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Cross-Cultural Adaptation and Psychometric Assessment of the Liver Disease Symptom Index 2.0 to Measure Health-Related Quality of Life Among Iranian Patients With Chronic Hepatitis B

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Abstract

Purpose: There are only a few measures to assess quality of life among patients with liver disorders. The aim of this study was to determine the psychometric properties of the Liver Disease Symptom Index Version 2.0 (LDSI 2.0), a disease specific measure of health-related quality of life (HRQOL), in Persian-speaking patients with chronic hepatitis B. **Method:** Using a cross-sectional design, 312 patients were recruited. Data were collected from the patients using the LDSI 2.0, Chronic Liver Disease Questionnaire, and EuroQol. Convergent and discriminant validity were investigated. Known-groups validity and factor structure of the scale were also determined. Receiver operating characteristics was used to discriminate patients based on their general health status. **Results:** Significant correlations were found between HRQOL measures. Disease duration, disease stage, and serum aspartate aminotransferase differentiated patients. Factor analysis determined a seven-factor solution that explained 70% of the total variance. Area under the curve in receiver operating characteristics analysis was 0.706; 95% confidence interval = [0.648, 0.764]. **Conclusions:** The LDSI2.0 is an appropriate HRQOL scale for use among Iranian patients with chronic hepatitis B based on its solid psychometric properties in this population.

Keywords

health-related quality of life, chronic hepatitis B, liver disease, validity, reliability

Introduction

Chronic hepatitis B (CHB) is a common liver disease that is present in every country around the world (Ott, Stevens, Groeger, & Wiersma, 2012). According to World Health Organization, 2 billion people may be infected by hepatitis B virus (HBV; World Health Organization, 2014). Statistics show that more than 350 million are chronically carriers of the disease and the majority live in Asia and developing countries (Franco et al., 2012; Hudu, Malik, Niazlin, Harmal, & Sekawi, 2013). For example, while 1.25 million people (approximately 400 per 100,000) with CHB are in the United States and average incidence of that in Europe varies from 1 to 15 per 100,000, the number in China exceeds 120 million (i.e., more than 9,000 per 100,000; Cui & Jia, 2013; Rantala & van de Laar, 2008; Spiegel et al., 2007). In a developing country like Iran, it is estimated that nearly 1.7% of the general population (approximately 1,700 per 100,000) suffers from the CHB (Poorolajal & Majdzadeh, 2009). This disease is a major health problem with serious and fatal complications such as cirrhosis and hepatocellular carcinoma (Spiegel et al., 2007). Overall, 0.5 to 1.2 million deaths occur annually because of HBV infection (Lavanchy, 2005).

Besides premature mortality, CHB may cause considerable health problems that threaten quality of life. Problems such as fatigue, pain, encephalopathy, ascites, depression, anxiety, reduced ability for daily activities, and communication issues may be experienced that negatively affect health-related quality of life (HRQOL; Gutteling et al., 2006; Spiegel et al., 2007). Therefore, measuring this construct as an essential component of health outcomes is important. HRQOL may also serve as an index of patient satisfaction and treatment success (Karaivazoglou et al., 2010). HRQOL instruments may

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be used in experimental studies to measure degree of change and evaluate efficacy of interventions being administered. Unfortunately, past research on liver disease emphasized treatment methods instead of HRQOL. However, it is now recognized that the best measures to assess therapeutic efforts are patient-reported outcomes such as HRQOL scales. Studies show that HBV infection even in the absence of complications decreases HRQOL significantly (Spiegel et al., 2007; Zhuang et al., 2014). Assessing this outcome, then, is necessary.

Although there are numerous instruments to assess overall HRQOL, use of a disease-specific measure may help better capture psychological, social, and health outcomes specific to CHB. Moreover, generic instruments may fail to address what patients with CHB feel are the most important domains that should be the targets of intervention. Otherwise, patients' perceptions regarding their clinical situations will go neglected (Ong, Lim, & Li, 2009). To date, a few disease-specific HRQOL measures have been developed such as the Chronic Liver Disease Questionnaire (CLDQ), the Liver Disease Quality of Life Instrument, and the Liver Disease Symptom Index (LDSI; Gralnek et al., 2000; van der Plas et al., 2003, 2004; Younossi, Guyatt, Kiwi, Boparai, & King, 1999). However, developing a culturally adapted scale for patients with various liver diseases is still a challenge. All these scales need to be translated and applied in different populations to adapt them to various cultural and socioeconomic factors related to the community being investigated. Although good translations of such scales (e.g., Persian CLDQ or HBQOL) are now available, the availability of other psychometrically sound, culturally appropriate disease-specific measures of HRQOL will expand researchers' toolbox in studying the overall health and well-being of those with liver disease.

The LDSI Version 1.0 was developed to address severity of liver disease symptoms and the problems caused by those symptoms that may affect HRQOL (van der Plas et al., 2003, 2004). Although other scales have also measured symptoms of disease, they did not assess the negative effects of those symptoms on daily activities. This measure addressed this issue by examining effects on ability to perform daily activities, and after amendments and minor changes to the original scale the final version of the measure (Liver Disease Symptom Index Version 2.0 [LDSI 2.0]) was developed and has shown considerable validity and reliability in a variety of settings (van der Plas et al., 2004, 2007; Youssef, Shepherd, Evans, & Wyke, 2012).

The purpose of present study was to develop a Persian language version of the scale and to examine the psychometric properties of this version in patients with the CHB.

Material and Method

Design and Sample

This was a cross-sectional study conducted in Tehran city of Iran. Data were collected between January and March 2014 from patients being seen at the Tehran Hepatitis Center. To improve the accuracy of data collection in both literate and illiterate patients, face-to-face interviews by trained health care professionals were conducted. An adequate sample size for conducting factor analysis was considered to be 300 participants (Furr & Bacharach, 2008). Consequently, a convenience sample of 330 patients was approached and asked to participate in the study, with 312 agreeing to take part (response rate of 94.5%). The following inclusion criteria were used to select the sample: diagnosis of CHB based on existing hepatitis B surface antigen for more than 6 months, age 18 years or older, and Farsi speaking. Patients with other types of hepatitis virus (A, C, D, and E), those with a history of liver transplantation, cognitive disorder, hepatic encephalopathy Grade II or higher, hepatic carcinoma, and other serious/end-stage diseases were excluded from the study. All patients received information about the aim of study and were ensured about confidentiality. This study was approved by institutional review board of Baqiyatallah University of Medical Sciences and ethical committee of the Gastroenterology and Liver Disease Research Center.

Measures

The EuroQOL and CLDQ were used to assess criterion validity of the LDSI 2.0.

EuroQoL (EQ-5D). The EQ-5D is a brief self-report scale that has been widely used to assess HEQOL among different groups of medical patients as well as in healthy people. This measure includes two sections. The first section (EQ-5D-3L) consists of five domains: mobility, self-care, regular activities, pain or discomfort, and anxiety or depression. Each domain includes a three-response option (*no problems* = 1, *moderate problems* = 2, and *extreme problems* = 3). The scores on theses domains can be summed and normalized to produce a utility score that ranges from 0.59 to 1.0 (higher scores indicate better state of general health). This score is calculated based on a value set derived from the U.S. general population (Shaw, Johnson, & Coons, 2005). For countries where there is no value set of preferred weights, a value set from the United Kingdom may be used (EuroQol, 2014). The second section of the measure is the EQ-5D-VAS. This is a visual analogue scale represented by a vertical line from 0 (*the worst imaginable health*) to 100 (*the best imaginable health*). The EQ-5D has been translated into many languages, and the Persian version of the scale has been used in previous studies (Rabin, Oemar, & Oppe, 2011; Saffari, Emami Meybodi, Koenig, Pakpour, & Rshidi Jahan, 2014).

Chronic Liver Disease Questionnaire. This is a disease-specific HRQOL questionnaire developed by Younossi et al. (1999) to investigate the medical issues that affect quality of life in patients with different types of chronic liver disease. This scale includes six subscales: abdominal symptoms, fatigue,

systemic symptoms, activity, emotional function, and worry. The overall scale contains 29 items with response options for each item ranging from 1 (*all of the time*) to 7 (*none of the time*) on a Likert-type scale. There is also a separate score for each subscale. Total score also can be computed by the sum of subscale scores divided by six (number of subscales). Higher scores indicate a better state of health. This scale has been shown to be valid and reliable in different studies (Younossi et al., 1999). The Persian version of the scale has also been developed and shown to be useful among Iranian patients with liver disease (Mahmoudi et al., 2012).

Liver Disease Symptom Index 2.0. The LDSI was originally developed by a group of hepatologists in the Netherlands. The scale assesses symptoms related to liver diseases and the adverse effects that these symptoms have on the daily activities. The scale includes 24 items and consists two main sections (a symptom index with 18 items and extra Dutch Liver Patients Association [NLV] with 6 items). The first section measures severity and hindrance of symptoms such as itching, joint pain, right upper abdominal pain, sleeping during the day, worry about family, decreased appetite, depression, and jaundice during the past week. Only severity related to "fear of complications" is also measured in this section. The second section includes items that were added by the NLV board as important supplemental items related to HRQOL for patients with liver disease. These are items that address issues related to memory problems, personality change, difficulty in financial affairs, time management, reduced sexual interest, and decreased sexual activity. Each item has a 5-level response option on a Likert-type scale that ranges from 0 (*not at all*) to 4 (*to a high extent*). Scores on each section or symptom may be calculated by summing the scores of items in the section or those related to a symptom and dividing by number of items. Lower scores demonstrate better situations. The original version of the LDSI 2.0 was validated in 1,175 patients with liver disease, of which less than half (42.5%) were in the noncirrhotic stage of the disease and only 25% had viral hepatitis (van der Plas et al., 2004). Dutch, English, and Arabic versions of the scale are available and it has been shown to have good psychometrics in prior studies (van der Plas et al., 2003, 2004; Youssef et al., 2012).

Demographic and Clinical Data. Data on age, sex, marital status, employment, education, accommodation, and number of children were collected. Clinical information including height, weight, cause of disease, stage of disease, comorbidity, history of interferon therapy, duration of disease, history of hospitalization, number of biopsies, and presence of ascites were retrieved by reviewing the medical records of patients and interviewing them by a trained researcher. Results of the latest laboratory tests relating to hepatic illness were also gathered from the medical records. These included blood tests such as serum albumin, hemoglobin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, total bilirubin, prothrombin time, international normalized ratio, and creatinine. The severity of disease was assessed by categorizing patients based on the Child–Pugh classification. This classification uses five clinical indices including three measures of liver function (i.e., albumin of serum, total bilirubin, and international normalized ratio) and two clinical indicators (i.e., levels of ascites and encephalopathy). Based on the average score obtained from these indices, three classes of severity are determined ranging A to C, where class C indicates the most severe liver disease (Pugh, Murray-Lyon, Dawson, Pietroni, & Williams, 1973). A single-item question was also asked about patients' overall health status: "In general, which of the following statements describe your current health status? (acceptable/appropriate or unacceptable/inappropriate)."

Translation and Adaptation of the LDSI 2.0

Permission to use the LDSI 2.0 in a psychometric study was obtained from one of the original developers. We used a standard method to forward- and backward-translate to scale to produce the Persian version of the LDSI 2.0 (Beaton, Bombardier, Guillemin, & Ferraz, 2000). First, the English version of the scale was translated into Persian by two bilingual translators who were experts in health education and internal medicine. Two independent bilingual translators unfamiliar with the original instrument then back-translated the Persian version into English. Face and content validity of the new version was discussed using a panel of experts. By consensus of these experts the next-to-last version of the scale was produced. This version, then, was pretested among 14 patients with the CHB. These patients were asked to rate each item on clarity, relevancy, appropriateness, and comprehension. Finally, these comments were used to adjust the scale and prepare the final Persian version. Speaking about sexual activity is a religious taboo for most Iranians who are Muslim. Consequently, several patients when pretesting the scale were embarrassed when asked about Items 14 and 15 of the questionnaire. Therefore, in order to address this cultural issue, we matched interviewers to patients by gender to relieve this concern. In addition, the importance of responding to all the items, especially regarding sexual activity, was emphasized in order to minimize missing data.

Data Analysis and Statistical Methods

Descriptive statistics were used to summarize characteristics of the sample. Internal consistency of the scale was examined using corrected item–total correlation. Items with higher than 0.2 correlation are considered acceptable (Kline, 1986). Floor and ceiling effect were measured to identify scale feasibility. The floor effect is present when probable considerable proportion of patients' responses fall below the lowest level of response for an item or scale, whereas a ceiling effect is present when a significant

proportion of responses exceed the highest level of response (Lewis-Beck, Bryman, & Liao, 2004). Time needed to complete the questionnaire was also considered an indicator of feasibility. The reliability of the scale was determined by test–retest reliability and Cronbach's alpha internal consistency. The test–retest statistic should be >.70 to indicate adequate stability of the scale (Aaronson et al., 2002). This correlation was computed using 26 patients that completed the LDSI 2.0 two times with a 1-week interval between measurements. Cronbach's alpha values greater than .70 are likewise considered appropriate (Aaronson et al., 2002). Convergent and discriminant validity of the scale were measured by the item-scaling test. This assesses the relationships between a subscale and its hypothesized items. When items have a sufficient correlation ($r > .40$) with their theoretical hypothesized subscale the convergent validity may be confirmed. Similarly, when the correlations of the item with nonhypothesized subscales are higher than its correlation to the hypothesized subscale, the discriminant validity will be established (Fayers & Machin, 2007). We evaluated concurrent validity of the LDSI 2.0 by examining Spearman correlations of its subscales with the CLDQ. Criterion validity was assessed also using a correlation matrix between EQ-5D subscales and domains of the LDSI 2.0. To establish construct validity of the scale both known-group method and factor analysis were conducted. Known-group validity should identify different results for the scale in various groups of individuals. When the scale can differentiate between different groups, this criterion is met. We used this method for both parts of the LDSI 2.0 (i.e., symptom index and extra NLV items). Principal component analysis with Varimax rotation was performed to explore and extract factors included in the scale. Kaiser–Mayer–Olkin and Bartlett's test of sphericity were run before factor analysis to investigate sample adequacy and overall significance of the correlations, respectively. We used scree plot and Kaiser–Guttman rule (eigenvalues greater than 1) to identify number of factors. To further assess discriminative validity of the scales, we performed a receiver operating characteristics (ROC) analysis. Area under the ROC curve (AUC) may demonstrate the scale's power of discrimination. According to Hosmer and Lemeshow guidelines, when the AUC is between 0.7 and 0.8, this is acceptable discrimination, and values greater than 0.8 indicate excellent discrimination (Hosmer & Lemeshow, 2000). This method has been shown to be useful for testing the performance of different measures against an external indicator. We used the participants' general assessment of their health status as an external indicator for this purpose (for the LDSI 2.0, CLDQ, and EQ-5D). The purpose of these analyses was to provide a comprehensive psychometric assessment of the LDSI 2.0 in this Iranian population. All statistical procedures were carried out by IBM SPSS for Windows Version 20, and the level of statistical significance was set at a p value of <.05.

Results

The mean age of the sample ($n = 312$) was 43.3 years ($SD = 11.3$), and the majority of patients were men ($n = 242$, 77.6%). Nearly 90% ($n = 283$) were married, and more than half of the sample were employed ($n = 175$, 56.1%). According to body mass index (BMI), 58.7% of patients ($n = 183$) were overweight or obese (BMI > 25), and only four persons (1.3%) were classified as underweight (BMI < 18). Most of the sample lived in urban areas ($n = 303$, 97.1%). Staging of the disease showed that most patients had not progressed to a cirrhotic stage ($n = 259$, 83%), and only 1.6% ($n = 5$) had ascites. The majority of patients ($n = 187$, 60%) had been diagnosed for more than 10 years to be hepatitis B surface antigen positive. More than half of patients ($n = 183$) did not understand what the primary cause of their disease was from (unknown etiology). Diabetes mellitus and cardiovascular disorders ($n = 24$, 7.7%, and $n = 19$, 6.1%, respectively) were the most prevalent comorbidities in the sample. Only 17.6% of the patients ($n = 55$) had received interferon therapy. More than 80% of patients ($n = 251$) had no history of liver biopsy. Results of recently reported laboratory blood tests revealed that the mean values of other tests were generally within the normal range, except for alkaline phosphatase ($M = 192.4$; $SD = 63.6$). The Child–Pugh classification demonstrated that among cirrhotic patients ($n = 53$, 17%), 44 persons were Grade A, and 9 persons were Grade B in disease severity. Demographic and clinical variables are described in Table 1.

Table 2 shows the results of descriptive item analysis of the LDSI 2.0. The means of all items with exception of the Items 5A and 12 ranged between 0 and 1. The overall floor effect is 69%, while the celling effect is 2.8%. The corrected item-to-total correlations range from .250 to .692. According to Cronbach's alpha for item deletion, removing any item does not help to significantly improve the overall Cronbach's alpha ($.886 < \alpha < .896$).

In Table 3, the subscales scores as well as evidence for convergent and discriminant validity are provided for the symptom index part of the LDSI 2.0.Variability of the subscale scores around the mean is considerable. The means ranged from 0.139 to 0.863, and the standard deviations ranged from 0.415 to 0.983. The average floor effect for these subscales is 59.5%, while the average ceiling effect is low (0.7%). The item-scaling test shows an appropriate range of correlations between the items and their hypothesized domains (.69-.94) that indicates convergent validity. Item discrimination shows that the correlations between items and nonhypothesized domains are all lower than their correlations with hypothesized domains, which is indicative of discriminant validity. The Cronbach's alpha for total scale was .896 and for the subscales of the symptom index ranged from .591 to .821. The alpha for extra NLV section was .769. The r value of the 1-week test–retest reliability in 26 patients was .84 (Pearson correlation).

Table 1. Demographic and Clinical Characteristics of the Patients (N = 312).

Characteristics	n (%)/(M ± SD)
Age	43.30 ± 11.34
Sex	
Male	242 (77.6)
Female	70 (22.4)
Marital status	
Single	26 (8.3)
Married	283 (90.7)
Widowed	3 (1.0)
Occupation	
Employed	175 (56.1)
Unemployed	137 (43.9)
Education level	
Primary	22 (7.1)
Secondary	165 (52.8)
University	125 (40.1)
Residence	
Urban	303 (97.1)
Rural	9 (2.9)
Number of children	2.02 ± 1.43
BMI (kg/m^2)	25.79 ± 3.80
Duration of disease in year	12.72 ± 7.58
Disease stage	
Noncirrhotic	259 (83.0)
Compensated cirrhosis	49 (15.7)
Decompensate cirrhosis	4 (1.3)
Hospitalization history	
No	274 (87.8)
Yes	38 (12.2)
Etiology	
Mother to child	122 (39.1)
Blood transfusion	7 (2.2)
Unknown	183 (58.7)
Comorbidities	
Diabetes mellitus	24 (7.7)
Cardiovascular	19 (6.1)
Respiratory	11 (3.5)
Gastrointestinal	18 (5.8)
Urological	9 (2.9)
Other	21 (6.7)
Interferon therapy	
No	257 (82.4)
Yes	55 (17.6)
Ascites	
No	307 (98.4)
Controlled (mild)	5 (1.6)
Number of biopsy	
None	251 (80.4)
Once	50 (16.0)
Twice or more	11 (3.6)
Recent lab tests[a]	
Serum albumin (g/dL) [NR = 3.4-5.4]	4.31 ± 0.438
Hemoglobin (g/dL) [MNR = 13.8-17.2; FNR = 12.1-15.1]	14.75 ± 1.56
AST [SGOT] (IU/L) [NR = 10-34]	32.08 ± 39.19
ALT [SGPT] (IU/L) [NR = 10-40]	38.33 ± 42.97
ALP (IU/L) [NR = 44-147]	192.47 ± 63.63
Total Bilirubin (mg/dL) [NR = 0.3-1.2]	1.08 ± 0.85
PT (seconds) [NR = 11-13.5]	13.11 ± 1.12
INR [NR = 0.8-1.1]	1.08 ± 0.16
Creatinine (mg/dL) [MNR = 0.7-1.3; FMR = 0.6-1.1]	1.00 ± 0.16
Severity of the liver disease	
No cirrhosis	259
Child–Pugh A	44
Child–Pugh B	9
Child–Pugh C	0

Note. NR = normal range; FNR = female's normal range; MNR = male's normal range; BMI = body mass index; AST = aspartate aminotransferase; ALT = alanine aminotransferase; ALP = alkaline phosphatase; PT = prothrombin time; INR = international normalized ratio.
[a]All reference values [normal ranges] have been adopted from U.S. National Library of Medicine and presented only as a basis for comparison to general normal levels. These values may be different in various laboratories.

Intercorrelations between the subscales of the LDSI 2.0 were all significant. The minimum correlation was .129 for itch and worry about family, and the maximum correlation was .612 for between fear of complications and depression. There were also significant correlations ($p < .01$) between all subscales of the LDSI 2.0 and its criterion scales (CLDQ and EQ-5D) with the exception of one (EQ-5D-VAS and itch subscale of the LDSI 2.0). These correlations ranged from −.088 to .680 (Table 4).

Known-group comparisons revealed that both parts of the scale (symptom index and extra NLV items) significantly differentiated between patients with various demographic and clinical characteristics, including characteristics such as disease duration, disease stage, and AST blood level. For the symptom index, there were differences among groups based on sex, BMI, comorbidity, and ALT blood level, whereas for the extra NLV section, groups were differentiated based on the characteristics of age, marital status, and education. All differences were significant at $p < .05$ with exception of the disease stage, which was significant at $p < .001$ for the extra NLV section (Table 5).

Results of the Kaiser–Mayer–Olkin and Bartlett's test were 0.830 and $p < .001$, respectively, indicating that the data were appropriate for analysis. Exploratory factor analysis revealed a seven-factor solution for the scale (Table 6): Component 1 = gastrointestinal conditions (GI) with Items

Table 2. Item Analysis of the LDSI 2.0.

Items/subscales	*M*	*SD*	Floor (%)	Ceiling (%)	CITC	α
Itch						
1A. Severity	0.59	0.92	64.4	1.3	0.311	.895
1B. Hindrance in daily activity	0.11	0.41	92.0	0.0	0.250	.896
1C. Hindrance in sleeping	0.22	0.61	85.3	0.6	0.517	.892
Joint pain						
2A. Severity	0.87	1.02	46.8	2.2	0.296	.896
2B. Hindrance in daily activity	0.45	0.94	76.6	2.6	0.502	.891
Pain in the right upper abdomen						
3A. Severity	0.48	0.84	68.3	1.6	0.456	.892
3B. Hindrance in daily activity	0.17	0.57	89.7	0.3	0.527	.892
Sleeping during the day						
4A. Severity	0.84	0.97	47.1	1.3	0.492	.891
4B. Hindrance in daily activity	0.40	0.77	73.4	0.3	0.562	.890
Worry about family situation						
5A. Severity	1.27	1.34	39.7	12.2	0.505	.892
5B. Hindrance in daily activity	0.46	0.91	73.7	2.2	0.540	.890
Decreased appetite						
6A. Severity	0.46	0.86	70.8	2.6	0.549	.890
6B. Hindrance in daily activity	0.21	0.62	86.5	1.3	0.612	.890
Depression						
7A. Severity	0.73	1.02	57.4	2.6	0.692	.886
7B. Hindrance in daily activity	0.41	0.88	76.9	1.9	0.659	.888
Fear of complication						
8. Severity	0.88	1.20	54.8	5.1	0.670	.886
Jaundice						
9A. Severity	0.21	0.57	85.3	1.3	0.438	.893
9B. Hindrance in daily activity	0.06	0.396	96.5	0.6	0.521	.893
Extra NLV (other aspects of HRQOL)						
10. Memory problems	0.77	1.11	58.0	4.2	0.488	.892
11. Change of personality	0.38	0.83	78.2	1.9	0.605	.889
12. Hindrance in financial affairs	1.04	1.38	55.8	9.0	0.469	.893
13. Change in use of time	0.72	1.13	63.8	3.5	0.535	.890
14. Decreased sexual interest	0.80	1.12	58.7	3.2	0.430	.893
15. Decreased sexual activity	0.84	1.15	56.7	4.2	0.468	.892

Note. LDSI 2.0 = Liver Disease Symptom Index Version 2.0; CITC = corrected item–total correlation, α = Cronbach's alpha if item deleted; NLV = Dutch Liver Patients Association; HRQOL = health-related quality of life.

6A, 6B, 9A, 9B; Component 2 = emotions and personality changes with Items 5A, 5B, 7A, 7B, and 8; Component 3 = day sleeping with Items 4A and 4B; Component 4 = sexual functioning with Items 14 and 15; Component 5 = joint pain with Items 2A and 2B; Component 6 = itch with Items 1A, 1B, and 1C; and Component 7 = abdominal pain with Items 3A and 3B. The item related to memory problem (Item 10) loaded on Component 5 (joint pain). These components explained about 70% of the total variance. The scree plot is depicted in Figure 1.

Figure 2 demonstrates the power of our HRQOL scales to distinguish between patients that reported their health status as appropriate from those who indicated it was not appropriate. The AUC for the LDSI 2.0, CLDQ, and EQ-5D-3L scales was 0.706, 0.720 and 0.686, respectively. The confidence interval for the AUC of the LDSI ranged from 0.648 to 0.764. Considering the point where the curve of LDSI 2.0 is nearest to the left upper corner of Figure 2, the best cutoff point for discrimination of the scale was at 0.604, which correctly detected 72% of patients with appropriate health status (sensitivity) and 41% of the patients with inappropriate health status (specificity).

Discussion

Based on the present results, the Persian version of the LDSI 2.0 is a psychometrically good, disease-specific measure of HRQOL in patients with CHB. This is a valid, reliable, sensitive, and specific scale when used in an Iranian population. Other internationally tested instruments such as the more

Table 3. Descriptive Analysis of Subscales (*M, SD*), Feasibility (Floor/Ceiling), Convergent and Discriminative Validity (Item-Scaling Test), and Reliability (Cronbach's α) of the Liver Disease Symptom Index.

					Convergent validity		Discriminant validity		
Subscales[a]	*M*	*SD*	Floor (%)	Ceiling (%)	Range (*r*)	Success (%)	Range	success	α
Itch	0.305	0.532	64.4	0.0	.69-.89	3/3 (100)	0.03-0.51	21/21 (100)	.669
Joint pain	0.657	0.879	45.8	0.6	.88-.90	2/2 (100)	0.10-0.39	14/14 (100)	.744
Abdominal pain	0.326	0.628	67.0	0.3	.84-.93	2/2 (100)	0.18-0.53	14/14 (100)	.693
Day sleeping	0.618	0.813	47.1	0.3	.91-.94	2/2 (100)	0.22-0.49	14/14 (100)	.821
Worry about family	0.863	0.983	38.8	1.9	.78-.91	2/2 (100)	0.05-0.53	14/14 (100)	.590
Decreased appetite	0.331	0.676	70.8	1.3	.88-.94	2/2 (100)	0.18-0.58	14/14 (100)	.763
Depression	0.568	0.876	56.7	1.3	.91-.93	2/2 (100)	0.22-0.58	14/14 (100)	.817
Jaundice	0.139	0.415	84.9	0.0	.79-.91	2/2 (100)	0.16-0.53	14/14 (100)	.591

[a]Subscales are including a given symptom severity along with its related symptom hindrance. All subscales have two items with exception of "Itch," which has three items. Extra NLV items were not included.

Table 4. Intercorrelations Between Subscales of LDSI 2.0, and With the CLDQ, and EQ-5D Subscales (Spearman Correlations).

Scale	Subscales	1	2	3	4	5	6	7	8	9	10
LDSI 2.0	1. Itch	—									
	2. Joint pain	.227**	—								
	3. Abdominal pain	.319**	.208**	—							
	4. Day sleeping	.445**	.359**	.325**	—						
	5. Worry about family	.129*	.228**	.330**	.287**	—					
	6. Decreased appetite	.371**	.231**	.503**	.451**	.401**	—				
	7. Depression	.249**	.283**	.426**	.477**	.586**	.566**	—			
	8. Fear of complication	.266**	.318**	.414**	.418**	.547**	.446**	.612**	—		
	9. Jaundice	.422**	.261**	.426**	.367**	.275**	.598**	.384**	.434**	—	
	10. Extra NLV	.264**	.324**	.367**	.302**	.536**	.381**	.561**	.508**	.336**	—
CLDQ	11. Abdominal symptoms	−.345**	−.218**	−.466**	−.251**	−.218**	−.346**	−.289**	−.296**	−.301**	−.404**
	12. Fatigue	−.387**	−.431**	−.371**	−.704**	−.331**	−.440**	−.523**	−.509**	−.379**	−.500**
	13. Systemic symptoms	−.548**	−.589**	−.360**	−.479**	−.320**	−.396**	−.399**	−.443**	−.354**	−.522**
	14. Activity	−.374**	−.342**	−.411**	−.373**	−.233**	−.484**	−.405**	−.485**	−.442**	−.428**
	15. Emotional function	−.275**	−.467**	−.371**	−.521**	−.445**	−.450**	−.639**	−.499**	−.314**	−.563**
	16. Worry	−.192**	−.232**	−.373**	−.374**	−.726**	.380**	−.580**	−.680**	−.311**	−.576**
EQ-5D	17. Index score	−.245**	−.451**	−.366**	−.373**	−.318**	−.319**	−.459**	−.349**	−.341**	−.508**
	18. VAS	−.088	−.389**	−.261**	−.303**	−.352**	−.309**	−.405**	−.248**	−.203**	−.247**

Note. VAS = Visual Analogue Scale; LDSI 2.0 = Liver Disease Symptom Index Version 2.0; EQ-5D = EuroQol; CLDQ = Chronic Liver Disease Questionnaire; NLV = Dutch Liver Patients Association.
*Significant at .05 level. **Significant at .01 level.

general EQ-5D and the more specific CLDQ helped us establish the psychometric properties of the LDSI 2.0. We also found that the factor structure of the scale indicated a seven-factor solution that explained almost 70% of the variance. These findings confirm the usefulness of this measure in liver disease patients.

Van der Plas and colleagues in their first attempts to develop the LDSI 2.0 emphasized the lack of a valid scale to assess symptom severity in patients with liver disease. They stressed the degree of disturbance that symptoms of liver disease generated in the daily activities of patients (van der Plas et al., 2004). Unfortunately, despite this being a very important issue in recognition of the quality of life among CHB patients, few studies have regarded the role of symptoms hindrance in activities of daily living among such patients. Our findings indicated that the hindrance related to symptoms such as worry about family situation, joint pain, depression, and sleeping during the day may be more considerable than other symptoms. Similarly, Posada et al. (2010) studying patients with hepatitis C infection found that apathy was higher in these patients compared with healthy controls and felt that this might be especially important in explaining the negative effects on activities of daily living.

In the present study, symptoms with a particularly high severity score were worry about family situation, fear of complications, joint pain, sleeping during the day, and

Table 5. Known-Group Validity of Symptom Index and Extra NLV Parts of LDSI 2.0.

		Symptom index			Extra NLV		
	n	*M*	*SD*	*p* value	*M*	*SD*	*p* value
Age (years)							
≤40	125	0.515	0.468	.457	0.632	0.722	**.019**
>40	187	0.472	0.508		0.841	0.797	
Sex							
Male	242	0.453	0.490	**.015**	0.759	0.789	.927
Female	70	0.615	0.483		0.750	0.724	
Marriage							
Single	29	0.592	0.533	.241	0.524	0.832	**.045**
Married	283	0.479	0.488		0.826	0.766	
Education							
High school or lower	187	0.506	0.523	.453	0.839	0.739	**.030**
University	125	0.464	0.443		0.645	0.817	
Disease duration							
≤10 years	125	0.411	0.444	**.010**	0.661	0.808	**.037**
>10 years	187	0.558	0.522		0.848	0.751	
Disease stage							
Noncirrhotic	259	0.464	0.501	**.043**	0.677	0.740	**.000**
Cirrhotic	53	0.614	0.432		1.147	0.823	
BMI							
≤25	129	0.435	0.612	**.023**	0.792	0.803	.509
>25	183	0.563	0.382		0.733	0.753	
Comorbidity							
No	227	0.413	0.509	**.013**	0.780	0.759	.870
Yes	85	0.569	0.447		0.796	0.807	
AST (SGOT)							
≤34	248	0.436	0.475	**.035**	0.700	0.756	**.015**
>34	64	0.582	0.555		0.976	0.806	
ALT (SGPT)							
≤40	235	0.440	0.485	**.036**	0.703	0.785	.250
>40	77	0.576	0.512		0.820	0.741	

Note. NLV = Dutch Liver Patients Association; LDSI 2.0 = Liver Disease Symptom Index Version 2.0; AST = aspartate aminotransferase; ALT = alanine aminotransferase; BMI = body mass index. Significant *p* values ($p < .05$) are in boldface.

depression. Most of these symptoms are related to the mental or emotional health of these patients. In the development of the LDSI 2.0, researchers also reported that these symptoms were those with the highest frequency (van der Plas et al., 2003, 2004). In another study from Iran on patients infected with HCV and HBV, anxiety and depression were identified as the important predictors of HRQOL (Ashrafi et al., 2012). This finding is not surprising because a life-threatening disease with an uncertain prognosis like CHB is likely to cause emotional distress that has a major impact on mental health as a main part of the HRQOL. Other studies of patients with HBV or HCV infection have also reported mental health problems in such patients that may lead to poor HRQOL (Foster, Goldin, & Thomas, 1998; Karaivazoglou et al., 2010; Ong, Mak, Aung, Li, & Lim, 2008).

Item analysis of the LDSI 2.0 in our study indicated a floor effect of 0.69%. This may seem to challenge the usefulness of the scale because the recommended value is only 15% (Terwee et al., 2007). However, the LDSI 2.0 was developed in order to be applied to a variety of people with liver disease. When this scale is administered to patients who are candidates for liver transplantation, we expect the results would be different than when administered to patients in the initial stages of disease after diagnosis with HBV infection (because of severity of symptoms). Therefore, we attribute the high value for the floor effect on the scale to a lower proportion of patients in our study with advanced disease. The results of blood tests along with the Child–Pugh classification in this study suggest the overall severity of disease in our sample was not that severe and reflected the low percentage of patients at the cirrhotic stage.

We found that the LDSI 2.0 was stable over time and internally consistent and reliable. The Arabic translation of the scale has also reported a high range of kappa values (0.62 to

Table 6. Factor Loadings Derived From Exploratory Factor Analysis of the LDSI 2.0.

Item	Original class	Factor 1 (GI)	Factor 2 (EP)	Factor 3 (DS)	Factor 4 (SF)	Factor 5 (JP)	Factor 6 (IT)	Factor 7 (AP)
Q1A	IT	0.083	−0.084	0.369	0.267	−0.054	**0.719**	0.097
Q1B	IT	0.120	0.042	0.014	−0.045	0.070	**0.823**	0.156
Q1C	IT	0.538	0.141	0.188	0.040	0.262	**0.561**	−0.184
Q2A	JP	−0.034	0.027	0.117	0.067	**0.846**	−0.020	0.038
Q2B	JP	0.278	0.134	0.172	0.002	**0.802**	0.123	0.001
Q3A	AP	0.169	0.204	0.207	−0.043	0.083	0.102	**0.815**
Q3B	AP	0.514	0.171	−0.058	0.083	0.072	0.240	**0.649**
Q4A	DS	0.122	0.043	**0.824**	0.054	0.174	0.227	0.105
Q4B	DS	0.278	0.180	**0.725**	−0.073	0.256	0.186	0.009
Q5A	WO	0.026	**0.649**	0.284	0.151	0.121	−0.128	0.105
Q5B	WO	0.393	**0.581**	0.102	0.112	0.013	−0.012	0.034
Q6A	DA	**0.642**	0.136	0.390	0.056	−0.010	0.038	0.154
Q6B	DA	**0.776**	0.265	0.162	0.071	−0.006	0.074	0.177
Q7A	DP	0.308	**0.558**	0.449	0.175	0.104	−0.096	0.169
Q7B	DP	0.480	**0.581**	0.383	0.000	0.039	−0.046	0.055
Q8	FC	0.272	**0.440**	0.394	0.315	0.178	−0.047	0.320
Q9A	JA	**0.634**	−0.091	0.110	0.207	0.076	0.216	0.184
Q9B	JA	**0.750**	0.236	0.006	−0.126	0.252	0.144	0.035
Q10	NLV	0.209	0.234	0.121	0.284	**0.527**	0.053	0.181
Q11	NLV	0.300	**0.489**	0.213	0.227	0.175	−0.123	0.283
Q12	NLV	−0.028	**0.769**	−0.026	0.194	0.120	0.157	0.037
Q13	NLV	0.218	**0.735**	−0.073	0.079	0.093	0.075	0.182
Q14	NLV	0.125	0.184	−0.019	**0.907**	0.057	0.108	−0.005
Q15	NLV	0.028	0.244	−0.079	**0.888**	0.140	0.024	0.012
EV		3.504	3.424	2.322	2.118	2.025	1.843	1.548
% σ^2		14.60	14.26	9.67	8.82	8.43	7.68	6.45

Note. NLV = Dutch Liver Patients Association; LDSI 2.0 = Liver Disease Symptom Index Version 2.0; IT = itch; JP = joint pain; AP = abdominal pain; DS = day sleeping, WO = worry; DA = decreased appetite; DP = depression; FC = fear of complication; JA = jaundice. Factors in parenthesis were extracted by principal component analysis with varimax rotation. These were included factors other than original components: GI = gastrointestinal conditions; EP = emotions and personality changes, and SF = sexual function. Bold values show significant items loading on each factor.

0.94) and is consistent with our findings. In this study, Cronbach's alpha for all paired items was higher than .72 (Youssef et al., 2012). In addition, and not reported in the prior study, we computed the alpha for the total scale as well as for its subscales including the extra NLV section, finding that these also indicated high internal consistency for the measure. The only exception was for the domains of "worry about family" and "jaundice" for which the alpha value was just less than .6. This may be because of lower effect that these symptoms had on daily activities.

Several methods to assess the validity of the scale were employed in this study, many of which were not applied in the previous studies of the LDSI 2.0 (van der Plas et al., 2004; Youssef et al., 2012). While prior studies have generally focused on criterion validity, we also evaluated convergent, discriminant, known-group, factor analysis, and ROC curve characteristics of the scale. The developers of the LDSI 2.0 used the SF-36 and MFI-20 (instead of the EQ-5D and CLDQ) to assess correlations between subscales with similar results as in our study. In the Arabic version of the scale, only the SF-36 was administrated to evaluate criterion validity. In none of these studies was concurrent validity investigated by using a similar disease-specific scale like the CLDQ.

In the known-groups validity of the scale, we found that demographic and clinical characteristics may play an important role in affecting the score obtained by the LDSI 2.0. Teuber et al. (2008) in a study of patients with HCV found that severity of disease, age, gender, and ALT may be significantly associated with HRQOL when using a generic scale like the SF-36. A disease-specific measure like the LDSI 2.0 is more capable of detecting the effects of such variables. Another similar study as ours using the LDSI 2.0 has also reported there were noticeable relationships between the many of such characteristics and the scale (Gutteling et al., 2006). The role of demographic and clinical variables in determining HRQOL has been emphasized in the previous studies on patients with liver diseases (El Khoury, Vietri, & Prajapati, 2014; Kwan et al., 2008).

We also identified the major components of the LDSI 2.0 using factor analysis. Although the authors of the scale introduced subscales as only the items of severity along with their hindrance-related items we also included items of the extra

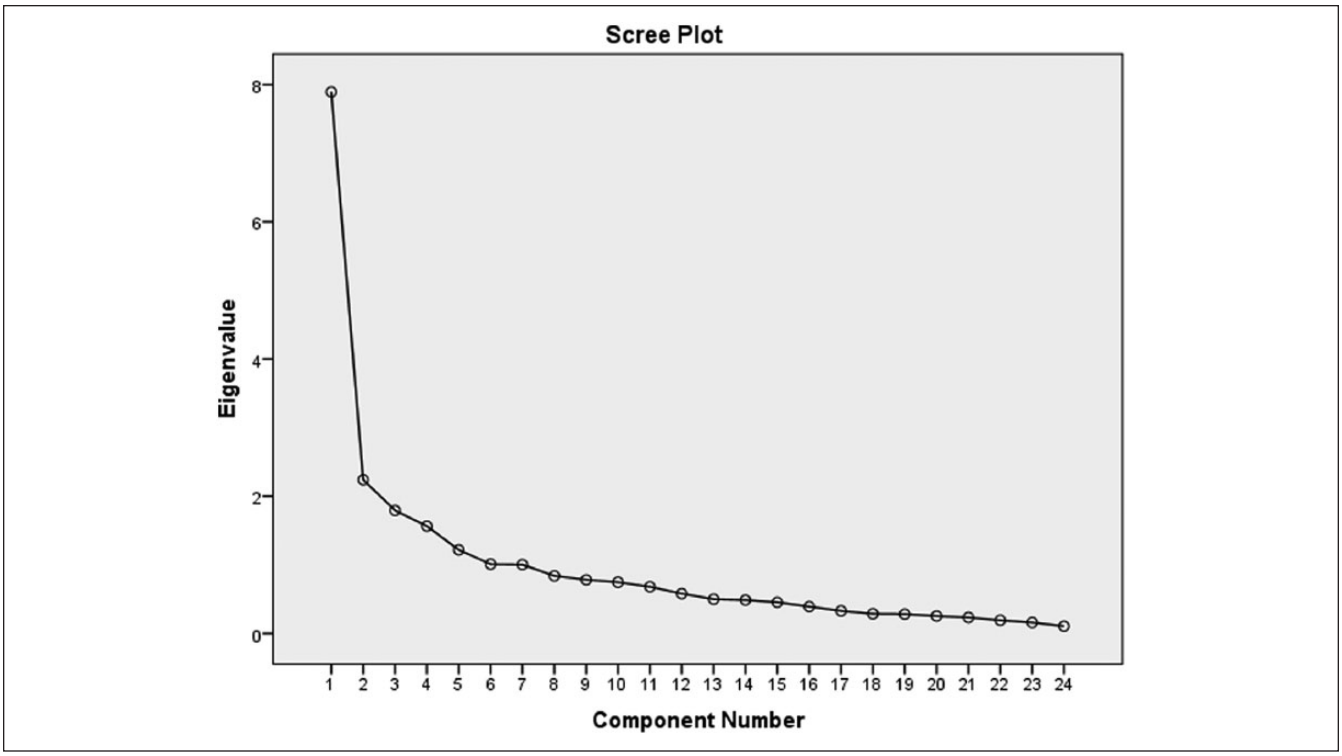

Figure 1. Scree plot of components including LDSI 2.0 with their eigenvalues.

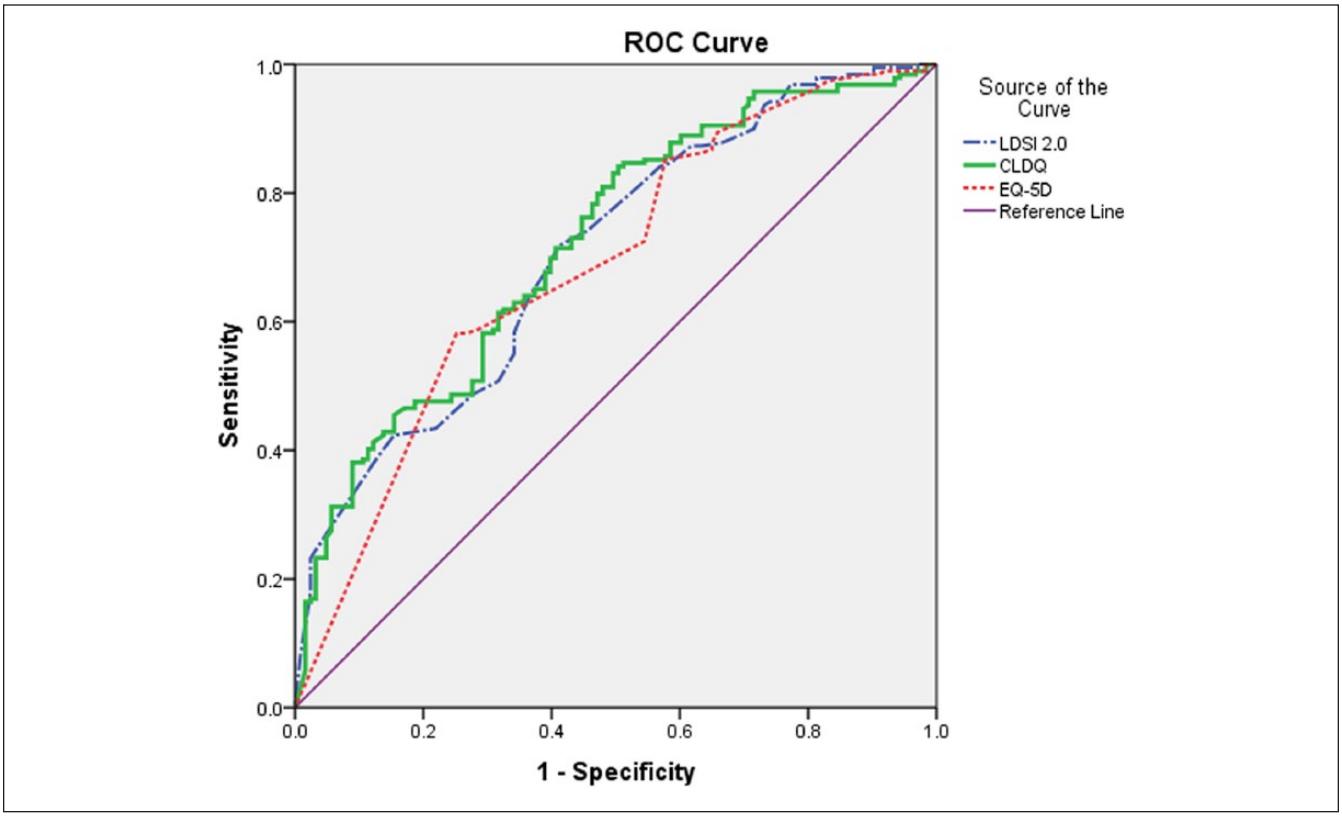

Figure 2. Diagram of ROC curve analysis for LDSI 2.0, EQ-5D, and CLDQ.

NLV section, making this a more comprehensive assessment. In our analysis three new factors may be presented that were including a gastrointestinal component, emotional and personality change component, and a sexual functioning component. We believed that including these components in the scale will significantly improve it. Our proposed structure of the scale with seven domains explained nearly 70% of the total variance that is sufficiently acceptable (Beavers et al., 2013). The only concern was that one of the items (Item 10) relating to memory problem ended up loading on the joint pain component, which may not make sense. However, this is not surprising since this was the only question that assessed memory function and had to load on one of the factors.

The high sensitivity and specificity of the LDSI 2.0 may be especially useful in identifying true positives and true negatives in terms of how patients perceive their health. We presented the ROC curves for the three measures used in the current study assuming that all measures had similar ability to discriminate between patients with acceptable health status and those who did not. As expected, the disease-specific measures achieved a higher discrimination power for health status than the generic measure used here. As others have suggested, more research is needed on using disease-specific measures that evaluate HRQOL in patients with hepatic disease (Gralnek et al., 2000; Younossi et al., 1999).

This study was designed to validate a disease-specific measure of HRQOL that may be useful in clinical practice. Those who use this measure, however, must considering the culture and religious beliefs of patients that may affect responses. As previously noted, health care professionals should be careful when assessing aspects of HRQOL related to sexual health, especially among Muslims. Asking such questions may cause embarrassment and be perceived as violating their privacy. Thus, the importance of asking about this area should be explained to patients and questions should be asked by same-sex health professionals. Second, we found that the mental health of individuals with a chronic liver disease may need more attention compared to other aspects of health. Given the frequent interactions of such patients with health care providers, the latter should carefully monitor patient mental health and establish good supportive relationships, which may have positive consequences for overall health and well-being.

There are also several limitations of this study that should be considered. One is that this was a sample of convenience. We used only patients who were readily available to us, which may affect the generalizability of our findings. However, the response rate among those whom we approached was high and there was very little missing data. Another limitation of the study is that we did not measure the scale's responsiveness to change. Although this responsiveness to change would help better understand the reaction of the scale to treatments and interventions, we were not able to do this in the present study and a high priority for future research should be establish this. However, Hauser, Schnur, Steder-Neukamm, Muthny, and Grandt (2004) believed that this should not be regarded as a weakness of the study. Finally, we used a self-report measure to assess the health status of patients. As a result, recall bias may have influenced the responses. However, to our knowledge, there is still no widely recognized objective measure of overall health status, and subjective self-reported of global health is commonly used and strongly correlated with a wide range of health outcomes including mortality (Haywood, Garratt, & Fitzpatrick, 2005).

In conclusion, the Persian version of the LDSI 2.0 is a valid and reliable scale for measuring disease-specific HRQOL among Iranian patients with hepatitis B infection. This instrument assesses both the symptoms of hepatic disease and the effects of those symptoms on important daily activities that influence quality of life. The scale is comparable with other disease-specific scales like the CLDQ that assess quality of life among patients with liver disease. There has been little research on the psychometric properties of the LDSI 2.0 when used in patients speaking languages other than English or different cultural contexts. Future research should investigate the responsiveness of the scale to change so that it can be used in intervention studies to assess changes in quality of life over time in patients with hepatic disease.

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