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ORIGINAL PAPER

Frailty in liver cirrhosis – insights into prevalence, determinants, and clinical impact from a tertiary center experience

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ABSTRACT

Introduction and aim. Frailty has emerged as a critical determinant of poor outcomes in patients with liver cirrhosis. This study aims to determine the prevalence and predictors of frailty in patients with liver cirrhosis and assess its clinical impact on disease severity.

Material and methods. This cross-sectional study included 460 patients with liver cirrhosis were classified into frail Clinical Frailty Scale (CFS) >4 and non-frail (CFS≤4) groups.

Results. The prevalence of frailty among the studied patients was 45.7%. Frail patients were significantly older (60.61±9.06 years), without gender predilection (43.7%, 47.9%). Patients with frailty exhibited significantly worse liver function; higher bilirubin (1.30 (0.90–2.0) vs 0.90 (0.66–1.30) mg/dL, p<0.001) and low albumin (3.9 (3.50–4.10) vs 3.2 (2.60–3.70) g/dL, p<0.001). Multivariate analysis identified age (OR=1.055, 95%CI: 1.023–1.088, p<0.001), body mass index (OR=9.803, 95%CI: 5.067–18.963, p<0.001), and high nutritional risk (OR=20.186, 95%CI: 8.456–48.191, p<0.001) as independent predictors of frailty.

Conclusion. Frailty is a significant concern in patients with liver cirrhosis, particularly those with advanced age, diabetes, and severe hepatic dysfunction. Optimizing outcomes for this patient population requires a multi-faceted approach that considers liver disease management, routine frailty assessment, and interventions to enhance physical resilience and address co-morbidities.

Keywords. cirrhosis, frailty, prevalence

Introduction

Frailty is a multidimensional syndrome characterized by diminished physiological reserves, increased vulnerability to stressors, and impaired ability to maintain homeostasis following minor health perturbations.[1] Originally studied in geriatric populations, frailty is now recognized as a pivotal determinant of clinical outcomes in various chronic diseases, including liver cirrhosis.[2]

In the context of cirrhosis, frailty arises from a complex interplay of sarcopenia, malnutrition, systemic inflammation, and hepatic encephalopathy, all of which compromise functional capacity.[3] Cirrhotic patients with frailty are at heightened risk for complications such as falls, infections, prolonged hospitalizations, and increased mortality.[4] Moreover, frailty adversely impacts candidacy and outcomes for liver transplantation, leading to higher delisting rates and poorer post-transplant survival.[5]

Recent studies report that frailty affects nearly 40–50% of patients with cirrhosis, even among those with compensated disease.[4-7] Despite this growing recogni-

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tion, frailty remains under-assessed in routine hepatology practice, particularly in low-resource settings. Standard liver disease severity scores such as Model for End-Stage Liver Disease (MELD) or Child-Pugh do not capture the functional and nutritional decline that defines frailty, underscoring the need for integrated prognostic models.

Multiple tools have been developed to evaluate frailty in cirrhosis, including performance-based measures [e.g., Liver Frailty Index (LFI)], self-reported scales, and clinician-administered tools such as the Clinical Frailty Scale (CFS).[8] The CFS offers the advantages of simplicity, feasibility, and reproducibility, making it suitable for real-world clinical settings.[9]

In Egypt and other Middle Eastern countries, limited data are available on the prevalence and implications of frailty in cirrhosis, despite high burdens of viral hepatitis and metabolic liver diseases. This gap hinders evidence-based interventions for risk stratification and patient optimization.

Aim

This study aims to determine the prevalence of frailty among patients with liver cirrhosis at a tertiary care center in Egypt, identify its demographic, clinical, and nutritional predictors, and explore its relationship with disease severity and transplant eligibility. By highlighting frailty's burden and correlates, we hope to inform better clinical decision-making and encourage routine frailty assessment in hepatology practice

Material and methods

This prospective cross-sectional study was conducted at the National Liver Institute (NLI), Menoufia University, Egypt, between September 15, 2023, and June 15, 2024. The study protocol was approved by the Institutional Review Board of NLI (IRB approval number: 0014014FWA00034015), and written informed consent was obtained from all participants.

Eligible participants were adults aged 18 years or older with a confirmed diagnosis of liver cirrhosis based on clinical, biochemical, and radiologic criteria, and/or liver biopsy when available.[10] Patients were required to be physically and cognitively able to participate in clinical and nutritional assessments.

Exclusion criteria included the presence of hepatocellular carcinoma or any other active malignancy, recent gastrointestinal bleeding (within the past two weeks), overt hepatic encephalopathy (Grade ≥2 based on West Haven criteria), neurological or musculoskeletal disorders impairing mobility, recent major surgery (within four weeks), advanced cardiopulmonary disease, prior liver transplantation, or life expectancy of less than six months due to non-hepatic causes.

The sample size was calculated using the normal approximation method for estimating a population proportion, assuming a 50% prevalence of frailty among patients with cirrhosis, consistent with prior studies such as Tandon et al.[3] and Padhi et al.[7] a 95% confidence level, and a ±5% margin of error. A minimum of 410 patients was required to achieve 80% power to detect a 10% difference. To account for potential exclusions or missing data, the target sample size was increased by 10–15%, resulting in a final enrollment of 460 patients.

Frailty was assessed using the Clinical Frailty Scale (CFS), a validated 9-point clinician-rated scale evaluating physical function, independence, and comorbidity burden. Patients were classified as frail (CFS >4) or non-frail (CFS ≤4).[11-13] Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared and classified according to WHO criteria.[14]

Nutritional status was evaluated using the Royal Free Hospital Nutritional Prioritizing Tool (RFHNPT), which categorizes patients into low (score 0), moderate (score 1), or high (score 2–7) nutritional risk.[15]

Liver disease severity was assessed using established scoring systems including the MELD, Child-Pugh score, and albumin-bilirubin (ALBI) score. Laboratory parameters used in these calculations were obtained on the same day as the frailty assessment.[10]

Data were collected through structured interviews and clinical examinations, including demographic data (age, sex), cirrhosis etiology, presence of comorbidities (diabetes mellitus, hypertension), and clinical features such as ascites, lower limb edema, and hepatic encephalopathy. The primary outcome was the prevalence of frailty (CFS >4). Secondary outcomes included associations between frailty and liver disease severity (MELD, ALBI, Child-Pugh scores), nutritional status (RFHNPT), BMI categories, and decompensating features.

This study is reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Statistical analysis

Data were analyzed using SPSS software, version 26.0 (IBM Corp., Armonk, NY, USA; 2019). Categorical variables were expressed as frequencies and percentages, and continuous variables as means ± standard deviations or medians with interquartile ranges, depending on distribution. Comparisons between groups (e.g., MELD <15 vs. ≥15; transplant-eligible vs. ineligible) were conducted using Chi-square or Fisher's exact test for categorical variables, and Student's t-test or Mann–Whitney U test for continuous variables. Univariate and multivariate logistic regression were performed to identify predictors of transplant eligibility, including CFS, age, MELD, diabetes, hypertension, and ascites. Spearman's rank correlation was used to examine the association between CFS and MELD score. A p-value <0.05 was considered statistically significant.

Results

A total of 460 patients with liver cirrhosis were enrolled. Based on the Clinical Frailty Scale (CFS), 210 patients (45.7%) were classified as frail (CFS >4), while 250 (54.3%) were non-frail. Demographic analysis revealed a median age of 61.0 years (IQR: 55.0–66.0) in frail patients and 56.0 years (IQR: 50.0–62.0) in non-frail patients (p<0.001). There was no significant sex difference between groups. Comorbid conditions such as diabetes mellitus (45.2% vs. 25.2%; p<0.001) and hypertension (42% vs. 21.7%; p=0.007) were more prevalent in the frail group. Ascites and lower limb edema were also significantly more common (82.1% vs. 17.9%; p<0.001) (Table 1).

Frail patients had significantly worse liver disease severity scores. Median MELD score was higher in frail vs. non-frail patients (11.0 vs. 8.0; p<0.001), and a greater proportion were classified as Child-Pugh Class C (17.6% vs. 1.2%; p<0.001). ALBI scores also correlated positively with frailty (rs=0.426, p<0.001) (Table 2).

Nutritional risk, assessed by the RFHNPT, was strongly associated with frailty. The RFHNPT score showed a robust correlation with CFS (rs=0.753, p<0.001) (Table 2, Figure 1).

BMI analysis revealed a U-shaped association with frailty. Among underweight individuals (BMI <18.5 kg/m²), 96.1% were classified as frail. Similarly, 95.5% of patients with obesity (BMI ≥30 kg/m²) were frail. In contrast, most patients with normal BMI (18.5–24.9 kg/m²) were non-frail, comprising 84.8% of that category. Overweight individuals (BMI 25–29.9 kg/m²) also showed a high prevalence of frailty (76.1%).

In multivariate logistic regression, independent predictors of frailty included: older age (OR=1.055; p=0.001), high nutritional risk (OR=20.186; p<0.001), and overweight/obese BMI categories (OR=9.803; p<0.001) (Table 3).

Table 1. Demographic and clinical characteristics of the two patients' groups

Variable	Non-frail (CFS≤4) n=250	Frail (CFS>4) n=210	Test	p
Age, years	56.0 (50.0–62.0)	61.0 (55.0–66.0)	18236.0	<0.001
Sex (Male)	138 (56.3%)	107 (43.7%)	0.827	0.363
Diabetes mellitus	63 (25.2%)	95 (45.2%)	20.322	<0.001
Ascites and lower limb edema	17 (6.8%)	78 (37.1%)	64.123	<0.001
Total bilirubin (mg/dL)	0.90 (0.66–1.30)	1.30 (0.90–2.00)	17119.5	<0.001
Albumin (g/dL)	3.90 (3.50–4.10)	3.20 (2.60–3.70)	14032.0	<0.001
MELD Score	8.0 (6.0–11.0)	11.0 (8.0–16.0)	16101.5	<0.001

Table 2. Correlation of frailty with liver disease severity and nutritional scores (Spearman's rank correlation)

Score	Test	p
MELD score	0.437	<0.001
ALBI score	0.426	<0.001
Child-Pugh score	0.433	<0.001
RFHNPT score	0.753	<0.001

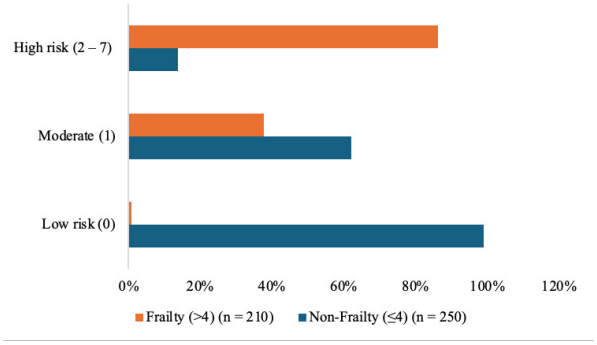

Fig. 1. Nutritional risk in frail vs. non-frail cirrhotic patients

Table 3. Logistic regression analysis for predictors of frailty (CFS >4)

Variable	Univariate OR (95%CI)	p	Multivariate OR (95%CI)	p
Age (per year increase)	1.061 (1.038–1.084)	<0.001	1.055 (1.023–1.088)	0.001
MELD Score	1.172 (1.118–1.228)	<0.001	1.153 (0.946–1.404)	0.158
Albumin	0.298 (0.221–0.402)	<0.001	0.517 (0.293–0.912)	0.023
RFHNPT (High risk)	19.864(11.78–33.48)	<0.001	20.186 (8.456–48.191)	<0.001
BMI (Overweight/ Obese)	10.238(5.96–17.58)	<0.001	9.803 (5.067–18.963)	<0.001

Discussion

This study highlights the high prevalence and clinical relevance of frailty in patients with liver cirrhosis and is associated with distinct demographic and clinical patterns. Older age and comorbidities such as diabetes and hypertension were significantly more common in the frail cohort, underscoring the interplay between systemic health and liver-related frailty. Our findings reinforce that frailty, as assessed using the CFS, is not merely a reflection of chronological aging but rather a multidimensional syndrome that correlates with liver disease severity, nutritional compromise, and reduced transplant eligibility. The Clinical Frailty Scale identified 45.7% of patients as frail, aligning with previous studies reporting frailty prevalence in cirrhosis ranging from 40% to 50%, even among patients with relatively preserved liver function.[7,11-13]

The CFS, adopted in our study due to its ease of implementation and real-world applicability, offers a pragmatic alternative as a validated simple screening tool to more complex tools such as the LFI.[12-13] While the LFI incorporates performance-based assessments (grip strength, chair-stands, balance), which enhances its predictive value for waitlist mortality and hospitalization[16], its routine use remains limited in many clinical settings due to time, training, and equipment constraints. Conversely, the CFS, being a clinician-judgment-based tool, enables rapid bedside assessment with proven prognostic relevance in liver disease populations.[12-13] However, the subjective nature of the CFS may render it less sensitive to subtle declines in physical function and more

vulnerable to inter-observer variability, thus potentially underestimating frailty in early stages.[17] Future research should explore the complementarity of both tools, especially in settings where resource limitations preclude objective measures.

Our study also underscores the intricate relationship between frailty and liver dysfunction. Frailty was more frequently observed in patients with features of hepatic decompensation, including ascites and hypoalbuminemia, and in those categorized within higher Child-Pugh and MELD score classes. This suggests a bidirectional interplay in which progressive liver dysfunction contributes to physiological decline and, conversely, frailty may exacerbate vulnerability to liver-related complications.[18] These findings support integrating frailty assessments into routine cirrhosis management to enhance risk stratification and inform decisions regarding transplant candidacy, inpatient care needs, and palliative approaches.

Importantly, the association between frailty and nutritional status emerged as particularly robust. The observed overlap between high frailty scores and elevated nutritional risk scores is consistent with the literature, where malnutrition is identified as both a contributor to and consequence of frailty in cirrhosis.[4,19] This highlights the importance of combining frailty screening with structured nutritional assessments. Early nutritional interventions – including adequate protein intake, branched-chain amino acid supplementation, and late evening snacks – have been shown to mitigate sarcopenia and improve physical reserve.[20-22]

Our findings also reveal a U-shaped relationship between body mass index (BMI) and frailty, where both underweight and obese individuals demonstrated elevated frailty prevalence. While under nutrition has long been recognized as a frailty determinant, obesity – particularly sarcopenic obesity – has emerged as a critical phenotype characterized by excess adiposity with reduced muscle mass and function.[14,23] This paradox may lead to misclassification of nutritional status if BMI alone is used and emphasizes the necessity of body composition analysis in cirrhotic populations.

Although sarcopenia and frailty are distinct entities, their overlap is considerable. Sarcopenia represents the physical dimension of frailty and shares pathophysiological underpinnings, including chronic inflammation, hormonal dysregulation, and metabolic imbalance.[24] While our study did not employ direct measures of sarcopenia, such as muscle mass or strength, the strong associations between frailty, nutritional risk, and BMI serve as surrogate indicators. Future studies incorporating imaging-based assessments or bioimpedance analysis may better delineate the interaction between these conditions.

The multivariate model identified age, advanced liver disease, and ascites as independent predictors of frailty. These findings mirror previous research and reinforce the notion that liver-specific factors outweigh traditional cardiovascular comorbidities, such as diabetes and hypertension, in determining frailty risk in cirrhosis.[4,7] This insight has important clinical implications, suggesting that even in patients without significant cardiometabolic burden, frailty may develop as a direct consequence of hepatic insufficiency and associated systemic effects.

A notable strength of this study is its relatively large sample size and comprehensive assessment of frailty using validated tools in conjunction with nutritional and hepatic parameters. However, several limitations should be acknowledged. The cross-sectional design precludes conclusions about the temporal evolution of frailty or its reversibility. Additionally, the exclusive use of the CFS may limit granularity in functional assessment compared to objective frailty indices. Our findings also reflect a single-center experience and may not be generalizable across diverse healthcare systems or populations.

Future research should focus on longitudinal frailty trajectories and the impact of targeted interventions, including pre-habilitation programs that integrate exercise, nutrition, and psychosocial support, especially for transplant candidates. Comparative studies of the CFS and LFI in diverse clinical settings would also help define optimal frailty assessment strategies

Conclusion

Frailty is a prevalent and clinically impactful condition among patients with liver cirrhosis, reflecting a convergence of physiological decline, malnutrition, and hepatic dysfunction. The Clinical Frailty Scale, owing to its practicality and validated utility, offers a feasible screening tool in routine hepatology practice, particularly in resource-limited settings. Our findings advocate for the systematic integration of frailty assessment into the management of cirrhotic patients to improve risk stratification, guide nutritional and rehabilitative interventions, and inform transplant eligibility decisions. Future multicenter and longitudinal studies incorporating objective frailty and sarcopenia measures are warranted to deepen our understanding of frailty's trajectory and its modifiability in liver disease.

Declarations

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Author contributions

Conceptualization, E.M. and E.M; Methodology, A.A.; Software, A.A.; Validation, E.M., E.M. and A.A.; Formal Analysis, E.M.; Investigation, A.A.; Resources, A.A.; Data Curation, E.M.; Writing – Original Draft Prepara-

tion, E.M.; Writing – Review & Editing, A.O. and E.M.; Visualization, A.O.; Supervision, A.O. and B.G.; Project Administration, A.O. and B.G.; Funding Acquisition, E.M. and A.A.

Conflicts of interest

The authors have no relevant financial or non-financial interests to disclose.

Data availability

Data is available upon request from the corresponding author.

Ethics approval

The study protocol was approved by the Institutional Review Board of NLI (IRB approval number: 0014014FWA00034015).

References

1. Martin FC, O'Halloran AM. Tools for Assessing Frailty in Older People: General Concepts. *Adv Exp Med Biol*. 2020;1216:9-19. doi: 10.1007/978-3-030-33330-0_2
2. Tandon P, Zanetto A, Piano S, Heimbach JK, Dasarathy S. Liver transplantation in the patient with physical frailty. *J Hepatol*. 2023;78(6):1105-1117. doi:10.1016/j.jhep.2023.03.025
3. Tandon P, Montano-Loza AJ, Lai JC, Dasarathy S, Merli M. Sarcopenia and frailty in decompensated cirrhosis. *J Hepatol*. 2021;75(1):S147-S162. doi:10.1016/j.jhep.2021.01.025
4. Lai JC, Tandon P, Bernal W, et al. Malnutrition, frailty, and sarcopenia in patients with cirrhosis: 2021 practice guidance by the American Association for the Study of Liver Diseases [published correction appears in *Hepatology*. 2021;74(6):3563. doi:10.1002/hep.32224]. *Hepatology*. 2021;74(3):1611-1644. doi: 10.1002/hep.32049
5. Harris SJ, Stine JG. Frailty in liver transplantation: exploring prescribing exercise as medicine to improve patient outcomes. *Liver Int*. 2024;44(9):2251-2262. doi: 10.1111/liv.15986
6. Niwa T, Saeki C, Saito M, et al. Impact of frailty and prevalent fractures on the long-term prognosis of patients with cirrhosis: a retrospective study. *Sci Rep*. 2025;15(1):186. doi: 10.1038/s41598-024-83984-2
7. Padhi BK, Gandhi AP, Sandeep M, et al. Prevalence of frailty and its impact on mortality and hospitalization in patients with cirrhosis: a systematic review and meta-analysis. *J Clin Exp Hepatol*. 2024;14(4):101373. doi: 10.1016/j.jceh.2024.101373
8. Deng Y, Sato N. Global frailty screening tools: review and application of frailty screening tools from 2001 to 2023. *Intractable Rare Dis Res*. 2024;13(1):1-11. doi: 10.5582/irdr.2023.01113
9. Wiedermann CJ, Barbieri V, Ausserhofer D, Engl A, Piccoliori G, Mahlknecht A. Sex bias in frailty screening: a cross-sectional analysis of PRISMA-7 and the Clinical Frailty Scale in primary care. *Diagnostics*. 2025;15(7):915. doi: 10.3390/diagnostics15070915
10. Kotak PS, Kumar J, Kumar S, Varma A, Acharya S. Navigating cirrhosis: a comprehensive review of liver scoring systems for diagnosis and prognosis. *Cureus*. 2024;16(3):e57162. doi: 10.7759/cureus.57162
11. Geladari E, Alexopoulos T, Vasilieva L, et al. Evaluation of five screening tools in detecting physical frailty in cirrhosis and their prognostic role. *J Clin Med*. 2024;13(17):5169. doi: 10.3390/jcm13175169
12. Kremer WM, Nagel M, Reuter M, et al. Validation of the Clinical Frailty Scale for the prediction of mortality in patients with liver cirrhosis. *Clin Transl Gastroenterol*. 2020;11(7):e00211. doi: 10.14309/ctg.0000000000000211
13. Schleicher EM, Kremer WM, Kalampoka V, et al. Frailty as tested by the Clinical Frailty Scale is a risk factor for hepatorenal syndrome in patients with liver cirrhosis. *Clin Transl Gastroenterol*. 2022;13(7):e00512. doi: 10.14309/ctg.0000000000000512
14. Montano-Loza AJ, Angulo P, Meza-Junco J, et al. Sarcopenic obesity and myosteatosis are associated with higher mortality in patients with cirrhosis. *J Cachexia Sarcopenia Muscle*. 2016;7(2):126-135. doi: 10.1002/jcsm.12039
15. Wu Y, Zhu Y, Feng Y, et al. Royal Free Hospital-Nutritional Prioritizing Tool improves the prediction of malnutrition in liver cirrhosis. *Br J Nutr*. 2020;124(12):1293-1302. doi: 10.1017/S0007114520002546
16. Lai JC, Covinsky KE, McCulloch CE, Feng S. The Liver Frailty Index improves mortality prediction of the subjective clinician assessment in patients with cirrhosis. *Am J Gastroenterol*. 2018;113(2):235-242. doi: 10.1038/ajg.2017.443
17. Singh S, Taneja S, Tandon P, et al. A comparison of different frailty scores and impact of frailty on outcome in patients with cirrhosis. *J Clin Exp Hepatol*. 2022;12(2):398-408. doi: 10.1016/j.jceh.2021.07.003
18. Elsheikh M, El Sabagh A, Mohamed IB, Bhongade M, Hassan MM, Jalal PK. Frailty in end-stage liver disease: understanding pathophysiology, tools for assessment, and strategies for management. *World J Gastroenterol*. 2023;29(46):6028-6048. doi: 10.3748/wjg.v29.i46.6028
19. Puri P, Dhiman RK, Taneja S, et al. Nutrition in chronic liver disease: consensus statement of the Indian National Association for Study of the Liver. *J Clin Exp Hepatol*. 2021;11(1):97-143. doi: 10.1016/j.jceh.2020.09.003
20. Loschi TM, Baccan MDTA, Della Guardia B, Martins PN, Boteon APCS, Boteon YL. Exercise training as an intervention for frailty in cirrhotic patients on the liver transplant waiting list: a systematic review. *World J Hepatol*. 2023;15(10):1153-1163. doi: 10.4254/wjh.v15.i10.1153
21. Duarte-Rojo A, Ruiz-Margáin A, Montaño-Loza AJ, Macías-Rodríguez RU, Ferrando A, Kim WR. Exercise and physical activity for patients with end-stage liver disease: improving functional status and sarcopenia while on the transplant waiting list. *Liver Transpl*. 2018;24(1):122-139. doi: 10.1002/lt.24958

22. Quint EE, Ferreira M, van Munster BC, et al. Prehabilitation in adult solid organ transplant candidates. *Curr Transplant Rep*. 2023;10(2):70-82. doi: 10.1007/s40472-023-00395-4
23. Jayanama K, Theou O, Godin J, Mayo A, Cahill L, Rockwood K. Relationship of body mass index with frailty and all-cause mortality among middle-aged and older adults. *BMC Med*. 2022;20(1):404. doi: 10.1186/s12916-022-02596-7
24. Wei S, Nguyen TT, Zhang Y, Ryu D, Gariani K. Sarcopenic obesity: epidemiology, pathophysiology, cardiovascular disease, mortality, and management. *Front Endocrinol (Lausanne)*. 2023;14:1185221. doi: 10.3389/fendo.2023.1185221