Decrease in grip strength is associated with the progression of sleep disturbances in chronic liver diseases

HIROKI NISHIKAWA[1,2*], KAZUNORI YOH[1*], HIRAYUKI ENOMOTO[1], TAKASHI NISHIMURA[1], SHUHEI NISHIGUCHI[3] and HIROKO IIJIMA[1]

[1]Department of Internal Medicine, Division of Gastroenterology and Hepatology, Hyogo College of Medicine; [2]Center for Clinical Research and Education, Hyogo College of Medicine, Nishinomiya, Hyogo 663-8501; [3]Department of Internal Medicine, Kano General Hospital, Osaka, 531-0041, Japan

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Abstract. The causal association between sarcopenia and sleep disorders in patients with chronic liver diseases (CLDs) is unclear. The present study aimed to examine the influence of sarcopenia-related factors [grip strength (GS) and muscle mass] on the progression of sleep disorders in patients with CLD (n=182, 46 cirrhotic cases; median age, 64 years). Sleep quality was evaluated by the Japanese version of Pittsburgh Sleep Quality Index (PSQI-J). A PSQI-J score >5 points was defined as a sleep disorder. In all analyzed patients, evaluation using the PSQI-J questionnaire was performed >2 times during the observation period. The time interval from the date of baseline PSQI-J and the first confirmed date of the elevation of PSQI-J score was calculated. The primary endpoint was the elevation of the PSQI-J score compared to the baseline PSQI-J score. The decline in GS was diagnosed with a GS of <26 kg for males and <18 kg for females. The loss of muscle mass was diagnosed by a skeletal muscle index (SMI) of <7.0 kg/m^2 for males and <5.7 kg/m^2 for females on bioelectrical impedance analysis. The median PSQI-J score was 5. A PSQI-J score of >5 points at baseline was found in 83 patients (45.6%). In patients with a decline in GS (n=48), the 3-year cumulative elevation rate of the PSQI-J score was 82.4%, while in patients with no decline in GS, it was 36.2% (P<0.0001). In patients with a decline in SMI (n=64), the 3-year cumulative elevation rate of the PSQI-J score was 60.6%, while in patients with no decline in SMI, it was 43.4% (P=0.1822). On the multivariate analysis of factors associated with the elevation of the PSQI-J score, only the decline in GS (P=0.0002) was a significant factor. On the whole, the present study demonstrates that a reduced GS rather than the loss of muscle mass is independently associated with an elevated risk for the progression of sleep disorders in patients with CLD.

Correspondence to: Dr Hiroki Nishikawa, Department of Internal Medicine, Division of Gastroenterology and Hepatology, Hyogo College of Medicine, Nishinomiya, Hyogo, 1-1, Mukogawacho, Nishinomiyashi, Hyogo 663-8501, Japan
E-mail: nishikawa_6392_0207@yahoo.co.jp

*Contributed equally

Abbreviations: CLD, chronic liver disease; PSQI, Pittsburgh Sleep Quality Index; PSQI-J, Japanese version of Pittsburgh Sleep Quality Index; GS, grip strength; BIA, bioelectrical impedance analysis; SMI, skeletal muscle index; JSH, Japanese Society of Hepatology; IQR, interquartile range; HR, hazard ratio; CI, confidence interval; HCV, hepatitis C virus; BMI, body mass index

Key words: chronic liver disease, sleep disorder, muscle strength, muscle mass, adverse predictor

Introduction

Sleep is pivotal for the maintenance of mental and physical health, and globally, research interests into sleep disorders are increasing. Some patients with chronic liver diseases (CLDs) complain of sleep disorders. Iwasa *et al* reported that out of 1,788 patients with CLD, 4.0% experienced severe sleep disorders, and 33.4% had moderate sleep disorders (1). Ghabril *et al* reported that 81% of patients with advanced cirrhosis had a disturbed sleep (2). One of the reasons for this is the disturbance of the sleep-regulating hormone (i.e., melatonin) and the appetite-regulating hormone (i.e., leptin) during the day. Itchy skin due to CLDs and anxiety regarding the illness can also cause insomnia (3-5). Shigiyama *et al* demonstrated that sleep disturbance was associated with fat accumulation in the liver and glucose intolerance in mice (6). Thus, sleep disorders can be a critical issue for patients with CLD. The Pittsburgh Sleep Quality Index (PSQI) is a widely used and well-validated patient-reported sleep questionnaire (7-9).

Skeletal muscle is also an endocrine organ that secretes myokines that regulate systemic glucose and lipid homeostasis, and regulate protein synthesis in muscle tissue (10). Sarcopenia is a condition accompanied by a decrease in skeletal muscle mass and strength or physical function (11). Primary sarcopenia is a condition in which skeletal muscle mass and strength or physical function decline with aging. 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 respiratory diseases, heart diseases, inflammatory diseases, malignancies, renal diseases and liver

diseases (12). As regards the mechanisms of the development of sarcopenia in patients with CLD, the involvement of various factors (aging, protein energy malnutrition, signal transduction related to protein synthesis and degradation, myokines and sex hormones, etc.) has been reported (13-15). Sarcopenia can result in a decreased quality of life (QOL) of affected patients and be associated with unfavorable outcomes in patients with CLD (13,16-18).

In a previous cross-sectional study, the authors demonstrated the close association between sarcopenia and sleep disorders in patients with CLD (19). There are several reports regarding the association between sarcopenia and sleep disorders (19-22). However, the causal association between sarcopenia and sleep disorders in patients with CLD is unclear. To clarify this association, the present study sought to examine the influence of sarcopenia-related factors (i.e., muscle strength and muscle mass) on the progression of sleep disorders in patients with CLD.

Patients and methods

Patients. Using a retrospective computerized database, a total of 182 individuals with CLD who visited the Hyogo College of Medicine Hospital between December, 2013 and April, 2018 were retrospectively analyzed. Clinical features, the Japanese version of PSQI (PSQI-J) scores and laboratory data recorded at baseline were collated. Diagnosis for cirrhosis was determined according to the current guidelines (23). In all analyzed patients, evaluation using PSQI-J questionnaire was performed twice or more during the observation period. The time interval from the date of baseline PSQI-J and the first confirmed date of the elevation of PSQI-J score was calculated in each subject. The most suitable intervention for each underlying liver disease was performed (23-26). The study protocol rigorously conformed to the 1975 Helsinki Declaration, and approval of ethics was obtained from the institutional review board in Hyogo College of Medicine Hospital. An opt out method was employed.

PSQI-J score and the present study cohort. Sleep quality was evaluated by PSQI-J, which is a screening tool for sleep disorders (7-9). PSQI-J consists of 7 categories (a total of 10 questions) as follows: i) Subjective sleep quality; ii) sleep latency; iii) sleep duration; iv) habitual sleep efficiency; v) sleep disorders; vi) use of sleep medications; and vii) daytime sleep disturbance. Each category was scored on a scale of 0 to 3, and the sum of PSQI-J scores for all categories was 21 points. Higher PSQI-J scores indicate a poorer sleep quality. Favorable sensitivity and specificity were reported to be found when the sum of PSQI-J scores exceeded 6 points (8). The patients in the present study was categorized as have normal skeep (0-5 points), mild sleep disorders (6-8 points), moderate to mild sleep disorders (9-11 points) and mild to severe sleep disorder (12 or more points) (7-9).

Muscle strength and muscle mass measurement. Muscle strength [grip strength (GS) in the present study] measurement and muscle mass measurements were performed based on previous findings (12). 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 the upper and lower extremities divided by height squared (kg/m^2). Based on the criteria of the Japanese Society of Hepatology (JSH), muscle strength weakness was diagnosed as a GS of <26 kg for males and <18 kg for females. Likewise, the loss of muscle mass was diagnosed by a SMI of <7.0 kg/m^2 for males and <5.7 kg/m^2 for females on BIA (12).

Statistical analysis. Continuous variables are presented as median value [interquartile range (IQR)] and compared using the Student's t-test. The primary endpoint was the elevation of the PSQI-J score compared to the baseline PSQI-J score. Cumulative elevation rates of the PSQI-J score were calculated by the Kaplan-Meier method and compared between groups using the log-rank test. Univariate and multivariate Cox proportional hazard models were employed for identifying significant factors associated with the elevation rates of PSQI-J score, and the results are presented as hazard ratios (HRs) and 95% confidence intervals (CIs) with corresponding P-values. In the univariate analysis, the cohort was divided into 2 categories using each median value. Variables with P-values <0.1 were entered into the multivariate analysis. JMP version 14.0 software (SAS Institute) was employed to analyze data statistically (significant level, P-value <0.05).

Results

Patient characteristics. Of the 182 patients with CLDs, 82 (45.1%) were males [age, median, 64 years; IQR, 55-71 years]. There were 136 patients (74.7%) with non-cirrhosis and 46 patients (25.3%) with cirrhosis. No patients were found to have overt hepatic encephalopathy, hepatocellular carcinoma, or severe ascites. The main liver disease etiology was hepatitis C virus (HCV, 155 cases, 85.2%). The median and IQR values for the PSQI-J score were as follows: Median, 5; IQR, 3-7. A PSQI-J score of 0-5 (normal) was observed in 99 (54.4%) patients, a score of 6-8 (mild sleep disorders) was found in 53 (29.1%) patients, a score of 9-11 (moderate sleep disorders) was found in 19 (10.4%) patients, and a score of ≥12 (severe sleep disorders) was observed in 11 (6.0%) patients. The median and IQR values for the PSQI-J scores in cirrhotic patients and non-cirrhotic patients were as follows: Cirrhotic patients: Media, 6; IQR, 4-9; non-cirrhotic patients: Median, 5; IQR, 3-7; P=0.0662. A decline in GS as defined by the JSH criteria was observed in 9 male patients (11.0%) and 39 female patients (39.0%). A decline in SMI as defined by the JSH criteria was observed in 25 male patients (30.5%) and 39 female patients (39.0%). Sarcopenia as defined by the JSH criteria was observed in 25 patients (13.7%). In patients with any grade of sleep disorder at baseline (PSQI-J score >5, n=83), 24 (28.9%) had a decline in GS, and 28 (33.7%) had a decline in SMI. The baseline clinical characteristics and laboratory data of all analyzed patients are summarized in Table I.

Cumulative elevation rate of PSQI-J score for all cases (n=182). During the observation period, 61 patients (33.5%) exhibited an elevation in the PSQI-J score. For all cases, the 1-, 2- and 3-year cumulative elevation rates of the PSQI-J score were 26.4, 35.2 and 49.3% (Fig. 1).

Table I. Patient baseline characteristics (n=182).

Variables	All cases (n=182)
Age (years)	64 (55-71)
Sex, male/female	82/100
Liver disease etiology	
HCV/HBV/others	155/13/14
Presence of sarcopenia, yes/no	25/157
PSQI-J score	5 (3-7)
Presence of cirrhosis, yes/no	46/136
Body mass index (kg/m^2)	22.7 (20.4-25.425)
SMI (kg/m^2), male	7.69 (7.0-8.07)
SMI (kg/m^2), female	5.9 (5.36-6.34)
Grip strength (kg), male	35.1 (29.8-42.1)
Grip strength (kg), female	20.35 (17.2-22.825)
Total bilirubin (mg/dl)	0.8 (0.6-1.1)
Serum albumin (g/dl)	4.2 (3.975-4.4)
Prothrombin time (INR)	1.07 (1.02-1.13)
Platelet count (x10^4/mm^3)	15.9 (11.8-20.05)
AST (IU/l)	29.5 (22-45.25)
ALT (IU/l)	27 (17-47)
ALP (IU/l)	243.5 (202.75-322)
GGT (IU/l)	26.5 (19-44)
eGFR (ml/min/1.73m^2)	82 (71.75-95)

Data are expressed as the number or median value (interquartile range). HCV, hepatitis C virus; HBV, hepatitis B virus; PSQI-J, the Japanese version of Pittsburgh Sleep Quality Index; SMI, skeletal muscle index; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transferase; eGFR, estimated glomerular filtration rate.

Table II. Univariate analysis of factors linked to the elevation of the PSQI-J score (n=182).

Variables	Number of each category	Univariate P-value
Age (years) ≥64, yes/no	98/84	0.0095
Sex, male/female	82/100	0.0292[a]
Cause of liver diseases, HCV/non-HCV	155/27	0.0632
Grip strength, high/low	134/48	<0.0001[a]
Skeletal muscle index, high/low	118/64	0.1822
Presence of cirrhosis, yes/no	46/136	0.1597
Presence of sleep disorder at baseline, yes/no	83/99	0.8226
AST ≥29.5 IU/l, yes/no	91/91	0.6134
ALT ≥27 IU/l, yes/no	93/89	0.5078
ALP ≥243.5 IU/l, yes/no	91/91	0.7334
GGT ≥26.5 IU/l, yes/no	91/91	0.2278
Serum albumin ≤4.2 g/dl, yes/no	100/82	0.0887
Total bilirubin ≥0.8 mg/dl, yes/no	108/74	0.6928
Prothrombin time (INR) ≥1.07, yes/no	93/89	0.4460
Platelet count ≤15.9 x10^4/mm^3, yes/no	91/91	0.7827
eGFR ≤82 ml/min/1.73m^2, yes/no	93/89	0.4019
Body mass index ≥22.7 kg/m^2, yes/no	93/89	0.8695

PSQI-J, the Japanese version of Pittsburgh Sleep Quality Index; HCV, hepatitis C virus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transferase; eGFR, estimated glomerular filtration rate. [a]P<0.05.

Cumulative elevation rates of the PSQI-J score according to the GS and SMI values. In patients with a decline in GS (n=48), the 1-, 2- and 3-year cumulative elevation rates of the PSQI-J score were 46.0, 67.1 and 82.4%, while in patients with no decline in GS (n=134), the 1-, 2- and 3-year cumulative elevation rates of the PSQI-J score were 19.1, 22.9 and 36.2% (P<0.0001; Fig. 2A).

In patients with a decline in SMI (n=64), the 1-, 2- and 3-year cumulative elevation rates of the PSQI-J score were 33.1, 39.3 and 60.6%, while in patients with no decline in SMI (n=118), the 1-, 2- and 3-year cumulative elevation rates of the PSQI-J score were 22.7, 33.0 and 43.4% (P=0.1822; Fig. 2B).

Predictors of the elevation of PSQI-J score in all patients by univariate and multivariate analyses. As per the univariate analyses, age >64 years (P=0.0095), sex (P=0.0292) and a lower GS (P<0.0001) were found to be significantly associated with the elevation of the PSQI-J score, while HCV or not (P=0.0632) and serum albumin ≤4.2 g/dl (P=0.0887) tended to be significant (Table II). As per the multivariate analyses, only a lower GS (P=0.0002) was identified to be a significant factor associated with the elevation of PSQI-J score (Table III). The HRs and 95% CIs for age >64 years, sex, a lower GS, HCV or not and serum albumin ≤4.2 g/dl are shown in Table III.

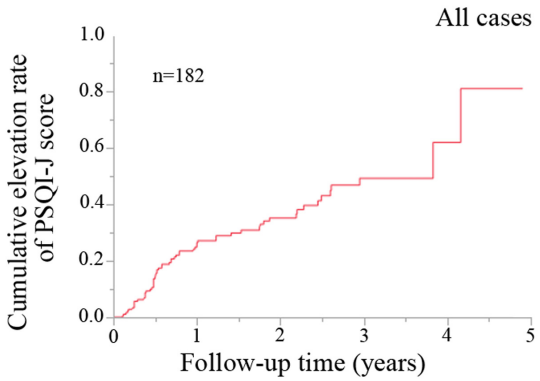

Figure 1. Cumulative elevation rate of the PSQI-J score for all cases (n=182). PSQI-J, Japanese version of Pittsburgh Sleep Quality Index.

Cumulative elevation rates of the PSQI-J score according to the GS and SMI values in cirrhotic patients and non-cirrhotic patients. Cirrhotic patients with a decline in GS (n=17) had significantly higher cumulative elevation rates of the PSQI-J score compared to those with no decline in GS (n=29) (P=0.0210; Fig. 3A). Cirrhotic patients with a decline in SMI (n=15) did not have a significantly higher cumulative elevation

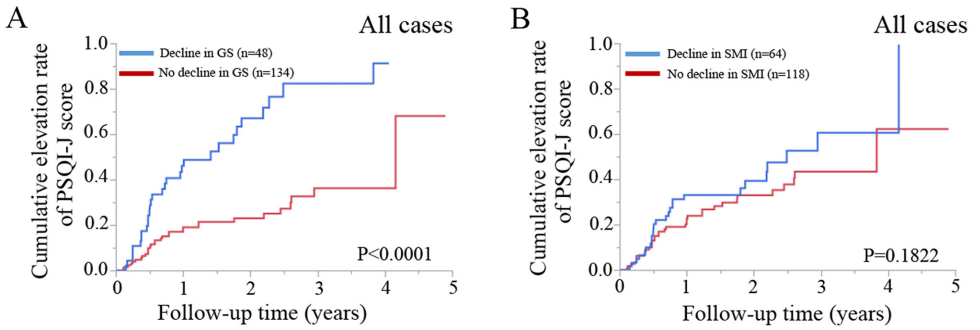

Figure 2. (A) Cumulative elevation rate of the PSQI-J score according to a decline in GS. (B) Cumulative elevation rate of the PSQI-J score according to a decline in SMI. PSQI-J, Japanese version of Pittsburgh Sleep Quality Index; GS, grip strength; SMI, skeletal muscle index.

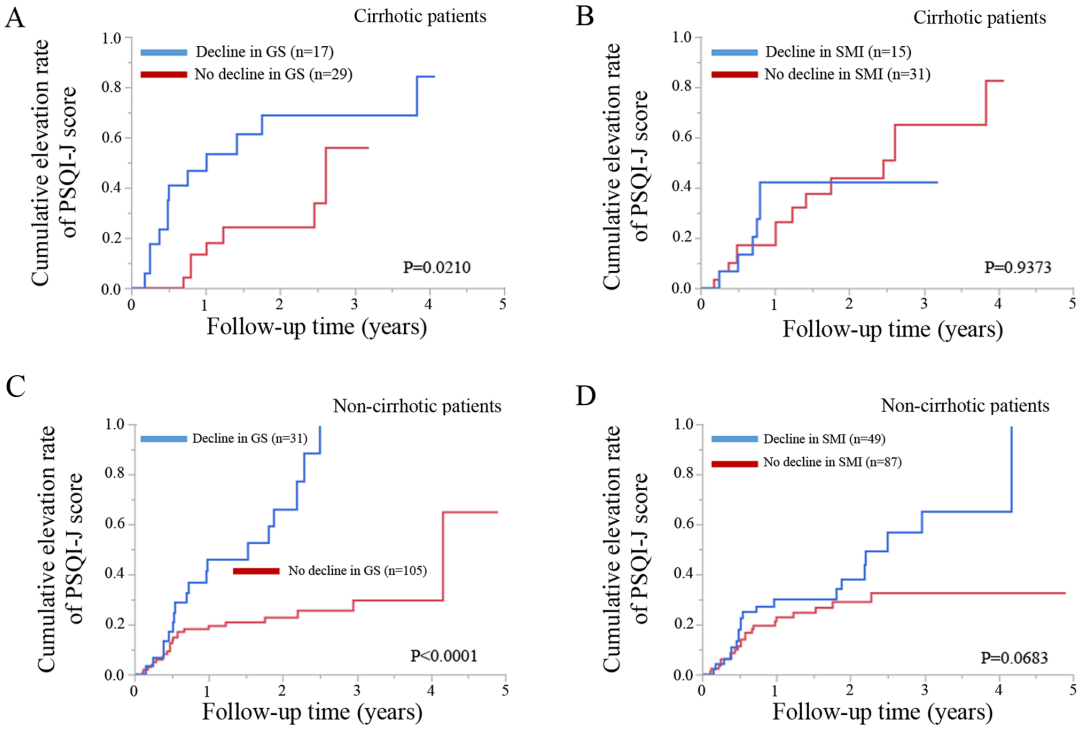

Figure 3. Cumulative elevation rate of the PSQI-J score according to (A) a decline in GS and (B) a decline in SMI in cirrhotic patients. Cumulative elevation rate of the PSQI-J score according to (C) a decline in GS and (D) a decline in SMI in non-cirrhotic patients. PSQI-J, Japanese version of Pittsburgh Sleep Quality Index; GS, grip strength; SMI, skeletal muscle index.

rates of the PSQI-J score compared to those with no decline in SMI (n=31) (P=0.9373; Fig. 3B).

Non-cirrhotic patients with a decline in GS (n=31) had significantly higher cumulative elevation rates of the PSQI-J score compared to those with no decline in GS (n=105) (P<0.0001; Fig. 3C). Non-cirrhotic patients with a decline in SMI (n=49) tended to have significantly higher cumulative elevation rates of the PSQI-J score compared to those with no decline in SMI (n=87) (P=0.0683; Fig. 3D).

Cumulative elevation rates of the PSQI-J score according to the GS and SMI values in patients aged ≥64 years and patients aged <64 years. Patients aged ≥64 years (median age in the present study) or with a decline in GS (n=37) had significantly higher cumulative elevation rates of the PSQI-J score compared to those with no decline in GS (n=61) (P<0.0001; Fig. 4A). However, patients aged ≥64 years with a decline in SMI (n=43) did not have significantly higher cumulative elevation rates of the PSQI-J score compared to patients with no decline in SMI (n=55) (P=0.6912; Fig. 4B).

Patients aged <64 years with a decline in GS (n=11) had significantly higher cumulative elevation rates of the PSQI-J score compared to those with no decline in GS (n=73) (P=0.0168; Fig. 4C). Patients aged <64 years with a decline SMI (n=21) tended to have significantly higher cumulative elevation rates of the PSQI score compared to patients with no decline in SMI (n=63) (P=0.0701; Fig. 4D).

Cumulative elevation rates of the PSQI-J score according to the GS and SMI values in male and female patients. Male patients with a decline in GS (n=9) had significantly higher cumulative elevation rates of PSQI-J score compared to those with no decline in GS (n=73) (P=0.0074; Fig. 5A). Likewise, male patients with a decline in SMI (n=25) had significantly

Table III. Multivariate analysis of factors linked to the elevation of the PSQI-J score.

	Multivariate analysis		
Variables	Hazard ratio	95% confidence interval	P-value
Age, ≥64 years	1.561	0.859-2.838	0.1443
Low-GS	2.984	1.685-5.285	0.0002[a]
Sex (female)	1.041	0.561-1.932	0.8990
Serum albumin ≤4.2 g/dl	1.126	0.625-2.029	0.6929
HCV	2.458	0.868-6.959	0.0902

PSQI-J, the Japanese version of Pittsburgh Sleep Quality Index; GS, grip strength; HCV, hepatitis C virus. [a]P<0.05.

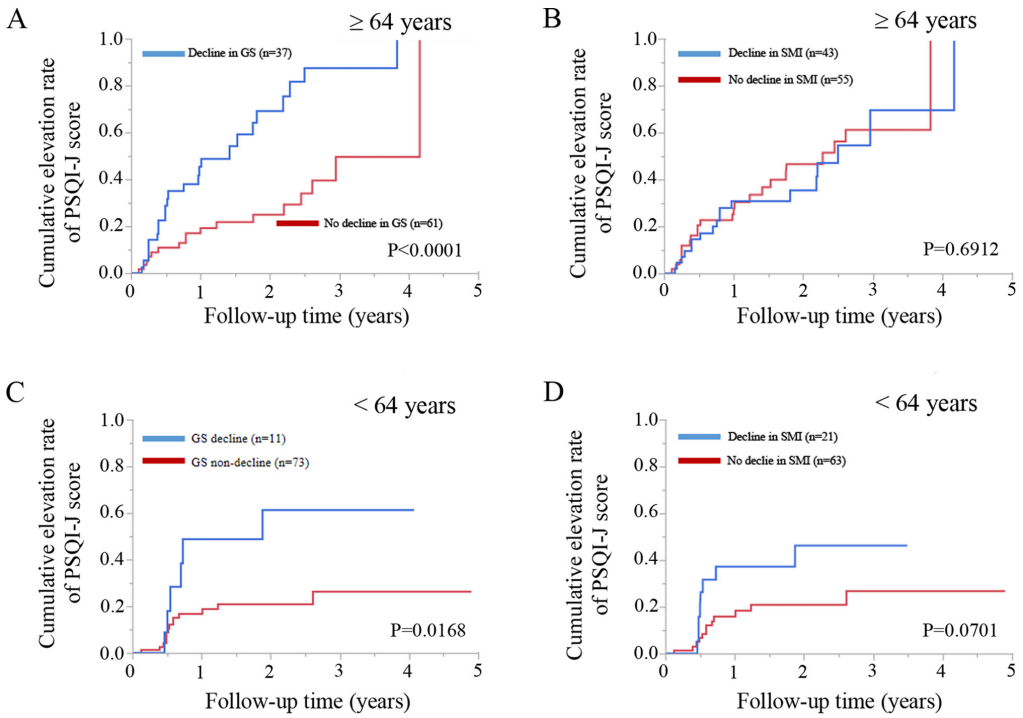

Figure 4. Cumulative elevation rate of the PSQI-J score according to (A) a decline in GS and (B) a decline in SMI in patients aged ≥64 years of age (median age). Cumulative elevation rate of the PSQI-J score according to (C) a decline in GS and (D) a decline in SMI in patients <64 years of age. PSQI-J, Japanese version of Pittsburgh Sleep Quality Index; GS, grip strength; SMI, skeletal muscle index.

higher cumulative elevation rates of the PSQI-J score compared to those with no decline in SMI (n=57) (P=0.0347; Fig. 5B).

Female patients with a decline in GS (n=39) had significantly cumulative higher elevation rates of the PSQI-J score compared to those with no decline in GS (n=61) (P<0.0001; Fig. 5C). However, female patients with a decline in SMI (n=39) did not have significantly higher cumulative elevation rates of the PSQI-J score compared to those with no decline in SMI (n=61) (P=0.9312; Fig. 5D).

Cumulative elevation rates of the PSQI-J score according to the GS and SMI values in patients with baseline PSQI score >5 (baseline) and baseline PSQI score <5 (baseline). Patients with baseline PSQI-J score >5 with a decline in GS (n=24) had significantly higher cumulative elevation rates of the PSQI score compared to those with no decline in GS (n=59) (P=0.0014; Fig. 6A). However, patients with a baseline PSQI score >5 with a decline in SMI (n=28) did not have significantly higher cumulative elevation rates of PSQI-J score compared to those with no decline in SMI (n=55) (P=0.4948; Fig. 6B).

Patients with baseline PSQI-J score ≤5 with a decline in GS (n=24) had significantly higher cumulative elevation rates of PSQI-J score compared to those with no decline in GS (n=75) (P<0.0001; Fig. 6C). Likewise, patients with baseline PSQI-J score ≤5 with a decline in SMI (n=36) had significantly higher cumulative elevation rates of PSQI-J score compared to those with no decline in SMI (n=63) (P=0.0240; Fig. 6D).

Discussion

The causal association between sleep disorders and sarcopenia-related factors in patients with CLD has not yet been fully examined. In patients with CLD, hepatic events or severity of liver fibrosis, as well as aging can be associated with

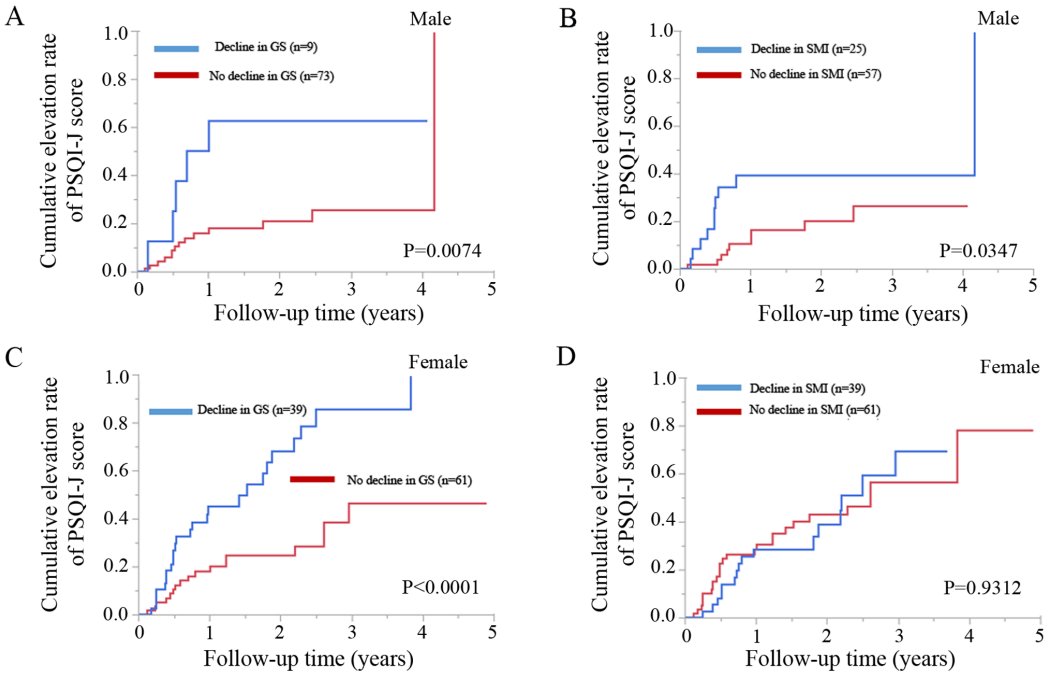

Figure 5. Cumulative elevation rate of the PSQI-J score according to (A) a decline in GS and (B) a decline in SMI in male patients. Cumulative elevation rate of the PSQI-J score according to (C) a decline in GS and (D) a decline in SMI in female patients. PSQI-J, Japanese version of Pittsburgh Sleep Quality Index; GS, grip strength; SMI, skeletal muscle index.

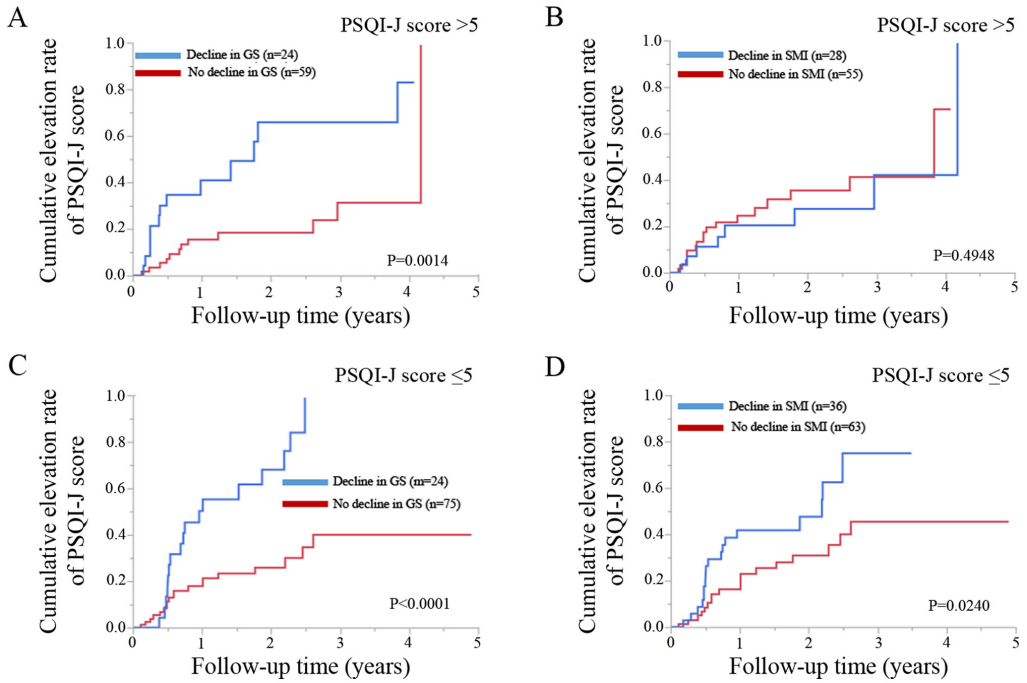

Figure 6. Cumulative elevation rate of the PSQI-J score according to (A) a decline in GS and (B) a decline in SMI in patients with baseline PSQI-J score >5. Cumulative elevation rate of the PSQI-J score according to (C) a decline in GS and (D) a decline in SMI in patients with baseline PSQI-J score ≤5. PSQI-J, Japanese version of Pittsburgh Sleep Quality Index; GS, grip strength; SMI, skeletal muscle index.

a decline in GS (27,28). In the present study, comprehensive analyses regarding the influence of sarcopenia-related factors on the elevation of PSQI-J score in patients with CLDs were performed. Multivariate analysis identified only GS decline as a significant adverse predictor associated with the elevation of PSQI-J score. To conclude, reduced GS rather than muscle mass was associated with the elevation of the PSQI-J score independent of age, cirrhosis status, sex and baseline sleep condition. The causal association between sleep disorders and sarcopenia-related factors in patients with CLD was clarified to some extent through the present study. To the best of our knowledge, this is the first report demonstrating the impacts of sarcopenia-related factors on the progression of sleep disorder in patients with CLDs.

It is unclear why the weakness of muscle strength can better predict the exacerbation of sleep status in patients with CLDs compared to muscle mass loss. One possible reason for this is that a decline in muscle strength occurs 2-5-fold faster than muscle mass loss, which can be linked to a decline in QOL, resulting in the elevation of the PSQI-J score (29). Another possible reason is that muscle strength decline is associated with hormonal changes, such as insulin-like growth factors 1 and testosterone, potentially leading to the exacerbation of sleep status (30). GS is representative of whole-body muscle strength and has been shown to be an independent marker of nutrition (31). However, in the present study, in male patients and in patients with baseline PSQI-J score ≤5, the group with a decline in SMI had significantly higher cumulative elevation rates of PSQI-J score compared to the SMI non-decline group. While the current study emphasizes the significance of GS on the progression of sleep disorder, it does not deny the significance of muscle mass on prognosis.

In the present study, 83 patients (45.6%) out of the analyzed subjects had a baseline PSQI-J score >5. In patients with cirrhosis (n=46), 27 patients (58.7%) had baseline PSQI-J score >5. Samanta *et al* reported that 60 out of 100 cirrhotic patients (60%) had PSQI score >5, which was in agreement with the present data (32). Clinicians should be aware of the high prevalence of sleep disorder in CLDs. During the observation period, 20 cirrhotic patients (43.5%) had the elevation of PSQI score, while 41 non-cirrhotic patients (30.1%) had the elevation of PSQI score, which was largely different from cirrhotic patients. In addition, the median baseline PSQI-J score in cirrhotic patients tended to be higher than that in non-cirrhotic patients in the present study cohort (P=0.0662). Longer liver disease duration in cirrhotic patients and anxiety about having cirrhosis may be linked to the current results.

HCV tended to be significant in our multivariate analysis (P=0.0902). In patients with HCV (n=155), 57 patients (36.8%) had the elevation of PSQI-J score during the observation period. Most of these 57 patients received antiviral therapies with sustained virological response (SVR). SVR does not eliminate the possibility of liver carcinogenesis (33). Similarly, SVR does not solve the sleep problems in patients with HCV considering the current data. Clinicians should be fully aware of these, and post SVR surveillance in HCV patients will be needed. On the other hand, obstructive sleep apnea is frequently seen in patients with non-alcoholic fatty liver disease with obesity (34). In the present study, the median body mass index (BMI) was 22.7 kg/m^2 and the number of patients with BMI ≥30 kg/m^2 was only 4 (2.2%). The PSQI-J score in these 4 obese patients were 0 or 1. Therefore, it is likely that obstructive sleep apnea is not included in the analyzed subjects, and sleep disorder shown in this study may be due to disease itself or other causes than obstructive sleep apnea.

PSQI-J question 8 is a question regarding the frequency of falling asleep while driving, eating and social activities. In the present study, 19 patients (10.4%) had a scale of ≥1 (i.e., experience of drowsiness at least once a week) in the question 8 of PSQI-J. Excessive drowsiness, particularly while driving, can lead to major accidents, so caution should be exercised for such patients (35,36). On the other hand, QOL can be influenced by sex (37). The role of menopause in the risk of a decline in GS or sleep disturbance warrants further investigations (37).

The limitations of the present study must be acknowledged. First, the retrospective nature of the study limits the evaluation of factors influencing the sleep condition such as life circumstances or sleep medications. Second, PSQI-J is a subjective assessment tool, and not objective one. Third, the data were derived from Japanese CLD patient data; further examinations on other cohorts will be required to extend the application. Finally, several interventions for patients with CLD during the observation period were performed, making bias for the disease progression. Thus, interpretation with caution to the results will be needed.

In conclusion, the present study would like to emphasize the significance of muscle strength on the sleep condition in CLDs. The findings involve essential implications in clinical practice as they highlight that a reduced GS rather than the loss of muscle mass is independently associated with an elevated risk for the progression of sleep disorder. Appropriate interventions for patients with CLD with a decline in GS will be necessary for improving patient QOL, including sleep conditions.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article or are available from the corresponding author on reasonable request.

Authors' contributions

All authors HN, KY, HE, TN, SN and HI were involved in the conception and design of the study. HN, KY, HE and TN were involved in data curation. HN was involved in the formal analysis. SN and HI supervised the study. HN and KY were involved in the writing of the original draft. HE, SN and HI were involved in the writing, reviewing and editing of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol rigorously conformed to the 1975 Helsinki Declaration, and approval of ethics was obtained from the institutional review board in Hyogo College of Medicine Hospital. An opt out method was employed.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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