## Title

A chair-stand time of greater than 15 seconds is associated with an increased risk of death and hospitalization in cirrhosis



## Journal

Canadian Liver Journal, 6(3)

## ISSN

2561-4444

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## Publication Date

2023-11-03

## DOI

10.3138/canlivj-2022-0021

Peer reviewed

CLINICAL BRIEF REPORT

# A chair-stand time of greater than 15 seconds is associated with an increased risk of death and hospitalization in cirrhosis

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## ABSTRACT

**BACKGROUND:** Frailty is a clinical state of increased vulnerability and is common in patients with cirrhosis. The liver frailty index (LFI) is a validated tool to evaluate frailty in cirrhosis, comprising of grip strength, chair stands, and balance tests. The chair-stand test is an easy to conduct frailty subcomponent that does not require specialized equipment and may be valuable to predict adverse clinical outcomes in cirrhosis. The objective of this study was to determine if the chair-stand test is an independent predictor of mortality and hospitalization in cirrhosis. **METHODS:** A retrospective review of 787 patients with cirrhosis was conducted. Chair-stand times were collected at baseline in person and divided into three groups: <10 seconds (*n* = 276), 10–15 seconds (*n* = 290), and >15 seconds (*n* = 221). Fine-Gray proportional hazards regression models were used to evaluate the association between chair-stand times and the outcomes of mortality and non-elective hospitalization. **RESULTS:** The hazard of mortality (HR 3.21, 95% CI 2.16%–4.78%, *p* <0.001) and non-elective hospitalization (HR 2.24, 95% CI 1.73%–2.91%, *p* <0.001) was increased in group 3 in comparison to group 1. A chair-stand test time >15 seconds had increased all-cause mortality (HR 2.78, 95% CI 2.01%–3.83%, *p* <0.001) and non-elective hospitalizations (HR 1.84, 95% CI 1.48%–2.29%, *p* <0.001) compared to <15 seconds. **CONCLUSIONS:** A chair-stand test time of >15 seconds is independently associated with mortality and non-elective hospitalizations. This test holds promise as a rapid prognostication tool in cirrhosis. Future work will include external validation and virtual assessment in this population.

**KEYWORDS:** cirrhosis; frailty; mortality

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## INTRODUCTION

Frailty is a clinical state of increased vulnerability to health and age associated stressors caused by decline across multiple physiological systems (1). Frailty is common in cirrhosis and is associated with increased morbidity and mortality (2). Routine assessment of frailty in cirrhosis is recommended due to its prognostic implications (3). The liver frailty index (LFI), composed of three measurements including grip strength, chair stands, and balance testing, is an objective and validated tool to evaluate frailty in cirrhosis (4,5). In some settings, evaluation of the full LFI may be limited by the need for a hand-grip dynamometer and the perceived challenge of testing three separate components. Intuitively, the chair-stand subcomponent is easy to conduct and has demonstrated high reliability across other populations (6). The aim of this study was to determine if the chair-stand test is an independent predictor of mortality and hospitalization in patients with cirrhosis.

## METHODS

A retrospective review of data was conducted from 787 adult patients with cirrhosis consecutively enrolled from five centres in outpatient clinics (3 in Canada, 1 in the USA, and 1 in India) between June 2013 to May 2019. Inclusion criteria: adults with cirrhosis was defined by compatible clinical, radiologic, or histologic criteria. For all centres, patients were excluded if they were unable to provide consent, had overt hepatic encephalopathy, or hepatocellular carcinoma outside of transplant criteria. Other exclusion criteria were advanced extra-hepatic organ failure including lung disease, end-stage renal disease with a GFR <15 ml/min/1.73m2, on dialysis, congestive heart failure with an ejection fraction <40%, active malignancy, pregnancy, or recent (<6 weeks) intake of drugs affecting psychometric performances. The chair-stand test is the time in seconds that a patient takes to stand up and sit down in a chair five times with their arms folded across their chest (4). Testing was carried out in person and completion times were divided into three categories for clinical ease of use, <10 seconds, 10–15 seconds, and >15 seconds. Patients who could not complete five chair stands were classified in the >15 seconds category. The primary outcome was all-cause mortality. The secondary outcome was non-elective all-cause hospital admission.

## STATISTICAL ANALYSIS

Fine-Gray proportional hazards regression models were used to evaluate the association between timed chair stands and the outcomes. Models were adjusted for age, sex, and MELD Na scores, and liver transplantation was accounted for as a competing risk. Hazard ratios were reported with 95% CIs for all chair-stand category comparisons. Cumulative incidence functions were used to create a graphical representation of the survival analysis for each chair-stand category. The association between chair-stand times as a continuous measure (per 1 second increase) with mortality and non-elective hospitalizations was also reported. SAS 9.4 (SAS Institute Inc., Cary, NC, USA) was used for the analysis.

## RESULTS

787 patients were enrolled retrospectively: 65.9% males ($n$ = 519), a mean age of 54.9 years, MELD-Na score 15.4, and Child-Pugh score of 8.1. Additional baseline characteristics and clinical outcomes are presented in Table 1. Baseline chair-stand times were divided into the following three groups: group 1, <10 seconds ($n$ = 276, 35.1%); group 2, 10–15 seconds ($n$ = 290, 36.8%); and group 3, >15 seconds ($n$ = 221, 28.1%). Adjusted competing risk analysis demonstrated increased mortality in group 3 in comparison to group 1 (HR 3.21, 95% CI 2.16%–4.78%, $p$ <0.001). Non-elective hospitalization was also increased in group 3 in comparison to group 1 (HR 2.24, 95% CI 1.73%–2.91%, $p$ <0.001). There was no significant difference in these outcomes between groups 1 and 2. Overall, patients with chair-stand test times >15 seconds experienced an increased risk of all-cause mortality (HR 2.78, 95% CI 2.01%–3.83%, $p$ <0.001) and non-elective hospitalization (HR 1.84, 95% CI 1.48%–2.29%, $p$ <0.001) compared to <15 seconds (Figure 1). There was also a significant association between the chair stand as a continuous measure (per 1 second increase) with mortality (HR 1.05, 95% CI 1.03%–1.06%, $p$ <0.001) and non-elective hospitalizations (HR 1.03, 95% CI 1.02%–1.05%, $p$ <0.001).

## DISCUSSION

In our multi-centre study of 787 patients, a chair-stand test time >15 seconds was independently associated with nearly three-fold increased mortality and nearly two-fold non-elective hospitalizations.

**Table 1:** Baseline patient characteristics and clinical outcomes across all centres

| | Canadian centres (*n* = 427) | US centre (*n* = 244) | India centre (*n* = 116) | Total (*n* = 787) |
|---|---|---|---|---|
| **Age (mean)** | 55.9 | 55.4 | 50.2 | 54.9 |
| **Males: *n* (%)** | 277 (64.9) | 142 (58.2) | 100 (86.2) | 519 (65.9) |
| **Females: *n* (%)** | 150 (35.1) | 102 (41.8) | 16 (13.8) | 268 (34.1) |
| **BMI** | 28.3 | 29.2 | 25.4 | 28.2 |
| **MELD-Na score** | 13.4 | 18.5 | 16.0 | 15.4 |
| **Child-Pugh score** | 7.5 | 9.1 | 8.1 | 8.1 |
| **Etiology of cirrhosis: *n* (%)** | | | | |
| Alcohol | 123 (28.8) | 81 (33.1) | 63 (54.3) | 267 (33.9) |
| NAFLD/Cryptogenic | 71 (16.6) | 72 (29.5) | 20 (17.2) | 163 (20.7) |
| Hepatitis C | 103 (24.1) | 29 (11.9) | 16 (13.8) | 148 (18.8) |
| Auto-immune, PBC, PSC | 58 (13.6) | 36 (14.8) | 4 (3.4) | 98 (12.5) |
| Hepatitis C & alcohol | 36 (8.4) | 13 (5.3) | 3 (2.6) | 52 (6.6) |
| Hepatitis B | 18 (4.2) | 9 (3.7) | 10 (8.6) | 37 (4.7) |
| Other | 18 (4.2) | 4 (1.6) | 0 | 22 (2.8) |
| **Complications of cirrhosis: *n* (%)** | | | | |
| Ascites | 167 (39.1) | 189 (77.5) | 84 (72.4) | 440 (55.9) |
| Hepatic encephalopathy | 133 (31.1) | 176 (72.1) | 40 (34.5) | 349 (44.3) |
| Variceal bleed | 131 (30.7) | 73 (30.0) | 35 (30.2) | 239 (30.4) |
| TIPS | 33 (7.7) | 23 (9.4) | 0 | 56 (7.1) |
| **Total hospitalizations: *n* (%)** | 267 (62.5) | 133 (54.5) | 50 (43.1) | 450 (57.2) |
| **Cause of hospitalization: *n* (% of hospitalizations)** | | | | |
| Non-liver cause | 88 (33.1) | 9 (6.8) | 0 | 97 (21.6) |
| Infection | 22 (8.2) | 37 (27.8) | 34 (68.0) | 93 (20.7) |
| Worsening liver function | 29 (10.9) | 25 (18.8) | 0 | 54 (12.0) |
| Volume overload | 26 (9.7) | 25 (18.8) | 3 (6.0) | 54 (12.0) |
| Hepatic encephalopathy | 33 (12.4) | 11 (8.3) | 4 (8.0) | 48 (10.7) |
| Gastrointestinal bleed | 24 (9.0) | 13 (9.8) | 9 (18.0) | 46 (10.2) |
| Other liver related | 41 (15.4) | 4 (3.0) | 0 | 45 (10.0) |
| Abdominal pain | 4 (1.5) | 3 (2.3) | 0 | 7 (1.6) |
| Unknown | 0 | 6 (4.5) | 0 | 6 (1.3) |
| **Total deaths: *n* (%)** | 118 (27.6) | 35 (14.3) | 23 (19.8) | 176 (22.4) |
| **Cause of death: *n* (% of deaths)** | | | | |
| Multiorgan failure | 38 (32.2) | 16 (45.7) | 0 | 54 (30.7) |
| Sepsis | 18 (15.2) | 10 (28.6) | 17 (73.9) | 45 (25.6) |
| Unknown | 31 (26.3) | 2 (5.7) | 0 | 33 (18.8) |
| Non-liver cause | 24 (20.3) | 7 (20.0) | 0 | 31 (17.6) |
| Gastrointestinal bleed | 7 (5.9) | 0 | 6 (26.1) | 13 (7.4) |

*BMI = Body mass index; MELD-Na = Model for end stage liver disease-sodium; NAFLD = Non-alcoholic fatty liver disease; PBC = Primary biliary cholangitis; PSC = Primary sclerosing cholangitis; TIPS = Transjugular intrahepatic portosystemic shuntv*

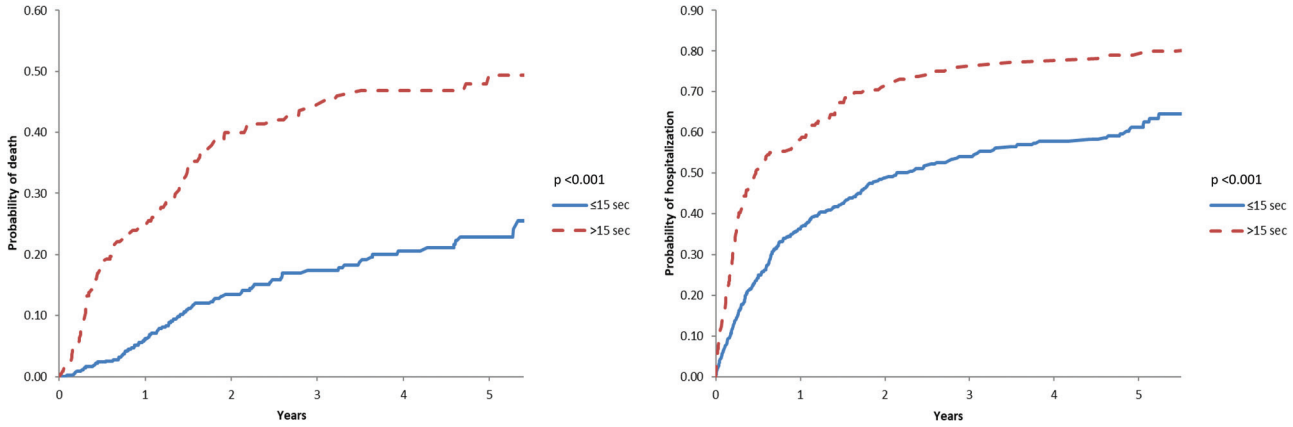


**Figure 1:** Cumulative incidence of death (1a) and hospitalization (1b) stratified by chair-stand time of 15 seconds

Our study supports the use of the chair stand as an independent frailty assessment tool in cirrhosis. Although the full LFI is recommended given the extensive validation work that accompanies it (5), the chair-stand component is easy to conduct and may be considered if the full test is not possible.

The predictive value of a chair-stand test time of greater than 15 seconds is consistent with the European Working Group on Sarcopenia in Older Patient's cut-off for prognostication in the geriatric population, supporting the applicability of our findings (6). Specifically in cirrhosis, in smaller studies of 299, 249, and 309 patients, respectively, the chair-stand test was associated with falls (7), development of hepatic encephalopathy (8), and transplant waitlist mortality (9).

Frailty assessment is recommended as a routine part of cirrhosis care (3). While a variety of tools for frailty in cirrhosis have been validated, many are limited by the need for equipment (eg, Grip strength), space (eg, 6-minute walk test), and time (eg, Fried frailty instrument) (3,5). The chair-stand test incorporates coordination, strength, and balance, takes <30 seconds to complete after instructions, and requires no additional equipment. Notably, evaluation of the chair-stand test in a senior Veterans population supports its usability and reliability across health conditions, even on a virtual platform (10). This ability to evaluate frailty virtually using the chair-stand test may become especially relevant as our learnings from the COVID-19 pandemic shift health care delivery to hybrid models involving virtual platforms.

Despite the large sample size, study limitations include the lack of external validation and the measurement of chair stands at only one timepoint. Acknowledging these limitations, our findings support the chair-stand test as an objective tool that is independently associated with mortality and unplanned hospitalization. Future studies will allow for external validation, explore virtual assessment, evaluate the prognostic value of repeated tests over time, and assess the impact on additional clinical outcomes in cirrhosis.

**CONTRIBUTIONS:** Data Curation, S Wang, R Whitlock, C Xu, S Taneja, S Singh, JG Abraldes, K Burak, RJ Bailey, JD Grab, JC Lai, P Tandon; Formal Analysis, R Whitlock; Investigation, JC Lai, P Tandon; Project Administration, P Tandon; Supervision, JC Lai, P Tandon; Writing–Original Draft, VV Nguyen, S Wang, S Taneja, JC Lai, P Tandon; Writing–Review & Editing, VV Nguyen, S Wang, P Tandon.

**ETHICS APPROVAL:** Ethics approval was obtained at each participating centre for the original studies. Ethics approval for the compilation of data was obtained from the Health Research Ethics Board at the University of Alberta (Pro00099666).

**INFORMED CONSENT:** We confirm that informed patient consent has been secured from all patients whose personal information is included in the manuscript or the parents or guardians of minors.

**REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL:** N/A

**FUNDING:** No funding was received for this work.

**DISCLOSURES:** The authors have nothing to disclose.

**PEER REVIEW:** This manuscript has been peer reviewed.

**ANIMAL STUDIES:** N/A

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