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Inpatient Frailty Assessment Is Feasible and Predicts Nonhome Discharge and Mortality in Decompensated Cirrhosis

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Abstract

Objective inpatient frailty assessments in decompensated cirrhosis are understudied. We examined the feasibility of inpatient frailty measurements and associations with nonhome discharge, readmission, and all-cause mortality among patients admitted for cirrhosis complications. We conducted a prospective study at 3 liver transplantation (LT) centers. Frailty was assessed using the liver frailty index (LFI). Multivariable logistic and competing risk models evaluated associations between frailty and clinical outcomes. We included 211 patients with median MELD-Na score 21 (interquartile range [IQR],15–27); 96 (45%) were women, and 102 (48%) were on the LT waiting list. At a median follow-up of 8.3 months, 29 patients (14%) were nonhome discharged, 144 (68%) were readmitted, 70 (33%) underwent LT, and 44 (21%) died. A total of 124 patients (59%) were frail, with a median LFI of 4.71 (IQR, 4.07–5.54). Frail patients were older (mean, 59 versus 54 years) and more likely to have chronic kidney disease (40% versus 20%; $P = 0.002$) and coronary artery disease (17% versus 7%; $P = 0.03$). Frailty was associated with hospital-acquired infections (8% versus 1%; $P = 0.02$). In multivariable models, LFI was associated with nonhome discharge (odds ratio, 1.81 per 1-point increase; 95% confidence interval [CI], 1.14–2.86). Frailty (LFI≥4.5) was associated with all-cause mortality in models accounting for LT as competing risk (subhazard ratio [sHR], 2.4; 95% CI, 1.13–5.11); results were similar with LFI as a continuous variable (sHR, 1.62 per 1-point increase; 95% CI, 1.15–2.28). A brief, objective inpatient frailty assessment was feasible and predicted nonhome discharge and mortality in decompensated cirrhosis. Inpatient point-of-care frailty assessment prior to hospital discharge

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can be useful for risk stratification and targeted interventions to improve physical fitness and reduce adverse outcomes.

Frailty is defined as a distinct biologic state of decreased physiologic reserve with increased vulnerability to stress.[1] The causes of frailty are tightly associated with malnutrition, sarcopenia (loss of skeletal muscle mass/function), sedentary lifestyle, and complications of portal hypertension including hepatic encephalopathy (HE).[2–4] Frailty in decompensated liver disease portends a dismal prognosis including increased risk for falls, hospitalization, institutionalization, removal from the transplant waiting list, posttransplant complications, and increased waitlist mortality.[5–8] Frailty is also associated with increased cost of care and disability. [7,9] The liver frailty index (LFI) is a widely used tool specifically validated to assess physical frailty in cirrhosis.[10] Frailty measured by the LFI has a prevalence of approximately 25% among patients with cirrhosis in ambulatory settings.[10] However, the feasibility and predictive validity of LFI have not been assessed in acute care settings.

Hospitalizations are common in cirrhosis and among patients on the liver transplantation (LT) waiting list.[11] Cirrhosis-associated hospitalizations have higher costs and post–acute care needs than those for heart failure and chronic obstructive pulmonary disease (COPD). [12] However, the impact of objective measures of frailty on postdischarge needs is not well quantified.

As a dynamic condition, frailty generally worsens with more advanced hepatic decompensation and has been shown to double from the time of waitlisting to the time of LT. [13,14] A recent consortium study showed that changes in LFI are as impactful on mortality as the baseline assessment.[15] Hospitalization may negatively modify frailty because of the pathogenic processes that led to the admission (eg, infection, acute kidney injury [AKI], HE). In addition, hospitalized patients may have restricted nutrition and mobility, further exacerbating frailty. Thus, LFI values obtained during a hospital admission may have different prognostic characteristics than those obtained in outpatient clinics.

Self-reported or clinician-observed frailty assessments have been shown to be associated with mortality and readmissions in a retrospective cohort.[7] However, it is not known whether a brief, objective measure of frailty using the LFI in the acute care setting can be feasibly implemented or predicts outcomes in cirrhosis. To address these gaps in knowledge, we conducted a prospective study to assess the feasibility of a brief, objective inpatient frailty assessment, quantify physical frailty among patients admitted for complications of cirrhosis, and investigate associations between frailty, nonhome discharge, hospital readmissions, and all-cause mortality.

Patients and Methods

STUDY DESIGN

This was a prospective multicenter cohort study involving the following 3 large LT centers: University of Pittsburgh Medical Center (UPMC), Hospital of the University of Pennsylvania (UPENN), and University of California San Francisco (UCSF) Medical Center. Adult patients hospitalized with cirrhosis complications (HE; volume

overload, which included edema and ascites; AKI/electrolyte disturbances; any infection; gastrointestinal bleeding) between September 2018 and December 2019 were enrolled and followed through June 2020. A patient's first admission during this timeframe was determined to be his or her index admission. Patients with any history of liver or other abdominal transplantation (ie, kidney, small bowel) prior to index admission or those undergoing LT at index admission were excluded. Admissions for LT or those resulting in hospice or palliative care were excluded from the readmission outcomes analysis. Follow-up was censored at transplantation. Local institutional review boards approved the study at all institutions with verbal and written consent obtained at UPENN and UCSF Medical Center, respectively. Inpatient LFI assessments were part of routine standard of care at UPMC, and the project was considered quality improvement; therefore, no informed consent was required.

Patient demographics (age, sex, race/ethnicity), body mass index (BMI), medical comorbidities, cirrhosis-related complications, and clinical endpoints were abstracted from the electronic health records (EHRs) at each site by trained research coordinators with oversight from study investigators. The cirrhosis comorbidity index (CirCom) score, a previously validated scoring system for the prediction of all-cause mortality specific to cirrhosis,[16] was calculated for each patient based on the presence or absence of COPD, acute myocardial infarction, peripheral arterial disease, epilepsy, substance abuse, heart failure, nonmetastatic cancer, metastatic cancer, and chronic kidney disease (CKD). In addition, the Model for End-Stage Liver Disease–sodium (MELD-Na) score prior to hospital discharge, discharge disposition, death, transplantation, and readmission data (including primary admission reason) were recorded. Infectious complications as a reason for admission (eg, urinary tract infection, gastrointestinal infections such as *Clostridium difficile*, primary bloodstream infections) or hospital-acquired infections (eg, ventilator-associated pneumonia) during the index admission were ascertained from the EHR.

Physical frailty assessments were performed by trained research coordinators or physical therapists during the patient's index hospitalization at a point when the patient's active issues leading to hospitalization had resolved and the patient was deemed medically stable for discharge. Notably, the date of the LFI assessment did not necessarily correspond to the patient's day of discharge but could occur earlier than the discharge date, depending on other factors that impacted discharge (eg, arrangement of home physical therapy, need for additional medical procedures or testing for transplant evaluation).

Frailty assessments included dynamometer-assessed dominant-hand grip strength (average of 3 trials), timed chair stands (number of seconds it takes to do 5 chair stands with patient arms folded across the chest), and balance testing (number of seconds it takes the patient to balance in side-by-side, semitandem, and tandem positions). Participants not able to complete assessments in a particular category received a score of 0 for that category. The LFI score was calculated by entering observed performance (including 0 when applicable) into the UCSF Medical Center LFI online calculator (https://liverfrailtyindex.ucsf.edu).[10] Disposition to home or nonhome discharge (physical rehabilitation, skilled nursing facility) were assessed. Additional study endpoints were hospital readmission and all-cause mortality following discharge from the index hospitalization.

STATISTICAL ANALYSIS

Descriptive statistics were obtained for all variables using mean ± standard deviation or median (interquartile range [IQR]), depending on the distribution of data (Shapiro-Wilk test). The chi-square test was used to compare proportions, whereas the Student *t* test, Mann-Whitney U test, Wilcoxon matched pairs test, or Kruskal-Wallis test were used for continuous variables. Frailty, the main exposure variable, was evaluated both as a dichotomous (LFI≥4.5 for frail and <4.5 for nonfrail) and as a continuous variable.[10] Kaplan-Meier curves were generated to examine the relationships between frailty, readmission, and mortality. Multivariable models were fit for clinical outcomes (logistic regression for nonhome discharge and Fine and Gray competing risk models with LT as competing risk for all-cause mortality).[17] Results are presented for 1-unit increase and for 0.3-unit increase given that the latter is considered the minimum clinically meaningful LFI change per observational and physical activity intervention studies.[15] MELD-Na was selected a priori in the multivariable models, whereas age and CirCom were considered on the basis of significant associations in univariable analyses ($P > 0.2$) and the number of clinical events. Additional analyses were performed evaluating frailty as a risk factor for time to readmission (Cox proportional hazards models) and 7-day and 30-day readmissions (logistic regression models) adjusted for age and MELD-Na and CirCom scores. Statistical analyses were carried out using Stata version 15 (StataCorp, College Station, TX).

Results

BASELINE CHARACTERISTICS

Baseline characteristics for all patients and according to frailty status are shown in Table 1 (characteristics by study site are in Supporting Table 1). A total of 211 patients with LFI assessments were included (107 for UPMC, 82 for UPENN, and 22 for UCSF Medical Center). The median follow-up time was 8.3 (4.4–12.2) months. Inpatient LFI assessment identified frailty in 124 (59%) patients prior to hospital discharge. The mean age of the study cohort was 57 ± 12 years, and the median LFI was 4.71 (IQR, 4.07–5.54). Patients with frailty were slightly older (mean of 59 versus 54 years; $P = 0.004$). Other demographic factors such as sex, BMI, and race/ethnicity were similar between the frail and nonfrail groups. Alcohol-related liver disease and nonalcoholic steatohepatitis (NASH), comprising nearly 70% of the study cohort, were the 2 most common etiologies for cirrhosis for patients who were frail and nonfrail. Patients who were frail were less likely to be on the waiting list than nonfrail patients (40% of patients on the waiting list were frail versus 60% nonfrail patients; $P = 0.005$).

The prevalence of prior hepatic decompensation such as HE, gastrointestinal bleeding, or ascites requiring large-volume paracentesis was similar between the frail and nonfrail groups. Patients who were frail were more than 2 times as likely to be taking β-blockers prior to their index admission compared with nonfrail patients (49% versus 23%; $P = 0.04$). In terms of comorbidities, patients who were frail had higher cirrhosis-specific comorbidity scores (44% versus 25% with CirCom 3+0 or greater; $P = 0.01$) and were more likely to have CKD (40% versus 20%; $P = 0.002$) and coronary artery disease (CAD; 17% versus 7%, $P = 0.03$) compared with nonfrail patients. Laboratory parameters such as MELD-Na

score and bilirubin level were similar between frail and nonfrail groups. Patients who were frail had slightly higher serum creatinine levels (1.0 mg/dL versus 0.9 mg/dL; $P = 0.04$) and slightly lower hemoglobin compared with nonfrail patients (8.8 g/dL versus 9.4 g/dL; $P = 0.04$). The most common primary reason for the index admission (Fig. 1A) was volume overload (n = 70, 33%) followed by HE (n = 41, 19%). Patients admitted for HE were more likely to be frail ($P = 0.03$). Reasons for readmission were similar between frailty groups except for HE where the proportion of patients who were frail was numerically higher (25% versus 13%; Fig. 1B).

LFI DISTRIBUTIONS BY KEY PATIENT CHARACTERISTICS

Figure 2 shows the distributions of LFI scores by liver disease etiology; patients with NAFLD/NASH had significantly higher LFI scores (were more likely to be frail) than patients with other liver diseases ($P < 0.05$). Figure 3 shows box-and-whisker plots for LFI values by key characteristics and medical comorbidities. Patients aged older than 65 years and those on dialysis with CKD, peripheral arterial disease, and heart failure were more likely to have higher LFI values (all $P < 0.05$).

FEASIBILITY OF FRAILTY ASSESSMENTS

Among the 211 study participants, 210 (99%) performed grip strength assessments, 170 (81%) did at least 1 form of balance testing position, and 140 (66%) completed timed chair stands. A total of 136 (64%) participants were able to perform the 3 tests, whereas 183 (87%) did at least 2 of the assessments; only 1 participant failed to do the 3 components. Not surprisingly, the ability to complete all assessments correlated with nonfrail status. Older age (odds ratio [OR], 0.95; 95% confidence interval [CI], 0.93–0.98; $P = 0.001$), CKD (OR, 0.54; 95% CI, 0.29–0.98; $P = 0.04$), and use of β-blockers (OR, 0.42; 95% CI, 0.23–0.77; $P = 0.005$) were associated with lower odds of performing all 3 assessments, whereas being listed for LT increased the odds (OR, 2; 95% CI, 1.12–3.56; $P = 0.01$); no other clinical characteristics were associated with completion.

LENGTH OF STAY AND TIMING OF FRAILTY ASSESSMENT

Total length of stay was 6 (IQR, 4–12) days with no differences across centers (Supplemental Data). Patients who were frail had a longer hospital stay when compared with the nonfrail patients (7 [IQR, 5–14] versus 5 [IQR, 3–8] days; $P < 0.001$), mainly related to time required to secure disposition. In fact, hospital discharge occurred 1 (IQR, 0–5) day following LFI assessment (ie, when medical concerns had resolved), with a longer time to discharge in the patients who were frail (2 [IQR, 0–6] versus 1 [IQR, 0–4]; $P = 0.014$). Across centers, UPENN showed the longest time between LFI assessment and discharge (Supplemental Data). These differences were not considered clinically relevant and likely speak of variations in hospital disposition options and discharge protocols. The correlation between total length of stay and LFI score and between LFI assessment to discharge interval and LFI score were poorly correlated ($\rho = 0.30$ [$P < 0.001$] and $\rho = 0.22$ [$P = 0.001$], respectively).

INFECTIOUS COMPLICATIONS AND SUBSEQUENT CLINICAL OUTCOMES

Table 2 shows infectious complications during the index hospital admission and subsequent clinical outcomes. A total of 29 (23%) patients who were frail had an infectious complication compared with 16 (18%) nonfrail patients with a significant difference in hospital-acquired infections during the index admission (frail, 8% versus nonfrail, 1%; $P = 0.02$). Frailty was associated with nonhome discharge, with 16% of patients who were frail being discharged to post–acute care facilities compared with 5% of nonfrail patients ($P = 0.01$). Unadjusted Kaplan-Meier curves for the outcome of readmissions are shown in Fig. 4. Patients with frailty at the index admission were more likely to be readmitted (unadjusted log rank test, $P = 0.003$). There were 144 (68%) patients readmitted following the index hospitalization, with a median time to readmission of 25 days (IQR, 10–50 days); the 7-day readmission rate was 10%, and the 30-day readmission rate was 38%. The 30-day readmissions were numerically higher among frail (40%) versus nonfrail patients (34%). In additional multivariable analyses adjusted for age, MELD-Na score, and CirCom score, frailty as a categorical variable (hazard ratio [HR], 1.53; 95% CI, 1.06–2.22; $P = 0.024$) was associated with time to readmission, whereas frailty as a continuous variable was not (HR, 1.15; 95% CI, 0.96–1.37; $P = 0.13$). Frailty was not significantly associated with 7-day or 30-day readmissions.

Unadjusted Kaplan-Meier curves for all-cause mortality are shown in Fig. 5. Frailty was significantly associated with death, with 29% of patients who were frail dying during the interval follow-up compared with 12% of nonfrail patients ($P = 0.002$). A smaller proportion of patients who were frail underwent LT compared with nonfrail patients (28% versus 40%; $P = 0.07$); patients who were frail were less likely to undergo living donor LT (7% frail versus 15% nonfrail; $P = 0.04$).

Multivariable models of the associations between frailty measured by LFI, nonhome discharge, and all-cause mortality are shown in Table 3. After adjusting for age, MELD-Na score, and CirCom score, LFI as a continuous measure was independently associated with nonhome discharge (adjusted OR [aOR], 1.81; 95% CI, 1.14–2.86 per 1-point increase in LFI; aOR 1.21, 95% CI, 1.04–1.42 per 0.3-point increase). LFI was independently associated with all-cause mortality in models accounting for LT as a competing risk when analyzed as both a dichotomous (subhazard ratio [sHR], 2.40; 95% CI, 1.13–5.11) and continuous variable (sHR, 1.62; 95% CI, 1.15–2.28 per 1-point increase in LFI; sHR, 1.17; 95% CI,1.04–1.31 per 0.3-point increase). Adjusting for site of enrollment as a covariable did not change results (data not shown). Univariable associations between frailty, nonhome discharge, and mortality are shown in Supporting Tables 2 and 3. In addition to chosen variables in multivariable models, CKD and paracentesis during admission were associated with higher odds of nonhome discharge, whereas LT candidacy was associated with lower odds of nonhome discharge. Higher serum creatinine was associated with higher likelihood of mortality in univariable analyses whereas LT candidacy and history of prior gastrointestinal bleed were associated with lower mortality. Hand grip alone as a measure of frailty was not associated with nonhome discharge or mortality in unadjusted or adjusted analysis (data not shown).

Discussion

Frailty, as measured by LFI in the outpatient setting, has been previously shown to predict the risk for hospitalization, removal from the transplant waiting list, and mortality in decompensated cirrhosis.[4,8,15,18] However, its predictive validity has not been studied in the inpatient setting.[4] We found that a brief, validated, and objective performance-based assessment, specifically the LFI, was feasible and valid among patients admitted for decompensated cirrhosis, about half of whom were on the LT waiting list at 3 large and diverse tertiary care centers. The LFI was largely conducted by physical therapists and was able to be implemented among patients with serious complications of cirrhosis such as HE, ascites, and infections, including those with high Model for End-Stage Liver Disease (MELD) scores. Furthermore, the predictive validity of this assessment was substantiated given its associations with patient-centered outcomes and hard clinical endpoints, namely, discharge to post–acute care facilities and mortality. These findings add to the growing body of literature of the predictive value of objective frailty assessments and expand the role of such measures to the inpatient setting.

The prevalence of frailty using LFI ≥4.5 was 59%. This is higher than the 25% previously described in the literature in the ambulatory setting.[2] A recent multicenter study evaluating outpatient frailty trajectories among >1000 patients eligible or on the LT waiting list showed subgroups with comparable frailty scores. These were patients with downward physical function trajectories as is often observed with decompensated cirrhosis.[15] Expectedly, a higher degree of frailty was found among patients who were older and had concomitant comorbidities (CAD and CKD).[19] More than one-third of patients with alcohol-related liver disease and NASH were frail, which was not unexpected given the high prevalence of sarcopenia and sedentary lifestyles in these groups.[20,21]

Unlike what has been observed in outpatient settings where frailty correlates with MELD, MELD-Na scores were similar between patients who were frail and nonfrail patients, again showing that frailty assessment can be complementary to MELD-Na, capturing overall health status, improving risk prediction, and identifying patients in need of intervention or a close follow-up visit to clinic after hospital discharge.

We found increased β-blocker use in patients who were frail compared with the patients who were not frail, and in fact, β-blockers were associated with a failure to perform the 3 components of LFI. It is possible that β-blocker adverse effects such as fatigue and weakness may contribute to sedentarism and decreased exercise tolerance, all of which are factors that play into the frailty phenotype.[1] Conversely, patients on β-blockers may have more severe portal hypertension and portosystemic shunting, resulting in more significant physical frailty. It is also possible that the association with β-blocker use was attributed to CAD, a comorbidity associated with frailty in this cohort. Future studies should examine in detail whether β-blockers could exert negative or positive consequences on physiologic reserve, symptoms, and ability to tolerate physical activity interventions to reduce physical frailty and increase muscle mass.

With regard to clinical outcomes, we found that frailty was associated with higher rates of hospital-acquired infections. The reasons for this difference could be attributed to bed-bound status among patients who were frail, leading to other risk factors for infection, such as prolonged indwelling catheter use, aspiration pneumonia, and so on. We noted numerically higher readmission rates among the frail versus the nonfrail, and this was at least in part driven by HE. Although frailty and HE independently affect mortality in decompensated cirrhosis, they are interrelated and likely potentiate each other through shared lifestyle, nutritional, and neurocognitive mechanisms; we confirmed findings of previous studies showing that patients with HE during the index admission had twice the prevalence of frailty.[20]

We observed that inpatient frailty had significant clinical and financial implications. First, patients who were frail were less likely than their nonfrail counterparts to be discharged home, with 20% in the frail group compared with 5% in the nonfrail group being discharged to physical rehabilitation, a skilled nursing facility, or hospice. This observation is especially informative as it pertains to health care usage given the higher costs associated with caring for patients in long-term, post–acute care facilities.[22,23] Second, frailty (LFI ≥4.5) more than doubled the risk of all-cause mortality after adjusting for age, MELD-Na score, and CirCom score, with a 60% increase in mortality risk for each additional point increase in LFI. Such increased mortality has been previously noted in patients who were ambulatory.[24] Third, patients who were frail were less likely to be on the LT waiting list and less likely to undergo living donor LT; waitlist mortality and attrition have previously been noted with frailty.[8] Whether frailty can be reduced among potential LT candidates is a challenging and highly important area for future investigations. Lastly, our sensitivity analysis using hand grip as the sole metric of frailty failed to show an association with nonhome discharge and mortality, further validating a composite metric that encompasses objective assessment of upper and lower body muscular groups such as LFI.

We must acknowledge certain study limitations. Physical frailty was assessed at a single time point, once the patient's acute medical issues leading to hospitalization had resolved and when the patient was deemed medically stable for discharge (ie, aiming to reflect the patient's health status at its best). Given that LFI measurements have not been routinely performed in the inpatient population, there is no current standard window or guidance for when LFI is best performed. Future studies could help define the standard window that would be most predictive of subsequent outcomes. Longitudinal frailty measures during hospitalization should also be performed in the future, although it is clear that not all patients (eg, patients with HE or other complications with immobility) could participate in physical assessments on admission. We were not able to assess the degree of physical therapy during hospitalizations or how this may impact frailty throughout the hospital stay or changes in frailty following ambulatory care transition or on subsequent hospitalizations. It is expected for patients who are frail to have longer hospital stays and use more hospital resources, and thus it will be important to learn whether strategies reversing the metrics of frailty have an impact on health care use and home versus specialized facility disposition. Although we documented the use of β-blockers, we did not assess whether patients were properly β-blocked, a difference that carries physiologic differences in terms of cardiac adaptation. We may have been underpowered to detect differences in readmission and

transplant rates between patients who were frail and patients who were not frail, and further studies are needed to better clarify these associations. Despite a diverse, multicenter cohort, there is a potential for limited generalizability to community hospitals and other diverse practice settings.

Conclusion

We describe that inpatient LFI assessment is feasible and can be implemented as part of routine clinical care by trained physical therapists or other staff. We observe that medical comorbidity and HE are associated with physical frailty prior to hospital discharge. Furthermore, we find that inpatient frailty is associated with lower rates of waitlisting, living donor transplantation, and age-adjusted and MELD-Na–adjusted mortality. Given its ease of implementation and prognostic utility, routine inpatient LFI measurement prior to discharge can potentially inform decisions regarding discharge disposition and identify patients at high risk for decompensation, death, and waitlist attrition in whom targeted interventions such as the prescription of outpatient rehabilitation or outpatient nutritional services may have the greatest impact on outcomes.[12]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

AKI	acute kidney injury
ALT	alanine aminotransferase
aOR	adjusted odds ratio
AST	aspartate aminotransferase
BMI	body mass index
CAD	coronary artery disease
CHF	congestive heart failure
CI	confidence interval
CirCom	cirrhosis comorbidity index
CKD	chronic kidney disease

COPD	chronic obstructive pulmonary disease
EHR	electronic health record
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HE	hepatic encephalopathy
HR	hazard ratio
INR	international normalized ratio
IQR	interquartile range
LFI	liver frailty index
LT	liver transplantation
MELD	Model for End-Stage Liver Disease
MELD-Na	Model for End-Stage Liver Disease–sodium
NAFLD	nonalcoholic fatty liver disease
NASH	nonalcoholic steatohepatitis
OR	odds ratio
PVD	peripheral vascular (arterial) disease
sHR	subhazard ratio
UCSF	University of California San Francisco
UPENN	Hospital of the University of Pennsylvania
UPMC	University of Pittsburgh Medical Center

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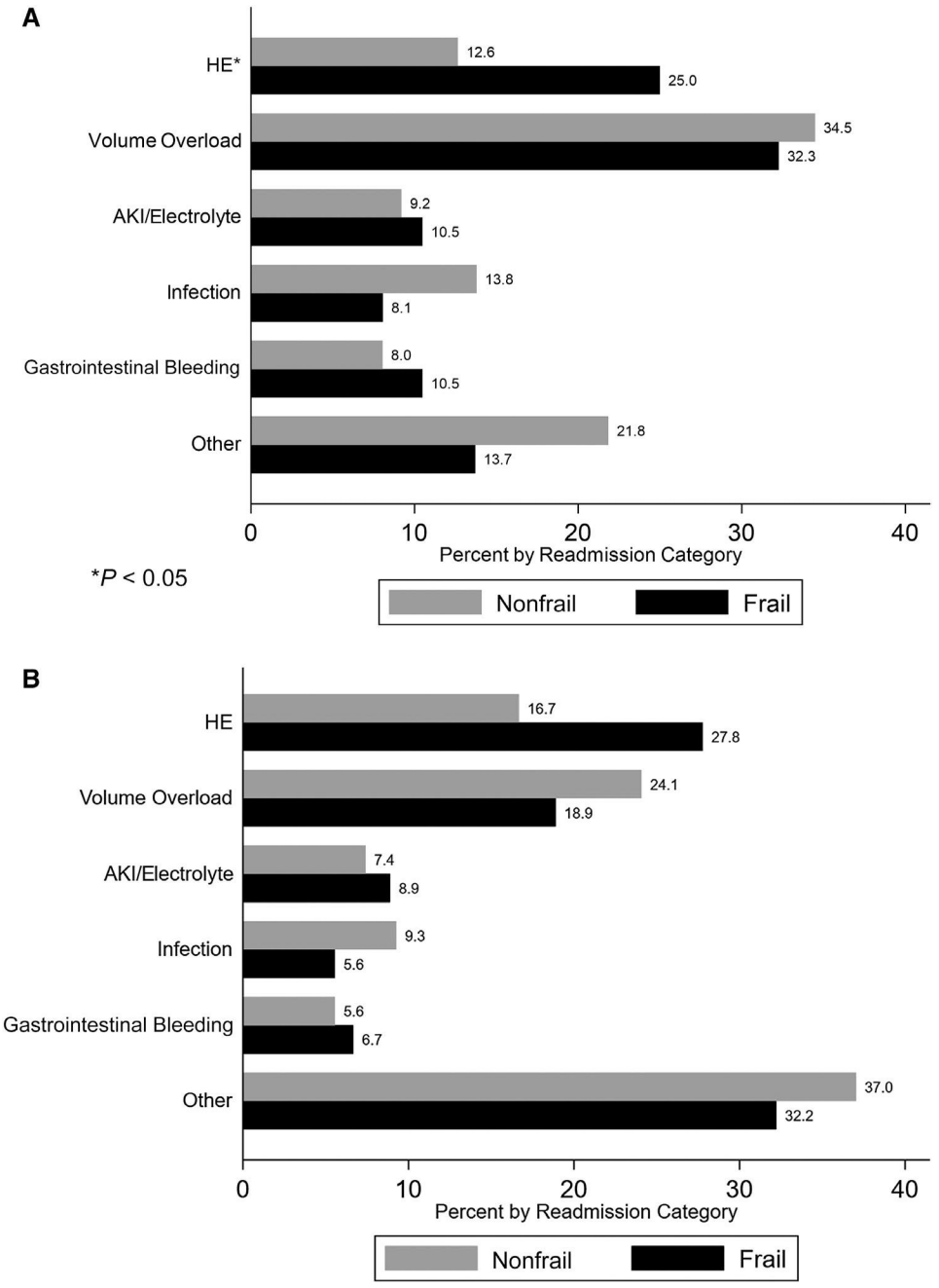

FIG. 1.

(A) Primary admission reason by frailty category (n = 211). “Other” admission reason includes splanchnic thrombosis, abdominal pain, worsening liver tests, ileus, symptomatic anemia, lightheadedness, chest pain, choledocholithiasis, acute coronary syndrome, post–transjugular intrahepatic portosystemic shunt monitoring, and alcoholic hepatitis. (B) Primary readmission reason by frailty category (n = 144). “Other” readmission reasons include arrhythmia, fall, alcoholic hepatitis, cholecystitis, worsening liver function, anemia, small bowel obstruction, ventral hernia repair, potential/cancelled liver transplantation, depression, diabetic ketoacidosis, respiratory failure.

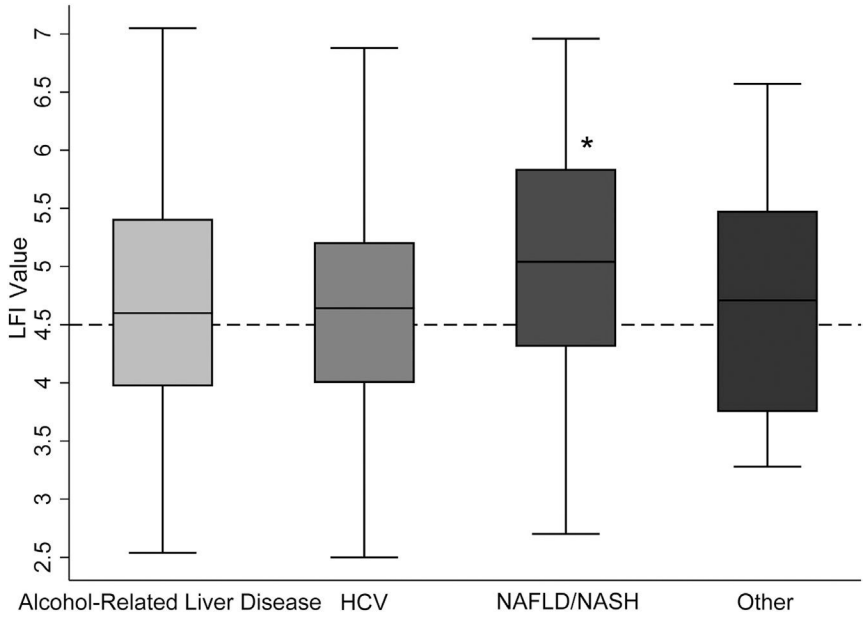

FIG. 2.

Box-and-whisker plots of inpatient LFI scores by liver disease etiology. The line through each box indicates the median (50th percentile) of LFI values with the outside borders showing the 25th (lower border) and 75th (upper border) percentiles. LFI threshold for frailty (4.5) is denoted with a dashed line. *$P < 0.05$ for LFI with NAFLD/NASH versus other liver disease etiologies.

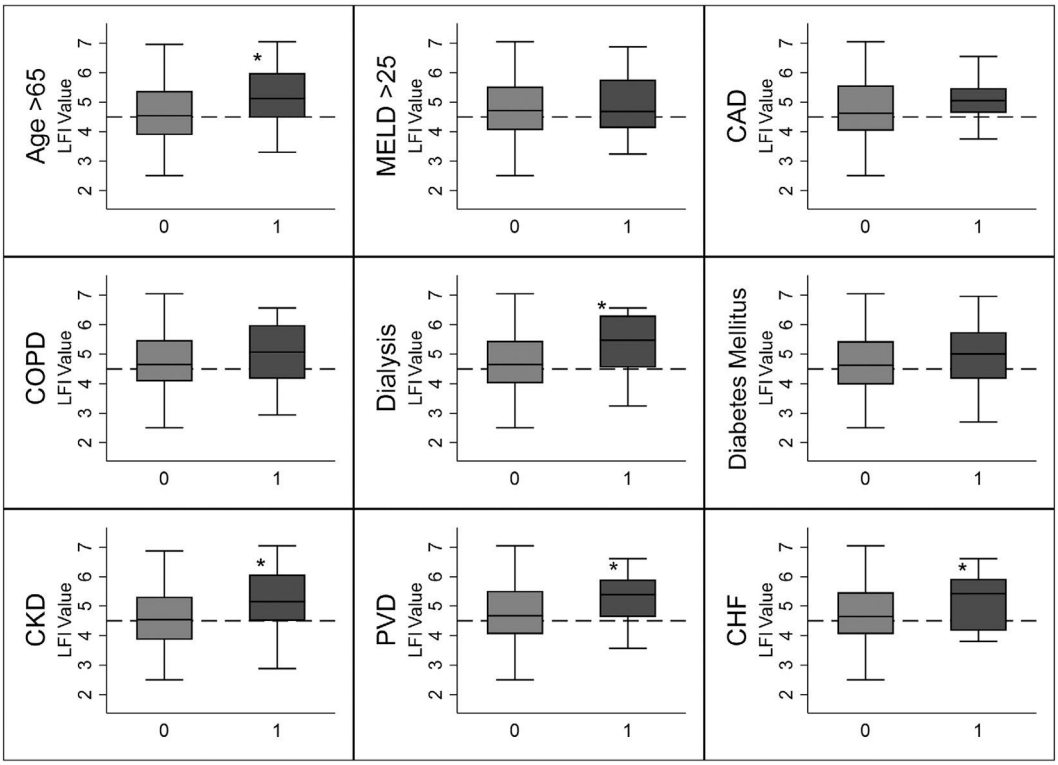

FIG. 3.

Box-and-whisker plots of inpatient LFI scores stratified by presence of medical comorbidities. The line through each box indicates the median (50th percentile) of LFI values with the outside borders showing the 25th (lower border) and 75th (upper border) percentiles. LFI threshold for frailty (4.5) is denoted with a dashed line. $*P < 0.05$ in bivariate comparisons.

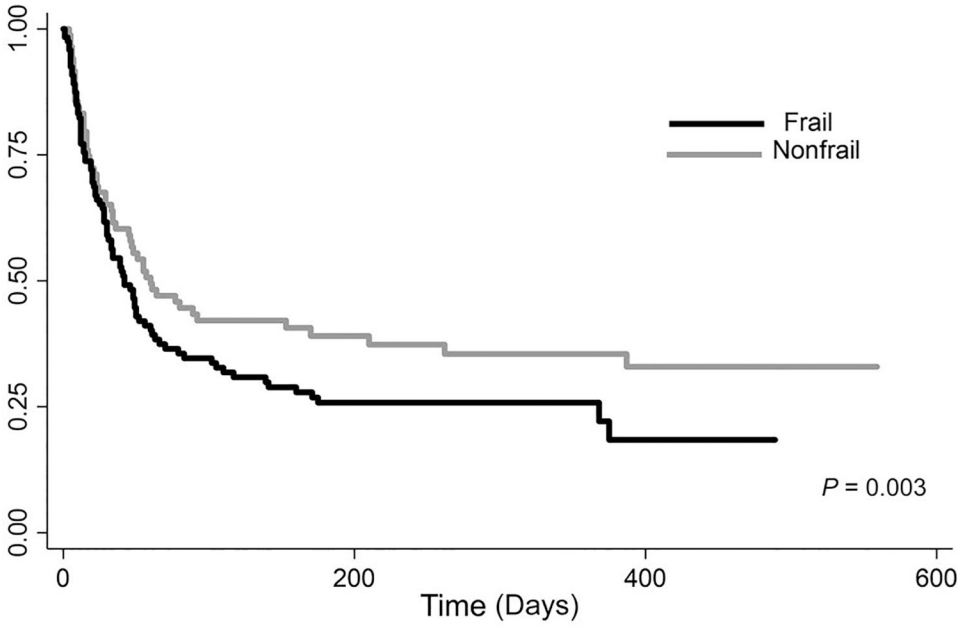

FIG. 4.

Kaplan-Meier curves of readmissions after index hospitalization based on frailty status (nonfrail with LFI <4.5, frail with LFI ≥4.5). The *y* axis indicates the percentage free from readmission. The *x* axis indicates the time in days after index hospital discharge.

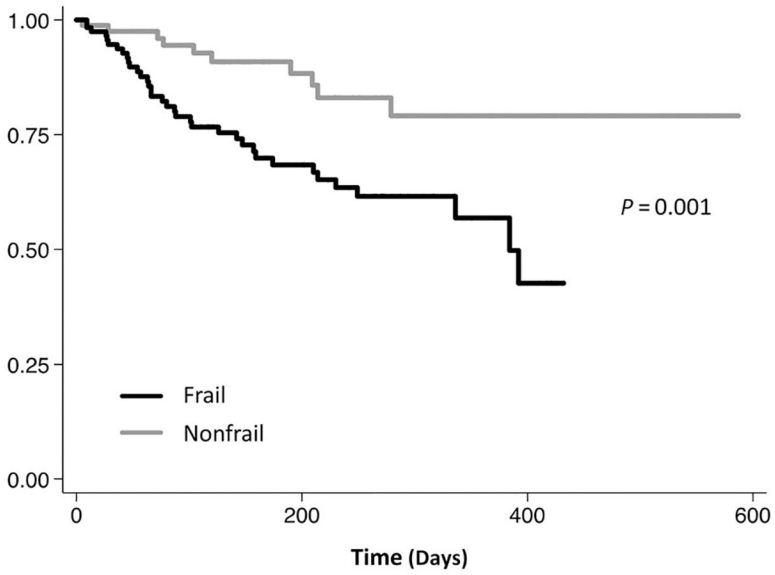

FIG. 5.

Kaplan-Meier curves of all-cause mortality after index hospitalization based on frailty status (nonfrail with LFI <4.5, frail with LFI ≥4.5 The *y* axis indicates the percentage free from mortality. The *x* axis indicates the time in days after index hospital discharge.

TABLE 1.

Baseline Characteristics of the Study Cohort Stratified by Frailty Status

	Total Cohort (n = 211)	Nonfrail, LFI <4.5 (n = 87)	Frail, LFI ≥4.5 (n = 124)	*P* Value
Demographic and anthropometry				
Age, years	57 ± 12	54 ± 12	59 ± 12	**0.004**
Male	115 (55)	49 (56.3)	66 (53.2)	0.68
Race/ethnicity				
White	184 (87)	74 (85)	110 (89)	0.57
Asian	5 (2)	2 (2)	3 (2)	
Black	11 (5)	7 (8)	4 (3)	
Latinx	9 (4)	3 (4)	6 (5)	
Other/unknown	2 (1)	1 (1)	1 (1)	
BMI (kg/m^2)	30.0 ± 7.0	30.5 ± 6.8	29.7 ± 7.1	0.44
Study sites				
Site 1, UPMC	107 (51)	47 (54)	60 (48)	0.06
Site 2, UPENN	82 (39)	27 (31)	55 (44)	
Site 3, UCSF Medical Center	22 (10)	13 (15)	9 (7)	
Cirrhosis etiology				
Alcohol-related cirrhosis	84 (40)	37 (42)	47 (38)	0.35
Chronic HCV	25 (12)	12 (14)	13 (10)	
NAFLD/NASH	65 (31)	21 (24)	44 (36)	
Other	37 (18)	17 (20)	20 (16)	
HCC	26 (12)	11 (13)	15 (12)	0.92
On the LT waiting list	102 (48)	52 (60)	50 (40)	**0.005**
Past medical history/ comorbidities				
Diabetes mellitus	74 (35)	26 (30)	48 (39)	0.19
CKD	66 (31)	17 (20)	49 (40)	**0.002**
Dialysis	25 (12)	6 (7)	19 (15)	0.06
COPD	29 (14)	10 (11)	19 (15)	0.42
CAD	27 (13)	6 (7)	21 (17)	**0.03**
Prior hepatic decompensations				
HE	159 (75)	66 (76)	93 (75)	1.00
Variceal bleeding	76 (36)	29 (33)	47 (38)	0.56
Ascites	176 (83)	71 (82)	105 (85)	0.55
Paracentesis	126 (60)	47 (54)	79 (64)	0.20
β-blocker use	72 (34)	23 (26)	49 (40)	**0.04**
CirCom score 0	72 (34)	37 (42)	35 (28)	**0.01**
1+0	44 (21)	17 (20)	27 (22)	
1+1	19 (9)	11 (13)	8 (6)	
3+0	68 (32)	20 (23)	48 (39)	
3+1	3 (1)	2 (2)	1 (1)	
5+0	0	0	0	

	Total Cohort (n = 211)	Nonfrail, LFI <4.5 (n = 87)	Frail, LFI ≥4.5 (n = 124)	*P* Value
5+1	5 (2)	0	5 (4)	
MELD-Na score prior to discharge				
<9	47 (23)	21 (24)	26 (21)	0.96
10–19	98 (47)	39 (45)	59 (48)	
20–29	53 (26)	22 (26)	31 (25)	
30–39	10 (5)	4 (5)	6 (5)	
MELD score	19 (12–23)	19 (12–23)	19 (12–24)	0.37
MELD-Na score	21 (15–27)	21 (15–26)	21 (15–28)	0.72
Laboratory parameters prior to discharge				
Total bilirubin, mg/dL	2.9 (1.6–7.6)	3.1 (1.5–8.7)	2.8 (1.7–6.7)	0.47
AST, units/L	47 (32–74)	51 (32–83)	47 (31–67)	0.23
ALT, units/L	23 (16–40)	28 (17–45)	23 (16–37)	0.08
Albumin, g/dL	2.8 (2.4–3.3)	2.8 (2.3–3.2)	2.9 (2.4–3.5)	0.26
INR	1.7 (1.4–2.2)	1.7 (1.5–2.2)	1.7 (1.4–2.2)	0.91
Sodium, mEq/L	135 (131–138)	136 (132–139)	135 (1 31 –1 38)	0.57
Creatinine, mg/dL	0.9 (0.7–1.5)	0.9 (0.7–1.2)	1.0 (0.7–1.9)	**0.04**
Hemoglobin, g/dL	9.0 (8.0–10.6)	9.4 (8.0–11.5)	8.8 (8.0–10.1)	**0.04**
Platelet count, × 10^{9}/L	79 (54–126)	83 (52–118)	76 (56–1 34)	0.72

NOTE: Data are provided as mean ± SD, n (%), or median (IQR). *P* values indicate comparisons across frailty categories. Bolded *P* values represent statistically significant comparisons.

TABLE 2.

Infectious Complications and Clinical Outcomes After the Index Admission Stratified by Frailty Status

	Total Cohort (n = 211), n (%)	Nonfrail, LFI <4.5 (n = 87), n (%)	Frail, LFI ≥4.5 (n = 124), n (%)	*P* Value
Infectious complications during index admission				
At least 1 infectious complication	45 (21)	16 (18)	29 (23)	0.38
Hospital-acquired infection	11 (5)	1 (1)	10 (8)	**0.029**
Ventilator-associated pneumonia	2 (1)	0 (0)	2 (2)	0.51
Surgical site infection	3 (1)	3 (3)	0 (0)	0.069
Gastrointestinal infection, for example, clostridium difficile	13 (6)	7 (8)	6 (5)	0.39
Urinary tract infection	16 (8)	5 (6)	11 (9)	0.44
Primary bloodstream infection	6 (3)	3 (3)	3 (2)	0.69
Outcomes after index admission				
Disposition				
Home discharge	182 (86)	80 (95)	102 (80)	**0.025**
Nonhome discharge, for example, skilled nursing facility, rehabilitation, hospice	29 (14)	4 (5)	25 (20)	
Readmission				
Any readmission	144 (68)	54 (62)	90 (73)	0.10
7-day readmission	21 (10)	7 (8)	14 (11)	0.43
30-day readmission	79 (38)	30 (34)	49 (40)	0.45
LT	70 (33)	35 (40)	35 (28)	0.076
Deceased donor	49 (23)	22 (25)	27 (22)	0.55
Living donor	21 (10)	13 (15)	8 (6)	**0.043**
Death without LT	44 (21)	10 (12)	34 (29)	**0.005**

NOTE: Bolded *P* values represent statistically significant comparisons.

TABLE 3.

Multivariable Models for the Associations Between Inpatient LFI, Nonhome Discharge, and All-Cause Mortality Adjusted for age and MELD-N Score

	Nonhome Discharge		All-Cause Mortality	
	Model 1, LFI ≥4.5 versus <4.5; aOR (95% CI)	**Model 2, LFI per 1-point increase; aOR (95% CI)**	**Model 1, LFI ≥4.5 versus <4.5; sHR (95% CI)**	**Model 2, LFI per 1-point increase; sHR (95% CI)**
Age	1.03 (0.99–1.07)	1.02 (0.98–1.06)	1.05 (1.01–1.08) *	1.04 (1.00–1.08)
Frailty	1.74 (0.67–4.49)	1.81 (1.14–2.86) *	**2.40 (1.13–5.11)** *	**1.62 (1.15–2.28)** *
MELD-Na	1.04 (0.99–1.10)	1.04 (0.98–1.09)	1.04 (1.00–1.07)	1.03 (1.00–1.07)
CirCom, ≥3+0 versus <3+0[a]	2.33 (0.97–5.58)	2.01 (0.82–4.95)	0.65 (0.33–1.29)	0.60 (0.30–1.21)

NOTE: Model 1 evaluates the LFI as a dichotomous variable (frail versus nonfrail). Model 2 evaluates LFI as a continuous variable.

[a]Higher values indicate higher comorbidity.

*$P < 0.05$.

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