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RESEARCH LETTER

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Validation of the Hospital Anxiety and Depression Scale in patients with decompensated cirrhosis

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INTRODUCTION

Patients with decompensated cirrhosis (DC) experience substantial psychological distress. Accurate screening of psychological distress in this population is a critical first step toward reducing their morbidity. The Hospital Anxiety and Depression Scale (HADS) is a self-administered questionnaire designed to identify psychological distress.[1] However, there is no research into the performance of HADS in DC. The overall goal of this study is to evaluate the psychometric properties of the HADS for patients with DC.

METHODS

Study design and population

This is a secondary data analysis of a longitudinal cohort study of adult outpatients with DC recruited from Massachusetts General Hospital between August 2018 and September 2022, details of which have been reported elsewhere.[2] All patient-reported outcomes were collected consistently across the study period (baseline, weeks 6, 12, 24, 26, and 48)—this study used data collected at baseline and week 6. All patients provided informed consent, and the Mass General Brigham Institutional Review Board approved this study.

Patient-reported outcome measures

HADS

We assessed self-reported anxiety and depression using the 14-item HADS.[1] The HADS has two 7-item subscales assessing anxiety (HADS-Anxiety) and depression (HADS-Depression) symptoms, with subscale scores ranging from 0 (no distress) to 21 (maximum distress).

Abbreviations: DC, decompensated cirrhosis; HADS, Hospital Anxiety and Depression Scale; PHQ-9, Patient Health Questionnaire-9; SF-LDQOL, Short-Form Liver Disease Quality of Life.

Keywords: behavioral health, emotional distress, end-stage liver disease, palliative hepatology, psychometric evaluation

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Other patient-reported outcome measures included depression (Patient Health Questionnaire-9, [PHQ-9]) and health-related quality of life (Short-Form Liver Disease Quality of Life [SF-LDQOL] questionnaire).[3,4]

Statistical Methods

We calculated Cronbach's alpha at baseline and week 6 for HADS-Anxiety and HADS-Depression separately to evaluate reliability. We evaluated floor and ceiling effects using the commonly accepted thresholds of 15% of patients achieving total scores between 0–1 (floor effect) or 20–21 (ceiling effect).[5]

A confirmatory factor analysis with 2 correlated latent variables (depression and anxiety) was performed to evaluate structural validity. We evaluated model fit using the comparative fit index (cutoff value >0.95), Tucker-Lewis index (cutoff value >0.95), root mean square error of approximation (cutoff value <0.06), and/or standardized root mean square residual (cutoff value <0.08).[6] Convergent validity was evaluated by calculating the correlations of HADS subscale scores with PHQ-9 scores at both baseline and week 6. Predictive validity was assessed through a regression analysis examining whether the change in overall SF-LDQOL was predicted by the changes in HADS-Anxiety and HADS-Depression subscale scores from baseline to week 6, adjusting for confounders as previously described (age; Model for End-Stage Liver Disease-Sodium score; the presence of ascites, HE, or HCC; diagnosis of alcohol-associated cirrhosis; transplant listing status; and cirrhosis-specific comorbidity scoring system comorbidity [CirCom] score).[2] Known-groups validity was assessed using ANOVA to evaluate if baseline HADS subscale scores differed based on Child-Pugh classes as they reflect the varying degrees of DC.

Internal responsiveness of HADS-Depression was evaluated by calculating the mean differences and 95% CIs in total scores between baseline and week 6 for patients who experienced clinically meaningful changes on PHQ-9 and SF-LDQOL.[2] For HADS-Anxiety, responsiveness was assessed only using SF-LDQOL as a criterion. The minimal clinically important difference is 1.5 points for HADS-Anxiety and HADS-Depression, 5 points for PHQ-9, and 8 points for SF-LDQOL.[7–9]

RESULTS

Overview

In the 218 patients at baseline, the median age was 60 years (IQR: 51–65). Half of the patients were actively listed for liver transplantation (n = 109, 50%). Median Child-Pugh score was 9 (IQR: 7–10), with the following distribution of classes: A (n = 19, 8.7%), B (n = 129, 59.2%), and C (n = 70, 32.1%). Mean scores for HADS-Depression and HADS-Anxiety at baseline were 6.7 (SD: 4.1) and 7.2 (SD: 4.3), respectively. In total, 145 patients were included in the week 6 analysis.

Reliability, floor, and ceiling effects

Both HADS-Depression and HADS-Anxiety demonstrated strong internal consistency (Cronbach alpha value >0.8) at baseline and week 6. Both HADS-Depression and HADS-Anxiety demonstrated minimum floor (8.1% and 9.4%, respectively) and ceiling effects (0% for both) at baseline.

Structural, convergent, known-groups, and predictive validity

The confirmatory factor analysis model estimated for HADS had a good model fit (comparative fit index: 0.95, Tucker-Lewis index: 0.94, root mean square error of approximation: 0.05, and standardized root mean square residual: 0.06). The correlation between HADS-Depression and HADS-Anxiety subscales was 0.71 ($p < 0.001$). At both baseline and week 6, strong correlations were observed between the PHQ-9 scores and HADS-Depression and HADS-Anxiety ($r \geq 0.70$).

There was a statistically and clinically significant difference in HADS-Depression scores among patients with varying levels of DC severity at baseline (Child-Pugh A: 3.8 vs. B: 6.8 and C: 7.5; $p < 0.001$). However, there was no statistically or clinically significant difference in HADS-Anxiety scores (Child-Pugh A: 6.6 vs. B: 7.0 and C: 7.7; $p = 0.45$).

Among patients who completed the week 6 assessment, results of regression analysis revealed that the changes in HADS-Depression ($\beta = -1.71$ [95% CI: −2.27 to −1.15], $p < 0.001$) and HADS-Anxiety ($\beta = -1.08$ [95% CI: −1.60 to −0.55], $p < 0.001$) scores were significantly and negatively associated with the change in SF-LDQOL (Table 1).

Responsiveness

The HADS-Depression score demonstrated significant changes corresponding to clinically meaningful changes in depression as measured by PHQ-9 from baseline to week 6, with a mean difference of −4.0 (95% CI: −5.4 to −2.6) among patients who showed a decrease of 5 points or more in the PHQ-9 and a mean difference of 2.4 (95% CI: 1.2 to 3.5) among those with an increase of 5 points or more in the PHQ-9.

Using SF-LDQOL as a criterion, we found that both HADS-Depression (2.2 [95% CI: 1.0 to 3.4]) and HADS-Anxiety (1.8 [95% CI: 0.5 to 3.2]) scores increased

TABLE 1 Regression analyses of change in SF-LDQOL predicted by the changes in HADS-Depression and HADS-Anxiety from baseline to week 6 (N = 145)[a]

Predictors	β (95% CI)	*t* Value	*p*
Age at baseline	0.00 (−0.16, 0.17)	0.01	0.994
MELD-Na score at baseline	−0.19 (−0.49, 0.11)	−1.28	0.204
Ascites	1.53 (−4.37, 7.43)	0.51	0.609
HE	−3.81 (−7.76, 0.13)	−1.91	0.058
Alcohol-associated cirrhosis	1.40 (−2.01, 4.81)	0.81	0.419
Listed for transplant at enrollment	−1.94 (−5.50, 1.62)	−1.08	0.284
HCC at enrollment	5.13 (−0.52, 10.77)	1.80	0.075
CirCom score	−2.21 (−3.83, −0.59)	−2.70	0.008
Change in HADS-Depression	**−1.71 (−2.27, −1.15)**	**−6.06**	**< 0.001**
Age at baseline	0.01 (−0.17, 0.19)	0.11	0.915
MELD-Na score at baseline	−0.18 (−0.49, 0.13)	−1.14	0.256
Ascites	1.64 (−4.52, 7.80)	0.53	0.600
HE	−4.04 (−8.23, 0.15)	−1.91	0.059
Alcohol-associated cirrhosis	1.27 (−2.40, 4.94)	0.68	0.495
Listed for transplant at enrollment	−2.71 (−6.50, 1.08)	−1.42	0.159
HCC at enrollment	3.93 (−2.00, 9.87)	1.31	0.192
CirCom score	−2.56 (−4.27, −0.85)	−2.96	0.004
Change in HADS-Anxiety	**−1.08 (−1.60, −0.55)**	**−4.04**	**< 0.0001**

[a]Unless specified. For the analysis of HADS-Depression, 134 patients were included due to the missingness in the HADS-Depression score (n = 3), MELD-Na score (n = 1), and SF-LDQOL score (n = 7). For the analysis of HADS-Anxiety, 135 patients were included due to the missingness in the HADS-Anxiety score (n = 2), MELD-Na score (n = 1), and SF-LDQOL score (n = 7). Abbreviations: CirCom score, cirrhosis-specific comorbidity scoring system comorbidity score; HADS, Hospital Anxiety and Depression Scale; MELD-Na, Model for End-Stage Liver Disease-Sodium; SF-LDQOL, Short-Form Liver Disease Quality of Life.

significantly in patients with clinically meaningful decreases in SF-LDQOL. In patients with clinically meaningful increases in SF-LDQOL, we did not find significant decreases in their HADS-Depression and HADS-Anxiety scores (Supplemental Table, http://links.lww.com/HC9/B92).

DISCUSSION

Both the HADS-Depression and HADS-Anxiety subscales showed strong psychometric performance, confirming the use of HADS as a screening tool for psychological distress among patients with DC. Both HADS-Anxiety and HADS-Depression domains demonstrated comparable floor/ceiling effects, reliability, structural validity, and convergent validity, which aligns with empirical evidence.[10]

Limitations include not evaluating the test-retest reliability of the HADS subscales and not having a second measure of anxiety to evaluate the convergent validity of HADS-Anxiety.

CONCLUSIONS

The HADS-Depression and HADS-Anxiety subscales within HADS are reliable, valid, and responsive tools for assessing psychological distress among patients with DC.

DATA AVAILABILITY STATEMENT

The data presented in this study are available on request from the corresponding author.

AUTHOR CONTRIBUTIONS

Chengbo Zeng, Raymond T. Chung, Areej El-Jawahri, Maria O. Edelen, and Nneka N. Ufere were involved in the concept design and conduct of the study. John Donlan, Teresa Indriolo, Lucinda Li, Enya Zhu, Joyce C. Zhou, Malia E. Armstrong, and Nneka N. Ufere helped with patient recruitment and data curation. Chengbo Zeng, Kedie Pintro, Nora Horick, Maria O. Edelen, and Nneka N. Ufere performed the data analysis. Chengbo Zeng, Maria O. Edelen, and Nneka N. Ufere wrote the initial draft and revised the manuscript. All authors were involved in interpreting the data and providing critical input regarding the analysis and manuscript. All authors approved the manuscript.

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CONFLICTS OF INTEREST

The authors have no conflicts to report.

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