

# Falls are an Underappreciated Driver of Morbidity and Mortality in Cirrhosis

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Cirrhosis is common and morbid, afflicting over one million Americans, and causing over 60,000 deaths annually.<sup>1</sup> As the epidemiology of cirrhosis shifts to account for increasing alcohol-related liver disease (ALD) and nonalcoholic fatty liver disease (NAFLD), so will cirrhosis's public health burden.<sup>1</sup> Rising rates of NAFLD and ALD will result in an older patient population with a high prevalence of metabolic complications, extrahepatic comorbidities, sarcopenia, polypharmacy, and cognitive dysfunction (CD). These factors will each increase the rate of falls, however, there is limited awareness among clinicians of fall risk, risk assessment, and prevention in cirrhosis.

### **Falls epidemiology**

Falls are an important and preventable cause of morbidity and mortality in cirrhosis. CD is the classic risk factor. Román et al. retrospectively investigated fall incidence in outpatients with cirrhosis and minimal hepatic encephalopathy (MHE).<sup>2</sup> Over 12 months, incidence of falls was 40% in those with MHE compared to 13% in those without ( $p < 0.001$ ).<sup>2</sup> Similarly, the probability of falls in patients with CD exceed 50% at 1 year compared to 7% in those without ( $p < 0.001$ ).<sup>3</sup> Tapper et al., prospectively followed 300 patients with cirrhosis and portal hypertension, but no prior HE, and found that probability of falls was 29% and 50% at 1 and 3 years, respectively.<sup>4</sup> The strongest risk factors were prior falls, lower serum sodium, poor chair-stand performance, and poor health-related quality of life (HRQOL), measured with the Short Form-8 (SF-8). Another study by Tapper et al. showed that among inpatients with cirrhosis, falls were frequent in those receiving benzodiazepines (51% vs 17%,  $p < 0.0001$ ) and antipsychotics (31% vs 7.3%,  $p < 0.0001$ ).<sup>5</sup>

### **Falls contribute to the morbidity and mortality of cirrhosis**

Falls are common and associated with increased risk of severe injuries and mortality. Tapper et al. showed that among compensated patients without prior HE, the risk of injurious falls was 9% and 17% at 1 and 3 years, respectively.<sup>4</sup> The probability of an injurious fall at 3 years was higher (at 20-40%) in patients with ALD and any dependence on others for activities of daily living or prior falls at baseline.<sup>4</sup> Falls are independently associated with a three-fold increased risk of mortality.<sup>4</sup> Ezaz et al. found that compared to those without cirrhosis, patients with cirrhosis were more likely to sustain severe injuries and die following falls.<sup>6</sup> Studying national data from England and Denmark, Otete et al. showed >5-fold increased risk of hip fracture and higher mortality after a fall in patients with ALD compared to those without.<sup>7</sup> Similarly in Taiwan, Tsai et al. report cirrhotic patients with and without HE had increased fracture incidence compared to controls ( $p < 0.05$ ). At 18 months, cumulative fracture incidence rate is 7% in patients with HE, 8% without HE, and 4% for the matched controls.<sup>8</sup> Injurious falls are of concern in cirrhosis given the high risk of surgery. As Cohen et al. found, orthopedic surgery in cirrhosis is more likely to have significant adverse outcomes, including decompensation, hemorrhage, cardiac arrest, and mortality when compared to controls (21% versus 3.2%,  $p=0.006$ ).<sup>9</sup> Emergent arthroplasty was associated with major complications in 80% and mortality in 60% of cases.<sup>9</sup> Finally, falls contribute strongly to poor HRQOL in cirrhosis.<sup>2,4,5</sup>

### **Why do patients fall?**

Common risk factors for falls include the use of sedating medications, older age, lower extremity weakness, alcohol intake, frailty, and cognitive deficits, all of which are more common among patients with cirrhosis.<sup>10,11</sup> Several physiologic changes associated with aging and present in cirrhosis include worsening postural control, body-orienting

reflexes, muscle tone, and step-height.<sup>12</sup> Fall avoidance requires accurate perception of perturbation prior to a successful response by generating enough torque in the hip and core muscles to adjust weight or shift foot placement.<sup>11</sup> Three separate domains—sensory, neurocognitive, and muscular play a physiologic role in fall avoidance (**Figure 1**). HE and alcohol use both cause peripheral neuropathy impairing sensation and ability to avoid environmental hazards. CD with or without HE and alcohol can cause minimal to overt disorientation and predispose patients to falls.<sup>12</sup> CD due to HE, poor nutrition, physical inactivity, and substance use contribute to frailty and the inability to generate a protective shift in weight to prevent falling.<sup>12,13</sup> Tapper et al. recently found that deprescribing zolpidem can reduce the risk of falls and fractures, highlighting the influence of sedating medications on falls risk.<sup>14</sup>

### **Screening for falls**

The CDC recommends screening for falls among those older than sixty-five with screening tools such as “Stay Independent: a 12-question tool” and asking three key questions: have you been worried about falling, unsteady, or had a prior fall over the past year? However, falls occur at younger ages in cirrhosis, and guidelines are lacking for this high-risk population. Tapper et al. proposed a model for predicting those at highest risk of falls—FallSSS.<sup>4</sup> In **Figure 2**, Tapper illustrates the strongest predictors (sHR)—fall history (4.08), chair-stands (0.92), serum sodium (0.92 per mEq/L), and SF-8 (0.97 per point) with an area-under-the-curve of 0.79, far greater than measures of liver or cognitive function.<sup>4</sup> This model offers an opportunity to predict the risk of falls over the next year and employ measures to mitigate that risk.

### **What can we do to decrease the incidence of falls?**

We advocate for increasing screening with measures such as our FallSSS model, for patients with prior falls, frailty, or HE. Identification of at-risk patients can lead to effective interventions. Interventions should focus on eliminating as many risk factors as possible in each individual patient, as well as provide support for the domain (sensory, neurocognitive, or physical) in which patients are weakest. In **Figure 3**, we highlight evidence-based options specific to this population to prevent falls including HE-directed therapy, Tai-chi and other exercise programs, personalizing footwear, eye exams, alcohol cessation and reduction of polypharmacy.

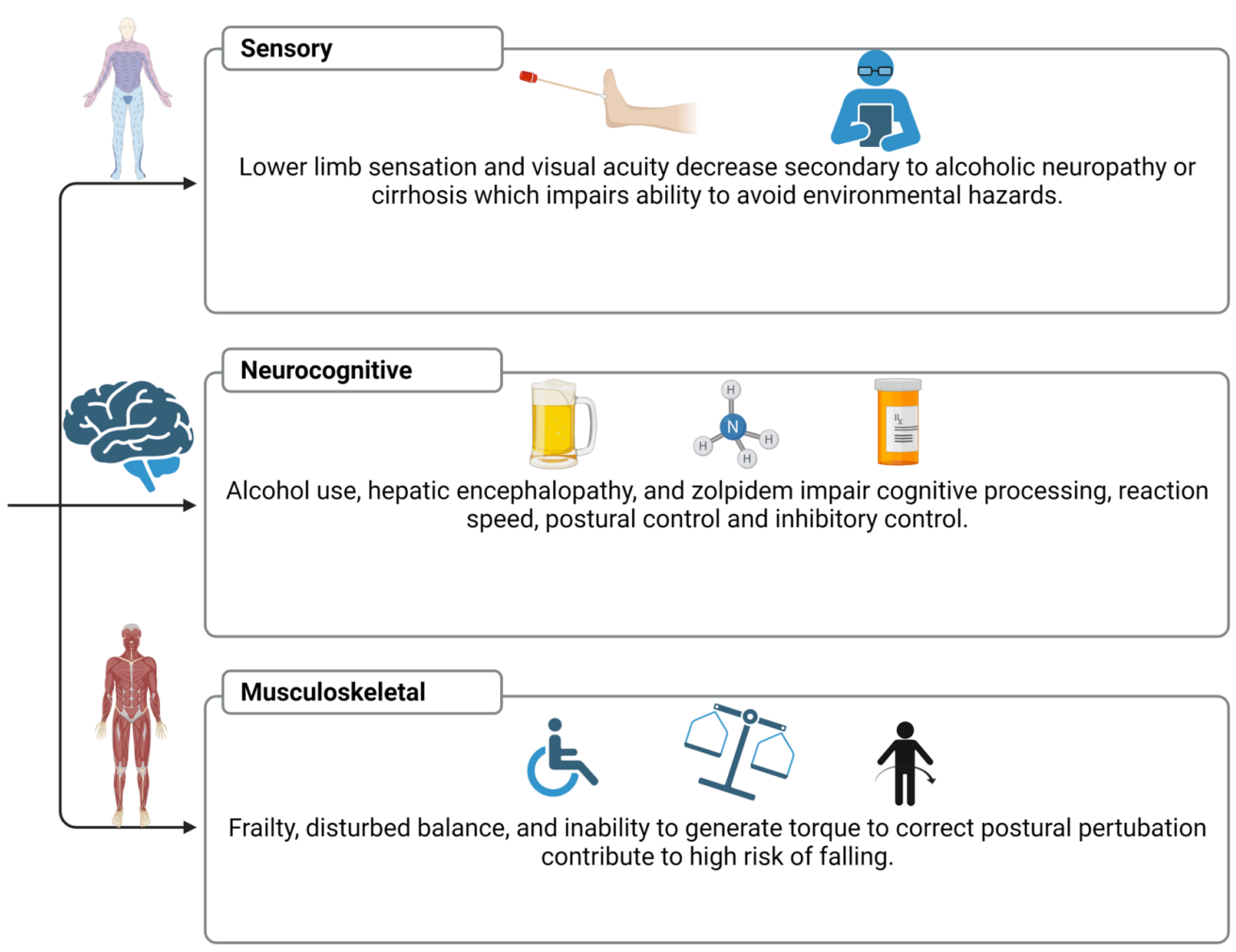
### **Conclusion**

As the prevalence of cirrhosis continues to rise each year, disease associated complications also increase. Falls are an underappreciated cause of significant morbidity and mortality in patients with cirrhosis. Reduction of fall-risk in this vulnerable population through improving screening, reducing risk factors, and implementing exercise in the form of Tai-chi is paramount to preserving HRQOL.

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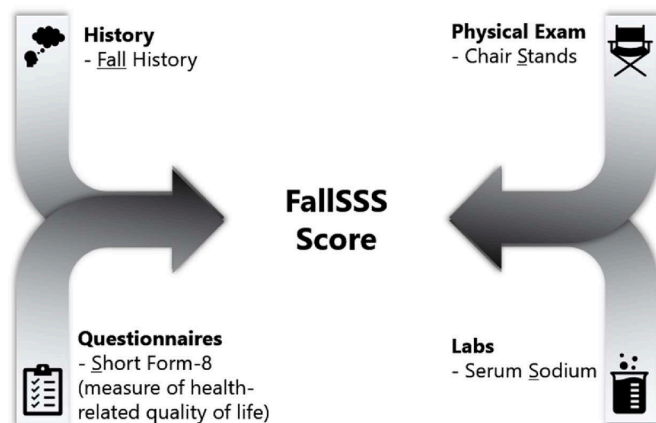
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CLD\_1246\_Figure 1 Domains Contributing to Falls.tiff





CLD\_1246\_Figure 2 FallSSS.tiff

# Preventing Falls in Patients with Cirrhosis



CLD\_1246\_Figure 3 Preventing Falls in Cirrhosis.tiff

**Figure 1.** The three domains that contribute to falls in patients with cirrhosis. Aspects of the sensory domain such as lower limb sensation and visual acuity are impaired in patients with cirrhosis. Alcohol use, hepatic encephalopathy and zolpidem use impair neurocognition and increase likelihood of falls. Frailty, lack of balance and inability to correct posture when tripping increases fall-risk.

**Figure 2.** The FallSSS score compiles the strongest predictors of falls over the next year: fall history (sHR = 4.08), chair-stands (sHR = 0.92), serum sodium (sHR = 0.92 per mEq/L), and SF-8 (sHR = 0.97 per point) with an area-under-the-curve of 0.79. By better predicting falls, we can employ measures to mitigate the risk in those who need it most.

**Figure 3.** Many factors can contribute to high fall-risk in individuals. Addressing some of these by alcohol cessation, reducing polypharmacy, incorporating Tai-chi and other strength building exercises, starting HE-directed therapy, personalizing footwear, and having annual eye exams will prevent falls in patients with cirrhosis.