

# A Claims-Based Frailty Risk Score Is Associated With Hospitalization for Acute-on-Chronic Liver Failure: But Is It Frailty?

SEE ARTICLE ON PAGE 16

Frailty is a multidimensional construct that broadly refers to a health state of diminished physiological reserve resulting in a reduced tolerance to health stressors.<sup>(1)</sup> Although the concept of frailty has its roots in geriatrics, it has flourished in hepatology. Indeed, many patients with cirrhosis are frail, which portends an increased risk of hospitalizations and mortality.<sup>(2,3)</sup> It is recommended that we evaluate all patients with decompensated cirrhosis or undergoing transplant evaluation for frailty with a toolbox that includes

physical performance measures and validated disability scales.<sup>(1)</sup> Despite its importance, there are 3 persistent challenges facing frailty research. First, frailty assessments are infrequently used due to time constraints and the need for specialized tools or staff.<sup>(1)</sup> Second, because of the need for performance measures, population-based studies of frailty are lacking. Third, given the difficulties in assessing hospitalized patients for physical frailty, tools beyond disability measures are limited.<sup>(3)</sup> For all of these reasons, we welcome the important study by Shah et al. in this issue that examines the potential role of claims-based indices of frailty in chronic liver disease in a cohort of recently hospitalized patients with cirrhosis.<sup>(4)</sup>

*Abbreviations: ACLF, acute-on-chronic liver failure; HFRS, hospital frailty risk score; ICD, International Classification of Diseases, Tenth Revision; VOCAL, Veterans Outcomes and Costs Associated with Liver Disease.*

*Address reprint requests to Elliot B. Tapper, M.D., Division of Gastroenterology and Hepatology, University of Michigan, 3912 Taubman, SPC 5362, 1500 East Medical Center Drive, Ann Arbor, MI 48109. Telephone: 734-647-9252; FAX: 734-936-7392; E-mail: etapper@umich.edu*

*Elliot B. Tapper receives funding from the National Institutes of Health through the National Institute of Diabetes and Digestive and Kidney Diseases (1K23-DK-117055-01A1).*

*Elliot B. Tapper has served as a consultant to Novartis, Kaleido Biosciences, and Allergan; has served on advisory boards for Takeda, Mallinckrodt Pharmaceuticals, Rebiotix, and Bausch Health; and has received unrestricted research grants from Gilead Sciences.*

*Jeremy Louisaint wrote the manuscript. Elliot B. Tapper was responsible for the revision of the manuscript. Both authors contributed to the concept and analysis given in the article.*

*Received October 1, 2020; accepted October 8, 2020.*

*Copyright © 2020 by the American Association for the Study of Liver Diseases.*

*View this article online at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).*

*DOI 10.1002/lt.25921*

## Finding Frailty in Claims Data

Multiple investigators have sought to estimate frailty from claims-based administrative billing codes. One such risk score is the hospital frailty risk score (HFRS), which is the cumulative weighted sum of 109 International Classification of Diseases, Tenth Revision (ICD-10) codes.<sup>(5)</sup> The HFRS was derived from a retrospective cohort of hospitalized patients age  $\geq 75$  years in the United Kingdom using cluster analyses linking ICD-10 codes to hospital days and costs. People with scores  $< 5$  are considered low risk and those with scores  $> 15$  are considered high risk. Higher scores are associated with readmissions and mortality. Interestingly, however, when it was compared with the gold-standard Fried Frailty Index, there was no meaningful association ( $\kappa = 0.22$ ). The HFRS was recently applied to patients with inflammatory bowel disease where it was associated with increased hospitalizations and mortality.<sup>(6)</sup> The HFRS has not, nor has any administrative frailty score, been

validated using established frailty indices in patients with cirrhosis.

## The First Use of Claims-Based Frailty Scores in Cirrhosis

Using a large ( $n = 16,561$ ) cirrhosis cohort with at least 1 hospitalization curated from the Veterans Health Administration by the Veterans Outcomes and Costs Associated with Liver Disease (VOCAL) group, Shah et al. examined the impact of claims-based frailty on the risk of acute-on-chronic liver failure (ACLF) hospitalizations (versus non-ACLF hospitalizations) and short-term mortality in cirrhosis. Median HFRSs were higher in those with an ACLF hospitalization compared with those with a non-ACLF hospitalization (11.8 versus 9.2). Interestingly, frailty scores increased with decreasing ACLF severity (ACLF 1 versus ACLF 3, 12.2 versus 10.8). The HFRS was associated with an increased risk of mortality (odds ratio 1.02 per 5-point HFRS increase,  $P = 0.004$ ). In the subgroup of patients with an ACLF hospitalization, however, the HFRS did not predict mortality.

## Is This Frailty?

This study has revealed that a claims-based frailty score is associated with incident ACLF hospitalizations and overall mortality in cirrhosis. However, it is unclear if our conclusion ought to be that frailty is associated with incident ACLF. We do not know whether the HFRS is detecting the physiological deficits measured when a patient performs chair stands, hand-grip tests, or walk-speed assessments. It turns out that there is poor agreement between the HFRS and established frailty measures.<sup>(5)</sup> Furthermore, the authors' observed association between the HFRS and lower-grade ACLF is in contrast to prior work showing that a traditional frailty/disability measure (Karnofsky Performance Status) worsens with increased ACLF severity.<sup>(7)</sup> Instead of frailty, the HFRS is likely best described as an expanded measure of comorbidity, not unlike the Charlson comorbidity index.<sup>(5,6)</sup>

## Can This Score Be Applied to Cirrhosis?

There are 4 reasons why any new comorbidity index or claims-based frailty score for patients with cirrhosis should be derived from patients with cirrhosis. First, a frailty index must discriminate robust from frail.<sup>(1)</sup> In contrast, using the cutoffs proposed by the HFRS, all subgroups studied by Shah et al. (non-ACLF hospitalization, ACLF 1 to 3 hospitalization) would have been classified as frail.

Second, the weighting of each code within the index must reflect frailty in cirrhosis. Instead, the HFRS lacks representation by key conditions known to impact frailty in cirrhosis, such as malnutrition, sarcopenia, ascites, and hepatic encephalopathy,<sup>(1,2)</sup> while nearly universal features of decompensated cirrhosis are heavily weighted: volume depletion, acute and chronic renal failure, hypotension, edema, and abnormal blood chemistries.

Third, because increasing frailty scores correlate with an increased risk of adverse outcomes, changes in frailty over time are meaningful in predicting future events.<sup>(8)</sup> The HFRS, however, is relatively static because it is calculated based on 2 years of preceding diagnostic codes which follow the patient in perpetuity.

Finally, patients with cirrhosis experience fragmented care, frequently dispersing their claims data across multiple health care systems.<sup>(9)</sup> Yet, the HFRS relies on 2 years of complete claims-based data. Shah et al. reveal that even in a centralized health care system, only 53% of the cohort have such complete data.

In conclusion, a claims-based risk score is associated with the risk of ACLF hospitalization and overall survival in chronic liver disease. The authors have initiated an exciting line of inquiry. However, we do not know if the chosen risk score truly captures frailty. Further study is needed to evaluate scores specific to patients with cirrhosis.

Jeremy Louissaint, M.D.<sup>1</sup>

Elliot B. Tapper, M.D. <sup>1,2</sup>

<sup>1</sup>Division of Gastroenterology and Hepatology  
University of Michigan  
Ann Arbor, MI

<sup>2</sup>Gastroenterology Section  
VA Ann Arbor Healthcare System  
Ann Arbor, MI

## REFERENCES

- 1) Lai JC, Sonnenday CJ, Tapper EB, Duarte-Rojo A, Dunn MA, Bernal W, et al. Frailty in liver transplantation: an expert opinion statement from the American Society of Transplantation Liver and Intestinal Community of Practice. *Am J Transplant* 2019;19:1896-1906.
- 2) Tapper EB. Frailty and outcomes after liver transplantation. *Curr Transplant Rep* 2019;6:1-6.
- 3) Tapper EB, Finkelstein D, Mittleman MA, Piatkowski G, Lai M. Standard assessments of frailty are validated predictors of mortality in hospitalized patients with cirrhosis. *Hepatology* 2015;62:584-590.
- 4) Shah S, Goldberg DS, Kaplan DE, Sundaram V, Taddei TH, Mahmud N. Patient frailty is independently associated with the risk of hospitalization for acute-on-chronic liver failure. *Liver Transpl* 2021;27:16-26.
- 5) Gilbert T, Neuberger J, Kraindler J, Keeble E, Smith P, Ariti C, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet* 2018;391:1775-1782.
- 6) Qian AS, Nguyen NH, Elia J, Ohno-Machado L, Sandborn WJ, Singh S. Frailty is independently associated with mortality and readmission in hospitalized patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol* 2020. <https://doi.org/10.1016/j.cgh.2020.08.010>.
- 7) Sundaram V, Jalan R, Wu T, Volk ML, Asrani SK, Klein AS, Wong RJ. Factors associated with survival of patients with severe acute-on-chronic liver failure before and after liver transplantation. *Gastroenterology* 2019;156:1381-1391.
- 8) Lai JC, Dodge JL, Kappus MR, Dunn MA, Volk ML, Duarte-Rojo A, et al.; for Multi-Center Functional Assessment in Liver Transplantation (FrAILT) Study. Changes in frailty are associated with waitlist mortality in patients with cirrhosis. *J Hepatol* 2020;73:575-581.
- 9) Cohen-Mekelburg S, Waljee AK, Kenney BC, Tapper EB. Coordination of care is associated with survival and health care utilization in a population-based study of patients with cirrhosis. *Clin Gastroenterol Hepatol* 2020;18:2340-2348.