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Association between hand-grip strength and depressive symptoms; Locomotive Syndrome and Health Outcomes in the Aizu Cohort Study (LOHAS)

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Running title: Low hand-grip strength associates with depression

Key words: hand-grip strength; depressive symptoms; mental health; muscular weakness; older patients; population-based study

Key points:

1. The aim of this study is to evaluate the relationship between baseline hand-grip strength and subsequent risk of depressive symptoms at one year follow up.

2. Lower hand-grip strength was associated with depressive symptoms in both cross-sectional and longitudinal analysis.

3. The relationship between lower hand-grip strength and depressive symptoms was robust with adjustment for potential confounders.

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ABSTRACT

Background

No study has examined the longitudinal association between hand-grip strength and mental health, such as depressive symptoms.

Objective

We investigated the relationship between baseline hand-grip strength and the risk of depressive symptoms.

Design

A prospective cohort study

Setting & Subjects

A prospective cohort study with a one-year follow-up was conducted using 4314 subjects from community-dwelling individuals aged 40-79 years old in 2 Japanese municipalities, based on the Locomotive Syndrome and Health Outcomes in Aizu Cohort Study (LOHAS, 2008-2010).

Method

We assessed baseline hand-grip strength standardized using national representative data classified by age and gender, and depressive symptoms at baseline and after the follow-up using the five-item version of the Mental Health Inventory (MHI-5).

Results

The 4314 subjects had a mean age of 66.3 years, 58.5% were women, and mean unadjusted hand-grip strength was 29.8 kg. Multivariable random-effect logistic regression analysis revealed that subjects with lower hand-grip

strength (per 1SD decrease) had higher odds of having depressive symptoms at baseline [Adjusted odds ratio (AOR) 1.15, 95% Confidence interval (CI) 1.06-1.24; *P* =0.001]. Further, lower hand-grip strength (per 1SD decrease) was associated with the longitudinal development of depressive symptoms after one year (AOR 1.13, 95% CI 1.01-1.27; *P* =0.036).

Conclusion

Using a large population-based sample, our results suggest that lower hand-grip strength, standardized using age and gender, is both cross-sectionally and longitudinally associated with depressive symptoms.

INTRODUCTION

A considerable number of older patients suffer from a decline in physical function due to age-related muscular weakness, the after effects of strokes, and degenerative neurological disorders such as Alzheimer disease [1, 2]. Previous studies reveal that patients with a decline in physical function are at great risk of falls, cardiovascular disease, and other complications [3-6]. Moreover, a decline in physical function is reportedly associated with mental health issues such as depression. For example, a recent study suggests a close relationship between depressive symptoms and activity of daily living in older persons, suggesting that a decline in physical function might predict the risk of having depressive symptoms [4].

However, the application of these findings in clinical settings requires the settling of two key issues: first, while a previous study demonstrated a longitudinal relationship between depressive symptoms and physical decline such as decrease in walking speed [5], the causal relationship between hand grip strength and depressive symptoms has not been well investigated. Second, because the previous studies used discrete and complicated definitions of physical function, such as the muscle strength of lower limbs and walking speed, interpretation of the results is not easy for general healthcare providers, indicating the need for a more convenient method of evaluating physical function in actual clinical settings.

Hand-grip strength, which is strongly correlated with systemic muscle strength, one of the promising candidate for the brief evaluation of physical function. Moreover, hand-grip strength is also used to predict future activities of daily life [7, 8]. While previous studies have suggested a cross-sectional association between hand-grip strength and depressive symptoms [9, 10], the longitudinal relationship between lower hand-grip

strength and the development of depressive symptoms has not been evaluated. In addition, assessment of the effect of hand-grip strength in the previous studies was done using models with insufficient adjustment, without normal population-based standardized values classified by age and sex [4, 11-15] .

Here, we investigated the relationship between the hand-grip strength, with adjustment using normal population-based standardized values, and both baseline depressive symptoms and the longitudinal development of depressive symptoms, using data from the Locomotive Syndrome and Health Outcome in Aizu Cohort Study (LOHAS) [16].

METHODS

Study Population

LOHAS (2008-2010) is a population-based cohort study conducted in two municipalities in Fukushima Prefecture, Japan [16]. The source population of LOHAS consisted of the general population of the region. Participations were limited to subjects aged 40-79 years who received annual health check-ups conducted by the local government in 2008-2010. The original aim of the study is to examine the relationship between locomotive syndrome and metabolic syndrome. Locomotive syndrome is a concept which denotes the vulnerable conditions in older patients due to functional decline in the locomotive organs [17]. All participants provided written informed consent, and the study protocol was approved by the institutional review board of Fukushima Medical University School of Medicine and Kyoto University Graduate School and Faculty of Medicine, Ethics Committee. Additional details on LOHAS sampling and study methods have been

previously described [16, 18].

Data Collection

The main variables evaluated were hand-grip strength and depressive symptoms. In LOHAS, hand-grip strength was measured using a digital dynamometer (Takei Scientific Instruments Co., Ltd, Japan). Strength was measured once for each hand in a monitored setting, with the forearm held parallel to the body in the standing position. In the present study, hand-grip strength was evaluated using the mean value of the data of both hands, unless only one of them was available. Then, to enable comparison of hand-grip strength regardless of sex and age, standardized hand-grip strength with adjustment for sex and age was calculated, using data from the Survey on Physical Strength and Physical Exercise Capability, which provided the national-representative mean and standard deviation of hand-grip strength classified by sex and age. In the main analysis, scores less than or equal to 50 and those more than 50 were defined as lower and higher hand-grip strength, respectively [19].

Depressive symptoms were assessed using the five-item version of the Mental Health Inventory (MHI-5), a 5-item questionnaire about depression which has been validated against the 20-item Zung Self-rating Depression Scale (ZSDS) and is considered highly reliable among the general population and patients with various psychiatric disorders[20]. In the MHI-5, a score of 60 or less suggests moderate or severe depression, which in our study is defined as having depressive symptoms.

Statistical Analysis

In the cross-sectional analysis, the relationship between standardized hand-grip strength, treated as a continuous variable, and odds of having depressive symptoms at baseline was examined by random-effect logistic regression analysis, with adjustment for age, sex, body mass index, smoking status, daily activities [moderate activities (e.g. carrying light loads) or severe activities (e.g. heavy lifting, digging, and climbing upstairs) more than once a week], and comorbid conditions (coronary artery disease, respiratory disease, stroke). Body Mass Index was assessed at the annual regular health check-up. Smoking status, daily activities, and comorbid conditions were assessed using the self-administered questionnaires. In the present study, random-effect models were employed to treat repeated measures between the same subjects at baseline (in 2008 and 2009), using the stata command xtlogit.

In the longitudinal analysis, assuming that lower hand-grip strength may predict the future risk of developing depressive symptoms, the relationship between lower standardized hand-grip strength at baseline (treated as a continuous variable) and development of depressive symptoms after one year was evaluated in subjects not having depressive symptoms at baseline using the random-effect logistic regression model described above, with adjustment for possible confounders aforementioned plus baseline MHI scores.

To examine the dose-dependency of the relationship, three categorical dummy variables were prepared according to quartile of score for standardized hand-grip strength from each participant. Random-effect logistic regression analysis was performed to evaluate the relationship between categorized standardized hand-grip strength at baseline and the odds of having depressive symptoms at baseline, and to evaluate subjects not having depressive symptoms at baseline between categorized standardized hand-grip strength at

baseline and the odds of developing depressive symptoms after one year. The first, second, and third quartiles were compared to the fourth quartile and results were expressed as an odds ratio of patients presenting depressive symptoms. Models were adjusted for the same possible confounders mentioned above. A test of linear trend across these four quartiles was performed using random-effect logistic regression models based on a previously reported method [21]. All analyses were performed using Stata SE version 13.1 (StataCorp LP, USA).

RESULTS

Of the 5347 participants enrolled in LOHAS, baseline data for standardized hand-grip strength and depressive symptoms were available for 4314 subjects (80.7%) (Figure 1). These 4314 subjects had a mean age of 66.3 years, 58.5% were women, and mean unadjusted hand-grip strength was 29.8 kg. Table 1 shows subject characteristics categorized by lower or higher average hand-grip strength, and characteristics of the 2479 (57.5%) of 4314 subjects with lower standardized hand-grip strength at baseline.

Cross-sectional relationship between depressive symptoms and hand-grip strength

Results showed that depressive symptoms were reported by 31.3% of patients with lower hand-grip strength and 25.8% of those with higher hand-grip strength ($P< 0.001$).

On multivariable random-effect logistic regression analysis, subjects with lower hand-grip strength (per 1SD decrease) had higher odds of having depressive symptoms at baseline [adjusted odds ratio (AOR) 1.15, 95%

confidence interval (CI) 1.06-1.24; *P* =0.001] (Table 2).

Compared with subjects in the fourth quartile of standardized hand-grip strength, those in the third, second, and first quartiles had significantly higher odds of having depressive symptoms at baseline, with AORs of 0.94, 1.20, and, 1.35, respectively (*P* for trend =0.005) (Figure 2).

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Association between longitudinal development of depressive symptoms and hand-grip strength

From the total 4314 subjects, data regarding depressive symptoms collected one year after baseline were available for 2512. Of those, data from 1936 subjects shown not to have depressive symptoms at baseline were used for longitudinal analysis. The 1936 subjects had a mean age of 67.2 years, 60.2% were female, and 1039 subjects (53.6%) had a lower hand-grip strength at baseline. Results showed that 25.5% of subjects with a lower hand-grip strength and 20.4% of those with a higher hand-grip strength had developed depressive symptoms during follow-up (*P*=0.01). Multivariable random-effect logistic analysis revealed that subjects with lower hand-grip strength at baseline (per 1SD decrease) had higher odds of developing depressive symptoms after one year (AOR 1.13, 95% CI 1.01-1.27; *P*=0.036, Table 3).

Further, a significant dose-dependent relationship was observed between lower hand-grip strength and risk of developing depressive symptoms, with AORs for third, second, and first standardized hand-grip strength quartiles of 1.11, 1.17, and, 1.73, respectively (*P* for trend =0.005) (Figure 2).

DISCUSSION

In this study, we showed a significant relationship between hand-grip strength standardized with age and sex and depressive symptoms as assessed by a self-administered questionnaire (MHI-5), based on a large population-based sample. In particular, our results revealed that subjects with below-average standardized hand-grip strength were at greater risk of subsequently developing depressive symptoms, which suggests that lower hand-grip strength may be a causative factor in the development of depressive symptoms, independent from age and sex.

Results also revealed that the association was clearly defined when categorized standardized hand-grip strength were used for analysis, with the odds of presenting depressive symptoms at baseline increasing with decreasing standardized hand-grip strength in a dose-dependent manner. Further, this relationship was also observed between categorized standard hand-grip strength and the longitudinal development of depressive symptoms one year after baseline. Results from the present study were generalized through the use of a large population-based sample of older subjects. Additionally, the positive results, standardized using the national data may strengthen reliability of our main results.

A number of studies have identified an association between lower physical function, assessed using many indices such as the muscle strength of lower limbs, walking speed and self-perceived functional decline, and depressive symptoms[22, 23]. A recent study suggests a bidirectional association between walking speed and depressive symptoms, but most studies investigated merely cross-sectional relationships [23]. To our knowledge this is the first study to examine a longitudinal relationship between baseline hand-grip strength and the development of depressive symptoms.

In the present study, we focused on hand-grip strength as representative of general physical function. Rantanen et al. evaluated the association between hand grip strength and the strength of other muscle functions, and reported correlation coefficients with elbow flexion strength ($r = 0.672$), knee extension strength ($r = 0.514$), and trunk extension strength ($r = 0.541$) which indicate an approximation of total body muscle strength [8, 12]. Hand-grip strength may thus serve as useful and simple measure of total body muscle function.

The longitudinal analysis in the present study showed that lower hand-grip strength, representing lower motor functions, is associated with the future risk of worsening mental health. One cohort study have shown that patients treated for depressive symptoms who have lower hand-grip strength or felt physical handicaps remained in a depressive mood for several years [24]. This finding suggests that lower hand-grip strength may have had a direct effect on the decreased metal health of the participants. Growing evidences suggests that lower hand-grip strength is closely associated with decreased physical quality of life (QOL), which would in turn explain how hand-grip strength, representing states of motor functions, affects mental health via physical QOL. Contrarily, patients with depressive symptoms might be likely to develop lower hand-grip strength based on the possible hypothesis that depression might cause decline in systemic physical functioning. Demakakos et al. revealed a bidirectional association between walking speed and depressive symptoms, supporting the speculation the association between hand-grip strength and depressive symptoms was bidirectional [23].

Previous studies have shown that a significant proportion of community-dwelling residents have depressive symptoms [25, 26]. However, healthcare providers other than psychiatrists are not familiar with identifying

depression, and many patients remain undiagnosed and undertreated. In general, most questionnaires used to screen for depressive symptoms consist of items which are perceived as threatening by psychologically distressed patients, and thus likely to affect doctor-patient relationship. This highlights the difficulties of managing depressed patients in local settings. Given that hand-grip strength can be measured even at routine health check-ups, we speculate that hand-grip strength might be a candidate of predictors when developing clinical prediction rules to detect depressive symptoms. Further investigations are needed to apply the result into actual clinical settings.

Several limitations of our study warrant mention. Longitudinal analysis in the present study might have been biased by the exclusion of 34.6% of subjects from follow-up. We compared the baseline characteristics (age, sex, and depressive symptoms) between patients with follow-up and those lost to follow-up, but there have been no remarkable differences. Duration of the follow-up period was only one year, and we did not examine the long-term relationship between hand-grip strength and depressive symptoms. Although our results indicate that depressive symptoms are sufficiently measured by MHI-5, assessment using this method does not fulfill the criteria of definitive diagnosis of depression. Data on details of socioeconomic status were not recorded in the present study, so we could not take this potential confounding factor into account in the multivariable analyses. In addition, our study was limited to a Japanese population, and the extrapolation of our findings to other countries requires further investigation. Although the results reveal a longitudinal relationship between hand-grip strength and depressive symptoms, the test performance of screening depressive symptoms using hand-grip strength cannot be assessed in the present study. Finally, as a general limitation of observational

studies, we were unable to adjust for unknown confounding factors highly associated with the investigated relationship.

In conclusion, our results from a large population-based sample show a significant epidemiological association between hand-grip strength and both depressive symptoms at baseline and the longitudinal development of depressive symptoms.

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FIGURE LEGENDS

Figure 1 Flow chart of the study

Figure 2 Odds ratio of depressive symptoms (a) at baseline, and (b) after one-year follow-up, by quartile of standardized hand-grip strength

351 **TABLES**

352 **Table 1.** Characteristics of all subjects by hand grip strength in cross-sectional study

	Total (n=4314)	Hand grip strength High (n=1835)	Low (n=2479)
Age, mean ± SD, years	66.3 ± 9.0	65.5 ±9.0	66.9 ±8.9
Age groups			
40 - 49, %	6.1	7.0	5.4
50 - 59, %	14.6	15.6	13.8
60 - 69, %	36.3	37.7	35.3
70 - 79, %	43.0	40.0	45.5
Sex, female, (%)	58.5	55.7	60.6
Hand grip strength, mean ± SD, kg	29.8 ± 9.9	35.5 ± 9.5	25.6 ± 7.9
Mental Statement			
MHI, mean ± SD	74.7 ±18.43	76.4 ± 17.7	73.5±18.7
Depressive symptoms, %	29.0	25.8	31.3
Body mass index, mean ± SD	23.8 ± 3.2	24.2 ± 3.0	23.5 ± 3.2
Smoking status			
Current smoker, %	13.6	14.0	13.3
ex-smoker, %	21.7	23.5	20.3
Moderate or severe activities more than once a week, %	73.3	79.6	68.6
Comorbidities			
Heart disease, (%)	6.8	6.2	7.3
Respiratory disease, (%)	3.8	4.0	3.7
Stroke, (%)	4.2	3.3	4.8

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354 **Table 2.** Odds ratio of depressive symptoms by hand grip strength, age, sex, and comorbidities in

355 cross-sectional analysis

	Fully-adjusted model				Minimally-adjusted model			
	AOR	95% CI		*P* value	AOR	95% CI		*P* value
Hand grip strength (per 1SD decrease)	1.15	1.06	1.24	0.001	1.16	1.08	1.25	<0.001
Age categories								
40 – 49	Ref.				Ref.			
50 – 59	1.18	0.73	1.93	0.502	1.35	0.88	2.07	0.175
60 – 69	1.39	0.89	2.19	0.149	1.50	1.02	2.23	0.042
70 – 79	1.56	0.99	2.46	0.053	1.67	1.13	2.46	0.010
Sex								
Male	Ref.				Ref.			
Female	1.41	1.09	1.82	0.009	1.30	1.09	1.53	0.003
Body mass index (per 1 unit increase)	1.00	0.97	1.03	0.954				
Current smoker (vs. never-smoker)	1.24	0.90	1.71	0.183				
Ex-smoker (vs. never-smoker)	1.01	0.76	1.35	0.949				
Moderate or severe activities more than once a week (vs. no)	0.96	0.85	1.07	0.425				
Comorbidities (vs. none)								
Heart disease	1.21	0.85	1.72	0.292				
Respiratory disease	1.66	1.06	2.58	0.026				
Stroke	1.09	0.70	1.69	0.707				

AOR; adjusted odds ratio, CI; confidence interval

Age and sex were adjusted in the minimally-adjusted model

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359 **Table 3.** Odds ratio of depressive symptoms at 1 year by hand grip strength, age, sex, and comorbidities in

360 longitudinal analysis.

	Fully-adjusted model				Minimally-adjusted model			
	AOR	95% CI		*P* value	AOR	95% CI		*P* value
Hand grip strength (per 1SD decrease)	1.13	1.01	1.27	0.036	1.14	1.01	1.28	0.035
Age categories								
40 – 49	Ref.				Ref.			
50 – 59	3.45	1.06	11.28	0.04	3.65	1.17	11.36	0.025
60 – 69	5.81	1.82	18.60	0.003	5.92	1.96	17.89	0.002
70 – 79	9.37	2.82	31.17	<0.001	9.99	3.20	31.15	<0.001
Sex								
Male	Ref.				Ref.			
Female	1.76	1.20	2.57	0.004	1.88	1.41	2.52	<0.001
Body mass index (per 1 unit increase)	1.03	0.99	1.08	0.111				
Current smoker (vs. never-smoker)	1.38	0.86	2.23	0.183				
Ex-smoker (vs. never-smoker)	1.07	0.70	1.61	0.764				
Moderate or severe activities more than once a week (vs. no)	1.01	0.85	1.21	0.888				
Comorbidities (vs. none)								
Heart disease	1.35	0.83	2.18	0.226				
Respiratory disease	1.51	0.81	2.82	0.190				
Stroke	0.70	0.37	1.31	0.263				

AOR; adjusted odds ratio, CI; confidence interval

Age and sex were adjusted in the minimally-adjusted model

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