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Article type : Editorial

A Claims-based Frailty Risk Score is Associated with Hospitalization for Acute on Chronic Liver Failure – But is it *Frailty*?

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Keywords: Claims-based Frailty, Acute on Chronic Liver Failure, Hospitalizations

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Disclosure:

1. Elliot Tapper is the guarantor of this article

2. Roles

a. Concept: Louissaint, Tapper

b. Analysis: Louissaint, Tapper

d. Writing: Louissaint

e. Revision: Tapper

3. Conflicts of interest: Elliot Tapper has served as a consultant to Norvartis, Kaleido, and Allergan, has served on advisory boards for Takeda, Mallinckrodt, Rebiotix, and Bausch Health, and has received unrestricted research grants from Gilead.

4. Funding: Elliot Tapper receives funding from the National Institutes of Health through the NIDDK (1K23DK117055-01A1).

Frailty is a multidimensional construct that broadly refers to a health-state of diminished physiologic reserve resulting in a reduced tolerance to health stressors.(1) 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.(2,3) 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.(1) Despite its importance, there are three persistent challenges facing frailty research. First, frailty assessments are infrequently utilized due to time constraints and the need for specialized tools or staff.(1) Second, owing to 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.(3) For all these reasons, we welcome the important study by Shah and colleagues in this issue of *Liver Transplantation* examining the potential role of claims-based indices of frailty in chronic liver disease in a cohort of recently hospitalized patients with cirrhosis.(4)

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 ICD-10 codes.(5) The HFRS was derived from a retrospective cohort of hospitalized patients age ≥ 75 years in the United Kingdom using cluster analyses linking ICD-10 codes to hospital-days and costs. Persons with scores <5 are considered low-risk and those with scores >15 are considered high-risk, and higher scores are associated with readmissions and mortality. Interestingly, however, when it was compared to the gold-standard Fried Frailty Index (FFI), 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.(6) The HFRS has not, nor has any administrative frailty score, been validated using established frailty indices in persons with cirrhosis.

The first use of claims-based frailty scores in cirrhosis

Using a large (N=16,561) cirrhosis cohort with at-least one hospitalization curated from the Veterans Health Administration by the VOCAL group, Shah et al examined the impact of claims-based frailty on the risk of acute on chronic liver failure (ACLF) hospitalizations (vs non-ACLF hospitalizations) and short-term mortality in cirrhosis. Median HFRS were higher in those with an ACLF hospitalization compared to those with a non-ACLF hospitalization (11.8 vs. 9.2). Interestingly, frailty scores increased with decreasing ACLF severity (ACLF-1 12.2 vs ACLF-3

10.8). The HFRS was associated with an increased risk of mortality (OR 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 physiologic 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.(5) Further, 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.(7) Instead of *frailty,* the HFRS is likely best described as an expanded measure of comorbidity, not unlike the Charlson comorbidity index.(5,6)

Can this score be applied to cirrhosis?

There are four 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.(1) In contrast, using the cutoffs proposed by the HFRS, all subgroups studied by Shah (non-ACLF hospitalization, ACLF-1-3 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,(1,2) while nearly universal features of decompensated cirrhosis are heavily weighted: volume depletion, acute and chronic renal failure, hypotension, edema, and abnormal blood chemistries.

Third, since increasing frailty scores correlate with an increased risk of adverse outcomes, changes in frailty over time are meaningful in predicting future events.(8) The HFRS,

however, is relatively static as it is calculated based on two 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 healthcare systems(9); yet, the HFRS relies on 2-years of complete claims-based data. Shah et al reveal that even in a centralized healthcare system, only 53% of the cohort have such complete data.

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 persons with cirrhosis.

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