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ORIGINAL ARTICLE

Clinical validation of the chronic liver disease questionnaire for the Chinese population in Singapore

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Abstract

Background and Aim: Assessment of health-related quality-of-life (HRQOL) in patients with chronic liver disease (CLD) requires the use of validated instruments that are understood by patients in their native language. We previously translated the Chronic Liver Disease Questionnaire into the Singapore-Mandarin version (CLDQ-SG). This study aims to examine the internal consistency and validity of the CLDQ-SG in patients with CLD.

Methods: We conducted a cross-sectional study of adult patients with CLD seen in a tertiary center in Singapore who completed both the CLDQ-SG and Short Form Health Survey 36 version 2 (SF-36v2) questionnaires. Internal consistency of the CLDQ-SG was assessed using Cronbach's alpha coefficient. Convergent and divergent validity of the SF-36v2 was assessed using the Spearman correlation coefficient, while discriminant validity was assessed using the Jonckheere-Terpstra test for trend. Exploratory factor analysis was performed to evaluate the factor structure of the CLDQ-SG.

Results: We enrolled 242 subjects (68.2% males, median age 67 years). Predominant etiology of CLD was chronic hepatitis B. Severity of CLD was divided into non-cirrhotic (67.3%), compensated cirrhosis (24.0%), and decompensated cirrhosis (8.7%). Item convergent and discriminant validity of the CLDQ-SG was excellent, with 100% scaling success in all six domains. All domains exhibited good internal consistency, with Cronbach's $\alpha > 0.70$. We observed a consistent trend of a reduction in mean CLDQ-SG score in the three groups reflecting the discriminant validity of the CLDQ-SG to assess changes in HRQOL in different severities of CLD. Factor analysis of the CLDQ-SG demonstrated an independent factor assessing sleep.

Conclusion: The Singapore-Mandarin version of CLDQ-SG is a valid and reliable instrument to measure HRQOL in patients with CLD.

Introduction

Chronic liver disease (CLD) is a major health burden to society and is estimated to be the fifth most common cause of death worldwide.[1] Progression of CLD to cirrhosis, liver failure, and liver cancer is associated with increasing patient morbidity, frequency of hospitalizations, and worsening quality of life.[2] Beyond the management of the physical components of the disease, attention must be directed to thee patient's health-related quality of life (HRQOL), which contributes to their overall state of health.[3] HRQOL is defined as "the physical, psychological and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations and perceptions."[4]

To provide complete patient care, physicians involved in managing patients with CLD must assess patients' HRQOL in addition to physical symptoms. The assessment of HRQOL is conducted using generic and disease-specific instruments. Generic instruments such as the SF36[5] provide normative data that allow a cross-comparison between patient cohorts but are less sensitive to disease-specific changes. Conversely, disease-specific instruments provide a more accurate assessment of impairments caused by specific disease processes. The Chronic Liver Disease Questionnaire (CLDQ) is the most widely validated disease-specific HRQOL instrument developed for patients with CLD.[6] The CLDQ has been cross-culturally validated and translated into several different languages worldwide and has demonstrated excellent validity and reliability for the assessment of HRQOL in CLD irrespective of language, cultural differences, educational level, and etiology of liver disease.[7–16] Despite this, measurement of HRQOL is not commonly performed in clinical

practice. This could be due to unfamiliarity with HRQOL instruments or a lack of evidence to support locally validated HRQOL instruments. This creates an important need for the local adaptation and clinical validation of such HRQOL tools.

In Singapore, a majority of the population is Chinese, and the major burden of CLD is due to chronic hepatitis B, which is endemic in the region.[17] In addition, the rate of non-alcoholic fatty liver disease (NAFLD) has been rapidly increasing over the last two decades.[18] Coupled with a low rate of liver transplantation compared to the West, this translates to a large burden of CLD patients who require regular HRQOL assessment. Although a Mandarin version of the CLDQ has been previously validated in China,[19] the Singapore version of spoken and written Mandarin is different, thus limiting the utility of the China-Mandarin CLDQ in local clinical practice. To meet the need for a Singapore-Mandarin version of CLDQ, we performed a translation and cultural adaptation of the CLDQ to develop a Singapore-Mandarin version of the CLDQ (CLDQ-SG) (refer to Appendix S1, Supporting information), which was shown to be culturally acceptable by the Mandarin-speaking population in Singapore.[20]

In this study, we aim to validate the CLDQ-SG by examining the internal consistency and validity of this self-reported questionnaire in a population of CLD patients in a tertiary center in Singapore.

Methods

We performed a cross-sectional study of adult patients with CLD who were seen in the outpatient clinics in the Department of Gastroenterology & Hepatology, Singapore General Hospital between May 2014 and July 2015. A small proportion of the study cohort was admitted to the hospital directly from the outpatient clinics and was recruited during the participants' inpatient stay. Inclusion criteria for this study were adults ≥21 years of age with a diagnosis of CLD who were able to read and speak Mandarin. Exclusion criteria included patients with active hepatic encephalopathy or cognitive impairment, acute complications of CLD (e.g. acute variceal bleeding, acute liver failure, and spontaneous bacterial peritonitis), extrahepatic organ failure, active malignancy, and active psychiatric diseases.

Diagnosis of CLD was made on clinical grounds and included patients with chronic viral hepatitis B and C, alcoholic liver disease, autoimmune liver disease, NAFLD, methotrexate-related liver fibrosis, and cryptogenic liver cirrhosis. The presence of liver cirrhosis was based on radiological findings of coarse liver echogenicity with irregular margins and/or histopathological criteria. The severity of liver cirrhosis was determined clinically using the Child-Pugh criteria. The presence of ascites was determined either clinically or via abdominal ultrasound. The presence and severity of hepatic encephalopathy was assessed clinically using the West Haven criteria. CLD patients were categorized into three groups for comparison: noncirrhotic, compensated cirrhosis (Child-Pugh A), and decompensated cirrhosis (Child-Pugh B and C).

The study received ethical approval from the SingHealth Centralized Institution Review Board (CIRB Ref: 2014/359/A). All subjects provided written consent to participate in the study. Permission to adapt and translate the original and Mandarin versions of the CLDQ instrument was obtained from the original authors Younossi[6] and Zhou,[18] respectively. Patients who fulfilled the inclusion criteria for the study were asked to complete two questionnaires, the SF-36v2 and the CLDQ-SG, on their own but could seek clarification from a research coordinator if required. The original CLDQ is a disease-specific instrument developed by Younossi *et al.* to evaluate the HRQOL of patients with CLD. It consists of a 29-item self-administered questionnaire that assesses six separate domains—"Fatigue," "Emotional Function," "Abdominal Symptoms," "Systemic Symptoms," "Worry," and "Activity". The questions relate to symptoms or emotions experienced over the past 2 weeks and are rated on a 7-point scale ranging from 1 ("all of the time") to 7 ("none of the time"). The domain score represents the mean score of the items related to that domain. The overall CLDQ score represents the mean score for all six domains. A lower score (closer to 1) represents a poorer state of health compared to a higher score (closer to 7).

Statistical analysis

Descriptive statistics were computed for patient demographics and clinical characteristics and are given as frequencies with percentages (%) for categorical variables and medians with interquartile range for continuous data. For the SF36v2 scoring, Singapore norm-based T-scores were computed using the mean and standard deviation scale scores from published literature.[21]

Item-level analysis. We used Cronbach's alpha coefficient to assess the internal consistency of the items within each domain of the CLDQ-SG, with an alpha value >0.70 representing acceptable reliability.[22] To assess the item convergent validity of the CLDQ-SG, we considered scaling the success achieved when an item-scale correlation (corrected for overlaps) exceeded 0.40.[23] Conversely, item discriminant validity was considered to be achieved when an item correlated higher with its hypothesized scale (item-scale correlation ≥0.40) compared to another unrelated scale in the questionnaire.

Scale-level analysis. The convergent and divergent validity of the disease-specific CLDQ-SG domains in relation to the generic SF-36v2 domains were assessed via Spearman correlation coefficient, r. Convergent validity was supported whenever the correlation of the two instruments demonstrated a moderate (r = 0.40–0.70) to large ($r > 0.70$) correlation. We hypothesized moderate correlations between the following domains: (i) Fatigue (CLDQ-SG) and Vitality (SF-36v2); (ii) Systemic Symptoms (CLDQ-SG) and Bodily Pain (SF-36v2); (iii) Activity (CLDQ-SG) and Role Physical (SF-36v2); and (iv) Emotional Function (CLDQ-SG) and Mental Health (SF-36v2). In contrast, discriminant validity is the extent to which a domain correlates weakly ($r < 0.40$) with another domain intended to assess a different trait and was also considered supported when the correlation was lower than for the corresponding a priori hypothesis mentioned above.

Known-group validity. The ability of CLDQ-SG to distinguish HRQOL between noncirrhotic, compensated cirrhosis, and decompensated cirrhosis patients was tested using the Jonckheere-Tersptra test for testing trends in ordered comparison groups. The poorest, that is, lowest scale scores of CLDQ-SG, were expected from patients with decompensated cirrhosis,

followed by patients with compensated cirrhosis and then patients in the noncirrhotic group in this ascending order. Pairwise comparison between noncirrhosis and compensated cirrhosis and between non-cirrhosis and decompensated cirrhosis for each CLDQ-SG scale was performed using the Mann–Whitney test.

Factor analysis. Exploratory factor analysis using principal components with varimax rotation was performed to evaluate the factor structure of the CLDQ-SG. The criterion for factor extraction was fixing the number of factors to extract as 6. The scree plot was also used to verify the correctness of the number of factors chosen based on an eigenvalue criterion of ≥1.

Results

Patient characteristics. A total of 242 patients with CLD completed both questionnaires. The demographics and clinical characteristics of the patients are presented in Table 1. The median age was 67 years, with 68.2% of participants being male. Majority of the cohort had secondary or college education or higher. Median time taken to complete the CLDQ-SG was 10 min. Questionnaires were completed in the outpatient setting by 220 patients (90.9%), while 22 (9.1%) completed them in the inpatient wards.

The predominant etiology of CLD was chronic hepatitis B, which accounted for 78.9% of cases, in keeping with the expected etiological spectrum in the Singapore population.[16] The median duration of CLD was 9 years from the date of first diagnosis, with a range of 5–17 years. Among the 163 subjects in the noncirrhotic group, 147 (90.2%) had chronic viral hepatitis, 13 (8.0%) NAFLD, 1 (0.6%) autoimmune hepatitis, and 2 (1.2%) had another etiology of CLD.

Approximately a third of the cohort had liver cirrhosis (79 patients, 32.6%), of which 58 (73.4%) had compensated cirrhosis, and 21 (26.6%) had decompensated cirrhosis. Etiology of CLD in the cirrhotic cohort was related to chronic viral hepatitis (68.4%), alcohol (19.0%), NAFLD (3.8%), autoimmune disease (3.8%), and others (5.1%).

Table 1 Demographic and clinical characteristics of study subjects

Characteristics	Summary statistics (n = 242), n (%)
Age (years), median (IQR)	57 (49–63)
Gender	
Male	165 (68.2)
Female	77 (31.8)
Marital status	
Single	29 (12)
Married	207 (85.5)
Widowed	1 (0.4)
Divorced	5 (2.1)
Highest education	
Primary or less	46 (19)
Secondary or college	143 (59.1)
Degree or higher	53 (21.9)
Etiology of CLD	
Chronic hepatitis B	191 (78.9)
NAFLD	16 (6.6)
Alcoholic	15 (6.2)
Chronic hepatitis C	10 (4.1)
Autoimmune	4 (1.7)
Others	6 (2.5)
Years living with CLD	9 (5, 17)
Cirrhosis	
No	163 (67.3)
Yes	79 (32.6)
Child-Pugh category	
A	58 (73.4)
B	17 (21.5)
C	4 (5.1)
MELD score, median (IQR)	8 (7–11)
Time taken to complete CLDQ-SG (min), median (IQR)	10 (5–10)

CLDQ-SG, Chronic Liver Disease Questionnaire into the Singapore-Mandarin version; IQR, interquartile range.

Item-level analyses. Item convergent validity for the CLDQ-SG was excellent, with scaling success (item-scale correlation >0.40) observed in 100% of items for all six scales (Table 2). Item discriminant validity was also excellent, with scaling success of 100% for all scales. All CLDQ-SG scales exhibited good internal consistency with Cronbach's $\alpha > 0.70$, except for Activity (AC), which nevertheless had a consistency that was marginally close to 0.7 at $\alpha = 0.69$. The highest internal consistency was observed for the emotional function (EF) and worry (WO) domains, followed by fatigue (FA) and abdominal symptoms (AS). Systemic symptoms (SS) and activity (AC) had moderate internal consistency.

Scale-level analyses. Our results demonstrate moderate convergent validity between CLDQ-SG and SF36v2, indicating consistency in assessing similar traits (Table 3). Correlation between similar traits: (i) FA and vitality; (ii) SS and bodily pain; (iii) AC and role physical; and (iv) EF and mental health, as indicated by the shaded values in Table 3, were high (>0.50). Convergent and divergent validity were supported as the hypothesized correlations for similar traits were higher than other correlations most of the time (underlined correlation values, Table 3).

Known-group validity. Subgroup analyses of CLDQ-SG scores by severity of CLD are presented in Table 4. All six domains of the CLDQ-SG showed a consistent trend of a reduction in CLDQ-SG score from the noncirrhotic group to the compensated cirrhosis group and a further reduction in the decompensated cirrhosis group, reflecting a progressive deterioration in HRQOL with increasing severity of CLD. The decreasing trend across the CLD groups was statistically significant by the Jonckheere-Terpstra test in four domains—FA, SS, AC, and WO, with a trend toward significance for AS. However, we did not find any significant change in the EF domain despite increasing severity of liver dysfunction.

On cross-comparison between groups, decompensated cirrhosis patients had a significantly lower overall CLDQ-SG score compared to noncirrhotic patients (4.7 *vs* 5.5, $P = 0.008$). The difference was statistically significant in all domains except for EF. This is reinforced by the observation that the difference in

Table 2 Convergent validity, discriminant validity, and internal consistency of the CLDQ-SG

Items	Item-scale correlation†						No. of items	Reliability (Cronbach's α)
	AS	FA	SS	AC	EF	WO		
Abdominal symptoms (AS)								
Q1. Abdominal bloating	**0.69**‡	0.52	0.47	0.41	0.48	0.40	3	0.82
Q5. Abdominal pain	**0.65**‡	0.57	0.52	0.46	0.54	0.46		
Q17. Abdominal discomfort	**0.71**‡	0.57	0.58	0.51	0.62	0.49		
Fatigue (FA)								
Q2. Tiredness or fatigue	0.51	**0.73**‡	0.50	0.38	0.60	0.41		
Q4. Feel sleepy during the day	0.46	**0.72**‡	0.54	0.41	0.62	0.44	5	0.87
Q8. Decreased strength	0.58	**0.68**‡	0.57	0.68	0.67	0.52		
Q11. Decreased energy	0.57	**0.79**‡	0.57	0.56	0.73	0.47		
Q13. Drowsiness	0.47	**0.71**‡	0.55	0.53	0.64	0.44		
Systemic symptoms (SS)								
Q3. Bodily pain	0.50	0.55	**0.43**‡	0.42	0.50	0.36		
Q6. Shortness of breath	0.50	0.51	**0.61**‡	0.50	0.50	0.48	5	0.75
Q21. Muscle cramps	0.38	0.35	**0.52**‡	0.42	0.38	0.31		
Q23. Dry mouth	0.46	0.50	**0.52**‡	0.36	0.54	0.48		
Q27. Itching	0.30	0.43	**0.52**‡	0.39	0.38	0.35		
Activity (AC)								
7. Not able to eat as much as you would like	0.40	0.49	0.39	**0.49**‡	0.47	0.41		
9. Trouble in lifting or carrying heavy objects	0.42	0.49	0.54	**0.52**‡	0.45	0.40		
14. Bothered by a limitation of the diet	0.51	0.57	0.48	**0.52**‡	0.54	0.44	3	0.69
Emotional function (EF)								
10. Anxiety	0.58	0.70	0.53	0.51	**0.75**‡	0.54		
12. Unhappiness	0.52	0.68	0.47	0.54	**0.75**‡	0.50		
15. Irritability	0.50	0.63	0.50	0.47	**0.78**‡	0.48	8	0.92
16. Difficulty in sleeping at night	0.48	0.57	0.53	0.42	**0.67**‡	0.41		
19. Mood swings	0.53	0.63	0.46	0.45	**0.81**‡	0.65		
20. Difficulty in falling asleep at night	0.41	0.47	0.53	0.35	**0.59**‡	0.39		
24. Depression	0.51	0.60	0.52	0.48	**0.79**‡	0.61		
26. Problems with concentration	0.52	0.71	0.61	0.44	**0.72**‡	0.59		
Worry (WO)								
18. Worries about the impact of the liver disease	0.48	0.53	0.53	0.51	0.61	**0.78**‡		
22. Worries that symptoms will develop into major problem	0.44	0.47	0.47	0.40	0.59	**0.82**‡	5	0.91
25. Worries that the condition is getting worse	0.47	0.50	0.46	0.45	0.63	**0.84**‡		
28. Worries about never feeling any better	0.46	0.54	0.53	0.48	0.60	**0.84**‡		
29. Availability of a liver for transplant	0.35	0.29	0.38	0.35	0.36	**0.58**‡		

†Item-scale correlation is corrected for overlap when assessing convergent validity. Convergent validity is supported when the hypothesized item-scale correlation is ≥0.40.

‡Discriminant validity is supported when the hypothesized item-scale correlations are higher than the alternative ones.

Convergent validity is determined by the bold formatting, which represent correlation of each item with their hypothesized scale, corrected for overlap.

AB, Abdominal symptoms; CLDQ-SG, Chronic Liver Disease Questionnaire into the Singapore-Mandarin version; FA, fatigue; SY, systemic symptoms; AC, activity; EM, emotional function; WO, worry.

the median CLDQ-SG scores between these two groups exceeded the minimum clinically important difference (MCID) of 0.5 in all domains (except EF). The MCID reflects changes in HRQOL scores that are clinically meaningful to the patient and the treating physician.[24] Twenty-two patients completed the CLDQ-SG in the inpatient wards. Of these, 77% were admitted for management of decompensated cirrhosis, chiefly ascites. The overall CLDQ-SG score was lower in inpatients compared to the outpatient cohort (4.8 *vs* 5.3, $P = 0.04$).

In contrast, there was no significant difference in the median CLDQ-SG scores between noncirrhotic and compensated cirrhosis patients. Despite an observed trend toward lower CLDQ-SG scores in the latter group, the difference did not exceed the MCID of 0.5 and was not statistically significant.

Factor analysis. Exploratory factor analysis identified six factors with eigenvalues >1 that accounted for a total variance of 69.1%. Table 5 illustrates the rotated factor loadings between the CLDQ-SG items and the six factors. Almost all the items of CLDQ-SG loaded nicely on their hypothesized factors except for two items from the EF subscale (#16 and #20). These two items, "difficulty in sleeping at night" and "difficulty in falling asleep at

Table 3 Correlation matrix for CLDQ-SG domains with SF-36v2 domains

SF-36v2 domains	CLDQ domains					
	Abdominal symptoms (AS)	Fatigue (FA)	Systemic symptoms (SS)	Activity (AC)	Emotional function (EF)	Worry (WO)
Physical functioning	*0.25***	*0.23***	*0.33***	**0.36****	*0.21***	*0.13*
Role physical	*0.39***	*0.48***	*0.42***	***0.53****	*0.45***	*0.36***
Bodily pain	0.51***	0.51***	***0.54****	0.48***	*0.49***	*0.38***
General health	0.46***	*0.47***	*0.40***	*0.37***	*0.45***	0.51***
Vitality	*0.35***	***0.51****	*0.43***	0.42***	*0.51***	*0.39***
Social functioning	0.40***	*0.41***	*0.41***	0.49***	*0.43***	*0.37***
Role emotion	0.42***	*0.50***	*0.42***	***0.45****	*0.52***	0.41***
Mental health	*0.30***	*0.40***	*0.31***	*0.36***	***0.55****	0.43***

**Correlation is significant at the 0.05 level (two-tailed).

Entries in the table correspond to Spearman rank correlation between domains of SF-36 and domains of CLDQ. Convergent validity is determined by the shaded cells, which represent correlation of the two instruments when assessing the same trait. Convergent validity is supported when the bolded correlations are higher than other correlations along the same column. The unbolded cells represent divergent validity, that is, correlation of the two instruments when assessing different traits. Supported convergent and divergent hypothesis are in italics.

CLDQ-SG, Chronic Liver Disease Questionnaire into the Singapore-Mandarin version.

Table 4 CLDQ-SG scores in patients with different severity of chronic liver disease

CLDQ-SG domains	Patient group			Test for decreasing trend across all groups, *P*-value[†]	Noncirrhotic *versus* compensated cirrhosis, *P*-value	Non-cirrhotic *versus*. decompensated cirrhosis, *P*-value
	Noncirrhotic (*n* = 163), median (IQR)	Compensated cirrhosis (*n* = 58), median (IQR)	Decompensated cirrhosis (*n* = 21), median (IQR)			
Abdominal symptoms (AS)	6.0 (5.0–6.7)	5.7 (4.7–6.7)	5.0 (4.0–6.0)	0.059	0.641	0.010
Fatigue (FA)	5.2 (4.4–5.8)	4.8 (4.2–5.8)	4.4 (3.2–5.0)	0.025	0.193	0.031
Systemic symptoms (SS)	5.4 (4.8–6.0)	5.2 (4.4–5.8)	5.0 (4.4–5.6)	0.012	0.065	0.037
Activity (AC)	5.7 (5.0–6.3)	5.3 (4.7–6.0)	4.7 (4.0–5.3)	0.001	0.010	0.001
Emotional function (EF)	5.3 (4.6–6.0)	5.1 (4.5–5.9)	5.0 (4.0–6.0)	0.409	0.703	0.361
Worry (WO)	5.6 (4.8–6.6)	5.2 (4.0–6.6)	4.6 (4.2–6.0)	0.014	0.100	0.027
Overall CLDQ score	5.5 (4.9–6.0)	5.3 (4.5–6.0)	4.7 (4.0–5.4)	0.007	0.118	0.008

[†]Testing the alternative hypothesis that, as disease severity increases (non-cirrhotic → compensated cirrhosis → decompensated cirrhosis), there is a trend towards lower CLDQ-SG domain score; test performed using the Jonckheere-Tersptra test for ordered alternatives.

CLDQ-SG, Chronic Liver Disease Questionnaire into the Singapore-Mandarin version; IQR, interquartile range.

night," instead loaded heavily on a newly identified factor assessing Sleep. We observed that items from the FA and EF domains seemed to be measuring one common trait (FA + EF) that appeared to link features of FA and EF together.

Discussion

This is the first study to validate the Singapore-Mandarin version of the CLDQ-SG in a clinical setting. Our results confirm the validity of the CLDQ-SG for the reliable assessment of HRQOL in a large cohort of patients with CLD. The key finding in our study is the demonstration that the overall CLDG-SG score declines in tandem with declining liver function. We observed a statistically significant decreasing trend in five of the six domains in addition to the overall CLDQ-SG score across the three groups, from noncirrhotic to compensated cirrhosis and decompensated cirrhosis patients. This observation strongly supports the construct validity of the CLDQ-SG for the assessment of severity of liver disease in the different groups of CLD patients. Our findings are consistent with similar studies of translation and validation of the CLDQ in various ethnic populations.[7–16] Clinicians can thus rely on the CLDQ-SG to assess the deterioration of HRQOL as CLD progresses. Conversely, the CLDQ-SG can be used to evaluate the efficacy of therapeutic interventions on improving HRQOL.

When comparing HRQOL between the noncirrhotic and decompensated cirrhosis groups, the difference in the mean CLDQ-SG scores for almost all domains exceeded the minimal clinically important difference (MCID) of 0.5. The concept of MCID describes changes in patient-related outcome scores that are clinically meaningful to the patient and the physician. A change of 0.5 in the CLDQ domain score (on a 1–7 scale) has been suggested as the MCID.[24] Changes of this magnitude in the CLDQ score should signal to the managing physician that a change in treatment may be warranted. This provides the clinician with reassuring evidence that the CLDQ-SG is clinically useful to detect significant deterioration in the patient's HRQOL as his or her CLD progresses. This allows for early identification and therapeutic interventions to address these specific issues.

Table 5 Factor analysis of CLDQ-SG

Item[†]	Factor 1 FA + EF	Factor 2 WO	Factor 3 AC	Factor 4 AS	Factor 5 SS	Factor 6 Sleep
Abdominal symptoms (AS)						
Q1. Abdominal bloating	0.174	0.176	0.192	**0.711**	0.106	0.286
Q5. Abdominal pain	0.246	0.268	0.350	**0.666**	0.052	0.069
Q17. Abdominal discomfort	0.267	0.279	0.289	**0.566**	0.032	0.436
Fatigue (FA)						
Q2. Tiredness or fatigue	**0.702**	0.119	−0.024	0.403	0.260	0.093
Q4. Feel sleepy during the day	**0.698**	0.116	0.054	0.330	0.298	0.032
Q8. Decreased strength	0.433	0.234	**0.587**	0.252	0.199	0.181
Q11. Decreased energy	**0.611**	0.155	0.367	0.277	0.226	0.233
Q13. Drowsiness	**0.610**	0.134	0.250	0.140	0.384	0.139
Systemic symptoms (SS)						
Q3. Bodily pain	0.415	0.143	0.045	**0.563**	0.269	−0.065
Q6. Shortness of breath	0.184	0.276	0.258	0.345	**0.517**	0.115
Q21. Muscle cramps	0.056	0.144	0.213	0.135	**0.664**	0.190
Q 23. Dry mouth	0.318	0.334	0.069	0.157	0.415	0.282
Q 27. Itching	0.209	0.133	0.149	−0.006	**0.757**	0.106
Activity (AC)						
7. Not able to eat as much as you would like	0.199	0.220	**0.697**	0.140	0.085	−0.056
9. Trouble in lifting or carrying heavy objects	0.127	0.090	**0.714**	0.106	0.334	0.077
14. Bothered by a limitation of the diet	0.219	0.185	**0.526**	0.255	0.189	0.268
Emotional function (EF)						
10. Anxiety	**0.651**	0.313	0.358	0.192	0.079	0.137
12. Unhappiness	**0.642**	0.237	0.401	0.099	0.046	0.276
15. Irritability	**0.707**	0.271	0.265	0.091	0.035	0.253
16. Difficulty in sleeping at night	0.349	0.141	0.143	0.158	0.245	**0.760**
19. Mood swings	**0.655**	0.468	0.215	0.128	0.046	0.202
20. Difficulty in falling asleep at night	0.238	0.180	0.040	0.139	0.225	**0.805**
24. Depression	**0.628**	0.458	0.257	0.041	0.061	0.231
26. Problems with concentration	**0.645**	0.394	0.068	0.168	0.102	0.268
Worry (WO)						
18. Worries about the impact of the liver disease	0.291	**0.735**	0.222	0.123	0.185	0.107
22. Worries that symptoms will develop into major problem	0.297	**0.820**	0.106	0.119	0.080	0.134
25. Worries that the condition is getting worse	0.324	**0.781**	0.144	0.125	0.090	0.198
28. Worries about never feeling any better	0.273	**0.792**	0.135	0.161	0.222	0.077
29. Availability of a liver for transplant	0.006	**0.699**	0.139	0.198	0.152	0.029

[†]The notation for the items was as such, for example, AB5 means the item belongs to the AB subscale and is question number 5 in the CLDQ-SG.
AB, abdominal symptoms; AC, activity; CLDQ-SG, Chronic Liver Disease Questionnaire into the Singapore-Mandarin version; EF, emotional function; FA, fatigue; SS, systemic symptoms; WO, worry. The bold values indicate the correlation between the variables and the individual factors.

The CLDQ-SG is a valid instrument for evaluating the specific domains of interest in the assessment of HRQOL. The only domain in which a significant trend was not observed between the three groups was EF. This observation is not unique to our study. In the validation of the China-Mandarin version of the CLDQ, Bao et al. similarly reported the lack of a significant trend in the EF domain between noncirrhotic and cirrhosis patients with chronic hepatitis B.[10] The lack of significant change in the EF domain across severity of CLD was also reported in the Persian and Serbian cohorts.[14,15] This suggests that the CLDQ may not be sensitive enough to detect significant differences in the EF domain. Indeed, in the original development of the CLDQ, the EF domain showed the smallest changes in CLDQ score across the severity of disease when compared to the other five domains.[6]

Through exploratory factor analysis, we identified six factors that accounted for a total variance of 69.1%. However, compared to the original CLDQ study, we found that the items for the FA domain were not distinct and instead coloaded with the EF domain into a single factor. Poor factor loading of the FA domain was similarly observed by Lam[12] and Zhou[18] in the Cantonese and Mandarin versions of the CLDQ, respectively. However, in the German[11] and Spanish[9] validation studies of the CLDQ, items in the FA domain loaded well on a single factor, similar to the original description by Younossi.[6] This finding may suggest that, in Chinese-speaking populations, questions relating to FA (e.g. "feeling sleepy during the day," "feeling decreased strength," or "decreased level of energy") may be misinterpreted as affecting activity or emotional dysfunction instead, possibly due to linguistic peculiarities.

We identified a new factor that assessed sleep, which is unique from the original six factors described by Younossi *et al.*[6] However, this is not a unique finding and has been consistently described in previous validations of the original CLDQ instrument.[8–12,15] Our data thus add to the collective literature

that calls for a modification of the CLDQ to add a separate seventh domain specifically to assess sleep. In the original CLDQ construct, items #16 and #20 are included in the EF domain. However, sleep difficulties in patients with CLD may not be related to emotional concerns but may instead be caused by physical discomfort (e.g. from ascites) or by the disease process itself (e.g. hepatic encephalopathy).

We acknowledge several limitations of our study. First, being a single-center study, there may be concerns regarding the applicability of the results to the general Singapore population. However, as one of the two tertiary centers in the country, our hospital sees a large proportion of CLD and cirrhosis patients in Singapore, and the large sample size provides confidence in the validity of the study findings. Second, we did not assess test–retest reliability in this study as this has already been well established in previous studies. Finally, the relatively low numbers of decompensated cirrhosis patients may have limited the sensitivity of the CLDQ-SG to demonstrate meaningful differences between the various Child-Pugh classes.

In conclusion, this is the first study to validate the Singapore-Mandarin version of the CLDQ. The CLDQ-SG is easy to administer, easily understood, and acceptable to patients. Most importantly, our study provides evidence of the reliability and validity of the CLDQ-SG as a disease-specific HRQOL instrument for CLD patients. This will enable all health-care professionals involved in the management of CLD patients to routinely incorporate the assessment of HRQOL using this validated tool to optimize the holistic care of CLD patients.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

Appendix S1. Supporting Information.