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Association between mental health and bone mass among community-dwelling adults: Nagasaki Islands Study on bone health

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Osteoporosis and its related fractures are important public health issues. This study examined the association between the Kessler Psychological Distress Scale (K6) and low bone mass in middle-aged community-dwelling men and women. A cross-sectional study was nested in a prospective observational study of 1,101 participants (median age: 57 [49-62] years in men and 58 [50-62] years in women) residing in a rural city in western Japan. Participants were recruited during medical check-ups in 2016 and 2017 from the community-dwelling population. The bone mass of the calcaneus was evaluated using quantitative ultrasound.

Of the participants, 56 men (14.9%) and 144 women (19.9%) had a bone mass of less than 70% of the mean of young adults. Univariate analysis revealed that there was a trend toward lower body mass index (BMI) and higher prevalence of low bone mass with an increase in K6 scores in men but not in women. Logistic regression analysis, adjusting for possible confounders (age, BMI, smoking, drinking habits, exercise habits, diabetes, hyperlipidemia, and hypertension), showed significant associations between the K6 scores and low bone mass (odds ratio (OR) = 2.66 for the men with 5 to 12 points of K6, OR = 7.51 for men with ≥ 13 of K6, not for women).

We showed an association between psychological distress and low bone mass independent of cofounders among community-dwelling middle-aged men but not women. This suggests that healthy mental health in middle-aged men may be a possible target for the prevention of consequent osteoporosis or fragile bone fractures.

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Key words: Bone ultrasound, osteoporosis, community-dwelling adults, human association studies, Kessler Psychological Distress Scale

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Introduction

Osteoporosis and its related fractures are important public health issues. Osteoporosis is characterized by low bone mineral density (BMD) and altered bone microstructure, which cause bone fragility[1]. As the global population ages, the number of patients with osteoporosis and fragile fractures is increasing. In Japan, the annual incidence of hip fractures was estimated to be 190,000 in 2012 and is expected to reach 300,000 by 2040[2]. Quantitative ultrasound (QUS) is a convenient tool for predicting osteoporotic fractures[3, 4] without radiation exposure.

Mental health is an important aspect of well-being[5], and psychological distress, which is evaluated using the Kessler Psychological Distress Scale, is a reliable and validated indicator of mental health[6]. In addition, chronic psychological distress has been reported to affect various systems (cardiovascular disease[7], cancer[8], hypertension[9], and diabetes[10]). It has been reported that the hypothalamic-pituitary-adrenocortical axis has been implicated in the process of depressive symptoms and onset after experiencing stress in adolescents[11].

Potential mechanisms linking psychological distress and bone health have been derived from case-control studies. However, few studies have examined the association between psychological distress and bone health among community-dwelling individuals. We examined this association in a cross-sectional observational study of community-dwelling adults.

Materials and methods

Study design

A cross-sectional study of 1,101 participants (median age: 57 [49-62] years in men and 58 [50-62] years in women) was nested in a prospective observational study in a rural city in western Japan (Nagasaki Islands Study)[12]. The participants volunteered to participate in this cross-sectional study. Written consent forms were available in Japanese to ensure comprehensive understanding, and informed consent was obtained from all participants. This study was approved by the Ethics Committee for Human Use of Nagasaki University (project registration number 14051404-13). The survey targeted a population residing in rural communities in Goto City in western Japan who underwent a general medical check-up in 2016 and 2017, as recommended by the Japanese government. All procedures were performed in accordance with the ethical standards of the institutional and/or national research committees and the ethical standards of the 1964 Declaration of Helsinki and subsequent amendments or equivalents.

Physical examination and laboratory measures

The following demographic variables were evaluated. Height (cm) and weight (kg) were measured without wearing light clothing or shoes. Body mass index (BMI) was calculated as the weight/height squared (kg/m^2). In addition, current smoking habits (smoked/not smoked), drinking habits (average of more than 40 g/day in pure alcohol weight for men and 20 g/day for women)[13, 14], exercise habits (exercise for more than 30 min at a time, at least two days a week for more than one year), and the presence of diabetes (HbA1c≥6.5%, or on any medication against diabetes), dyslipidemia (triglycerides ≥ 150 mg/dl or more or on medication against dyslipidemia), and hypertension (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or on any medication against hypertension) were investigated.

QUS measurement of bone

Bone mass in the calcaneus was measured using the QUS method for ultrasound measurement. The QUS parameter (stiffness index) of the heel was measured using a Lunar Achilles device (Achilles InSight GE Lunar Corp., Madison, WI, USA). Previous studies have reported its usefulness as a tool for predicting fracture risk[15]. This study defined low bone mass as a low bone mass below 70% of the young adult average.

Psychological distress

Among the items for mental health, K6 is a reliable and validated scale developed by Kessler et al. to measure psychological distress[6]. It was developed to screen for psychiatric disorders and consists of six items. The K6 has been translated into Japanese and examined for reliability and validity[16]. The questions were as follows: In the past 30 days, how often did you experience the following? (i) Did you feel irritable? (ii) "Did you feel hopeless?"; (iii) "Did you feel fidgety or restless?" (iv) "Did you feel depressed, as if nothing would happen to make you feel better?" (v) "Did you feel that everything you did was a struggle?"; and (vi) "Did you feel that you are worthless?" A 5-point Likert scale from 0 to 4 was used: "always" (4 points), "usually" (3 points), "sometimes" (2 points), "a little" (1 point), and "not at all" (0 points). The score range was 0-24 points. The higher the K6 score, the more likely the patient is to have a mood/anxiety disorder. Total K6 scores of ≥ 5 and ≥ 13 were defined as moderate and severe psychological distress, respectively[17-19], and the patients were divided into four groups for analysis: 0, 1-4, 5-12, and ≥ 13 points.

Statistical analysis

Participants were divided by gender, and the chi-square test was performed to compare categorical variables (smoking, drinking habits, exercise habits, diabetes, hyperlipidemia, and hypertension). The Mann-Whitney U-test was performed to compare continuous variables (K6; 0, 1-4, 5-12, and ≥ 13 points) between the two groups of men and women. The Jonckheere-Terpstra test was performed to investigate the trends. For multivariate analysis, logistic regression analysis was performed with K6 divided into four groups (0, 1-4, 5-12, and ≥ 13 points). Model 1 was adjusted for age and BMI, whereas Model 2 was adjusted for age, BMI, smoking, drinking habits, exercise habits, diabetes, dyslipidemia, and hypertension. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA).

Results

Table 1 presents the characteristics of the participants. Of the participants, 56 men (14.9%) and 144 women (19.9%) had a bone mass of less than 70% of the mean of young adults. There were significant differences between men and women regarding the K6, BMI, smoking, drinking, and exercise habits, and the presence of diabetes, dyslipidemia, and hypertension. Since the characteristics were different among the sexes, the following analyses were conducted separately for men and women.

Table 2 shows the results of the univariate analysis for age, BMI, and prevalence of low bone mass among the four groups with different degrees of psychological distress. In men, there was a trend toward lower BMI and higher prevalence of bone mass as K6 increased. In women, age

Table 1. Characteristics of the participants

	Men (n=377)	Women (n=724)	*p*
Psychological distress: K6			
0	246 (65.3)	399 (58.6)	
1-4	86 (22.8)	215 (29.7)	
5-12	39 (10.3)	95 (13.1)	
≥ 13	6 (1.6)	15 (2.1)	0.01
Age (years)	57 (49-62)	58 (50-62)	0.49
BMI (kg/m^2)	23.7 (21.8-25.8)	21.8 (19.7-24.0)	<0.01
Smoking, n (%)	115 (30.5)	42 (5.8)	<0.01
Drinking	37 (9.8)	32 (4.4)	<0.01
Exercise	158 (41.9)	264 (36.5)	0.08
Hyperlipidemia	135 (35.8)	175 (24.2)	<0.01
DM	38 (10.1)	28 (3.9)	<0.01
HT	272 (72.1)	380 (52.5)	<0.01
Low bone mass	56 (14.9)	144 (19.9)	0.04

K6: Kessler psychological distress scale, BMI: Body mass index, DM: diabetes mellitus, HT: hypertension, Low bone mass was defined as bone mass less than 70% of young adults mean

Table 2. Association between psychological distress and bone mass (univariate analysis)

K6	0	1-4	5-12	≥ 13	*p*
Men (n)	246	86	39	6	
Age	57.5 (49.0-62.0)	57.0 (50.0-62.3)	53.0 (48.0-59.0)	53.0 (43.0-60.0)	0.13
BMI	23.9 (22.2-26.0)	23.6 (21.7-25.6)	22.7 (20.4-25.6)	20.8 (18.8-24.8)	0.05
Low bone mass	28 (11.4)	15 (17.4)	10 (25.6)	3 (50.0)	0.007
Women (n)	399	215	95	15	
Age	58.0 (52.0-62.0)	58.0 (49.0-62.0)	56.0 (46.0-61.0)	51.0 (44.0-58.0)	0.02
BMI	21.9 (19.8-23.8)	21.5 (19.5-24.2)	21.6 (20.1-24.3)	23.1 (21.2-27.9)	0.41
Low bone mass	84 (21.1)	42 (19.5)	17 (17.9)	1 (6.7)	0.52

median (Q1-Q3), n (%), Jonckheere-Terpstra test, Chi-square test, K6: Kessler psychological distress scale, BMI: Body mass index, Low bone mass was defined as bone mass less than 70% of young adults mean

tended to decrease with increasing K6 level.

Table 3 shows the results of a multivariate analysis of K6 and low bone mass in men. The variables adjusted were age and BMI in Model 1, as well as smoking, drinking habits, exercise habits, diabetes, hyperlipidemia, and hypertension in Model 2. In Model 1, the group with a K6 score of 5 to 12 points and the group with a K6 score of 13 or more points were significantly associated with low bone mass than that of the group with a K6 score of zero points (odds ratios of 2.51 and 6.26, respectively). In Model 2, after adjusting for other factors, groups with K6 scores between 5 and 12 and those with K6 scores of 13 or higher were significantly associated with low bone mass (odds ratios of 2.66 and 7.51, respectively). Similar to Model 1, the higher the BMI, the lower the bone mass, with an odds ratio of 0.83.

Table 4 shows the results of a multivariate analysis of K6 and low bone mass in women.

Both Model 1 and Model 2 of the logistic regression analysis showed significant associations with age (odds ratios of 1.10 and 1.10, respectively) but not psychological distress.

Table 3. Association between psychological distress and low bone mass among men

Men	Unit	OR (95% CI)	OR (95% CI)	OR (95% CI)
		Crude	MODEL1	MODEL2
Psychological distress				
K6 : 0	reference	1	1	1
K6 : 1-4	/ K6：0	1.64 (0.83 – 3.25)	1.55 (0.77 – 3.10)	1.57 (0.78 – 3.18)
K6 : 5-12	/ K6：0	2.68 (1.18 – 6.09)	2.51 (1.06 – 5.93)	2.66 (1.10 – 6.44)
K6 : ≥ 13	/ K6：0	7.79 (1.50 – 40.46)	6.26 (1.15 – 33.97)	7.51 (1.34 – 42.15)
Age	+1 year		1.03 (0.99 – 1.06)	1.03 (0.99 – 1.07)
BMI	+1 kg/m^2		0.84 (0.76 – 0.93)	0.83 (0.74 – 0.92)
Smoking	/ No			1.48 (0.79 – 2.78)
Drinking	/ No			0.42 (0.12 – 1.41)
Exercise	/ No			0.85 (0.46 – 1.58)
Hyperlipidemia	/ No			1.26 (0.65 – 2.43)
DM	/ No			0.64 (0.21 – 1.90)
HT	/ No			1.46 (0.71 – 3.01)

OR: odds ratio, K6: Kessler psychological distress scale, BMI: Body mass index, DM: diabetes mellitus, HT: hypertension, Logistic regression analysis, Dependent variable: Low bone mass was defined as bone mass less than 70% of young adults mean

Table 4. Association between psychological distress and low bone mass among women

Women	Unit	OR (95% CI)	OR (95% CI)	OR (95% CI)
		Crude	MODEL1	MODEL2
Psychological distress				
K6 : 0	reference		1	1
K6 : 1-4	/ K6：0	0.91 (0.60 – 1.38)	0.97 (0.63 – 1.49)	1.00 (0.65 – 1.54)
K6 : 5-12	/ K6：0	0.82 (0.46 – 1.46)	0.98 (0.54 – 1.78)	0.90 (0.49 – 1.66)
K6 : ≥ 13	/ K6：0	0.27 (0.03 – 2.07)	0.39 (0.05 – 3.15)	0.38 (0.05 – 3.12)
Age	+1 years		1.10 (1.07 – 1.14)	1.10 (1.07 – 1.14)
BMI	+1 kg/m^2		0.95 (0.89 – 1.00)	0.93 (0.87 – 0.99)
Smoking	/ No			1.55 (0.66 – 3.64)
Drinking	/ No			0.43 (0.12 – 1.52)
Exercise	/ No			0.67 (0.45 – 1.01)
Hyperlipidemia	/ No			1.57 (1.01 – 2.45)
DM	/ No			0.37 (0.11 – 1.28)
HT	/ No			1.16 (0.77 – 1.76)

OR: odds ratio, K6: Kessler psychological distress scale, BMI: Body mass index, DM: diabetes mellitus, HT: hypertension, Logistic regression analysis, Dependent variable: Low bone mass was defined as bone mass less than 70% of young adults mean

Discussion

We conducted a cross-sectional study among community-dwelling adults, and our results showed that mental and bone health were associated, independent of possible confounders. Men with a psychological distress (K6) score of 5-12 points were associated with low bone mass, compared with the reference group. Furthermore, men with a K6 score of ≥ 13 were also associated with low bone mass with a higher odds ratio than men of 5-12 points. However, no significant association was found among women.

Our result showed that a higher BMI was associated with healthier bones. There have been several reports[20-24] relating BMI to bone mass. The result that BMI was independently associated with low bone mass after adjustment for psychological distress, age, smoking, drinking, exercise and comorbidities (OR = 0.83 for men, 0.93 for women), was consistent with the association between BMI and bone mass.

There was no report which showed any association between the Kessler Psychological Distress Scale and low bone mass among community-dwelling participants. Two previous case-control studies that examined the association between the Kessler Psychological Distress Scale and osteoporosis were consistent with our results. First, a study of 26,376 Australian men and women reported a significant association with osteoporosis in men aged 50-64 years, with high scores on the Kessler Psychological Distress Scale but not in women[25]. Second, a study of 43,487 Japanese men and women showed an association between the Kessler Psychological Distress Scale and osteoporosis in men but not in women[26]. Without an evaluation of the Kessler Psychological Distress Scale, the results from a previous study examining the association between the Center for Epidemiologic Studies Depression Scale (CES-D) and lower BMD[27] were also consistent with our results.

Studies examining depression and BMD have shown mixed results. These include reports of an association with lower BMD in men and women with depressive or anxiety disorders[28] and an association with lower BMD only in men with depression and not in women[29].

Literature suggests possible mechanisms by which depression is associated with physical illness. Depression may be associated with physical disease through unhealthy behaviors (smoking[30], physical inactivity[31]) and increased hormone secretion (cortisol[32] and corticotropin-secreting hormone[33]). This mechanism might be consistent for glucocorticoid-induced osteoporosis.

In the present study, the K6 scores were higher in women than in men. Case-control studies have generally reported that women have nearly twice the prevalence of depression than men[34, 35]. However, in the present study, psychological distress was associated with lower bone mass in men but not women. Reports were suggested that men secrete twice as much adrenocorticotropic hormone and cortisol in response to stress than women[36] and that men secrete more cortisol in response to stress than women[37-40]. Therefore, although men had lower K6 score than women, psychological distress may be associated with low bone mass via higher cortisol secretion in men than that in women.

In the present study, no significant association was found in the analysis with K6 divided into three groups, but a significant association was found in the analysis with K6 divided into four groups. In other words, men with five or more points were significantly different from men with zero points but not significantly related to men with 0-4 points combined. This difference could be because the 0 and 1-4 scores were related to different health characteristics. In support of the above, the following groups were associated with low bone mass: 1-4 points, 5 or more points, and 13 or more points, in a graded order of odds ratios compared to zero points. There is a lack of studies on such a four-group analysis. It might be worthwhile to conduct a four-group analysis of other diseases.

This study has several limitations. First, because this was a cross-sectional study, it was not possible to determine the causal relationship between mental health and bone mass. Second, because the subjects underwent periodic physical examinations, selection bias might have occurred. Third, bone densitometry using dual-energy X-ray absorptiometry, which is used to diagnose osteoporosis, was not obtained, and the association between QUS parameters and the diagnosis of osteoporosis or osteopenia cannot be assessed, so it might be difficult to generalize the results of this study. Fourth, this study did not measure cortisol levels in the blood or saliva. Future studies should include laboratory measurements of the cortisol levels.

Conclusion

The results showed that mental health was associated with low bone mass independent of age, BMI, smoking, drinking habits, exercise habits, diabetes, hyperlipidemia, and hypertension among community-dwelling middle-aged men but, that it was not significantly associated with low bone mass among women. This suggests that healthy mental health in middle-aged men may be a possible target for the prevention of consequent osteoporosis or fragile bone fractures.

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