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Advancing adoption of frailty to improve the care of patients with cirrhosis: Time for a consensus on a frailty index

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Abstract

Frailty is a key determinant of outcomes in patients with cirrhosis. Two papers in this issue of the *American Journal of Gastroenterology* advance our understanding of the mechanism by which frailty impacts mortality – by increasing the risk of hospitalization for liver-related complications. We now have overwhelming justification to incorporate frailty into clinical practice, but this should be done in a systematic way to foster multi-center collaboration to accelerate research in this field. It's time for consensus on single frailty index to unify decision-making surrounding frailty and equalize outcomes for all cirrhotics across all centers.

Keywords

frailty index; cirrhosis; risk prediction; hospitalization

Patients with cirrhosis live in a precarious state of homeostasis, highly vulnerable to even the slightest of stressors. An unplanned hospitalization represents the disruption of this homeostasis. From the patient's perspective, a hospitalization frequently leads to precipitous decline in physical function with resultant disability that, at least transiently, if not permanently, reduces quality of life and increases risk of death. From a societal perspective, even a brief inpatient stay can increase the cost of a patient's care exponentially. Despite the clinical relevance of hospitalizations as an intervening event in the natural trajectory of a patient with cirrhosis, little is known of the factors that increase the risk of unplanned hospitalizations in this vulnerable population.

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In this issue of *American Journal of Gastroenterology*, one of these factors is unveiled. Through two original articles including 673 cirrhotics from two North American centers, we learn that frailty – measured by the performance-based gait speed or clinician-assessed Clinical Frailty Scale – is associated with an increased risk of hospitalizations.^{1,2} Specifically, Dunn *et al* report that every 0.1 meter/second decrease in gait speed (i.e., slower) was associated with 22% greater inpatient days. This is an enormous effect size for a minimally significant change in gait speed.³ Compared to an otherwise similar patient with cirrhosis and a gait speed of 1.0 meter/second, a cirrhotic with a gait speed of 0.5 meters/second is estimated to spend 15 *additional* days in the hospital at an estimated \$60,000 *increased* cost per year.¹ In the report by Tandon *et al*, cirrhotics rated as “mildly frail”, “moderately frail”, or “severely frail” on the Clinical Frailty Scale (i.e., score >4 out of 9) experienced nearly double the rate of unplanned hospital admissions as compared to patients with a Clinical Frailty Scale score ≤ 4 (39% versus 21%; $p=0.005$).²

These papers significantly advance our understanding of the mechanism by which frailty impacts patients with end-stage liver disease. Even after adjustment for liver disease severity, cirrhotics classified as frail were hospitalized more frequently for liver-related complications including volume overload, gastrointestinal bleeding, and hepatic encephalopathy in both studies.^{1,2} This reinforces one of the original conceptualizations of frailty as a biological syndrome of decreased physiologic reserve and increased vulnerability to adverse health outcomes in response to acute stressors.⁴ To put it another way, all cirrhotics are prone to fluid retention, but a frail one is less likely to tolerate the relatively slow diuretic adjustments as an outpatient and, as a result, more likely to be hospitalized for volume overload.

But, by introducing several additional frailty instruments (Clinical Frailty Scale, gait speed, and grip strength) into the hepatology literature, these studies also add to the confusion about the application of frailty in clinical practice. Can the frail phenotype, defined by an arbitrary cut-point on an ordinal scale that captures the clinicians’ assessment of the patient (i.e., Clinical Frailty Scale), really be the same as the frail phenotype defined by a continuous, performance-based assessment of gait speed? What should we conclude of the fact that neither hand grip strength nor the Braden Scale, tools that have previously been shown to predict mortality in cirrhotics,^{5,6} were *not* significantly associated with an increased risk of hospitalizations?¹

Herein lies the major shortcoming of the current state of the frailty literature in hepatology. The overarching conclusion from all of the studies involving frailty is that frailty is a key determinant of outcomes in cirrhotics,^{1,2,5,7-9} but the heterogeneity and sheer number of frailty instruments evaluated in these studies have impeded progress toward systematic and widespread adoption of a frailty index in clinical practice. A handful of transplant centers have already incorporated frailty into their initial transplant evaluations using tests as varied as the Fried Frailty Index, grip strength, Timed Up and Go test, or the six-minute walk test (personal communication). But this haphazard approach to implementing frailty in clinical practice will not position us to reconcile differences in results in the existing literature, accelerate research to further understand mechanisms underlying frailty, or collaborate to develop system-wide programs to address the needs of this vulnerable population.

Rather, we should seize this moment – before each center adopts a different frailty measure – to engage in a discussion about what we ideally want out of a frailty index. How many components (i.e., gait speed, chair stands, disability, physical activity) are we willing to measure in the clinic setting to capture frailty? There will be a trade-off between increasing predictive ability using a greater number of components and ease of clinical use with fewer components. Should the index be entirely performance-based or can it include self-reported components? Self-reported tests are easier to administer and collect longitudinally but performance-based tests are more objective. What is most important outcome for this index to predict? An index that predicts mortality may have use in a national liver allocation system but one that better predicts intermediate outcomes, such as unplanned hospitalizations or quality of life, may have greater impact on day-to-day clinical decision-making. In my opinion, an ideal frailty index would be a continuous index that consists of as few tests as possible, all performance-based, while still capturing multiple dimensions of physical frailty (i.e., nutrition, muscle strength, sensorimotor control, cardiopulmonary fitness) and predicts mortality in cirrhotics above and beyond liver disease severity. Ultimately, however, the “best” choice of a liver-specific frailty index is the single one that we can all agree to use.

With the addition of these reports by Dunn *et al* and Tandon *et al* to the existing frailty literature, the concept of frailty in hepatology is unequivocally here to stay. It is now our responsibility as clinicians to adopt frailty within our clinical practice to improve the care of our patients with cirrhosis. Let’s do this in a systematic way to unify decision-making surrounding frailty, equalize outcomes, and improve the care of all cirrhotics across all centers.

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