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REVIEW

Falls are an underappreciated driver of morbidity and mortality in cirrhosis

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INTRODUCTION

Cirrhosis is common and morbid, afflicting more than 1 million Americans and causing more than 60,000 deaths annually.[1] As the epidemiology of cirrhosis shifts to account for increasing alcohol-related liver disease (ALD) and nonalcoholic fatty liver disease, so will the public health burden of cirrhosis.[1] Increasing rates of nonalcoholic fatty liver disease 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. (Table 1) CD is the classic risk factor. Román et al.[2] retrospectively investigated fall incidence in outpatients with cirrhosis and minimal hepatic encephalopathy (MHE). Over 12 months, incidence of falls was 40% in those with MHE compared with 13% in those without ($p < 0.001$).[2] Similarly, the probability of falls in patients with CD exceeded 50% at 1 year compared with 7% in those without ($p < 0.001$).[3] Tapper et al.[4] 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. 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.[5] 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%; $p < 0.0001$).

FALLS CONTRIBUTE TO THE MORBIDITY AND MORTALITY OF CIRRHOSIS

Falls are common and associated with increased risk for severe injuries and mortality. (Table 1) Tapper et al.[4] showed that among compensated patients without prior HE, the risk for injurious falls was 9% and 17% at 1 and 3 years, respectively. 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.[4] Falls are independently associated with a 3-fold increased risk for mortality.[4] Ezaz et al.[6] found that compared with those without cirrhosis, patients with cirrhosis were more likely to sustain severe injuries and die following falls. Studying national data from England and Denmark, Otete et al.[7] showed >5-fold increased risk for hip fracture and higher mortality after a fall in patients with ALD compared with those without. Similarly, in Taiwan, Tsai et al.[8] reported patients with cirrhosis with and without HE had increased fracture incidence compared with control subjects ($p < 0.05$).

TABLE 1 Epidemiology of falls in cirrhosis

Román et al. (2011)[2]	Cirrhosis with MHE versus without MHE	
Incidence of falls at 1 year among outpatients	40% versus 13%; $p < 0.01$	
Soriano et al. (2012)[3]	Patients with Cognitive Dysfunction	Matched control subjects
Percentage of falls at follow-up	40.4% (17/42); $p < 0.001$	6.2% (5/80)
Probability of falls at 1 year	52.3%; $p < 0.001$	6.5%
Tapper et al. (2021)[4]	Compensated cirrhosis without prior HE	Patients with HE, ALD, any degree of disability, or prior falls
Overall probability of injurious falls at 1 year	9.1% ± 1.7%	
Overall probability of injurious falls at 3 years	17.2% ± 5.3%	1–2 in 5 (20%-40%)
Tapper et al. (2015)[5]	Benzodiazepine exposure versus benzodiazepine naive	Antipsychotic exposure versus antipsychotic naive
Incidence of falls in hospitalized patients with cirrhosis	50.9% versus 16.7%; $p < 0.0001$	30.9% versus 7.3%; $p < 0.0001$
Odds of fall after adjusting for HE in hospitalized patients with cirrhosis	OR 6.59 (95% CI: 3.76-11.59)	OR 3.72 (95% CI: 1.90-7.06)
Adjusted risk for injurious fall in hospitalized patients with cirrhosis	OR 3.45 (95% CI: 1.39-8.23)	OR 3.42 (95% CI: 1.08-8.99)
Ezaz et al. (2018)[6]	Patients with cirrhosis versus patients without cirrhosis	
Risk for severe injury complicating a fall requiring hospitalization	OR 2.15 (95% CI: 2.01-2.29)	
Risk for in-hospital death after fall requiring hospitalization	OR 2.14 (95% CI: 1.99-2.31)	
Otete et al. (2018)[7]	Patients with alcoholic cirrhosis versus patients without cirrhosis	
Hip fracture risk at 5 years	HR 5.5 (95% CI: 4.3-6.9)	
30-Day mortality after hip fracture risk in England	HR 2.8 (95% CI: 1.9-3.9)	
30-Day mortality after hip fracture risk in Denmark	HR 2.0 (95% CI: 1.5-2.7)	
Tsai et al. (2013)[8]	Cirrhosis with HE versus control	Cirrhosis without HE versus control
IRR of fracture	IRR 1.32 (1.02-1.72); $p < 0.05$	IRR 1.63 (1.29-2.05); $p < 0.001$
Incidence of fracture at 18 months	7.09% (4.05%); $p < 0.001$	7.72% (4.05%); $p < 0.001$
Cohen et al. (2005)[9]	Patients with cirrhosis	Matched controls
Adverse outcomes associated with total hip and knee arthroplasty	20.7% (6/29); $p = 0.006$	3.23% (3/93)
Emergent hip arthroplasty complications	80% (4/5); $p = 0.005$	0.07% (1/15)
Emergent hip arthroplasty mortality	60% (3/5); $p = 0.032$	0.07% (1/15)

At 18 months, cumulative fracture incidence rate is 7% in patients with HE, 8% without HE, and 4% for the matched control subjects.[8] Injurious falls are of concern in cirrhosis given the high risk for surgery. As Cohen et al.[9] found, orthopedic surgery in cirrhosis is more likely to have significant adverse outcomes, including decompensation, hemorrhage, cardiac arrest, and mortality, when compared with control subjects (21% vs. 3.2%; $p = 0.006$). Emergent arthroplasty was associated with major complications in 80% and mortality in 60% of cases.[9] Finally, falls contribute strongly to poor HRQOL in cirrhosis.[2,4,5]

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.[10,11] Several physiological changes associated with aging and present in cirrhosis include worsening postural control, body-orienting reflexes, muscle tone, and step height.[12] Fall avoidance requires accurate perception of perturbation before a successful response by generating enough torque in the hip and core muscles to adjust weight or shift

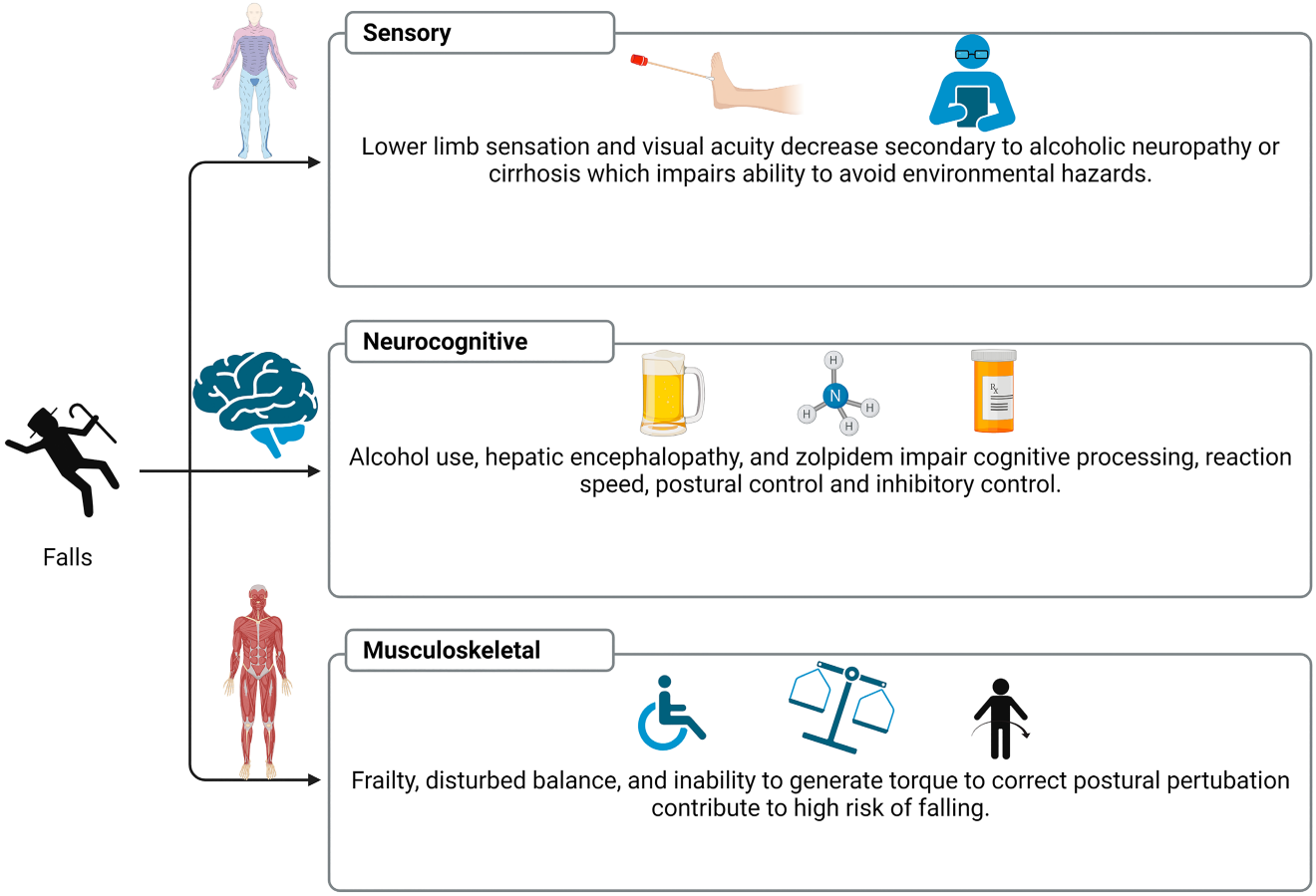

FIGURE 1 The three domains that contribute to falls in patients with cirrhosis. Aspects of the sensory domain, such as lower-limb sensation and visual acuity, are impaired in patients with cirrhosis. Alcohol use, HE, and zolpidem use impair neurocognition and increase likelihood of falls. Frailty, lack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

foot placement.[11] Three separate domains—sensory, neurocognitive, and muscular—play a physiological 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.[12] CD caused by HE, poor nutrition, physical inactivity, and substance use contribute to frailty and the inability to generate a protective shift in weight to prevent falling.[12,13] Tapper et al.[14] recently found that deprescribing zolpidem can reduce the risk for falls and fractures, highlighting the influence of sedating medications on falls risk.

SCREENING FOR FALLS

The Centers for Disease Control and Prevention recommends screening for falls among those older than 65 years 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.[4] proposed a model for predicting those at highest risk for falls: FallSSS. In Figure 2, Tapper illustrates the strongest predictors

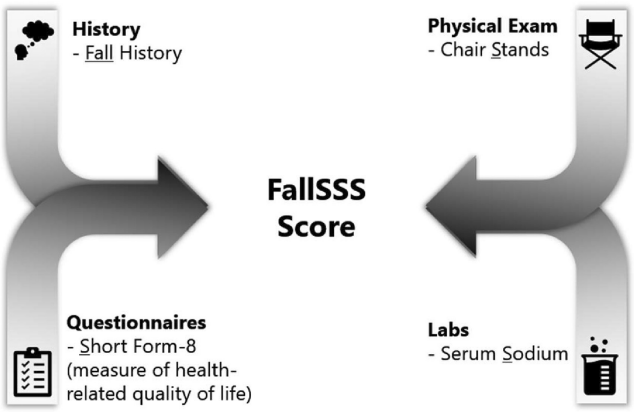

FIGURE 2 The FallSSS score compiles the strongest predictors of falls over the next year: fall history (sHR = 4.08), chair stands (sHR = 0.92), serum sodium (sHR = 0.92 per mEq/L), and SF-8 (sHR = 0.97 per point) with an area under the curve of 0.79. By better predicting falls, we can use measures to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

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 examinations will prevent falls in patients with cirrhosis.

(subdistribution hazard ratio)—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.[4] This model offers an opportunity to predict the risk for falls over the next year and use 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 allows for implementation of 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 examinations, 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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CONFLICTS OF INTEREST

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