	MetS (+) (n = 388)	P value	MetS (–) (n = 1261)	MetS (+) (n = 499)	P value
Age (years)	63 ± 12	62 ± 10	0.14	62 ± 13	67 ± 11	< 0.0001
Single or divorced (%)	11.7	11.6	0.95	27.5	31.9	0.07
History of cardiovascular disease (%)	8.4	10.6	0.21	2.6	4.8	0.02
Antihypertensive medication (%)	28.2	44.6	< 0.0001	23.2	50.1	< 0.0001
Antidiabetic medication (%)	7.2	17.0	< 0.0001	1.8	17.6	< 0.0001
Waist circumference (cm)	83.5 ± 7.2	92.6 ± 6.8	< 0.0001	81.3 ± 9.3	91.4 ± 9.3	< 0.0001
Systolic blood pressure (mmHg)	129 ± 17	144 ± 15	< 0.0001	125 ± 18	144 ± 16	< 0.0001
Diastolic blood pressure (mmHg)	79 ± 9	88 ± 9	< 0.0001	75 ± 10	84 ± 10	< 0.0001
Total cholesterol (mmol/L)	5.10 ± 0.87	5.34 ± 0.93	0.0001	5.57 ± 0.89	5.73 ± 0.93	0.0008
Triglycerides (mmol/L)	1.10(0.82–1.47)	2.02(1.47–2.84)	< 0.0001	0.93(0.69–1.23)	1.57(1.09–2.04)	< 0.0001
HDL cholesterol (mmol/L)	1.65 ± 0.42	1.39 ± 0.37	< 0.0001	1.95 ± 0.43	1.61 ± 0.42	< 0.0001
Fasting plasma glucose (mmol/L)	5.8 ± 1.2	6.7 ± 1.6	< 0.0001	5.3 ± 0.7	6.4 ± 1.5	< 0.0001
Smoking habit (%)	33.6	38.0	0.12	7.6	7.3	0.82
Alcohol intake (%)	68.0	71.4	0.22	33.7	26.7	0.004
Regular exercise (%)	13.7	12.9	0.70	10.1	12.6	0.12

MetS metabolic syndrome; *HDL* high-density lipoprotein.
Values are mean ± SD, median (interquartile range) or frequency.
The differences between subjects with and without MetS were tested by Wilcoxon tests for continuous variables and chi-square tests for categorical variables.

Table 2 Components of metabolic syndrome and elevated depressive symptoms in men and women

	N of cases/ participants	Age-adjusted prevalence (%)	Age-adjusted OR (95% CI)	P value
Men				
Central obesity				
No	34/912	3.6	Reference	
Yes	24/441	5.9	1.61 (0.94–2.77)	0.08
Elevated BP				
No	21/582	3.9	Reference	
Yes	37/771	4.9	1.26 (0.73–2.18)	0.41
Hypertriglyceridemia				
No	40/939	4.1	Reference	
Yes	18/414	4.8	1.17 (0.66–2.09)	0.60
Low HDL cholesterol				
No	51/1276	4.0	Reference	
Yes	7/77	8.3	2.55 (1.11–5.86)	0.03
Elevated FPG				
No	16/570	2.9	Reference	
Yes	42/783	5.5	1.90 (1.06–3.42)	0.03
Women				
Central obesity				
No	43/593	7.4	Reference	
Yes	68/1167	5.9	0.78 (0.53–1.16)	0.22
Elevated BP				
No	58/899	6.8	Reference	
Yes	53/861	6.2	0.91 (0.61–1.36)	0.65
Hypertriglyceridemia				
No	100/1471	6.8	Reference	
Yes	11/289	3.6	0.54 (0.28–1.01)	0.05
Low HDL cholesterol				
No	102/1607	6.3	Reference	
Yes	9/153	6.4	0.92 (0.45–1.85)	0.81
Elevated FPG				
No	71/1103	6.5	Reference	
Yes	40/657	6.3	0.93 (0.62–1.39)	0.71

OR odds ratio, 95% *CI* 95% confidence interval, *BP* blood pressure, *HDL* high-density lipoprotein, *FPG* fasting plasma glucose.
OR and P values were estimated using logistic regression models.

depressive symptoms (p = 0.17 for trend; OR 0.9 (95% CI 0.76-1.06) per 1 component increase; p = 0.04 for homogeneity between men and women).

Discussion

The present cross-sectional examination of a general population of Japanese demonstrated a higher prevalence of elevated depressive symptoms in male subjects with MetS compared to those without it. This association remained significant even after controlling for the effects of age, marital status, history of cardiovascular disease, smoking habit, alcohol intake, and regular exercise. Furthermore, the prevalence of elevated depressive symptoms rose with the number of MetS components. In female subjects, on the other hand, there was no clear association between MetS and depressive symptoms.

Although a number of observational studies have investigated the association between MetS and depressive symptoms, their conclusions have been inconsistent [11-29]. With regard to cross-sectional studies, a French study demonstrated elevated depressive symptoms in men and women with MetS [14]. The PPP-Bonita Study also showed close associations of MetS and its components with depressive symptoms in Finnish men and women [29]. With respect to longitudinal design research, the Whitehall II study demonstrated that the presence of MetS was associated with 38% increased risks of future depressive symptoms in men and women in London [16]. The Health in Men Study showed that MetS was a strong predictor of the future development of depression in elderly Australian men [17]. A positive association between MetS and the incidence of depression was also reported in an office-based study of 956 Japanese men [18]. On the other hand, a cohort study from France demonstrated no significant association between MetS and depressive symptoms in elderly subjects aged about 70–90 years old [24]. A recent systematic review and a meta analysis including all these studies, however, demonstrated a clear relationship between MetS and depression. Our findings from the Hisayama Study suggest that the concept of a link between MetS and depression is likely to be applicable to Japanese men.

Several population-based observational studies have reported the association between MetS and depression separately for men and women. A cross-sectional study in France demonstrated that depression and depressive symptoms were associated with MetS, irrespective of gender [14]. A cross-sectional study in Poland showed that MetS was observed more frequently among male subjects with depressive symptoms than those without, while there were no associations among women [12]. A cross-sectional study in the United States reported that women with a history of major depressive episode were twice as likely to have metabolic syndrome compared with those without such a history, but men with history of depression were not significantly more likely to have MetS [11]. A cohort study in Finland found that MetS was not associated with depression or anxiety in either men or women [13]. Therefore, there has been significant inconsistency in gender differences in the link between MetS and depression in Western populations. With regard to Asian populations, on the other hand, a cohort study of Japanese male employees showed a

Table 3 Metabolic syndrome and elevated depressive symptoms in men and women

	N of cases/participants	Age-adjusted			Multivariable-adjusted*	
		Prevalence (%)	OR (95% CI)	P value	OR (95% CI)	P value
Men						
MetS (–)	35/965	3.6	Reference		Reference	
MetS (+)	23/388	7.1	1.78 (1.03–3.08)	0.04	1.82 (1.05–3.15)	0.03
Women						
MetS (–)	87/1261	7.0	Reference		Reference	
MetS (+)	24/499	5.2	0.66 (0.41–1.06)	0.08	0.67 (0.42–1.08)	0.10

MetS metabolic syndrome, *OR* odds ratio, *95% CI* 95% confidence interval.
OR and P values were estimated using logistic regression models.
*Adjusted for age, marital status, history of cardiovascular disease, smoking habit, alcohol intake and regular exercise.

positive relationship between MetS and depression [18]. A cross-sectional study of Japanese subjects in Takarazuka City demonstrated that the mean depression score was higher for men with MetS than those without it, while depression was not associated with MetS in women [25]. In the present study of Japanese subjects, MetS was associated with elevated depressive symptoms in men but not in women. In Asian populations, MetS may be associated with depressive symptoms only in men.

One of the mechanisms underlying the association between MetS and depressive symptoms is thought to be the stress-induced hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, which is common in depression [30-32] and could lead to metabolic alterations [33-35]. Chronic stress has also been shown to increase the risk of metabolic disorders through elevated sympathetic activity [36]. Another potential mechanism is that cerebral small vessel disease associated with MetS [37] can increase the risk of late-life depression [38,39]. It is also possible that behavioral factors associated with depressive symptoms, such as physical inactivity and poor diet, contribute to central adiposity and metabolic disorders.

Another important finding from the present analysis is the lack of associations between MetS and depressive symptoms in women. This finding is consistent with a previous cross-sectional study. The SOPKARD project demonstrated clear associations between MetS and depressive symptoms in Polish men but not in Polish women [12]. The reason for this discrepancy has not been clearly resolved, but it may be attributable to heterogeneity in genetic factors, hormonal factors, socioeconomic factors and social roles between men and women.

There were several limitations to this study. Because of the cross-sectional nature of the study, we were unable to determine whether or not there was a causal association between MetS and the development of depressive symptoms. In addition, we were unable to address the potential mechanisms underlying the reported associations, the self-reported covariates had somewhat limited accuracy, and the study lacked definite diagnosis

Table 4 The number of metabolic syndrome components and elevated depressive symptoms in men and women

	N of cases/participants	Age-adjusted			Multivariable-adjusted*	
Number of MetS components		Prevalence (%)	OR (95% CI)	P trend	OR (95% CI)	P trend
Men						
0-1	20/567	3.5	Reference		Reference	
2	15/398	3.6	0.80 (0.44–1.45)		0.84 (0.46–1.55)	
3	12/250	5.8	1.17 (0.61–2.25)		1.20 (0.62–2.31)	
≥4	11/138	9.2	2.43 (1.22–4.86)	0.02	2.47 (1.22–4.96)	0.01
Women						
0-1	56/782	7.4	Reference		Reference	
2	31/479	6.3	1.03 (0.67–1.58)		1.05 (0.68–1.62)	
3	15/360	4.4	0.58 (0.33–1.01)		0.56 (0.32–0.99)	
≥4	9/139	7.5	1.01 (0.50–2.06)	0.12	1.10 (0.54–2.25)	0.17

MetS metabolic syndrome, *OR* odds ratio, *95% CI* 95% confidence interval.
OR and P values were estimated using logistic regression models.
*Adjusted for age, marital status, history of cardiovascular disease, smoking habit, alcohol intake and regular exercise.

of depression based on structured interviews with psychiatrists using standard criteria.

Conclusions

In conclusion, MetS was associated with elevated depressive symptoms in a general population of Japanese men. Screening of depressive symptoms in men with MetS is likely to aid in the early detection and treatment of depression, and might be able to provide additional protection against the enormous burden of mental disorders in Japan.

Abbreviations

MetS: Metabolic syndrome; CES-D: Center for epidemiologic studies depression scale; HDL: High-density lipoprotein; OR: Odds ratio; CI: Confidence interval; HPA: Hypothalamic-pituitary-adrenal.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

AS conducted the statistical analyses, wrote the manuscript, and reviewed and edited the manuscript. AS is the guarantor of this work, had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. HA contributed to discussion and reviewed and edited the manuscript. TN, TO and YD contributed to discussion. YH brushed up the accuracy of data. MF, JH, KY, YG, TK and SK contributed to discussion. YK is responsible for overall management of the Hisayama Study, and reviewed and edited the manuscript. All authors read and approved the final manuscript.

Acknowledgements

This study was funded in part by Grants-in-Aid for Scientific Research on Innovative Areas (22116010) and for Scientific Research (A) (22240073) and (C) (22590892, 23590797, 23590798, 23500842, 24590797, and 24590796) from the Ministry of Education, Culture, Sports, Science and Technology of Japan and by Health and Labour Sciences Research Grants of the Ministry of Health, Labor and Welfare of Japan (Comprehensive Research on Aging and Health: H20-Chouju-004; Comprehensive Research on Life-Style Related Diseases including Cardiovascular Diseases and Diabetes Mellitus: H22-Junkankitou [Seishuu]-Ippan-005, H22-Junkankitou [Seishuu]-Ippan-017, H23-Junkankitou [Seishuu]-Ippan-002, and H23-Junkankitou [Seishuu]-Ippan-005; and Comprehensive Research on Dementia: H23-Ninchisho-Ippan-004).

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Received: 13 February 2013 Accepted: 5 September 2013
Published: 18 September 2013

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doi:10.1186/1471-2458-13-862
Cite this article as: Sekita *et al.*: Elevated depressive symptoms in metabolic syndrome in a general population of Japanese men: a cross-sectional study. *BMC Public Health* 2013 **13**:862.