



Reduced grip strength is associated with progression of depressive status in chronic liver diseases

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Background: The causal relationship between sarcopenia and depression in chronic liver disease (CLD) patients is unclear. To elucidate these issues, we aimed to investigate the impacts of muscle strength as assessed by grip strength (GS) and muscle mass as assessed by bioelectrical impedance analysis (BIA) on the progression of depression in CLD patients (n=189, 49 cirrhotic cases, and 87 males).

Methods: The Beck Depression Inventory-2nd edition (BDI-II) was used for the evaluation of depression. Time interval from the date of baseline BDI-II and the first confirmed date of elevation of BDI-II score was calculated in each subject. We analyzed factors associated with the elevation of BDI-II score.

Results: The baseline mean BDI-II score was 8.4 (median value, 7). Depression (BDI-II score >11) was found in 63 patients (33.33%). GS decline at baseline was found in 13 male patients (14.9%) and 37 female patients (36.3%). Skeletal muscle index (SMI) by BIA decline at baseline was found in 25 male patients (28.7%) and 40 female patients (39.2%). During the follow-up period, 84 patients (44.4%) had the elevation of BDI-II score. For all cases, the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 39.2%, 46.6% and 54.9%. In patients with GS decline at baseline, the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 53.1%, 67.8% and 77.9%, while in patients with GS non-decline at baseline, the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 34.4%, 39.8% and 47.4% (P=0.0006). In patients with SMI decline at baseline, the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 43.5%, 50.8% and 62.1%, while in patients with SMI non-decline at baseline, the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 36.9%, 44.5% and 51.0% (P=0.2487). As per the multivariate analyses, only lower GS at baseline (P=0.0022) was identified to be a significant factor associated with the elevation of BDI-II score.

Conclusions: Reduced GS rather than loss of muscle mass can be independently associated with an elevated risk for the progression of depression.

Keywords: Chronic liver disease (CLD); depression; muscle function; muscle mass

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Introduction

Depressive state seen in patients with chronic liver diseases (CLDs) is common (1-10). Even in CLD patients with an earlier disease stage, depressive manifestations can be frequently recognized compared to healthy individuals, and depression is a leading mental illness in CLD patients (7). In patients with persistent hepatitis C virus (HCV) infection, anxiety, depression, and chronic fatigue are reported to be major psychiatric disorders (11,12). Decrease of quality of life (QOL) and increase of health care costs have been shown in CLD patients with depressive state (4,13). In cirrhotic patients, depression can be linked to adverse clinical outcomes. Pre-transplant depression can cause length of hospitalization and poorer survival after liver transplantation (14). However, it tends to be overlooked and this issue is not given full consideration in the current practice guidelines (1). Depression seems to be one of essential neurocognitive manifestations in CLD patients. The Beck Depression Inventory-2nd edition (BDI-II) is a representative screening tool for the severity of depression (15).

Sarcopenia is a condition in which skeletal muscle mass and strength or physical function are reduced (16). Primary sarcopenia is a condition in which skeletal muscle mass and strength or physical function decline with aging, while secondary sarcopenia is defined as a condition in which skeletal muscle mass and strength or physical function are impaired due to underlying diseases such as inflammatory diseases, malignancies, renal diseases, respiratory diseases, heart diseases and liver diseases (17). Regarding mechanisms of developing sarcopenia in patients with CLDs, involvements of various factors such as aging, protein energy malnutrition, signal transduction related to protein synthesis and degradation, cytokines such as myostatin (a myokine which inhibits skeletal muscle protein synthesis), hyperammonemia, chronic inflammation, and sex hormones have been reported (18-20). Sarcopenia can be associated with decreased QOL and adverse clinical outcomes such as mortality, increased length of hospital stay and severe infections in CLD patients (18,21-25). Thus, the relationship between sarcopenia and depression in CLD patients appears to be essential.

In our previous cross-sectional study, we demonstrated the close relationship between sarcopenia and depression in CLD patients (26). Chang *et al.* reported in their meta-analysis that sarcopenia was independently associated with depression in elderly people, while the causal relationship

between sarcopenia and depression needs further studies (27). The causal relationship between sarcopenia and depression in CLD patients is also unclear. To elucidate these issues, we aimed to investigate the impacts of sarcopenia-related factors (i.e., muscle strength and muscle mass) on the progression of depression in CLD patients.

We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/apm-20-2059>).

Methods

Patients

Using a retrospective computerized database, a total of 189 CLD individuals who visited our hospital between October 2012 and April 2018 were analyzed. Clinical features, BDI-II scores and laboratory data recorded at baseline were collated. Diagnosis for cirrhosis was determined according to the current guidelines (28). In all analyzed patients, evaluation using BDI-II questionnaire was performed twice or more during the observation period. The follow-up intervals were determined by the attending physician, and the patient's free will was used to make decisions regarding entries on the BDI-II questionnaire. Time interval from the date of baseline BDI-II and the first confirmed date of elevation of BDI-II score was calculated in each subject. The most suitable intervention for each underlying liver disease was performed (11,28-30). In this study, there was no patient receiving liver transplantation during the follow-up period. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and approval of ethics was obtained from the institutional review board in Hyogo College of Medicine Hospital (No. 3469) and individual consent for this retrospective analysis was waived. An opt out method was employed.

BDI-II score and our study

The BDI-II is a widely accepted screening tool for assessing the severity of depression (31,32). High reliability and internal consistency are involved in the BDI-II, and the Japanese version of the BDI-II has reported the similar internal reliability and validity compared to the original version (33). BDI-II is a self-administered questionnaire which consists of 21 items (31,34). Each answer is assessed on a four-point scale (0 to 3 points) (31,34). Higher BDI-II score indicates a severer depressive condition. A Japanese

researcher categorized patients into normal (BDI-II score, 0–10), minimal depressive state (BDI-II score, 11–16), mild depressive state (BDI-II score, 17–20), moderate depressive state (BDI-II score, 21–30), and severe depressive state (BDI-II score ≥ 31), and defined depression as BDI-II score ≥ 11 . In the current analysis, this classification system was applied. We analyzed factors associated with the elevation of BDI-II score (i.e., progression of depressive state).

Muscle strength and muscle mass measurement

Muscle strength [grip strength (GS) in this study] measurement and muscle mass measurement at baseline were done based on the previous reports (17). GS of the left hand and the right hand were measured twice each, and the mean value of the better of the two was adopted. For the evaluation of muscle mass, bioelectrical impedance analysis (BIA) was performed using InBody 720 to calculate appendicular muscle mass. Skeletal muscle index (SMI) was calculated as sum of muscle mass in upper and lower extremities divided by height squared (kg/m^2). Based on the criteria of Japanese Society of Hepatology (JSH), muscle strength weakness was diagnosed with a GS of < 26 kg for male and < 18 kg for female. Likewise, loss of muscle mass was diagnosed by a SMI of < 7.0 kg/m^2 for male and < 5.7 kg/m^2 for female on BIA (17). Impacts of baseline GS and SMI on the elevation of BDI-II score were examined.

Statistical analysis

Continuous variables were presented as mean value [\pm standard deviation (SD)]. Our primary endpoint was the elevation of BDI-II score compared to the baseline BDI-II score. Cumulative elevation rates of BDI-II score were calculated by the Kaplan-Meier method and compared between groups by the log-rank test. Univariate and multivariate Cox proportional hazard models were employed for identifying significant factors associated with the elevation rates of BDI-II score, and the results were presented as hazard ratios (HRs) and 95% confidence intervals (CIs) with corresponding P value. In the univariate analysis, the cohort was divided into two categories using each median value. The JMP version 14.0 software (SAS Institute, Cary, NC, USA) was employed to analyze data statistically (significant level, $P < 0.05$).

Results

Patient characteristics

Of the 189 patients with CLDs, 87 (46.0%) were males, and the mean (\pm SD) age was 61.8 ± 11.7 years. The mean (\pm SD) follow-up period was 1.3 ± 1.1 years. There were 140 patients (74.1%) with non-cirrhosis and 49 patients (25.9%) with cirrhosis. There was no patient with overt hepatic encephalopathy. The main liver disease etiology was HCV (160 cases, 84.7%). The baseline mean (\pm SD) BDI-II score was 8.4 ± 7.3 (median value, 7). Baseline BDI-II score 0–10 (normal) was observed in 126 (66.7%), 11–16 (minimal depressive state) in 41 (21.7%), 17–20 (mild depressive state) in 14 (7.4%), 21–30 (moderate depressive state) in 4 (2.1%), and ≥ 31 (severe depressive state) in 4 (2.1%). GS decline at baseline as defined by the JSH criteria was observed in 13 male patients (14.9%) and 37 female patients (36.3%). SMI decline at baseline as defined by the JSH criteria was observed in 25 male patients (28.7%) and 40 female patients (39.2%). Sarcopenia at baseline as defined by the JSH criteria was observed in 7 male patients (8.0%) and 19 female patients (18.6%). In patients with GS decline at baseline ($n=50$) and non-decline at baseline ($n=139$), there were 26 patients (52%) and 39 patients (28.1%) with SMI decline at baseline. In patients with depression at baseline (BDI-II score ≥ 11 , $n=63$), 20 (31.7%) had GS decline, and 24 (38.1%) had SMI decline. The baseline clinical characteristics and laboratory data of all analyzed patients are summarized in *Table 1*.

Cumulative elevation rate of BDI-II score for all cases (n=189)

During the observation period, 84 patients (44.4%) had the elevation of BDI-II score. For all cases, the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 39.2%, 46.6% and 54.9% (*Figure 1*).

Cumulative elevation rates of BDI-II score according to the cirrhosis status

In cirrhotic cases ($n=49$), the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 51.3%, 64.0% and 75.3% (*Figure 2A*). During the follow-up period, 30 cirrhotic patients (61.2%) had the elevation of BDI-II

Table 1 Baseline characteristics (n=189)

Baseline variables	All cases (n=189)
Age (years)	61.8±11.7
Gender, male/female	87/102
Liver disease etiology HCV/HBV/others	160/15/14
Presence of sarcopenia, yes/no	26/163
BDI-II score	8.4±7.3
Presence of cirrhosis, yes/no	49/140
Body mass index (kg/m ²)	23.0±3.4
SMI (kg/m ²), male	7.7±0.9
SMI (kg/m ²), female	5.9±0.6
Grip strength (kg), male	35.3±8.8
Grip strength (kg), female	19.7±4.4
Total bilirubin (mg/dL)	0.9±0.5
Serum albumin (g/dL)	4.1±0.4
Prothrombin time (INR)	1.11±0.16
Platelet count (×10 ⁴ /mm ³)	15.9±6.2
AST (IU/L)	39.4±25.2
ALT (IU/L)	39.2±33.4
eGFR (mL/min/1.73 m ²)	83.9±20.6

Data are expressed as number or mean value (standard deviation). HCV, hepatitis C virus; HBV, hepatitis B virus; BDI-II, Beck depression inventory II; SMI, skeletal muscle index; AST, aspartate aminotransferase; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate.

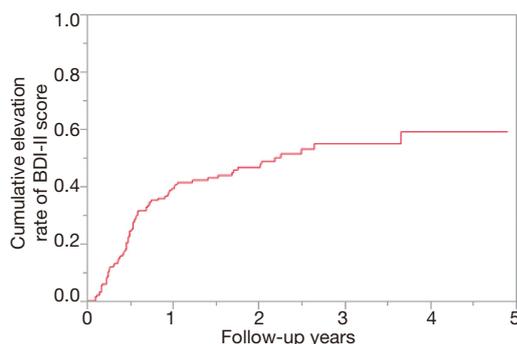


Figure 1 Cumulative elevation rate of BDI-II score for all cases (n=189). BDI-II, Beck Depression Inventory-2nd edition.

score. In non-cirrhotic cases (n=140), the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 34.6%, 40.4% and 46.8% (Figure 2B). During the follow-up period, 54 non-cirrhotic patients (38.6%) had the elevation of BDI-II score. The difference of cumulative elevation rates of BDI-II score between cirrhotic and non-cirrhotic cases was noted with significance (P=0.0112).

Cumulative elevation rates of BDI-II score according to the GS value and the SMI value

In patients with GS decline at baseline (n=50), the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 53.1%, 67.8% and 77.9%, while in patients with GS non-decline at baseline (n=139), the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 34.4%, 39.8% and 47.4% (P=0.0006, Figure 3A).

In patients with SMI decline at baseline (n=65), the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 43.5%, 50.8% and 62.1%, while in patients with SMI non-decline at baseline (n=124), the 1-, 2- and 3-year cumulative elevation rates of BDI-II score were 36.9%, 44.5% and 51.0% (P=0.2487, Figure 3B).

Predictors of the elevation of BDI-II score in all patients by univariate and multivariate analyses

As per the univariate analyses, lower GS at baseline (P=0.0006), presence of cirrhosis (P=0.0113), aspartate aminotransferase (AST) ≥ 31 IU/L (P=0.0193), and prothrombin time (PT-INR) >1.08 (P=0.0456) were found to be associated with the elevation of BDI-II score (Table 2). As per the multivariate analyses, only lower GS at baseline (P=0.0022) was identified to be a significant factor associated with the elevation of BDI-II score (Table 3). HRs and 95% CIs of lower GS at baseline, presence of cirrhosis, AST ≥ 31 IU/L and PT-INR >1.08 were shown in Table 3.

Cumulative elevation rates of BDI-II score according to the GS value and the SMI value in cirrhotic patients and non-cirrhotic patients

Cirrhotic patients with GS decline at baseline (n=17) had significantly higher cumulative elevation rates of BDI-II score

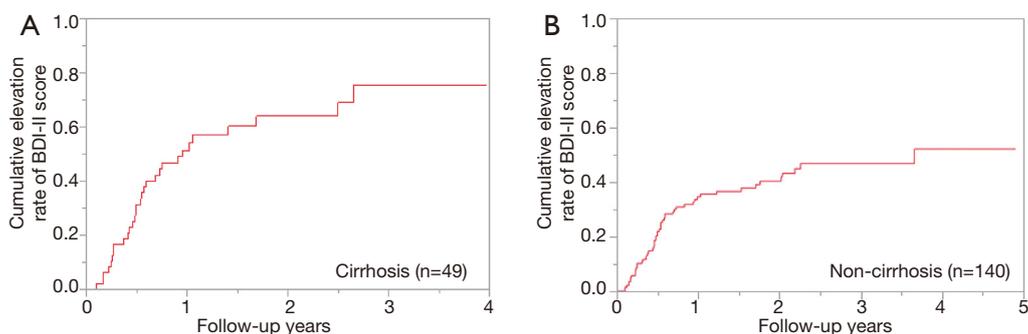


Figure 2 Cumulative elevation rate of BDI-II score in cirrhotic patients (n=49) (A) and non-cirrhotic patients (n=140) (B). BDI-II, Beck Depression Inventory-2nd edition.

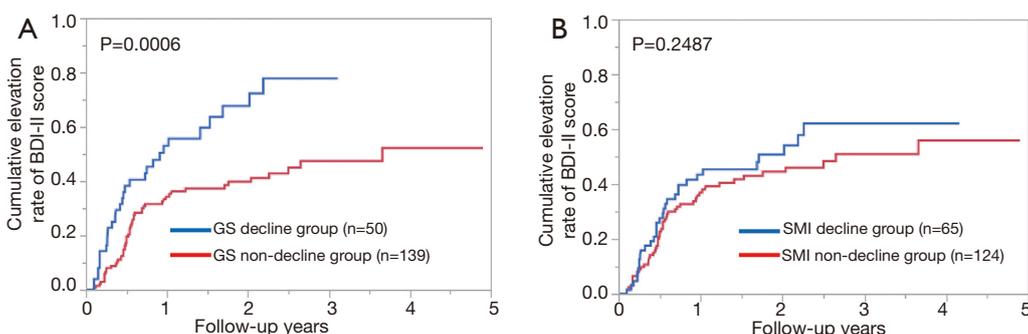


Figure 3 Cumulative elevation rate of BDI-II score according to the baseline GS decline (A) and according to the baseline SMI decline (B). BDI-II, Beck Depression Inventory-2nd edition; GS, grip strength; SMI, skeletal muscle index.

compared to those with GS non-decline at baseline (n=32) ($P=0.0247$, *Figure 4A*). Cirrhotic patients with SMI decline at baseline (n=16) tended to have significantly higher cumulative elevation rates of BDI-II score compared to those with SMI non-decline at baseline (n=33) ($P=0.0944$, *Figure 4B*).

Non-cirrhotic patients with GS decline at baseline (n=33) had significantly higher cumulative elevation rates of BDI-II score compared to those with GS non-decline at baseline (n=107) ($P=0.0335$, *Figure 4C*). However, non-cirrhotic patients with SMI decline at baseline (n=49) did not have significantly higher cumulative elevation rates of BDI-II score compared to those with SMI non-decline at baseline (n=91) ($P=0.5943$, *Figure 4D*).

Cumulative elevation rates of BDI-II score according to the GS value and the SMI value in patients aged 64 years or more and patients aged less than 64 years

Patients aged 64 years (median age in this study) or more with GS decline at baseline (n=37) had significantly higher

cumulative elevation rates of BDI-II score compared to those with GS non-decline at baseline (n=64) ($P=0.0109$, *Figure 5A*). However, patients aged 64 years or more with SMI decline at baseline (n=44) did not have significantly higher cumulative elevation rates of BDI-II score compared to patients with SMI non-decline at baseline (n=57) ($P=0.0944$, *Figure 5B*).

Patients aged less than 64 years with GS decline at baseline (n=13) had significantly higher cumulative elevation rates of BDI-II score compared to those with GS non-decline at baseline (n=75) ($P=0.0232$, *Figure 5C*). However, patients aged less than 64 years with SMI decline at baseline (n=21) did not have significantly higher cumulative elevation rates of BDI-II score compared to patients with SMI non-decline at baseline (n=67) ($P=0.1396$, *Figure 5D*).

Cumulative elevation rates of BDI-II score according to the GS value and the SMI value in male and female patients

Male patients with GS decline at baseline (n=13) had

Table 2 Univariate analyses of factors linked to the progression of depression (n=189)

Baseline variables	Number of each category	Univariate P value
Age (years) ≥ 64 , yes/no	101/88	0.3869
Gender, male/female	87/102	0.4173
Cause of liver diseases, HCV/HBV/others	160/15/14	0.2516
Grip strength at baseline, high/low	139/50	0.0006
Skeletal muscle index at baseline, high/low	124/65	0.2487
Presence of cirrhosis at baseline, yes/no	49/140	0.0113
Presence of depression at baseline, yes/no	63/126	0.3616
AST ≥ 31 IU/L, yes/no	97/92	0.0193
ALT ≥ 28 IU/L, yes/no	100/89	0.2008
Serum albumin ≤ 4.2 g/dL, yes/no	102/87	0.2095
Total bilirubin ≥ 0.8 mg/dL, yes/no	114/75	0.1216
Prothrombin time (INR) > 1.08 , yes/no	98/91	0.0456
Platelet count $\leq 16.1 \times 10^4$ /mm ³ , yes/no	95/94	0.8675
eGFR ≤ 83 mL/min/1.73 m ² , yes/no	96/93	0.4427
Body mass index ≤ 22.7 kg/m ² , yes/no	98/91	0.3971

HCV, hepatitis C virus; HBV, hepatitis B virus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate.

Table 3 Multivariate analyses of factors linked to the progression of depression.

Baseline variables	Multivariate analysis		
	Hazard ratio	95% confidence interval	P value
Presence of cirrhosis	1.362	0.806–2.300	0.2483
Low-GS at baseline	2.037	1.291–3.216	0.0022
AST ≥ 31 IU/L	1.443	0.904–2.302	0.1242
PT (INR) > 1.08	1.129	0.690–1.848	0.6288

GS, grip strength; AST, aspartate aminotransferase; PT, prothrombin time.

significantly higher cumulative elevation rates of BDI-II score compared to those with GS non-decline at baseline (n=74) (P=0.0113, *Figure 6A*). Likewise, male patients with SMI decline at baseline (n=25) had significantly higher cumulative elevation rates of BDI-II score compared to those with SMI non-decline at baseline (n=62) (P=0.0403, *Figure 6B*).

Female patients with GS decline at baseline (n=37) had significantly cumulative higher elevation rates of BDI-II score compared to those with GS non-decline at baseline (n=65) (P=0.0170, *Figure 6C*). However, female

patients with SMI decline at baseline (n=40) did not have significantly higher cumulative elevation rates of BDI-II score compared to those with SMI non-decline at baseline (n=62) (P=0.9134, *Figure 6D*).

Cumulative elevation rates of BDI-II score according to the GS value and the SMI value in patients with baseline BDI-II score ≥ 11 and baseline BDI-II score ≤ 10

Patients with baseline BDI-II score ≥ 11 with GS decline

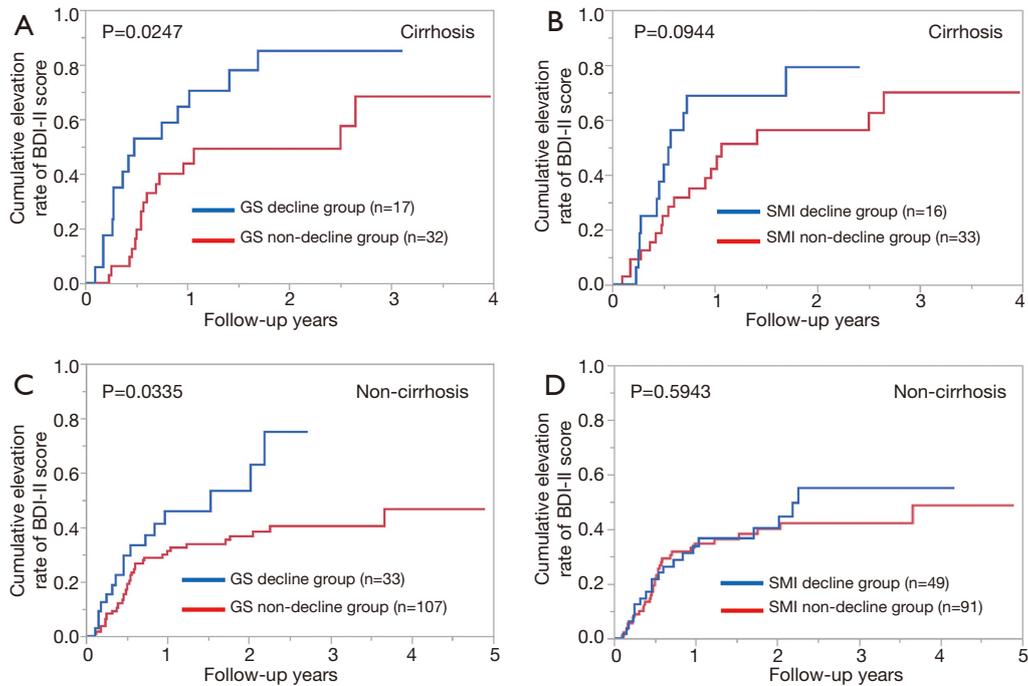


Figure 4 Cumulative elevation rate of BDI-II score according to the baseline GS decline (A) and the baseline SMI decline (B) in cirrhotic patients. Cumulative elevation rate of BDI-II score according to the baseline GS decline (C) and the baseline SMI decline (D) in non-cirrhotic patients. BDI-II, Beck Depression Inventory-2nd edition; GS, grip strength; SMI, skeletal muscle index.

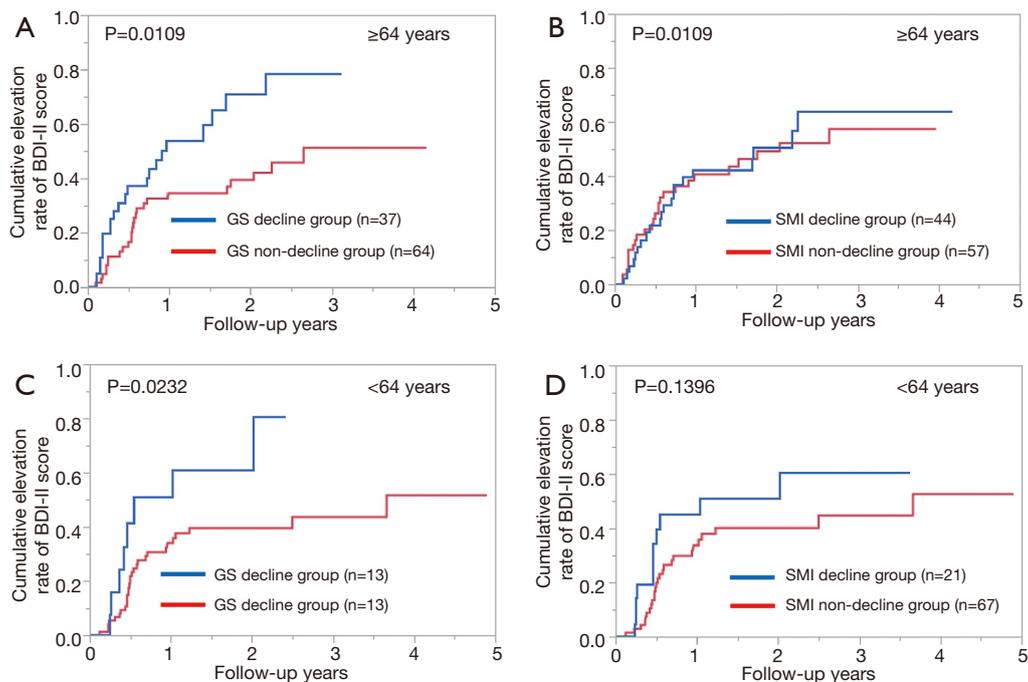


Figure 5 Cumulative elevation rate of BDI-II score according to the baseline GS decline (A) and the baseline SMI decline (B) in patients aged 64 years (median age) or more. Cumulative elevation rate of BDI-II score according to the baseline GS decline (C) and the baseline SMI decline (D) in patients less than 64 years. BDI-II, Beck Depression Inventory-2nd edition; GS, grip strength; SMI, skeletal muscle index.

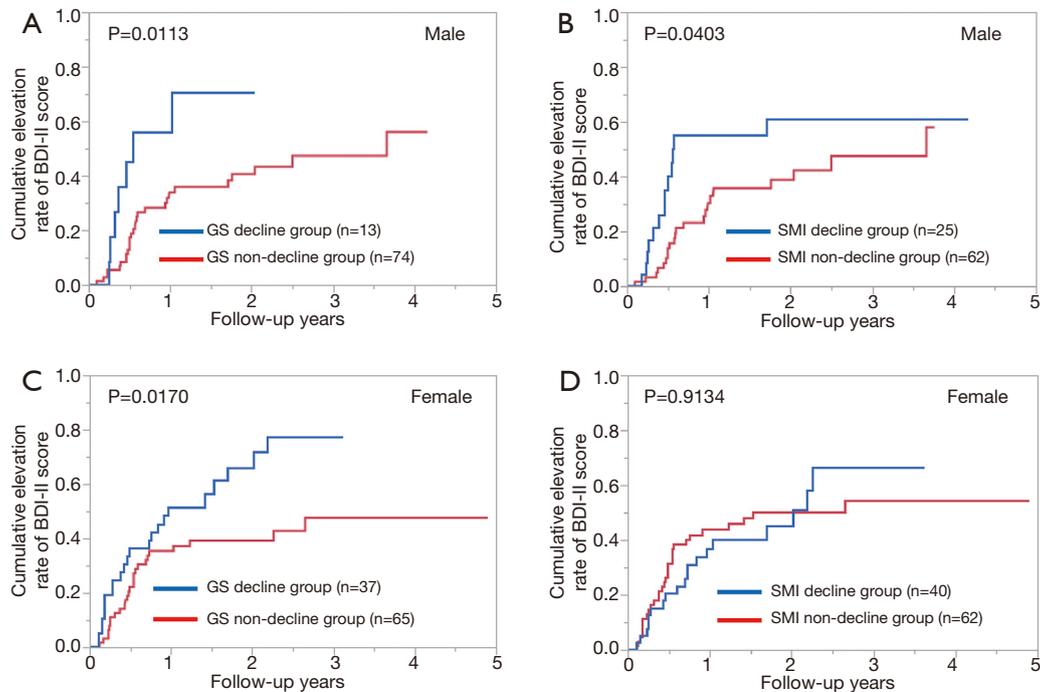


Figure 6 Cumulative elevation rate of BDI-II score according to the baseline GS decline (A) and the baseline SMI decline (B) in male patients. Cumulative elevation rate of BDI-II score according to the baseline GS decline (C) and the baseline SMI decline (D) in female patients. BDI-II, Beck Depression Inventory-2nd edition; GS, grip strength; SMI, skeletal muscle index.

at baseline (n=20) had significantly higher cumulative elevation rates of BDI-II score compared to those with GS non-decline at baseline (n=43) (P=0.0101, *Figure 7A*). Patients with baseline BDI-II score ≥ 11 with SMI decline at baseline (n=24) did not have significantly higher cumulative elevation rates of BDI-II score compared to those with SMI non-decline at baseline (n=39) (P=0.2837, *Figure 7B*).

Patients with baseline BDI-II score ≤ 10 with GS decline at baseline (n=30) had significantly higher cumulative elevation rates of BDI-II score compared to those with GS non-decline at baseline (n=96) (P=0.0187, *Figure 7C*). Likewise, patients with baseline BDI-II score ≤ 10 with SMI decline at baseline (n=41) had significantly higher cumulative elevation rates of BDI-II score compared to those with SMI non-decline at baseline (n=85) (P=0.0215, *Figure 7D*).

Discussion

It is well accepted that particular cohorts of patients with chronic illnesses such as malignancies, musculoskeletal diseases, cardiovascular diseases and respiratory disease

involve a much higher prevalence of affective disorders than the general population, which may be linked to poorer functional outcomes (35). Risk factors for the progression of depression in CLD patients are largely unknown. While skeletal muscle is also an endocrine organ that secretes myokines that regulate systemic glucose and lipid homeostasis and regulate protein synthesis and breakdown (i.e., protein turnover) in muscle tissue (36,37). The causal relationship between depression and sarcopenia-related factors in CLD patients is also unclear. In the current study, we performed comprehensive analyses regarding the influence of sarcopenia-related factors at baseline on the elevation of BDI-II score in patients with CLDs. The multivariate analysis identified only GS decline at baseline as a significant adverse predictor linked to the elevation of BDI-II score. We therefore concluded that reduced GS rather than muscle mass was associated with the elevation of BDI-II score independent of age, cirrhosis status, gender and baseline depressive condition. The causal relationship between depression and sarcopenia-related factors in CLD patients was clarified to some extent through the current study. Depression is possibly linked to sarcopenia due to its

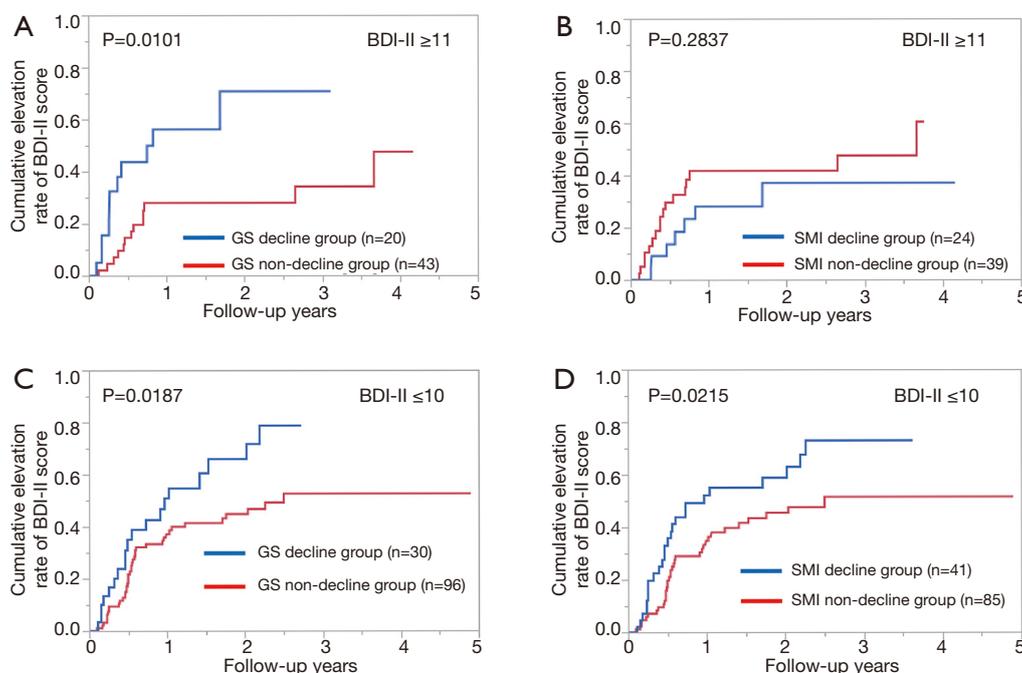


Figure 7 Cumulative elevation rate of BDI-II score according to the baseline GS decline (A) and the baseline SMI decline (B) in patients with baseline BDI-II score >11 . Cumulative elevation rate of BDI-II score according to the baseline GS decline (C) and the baseline SMI decline (D) in patients with baseline BDI-II score ≤ 10 . BDI-II, Beck Depression Inventory-2nd edition; GS, grip strength; SMI, skeletal muscle index.

association with reduced mobility and ability to complete daily activities. A reduction in ability to complete these daily activities has been found to reduce QOL, in particular the mental components of QOL, which infer a potential increase in susceptibility to depression (38,39). To the best of our knowledge, this is the first report demonstrating the impacts of sarcopenia-related factors on the progression of depression in patients with CLDs.

It is unclear why muscle weakness can better predict the exacerbation of depression in patients with CLDs compared to muscle mass loss. One possible reason for these is that muscle strength decline occurs 2–5 times faster than muscle mass loss, which can be linked to the QOL decline, resulting in the elevation of BDI-II score (40). GS is representative of whole-body muscle strength and has been demonstrated to be an independent indicator of nutritional status (41). However, in male patients and in patients with baseline BDI-II ≤ 10 , the SMI decline group had significantly higher cumulative elevation rates of BDI-II score compared to the SMI non-decline group. While the present study emphasizes the importance of GS on the progression of depression, it does not deny the importance

of muscle mass on prognosis. Disease progression and QOL decline can also affect prognosis (39).

In the present study, one-third of analyzed subjects had BDI-II score ≥ 11 at baseline. As mentioned earlier, presence of depression in CLDs tends to be overlooked despite of its prognostic impact. Clinicians should be aware of the high prevalence of depression in CLDs. During the follow-up period, 30 cirrhotic patients (61.2%) had the elevation of BDI-II score, while 54 non-cirrhotic patients (36.2%) had the elevation of BDI-II score, which was largely different from cirrhotic patients. Longer liver disease duration in cirrhotic patients and anxiety about having cirrhosis may be associated with the results. It is reported that over 30% of cirrhotic subjects had depressive features, and they experienced unfavorable clinical outcomes such as progression of depression or higher mortality than non-depressed cirrhotic subjects, which were in line with our data (9). In this study, sarcopenia as defined by the JSH criteria was observed in 7 men (8.0%) and 19 women (18.6%). The prevalence of sarcopenia, determined by the Asian Working Group of Sarcopenia 2014 criteria, was reported to be 9.6% for males and 7.7% for females in

the 949 randomly selected general elderly population in Japan (42). Therefore, it was suggested that sarcopenia has a higher prevalence in female patients with CLDs than in the general elderly population. The reason for these may be linked to the influence of underlying liver diseases on muscle.

In patients with HCV (n=160), 75 patients (46.9%) had the elevation of BDI-II score during the follow-up period. Most of these 75 patients received antiviral therapies with sustained virological response (SVR). SVR does not eliminate the possibility of liver carcinogenesis (43). Similarly, SVR does not solve the psychological problems in patients with HCV considering the current data. Clinicians should be fully aware of these. Post SVR surveillance in HCV patients will be needed.

The limitations of this study should be acknowledged. The retrospective nature of the study limits the evaluation of factors influencing the depressive state such as life circumstances or antidepressant medications. Additionally, our data were derived from Japanese CLD patient data; further examinations on other cohorts will be required to extend the application. Finally, several interventions for CLD patients during the follow-up period have been done, making bias for the disease progression. Thus, interpretation with caution to our results will be necessary.

In conclusion, we would like to emphasize the importance of muscle strength on depressive condition in CLDs. Our findings involve essential implications in clinical practice as they highlight that reduced GS rather than loss of muscle mass is independently associated with an elevated risk for the progression of depression.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and approval of ethics was obtained from the institutional review board in Hyogo college of medicine hospital (No. 3469) and individual consent for this retrospective analysis was waived. An opt out method was employed.

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