HHS Public Access

Author manuscript

Hepatology. Author manuscript; available in PMC 2016 February 26.

Published in final edited form as:

Hepatology. 2015 August ; 62(2): 584–590. doi:10.1002/hep.27830.

Standard Assessments of Frailty are Validated Predictors of Mortality in Hospitalized Patients with Cirrhosis

Elliot B. Tapper[1], **Daniel Finkelstein**[2], **Murray A. Mittleman**[3], **Gail Piatkowski**[4], and **Michelle Lai**[1]

Elliot B. Tapper: etapper@bidmc.harvard.edu; Daniel Finkelstein: dfinkelstein1@partners.org; Murray A. Mittleman: mmittlem@bidmc.harvard.edu; Gail Piatkowski: gpiatkow@bidmc.harvard.edu; Michelle Lai: mlai@bidmc.harvard.edu

[1]Division of Gastroenterology and Hepatology, Beth Israel Deaconess Medical Center, Harvard Medical School

[2]Massachusetts General Hospital, Harvard Medical School

[3]Cardiovascular Epidemiology Research Unit,,, Beth Israel Deaconess Medical Center, Harvard Medical School

[4]Decision Support, Beth Israel Deaconess Medical Center, Harvard Medical School

Abstract

The risk of morbidity and mortality for hospitalized patients with cirrhosis is high and incompletely captured by conventional indices. We sought to evaluate the predictive role of frailty in an observational cohort study of inpatients with decompensated cirrhosis between 2010 and 2013. The primary outcome was 90-day mortality. Secondary outcomes included discharge to a rehabilitation hospital, 30-day readmission and length of stay (LOS). Frailty was assessed with three metrics: activities of daily living (ADL), the Braden Scale (BS), and Morse fall risk score. A predictive model was validated by randomly dividing the population into training and validation cohorts. 734 patients were admitted 1358 times in the study period. The overall 90-day mortality was 18.3%. The 30-day readmission rate was 26.6% and the rate of discharge to a rehabilitation facility was 14.3%. Adjusting for sex, age, MELD, sodium and Charlson index, the odds ratio (OR) for the effect of an ADL score less than 12 of 15 on mortality is 1.83 95% CI (1.05 - 3.20). A predictive model for 90-day mortality including ADL and BS yielded an c-statistics of 0.83 95% CI (0.80 - 0.86) and 0.77 95% CI (0.71 – 0.83) in the derivation and validation cohorts, respectively. Discharge to a rehabilitation hospital is predicted by both the ADL (<12) and BS (< 16) with respective adjusted OR of 3.78 95% CI (1.97 - 7.29) and 6.23 95% CI (2.53 - 15.4). LOS was associated with the BS (< 16), hazard ratio 0.63 95% CI (0.44 - 0.91). No frailty measure associated with 30-day readmission.

Conclusions—Readily available, standardized measures of frailty predict 90 day mortality, LOS, and rehabilitation needs for hospitalized patients with cirrhosis.

Keywords

Activities of daily living; Model for Endstage Liver Disease; Braden Scale; Liver Disease

Corresponding author: Elliot B. Tapper MD, Division of Gastroenterology and Hepatology, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston, MA 02215, Phone: 617-667-5587, etapper@bidmc.harvard.edu.

Introduction

The morbidity and mortality of hospitalized patients with cirrhosis is very high.(1-3) Accurate prognostics are critical to support care planning, including decisions regarding liver transplant candidacy. Problematically, currently available prognostic indices such as the Model for Endstage Liver Disease (MELD) provide an incomplete picture of a given patient's risk of death and complications.(4-6)

The MELD score was developed to provide risk stratification prior to portosystemic shunting procedures and later adapted to allocate liver transplants on the organ waitlist.(7, 8) Its combination of bilirubin, creatinine and international normalized ratio (INR) is a proven, powerful prognostic tool for patients with cirrhosis.(9-11) Yet it can be improved further. Adding sodium to the MELD formula improves its predictive power significantly, but slightly.(12, 13) Severity-of-disease classification systems such as the APACHE or CLIF-SOFA scores improve its power even further. This is particularly true for patients hospitalized with a cirrhotic decompensation such as hepatic encephalopathy.(1, 3, 4, 11) However these scores are difficult to assess at the bedside and require extensive training as they are not routinely performed on the wards in American hospitals.(14)

Frailty or, as Lai and Colleagues write, “a patient's vulnerability to stress and decreased physiologic reserve” is increasingly seen as a major contributing factor to patient outcomes.(5) After controlling for standard biochemical indices such as MELD or sodium, a patient's functional status or frailty may play a significant role in a patient's prognosis. Frailty is a concept that originated in the geriatric literature and has since been validated in cohorts of outpatients with decompensated cirrhosis.(5, 15) In contrast to the severity-of-disease classification systems like APACHE, all American nurses are trained to assess each inpatient on admission for frailty. Furthermore, they do so using multiple different validated instruments.(16, 17) Herein, we test the hypothesis that frailty would add significantly to standard prognostic indices for inpatients with cirrhosis.

Methods

We performed retrospective cohort study of patients with cirrhosis at Beth Israel Deaconess Medical Center (BIDMC) in Boston, MA. The study took place on a liver transplant unit with an average of 600 annual admissions. Criteria for admission to this service entails an established diagnosis of decompensated cirrhosis or a medically complicated liver transplant. All clinical care was provided on the dedicated inpatient hepatology unit staffed by housestaff and a hepatologist. No changes in the number of staff, nursing and housestaff occurred during the time under study. This study was conducted in accordance with the Declaration of Helsinki and was approved by our Institutional Review Board. The cohort design and analysis of this study was performed consistent with STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines.(18)

Collection of data

All patients with cirrhosis admitted to or discharged from the dedicated liver unit from January 1st 2010 to September 1st 2013 were included. The population is described in Table 1. Patients were excluded (n = 90) if the medical record lacked complete data regarding frailty assessments.

The study exposure was an assessment of functional status performed at the time of admission. The admitting nurse performed three standardized assessments 1) activities of daily living (ADL), 2) The Braden Scale (Supplementary Figure 1), and 3) Morse fall risk scores (Supplementary Table 2). To determine a patient's ADL scale, the nurse assessed each patient's self-reported ability to feed, toilet, dress, bathe and transfer. Each of these 5 categories were scored as follows: independent (3 points), needs assistance (2 points), or dependent (1 point), giving a maximum potential score of 15. During an initial assessment, the nurse also determined the patient's Braden Scale using a standardized worksheet.(16) Traditionally used to risk stratify for pressure ulcers, the Braden Scale is a metric required by the Center for Medicare and Medicaid Services. It includes a physical exam and an assessment of 6 criteria: skin sensory perception, moisture, activity, mobility, nutrition, and friction (ability to hold a comfortable position in a chair and bed). A score of 23 indicates no risk of skin breakdown while a score of less than 16 requires as a nutrition or physical therapy consultation to forestall nosocomial complications. The Morse Fall Risk scale assigns a patient's risk to fall using a standard form based on the following: history of falling, secondary diagnoses, ambulatory aids, intravenous access, gait disturbances and mental status.(17)

The primary outcome was 90-day mortality assessed from the time of a patient's first admission. Mortality data is considered complete as it was confirmed using a validated online-search of the United States Social Security Death Index.(19) Secondary outcomes included hospital length of stay (LOS), discharge to a rehabilitation hospital and 30-day readmission to BIDMC. Patients who died during hospitalization were excluded from analyses of LOS and 30-day readmission.

Covariates included the MELD score, sodium(12), Charlson comorbidity index, the presence of decompensated cirrhosis(20, 21), active infection(22), hepatocellular carcinoma, admission within the past 30 days, as well as standard demographic features including age, sex, ethnicity and payor. All models were adjusted for whether a liver transplant was performed during the admission (n = 19). A quality improvement project to reduce readmissions occurred during the study period, the phases of which were adjusted for in the analysis. The MELD score was calculated using the United Network for Organ Sharing (UNOS) modification according to previously described algorithms.(9) The Charlson comorbidity index was calculated using ICD-9 codes as previously described.(23) Decompensations were defined by the presence of variceal hemorrhage, overt ascites and overt (West-Haven grade 2 or greater) hepatic encephalopathy. Infections included spontaneous bacterial peritonitis, bacteremia, pneumonia, infectious enterocolitis, urinary tract infections and skin and soft-tissue infections.

Analysis

Data were summarized as mean ± standard deviation for normally distributed, median [25th and 75th percentiles] for non-normally distributed continuous outcomes, or counts and percentages for categorical outcomes. For two-group comparisons, we compared means of normally distributed continuous outcomes medians of non-normally distributed continuous outcomes, and frequencies of categorical outcomes.

Multivariable regression models adjusted for gender, age, ethnicity, Charlson index, admission MELD, admission sodium, infection, cirrhotic decompensation, hepatocellular carcinoma and admitting Hepatologist. For multivariable modeling of the binary outcomes, we used logistic regression resorting to Generalized Estimating Equations in order take into account the multiple admissions within patients and admitting hepatologists (provider). For length of stay, a frailty model was used wherein the effects of patient and provider as random. The comparisons between predictive models were performed by using the method proposed by DeLong et al.(24) All two-tailed p-values < 0.05 were considered statistically significant. All statistical analyses were performed with SAS software, Version 9.3 of the SAS System for Windows. Copyright © 2012 SAS Institute Inc., Cary, NC, USA.

Validation Procedures

Internal validation was performed by randomly dividing the cohort into a training set (two-thirds of the cohort) and validation set (one-third). Two samples (a training set and a validation set) were constructed to develop and validate the prediction model. Two thirds of the subjects were randomly selected for the training set for model development, and the remaining one third were assigned to a validation set for evaluating the predictive performance of the model. Subjects were assigned a random value between 0 and 1. Those subjects with a value less than 0.6667 were assigned to the sample for the training model, and the remaining subjects were assigned to the validation sample. The predictive power of the model was assessed with two summary statistics. First, we examined the concordance rate, which reflects the percentage of events in which the observed outcome and the outcome predicted by the model were concordant. Second, we employed Harrell's c-statistic, which computes the probability that the predicted risk is higher for a case than for a non-case, to assess the goodness of fit for the model and each outcome.(25)

Results

Seven hundred and thirty-four unique patients were admitted a total of 1358 times to the liver unit. Demographics and markers of illness severity/complexity are detailed in Table 1. The 90-day all-cause mortality following an admission to the liver unit for all patients was 16.9 % (230 deaths). The median length of stay (LOS) for all patients was 4 (25th to 75th percentile: 2 - 8) days. Overall, 199 (14.7%) admissions resulted in a discharge to a rehabilitation hospital and 436 (32.1%) resulted in a readmission to our hospital within 30 days.

Table 2 details the association of clinical predictors with the primary and secondary outcomes in univariate and multivariate analyses. Ninety-day mortality is predicted by age,

Charlson index, MELD score, sodium, ADL and Braden score. The adjusted odds ratio (OR) for the effect of an ADL score less than 12 of 15 on mortality is 1.83 95% CI (1.05 - 3.20). An intermediate Braden score (16 to 18) was associated with increased mortality risk, OR 1.62 95% CI (1.03 - 2.56). By contrast, the OR associated with each point increase in the MELD and the Charlson index are 1.09 95% CI (1.06 - 1.12) and 1.11 95% IC (1.02 - 1.20), respectively. The Morse Fall Risk Score do not predict mortality in this population. Discharge to a rehabilitation hospital is predicted by low ADL and Braden Scores with respective OR of 3.78 95% CI (1.97 - 7.29) and 6.23 95% CI (2.53 - 15.4). LOS was significantly associated with low Braden scores, hazard ratio (HR) 0.63 95% CI (0.44 - 0.91). The ADL score did not have a significant association with LOS. In this context, the higher the score the lower the hazard of a longer LOS. None of the frailty measures were associated with 30-day readmission. In multivariate analysis, only MELD and Charlson index were associated with respective odds ratios of 1.05 95% CI (1.03-1.07) and 1.07 95% CI (1.01- 1.13) per unit increase.

The frailty measures were significantly different among patients with and without decompensations, particularly hepatic encephalopathy (HE). Only 348 (60.6%) patients with HE reported full independence with ADLs compared to 587 (81.9%) of those without HE ($p < 0.0001$). Similarly, patients with HE were more likely to have an ADL score < 12 than those without, 138 (24%) vs 66(9.2%) ($p < 0.0001$).Of those with HE, 424 (71.9%) had high/good Braden Scale scores (19-23) compared to 629 (86.3%) of those without ($p <0.0001$). The same pattern exists for the Morse Fall Risk score (median 35 vs 55, $p < 0.0001$).

The clinical variables shown in Table 3 were used to develop a prediction model for each outcome. The relative improvement in predictive power is shown by displaying the c-statistics for models without the frailty measures. Employing the models described Table 3, the AUROC for 90-day mortality, discharge to a rehabilitation facility and 30-day readmission were 0.83 95% CI (0.80 - 0.86), 0.85 95% CI (0.82 - 0.88) and 0.69 95% CI (0.66 - 0.72). For the analysis of 90 day morality, we found that there was a significant difference between the fit of the Model 1 (which included the ADL and Braden scores) and Model 2 ($p =.01$), but not between Model 2 (which included the Charlson index) and Model 3. For the analysis of discharge to a rehabilitation facility, we found that there was a significant difference between the fit of the Model 1 and Model 2 ($p<.0001$) but not between Model 2 and Model 3. For the analysis of 30 day readmission, there was no significant difference between the fit of the three models.

We next applied the model to a validation procedure. As shown in Table 4, the model appeared strongly predictive of 90-day mortality with a 83% concordance rate and a c-statistic of 0.77. Beyond that, for the secondary outcomes of discharge to a rehabilitation facility and 30-day readmission, the model was more predictive of the former than the latter. The concordance rate for rehabilitation facility discharge was 85% with a c-statistic of 0.77. Meanwhile, the 30-day readmission concordance rate was 69.0% with a c-statistic of 0.69.

Discussion

When a patient with cirrhosis requires hospitalization, they are at increased risk of death.(1, 3, 11) The tools established to assess that risk (e.g. MELD) incompletely capture its magnitude while investigational tools (e.g. APACHE) require expertise or require expertise and are unfamiliar to most clinicians.(1, 3, 11, 14, 26) Furthermore, we suspect that a shortcoming of the MELD score and its derivatives is that they do not include measures of a patient's frailty. Frailty measures such as functional status and sarcopenia have recently been validated to predict mortality in the pre-transplant population.(5, 15, 27, 28) In this study of frailty assessments performed upon admission to a liver unit, we show that measurement of frailty added significantly to the prediction of 90-day mortality for hospitalized patients with cirrhosis.

Frailty is a powerful prognostic sign for patients with cirrhosis for a number of reasons. First, previous studies have found that sarcopenia is associated with mortality as well as encephalopathy in patients with cirrhosis.(28, 29) Frailty and sarcopenia are likely correlated if not causally linked, though further study is required to confirm this. As sarcopenia advances, so too would frailty. Yet frailty is easy to assess while sarcopenia is difficult and costly to determine, often requiring advanced imaging.(28) Second, though we adjusted for overt encephalopathy, cognitive impairment would limit performance of ADLs and may reflect un- or under treated hepatic encephalopathy. Third and most importantly, frailty may be a modifiable risk factor that could respond to intensive nutritional support and physical therapy.

Our study extends the results of prior work with three novel findings. First, the ADL score is the simplest and most broadly predictive of the three nursing assessments evaluated. Other available predictive tools such as the APACHE or CLIF-SOFA are good predictors and could also be performed by nurses.(4, 26) However, these metrics are mainly familiar to clinicians and nurses in intensive care units. As a result, and in contrast to the scores assessed in this study, advanced indices such as the APACHE or CLIF-SOFA cannot be performed on most wards without extensive training and validation.(14, 26)

Second, Lai and colleagues previously showed that frailty as reflected by an ADL score is an independent predictor of mortality in outpatients with cirrhosis assessed by a dedicated research staff.(5) Our results underscore the generalizability and broad applicability of these assessments as they were drawn from the inpatient setting using assessments that were collected from nurses without specific training as part of clinical care.

Third, we confirm that the prediction of 30-day readmission rates for patients with cirrhosis is difficult. Prior work from Singal and colleagues generated a prediction model that yielded a c-statistic of 0.66 using a large number of clinical variables (30) including MELD, number of address changes and admissions in the prior year, insurance status, platelet count, hemoglobin, sodium and alanine aminotransferase level. Our c-statistic was a comparable 0.69. Despite assessing a novel clinical dimension (frailty), we were not able to improve the prediction of readmissions. Further study of additional variables using fundamentally

different approaches may be required to determine the predictors of readmission in this population.

Our data must be interpreted within the context of the study design. First, this study took place on a dedicated liver disease unit and as such the results may not be generalizable to other settings. On the other hand, the metrics assessed are familiar to most American nurses and there is nothing specific about the training of our nurses that would limit the translation of these results. Second, we did not power our study to determine whether this model applied best to specific subgroups, such as those with ascites or encephalopathy. Third, though in our healthcare market, patients with complex conditions are generally not cared for a multiple hospitals, we may not have been able to capture all 30-day readmissions, such as those to hospitals outside of our network. Fourth, though we provide statistically validated assessments of frailty, there is no gold-standard for frailty against which to compare the assessments performed.

In conclusion, simple assessments of frailty at admission have a powerful effect on the prediction of clinical events for patients with cirrhosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors would like to thank Dr. J. Thomas Lamont for his critical review of the manuscript and generous mentorship as well as Dr. Michael Howell for his critical input and advice.

Funding: This work was supported by a grant from the Carl J. Shapiro Institute for Education and Research. This work was conducted with support from Harvard Catalyst | The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award UL1 TR001102) and financial contributions from Harvard University and its affiliated academic healthcare centers. The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centers, or the National Institutes of Health.

References

1. Cordoba J, Ventura-Cots M, Simón-Talero M, Amorós À, Pavesi M, Vilstrup H, Angeli P, et al. Characteristics, risk factors, and mortality of cirrhotic patients hospitalized for hepatic encephalopathy with and without acute-on-chronic liver failure (ACLF). Journal of hepatology. 2014; 60:275–281. [PubMed: 24128414]
2. Ganesh S, Rogal SS, Yadav D, Humar A, Behari J. Risk factors for frequent readmissions and barriers to transplantation in patients with cirrhosis. PLoS One. 2013; 8:e55140. [PubMed: 23383085]
3. Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cordoba J, Durand F, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology. 2013; 144:1426–1437. e1429. [PubMed: 23474284]
4. Jalan R, Saliba F, Pavesi M, Amoros A, Moreau R, Ginès P, Levesque E, et al. Development and Validation of a Prognostic Score to Predict Mortality in Patients with Acute on Chronic Liver Failure. Journal of hepatology. 2014
5. Lai J, Feng S, Terrault N, Lizaola B, Hayssen H, Covinsky K. Frailty Predicts Waitlist Mortality in Liver Transplant Candidates. American Journal of Transplantation. 2014; 14:1870–1879. [PubMed: 24935609]

6. Lai JC, Feng S, Roberts JP. An examination of liver offers to candidates on the liver transplant wait-list. Gastroenterology. 2012; 143:1261–1265. [PubMed: 22841780]
7. Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, D'Amico G, et al. A model to predict survival in patients with end-stage liver disease. Hepatology. 2001; 33:464–470. [PubMed: 11172350]
8. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. 2000; 31:864–871. [PubMed: 10733541]
9. Kamath PS, Kim W. The model for end-stage liver disease (MELD). Hepatology. 2007; 45:797–805. [PubMed: 17326206]
10. Wiesner RH, McDiarmid SV, Kamath PS, Edwards EB, Malinchoc M, Kremers WK, Krom RA, et al. MELD and PELD: application of survival models to liver allocation. Liver transplantation. 2001; 7:567–580. [PubMed: 11460223]
11. Al Sibae MR, Cappell MS. Accuracy of MELD scores in predicting mortality in decompensated cirrhosis from variceal bleeding, hepatorenal syndrome, alcoholic hepatitis, or acute liver failure as well as mortality after non-transplant surgery or TIPS. Digestive diseases and sciences. 2011; 56:977–987. [PubMed: 20844956]
12. Biggins SW, Kim W, Terrault NA, Saab S, Balan V, Schiano T, Benson J, et al. Evidence-based incorporation of serum sodium concentration into MELD. Gastroenterology. 2006; 130:1652–1660. [PubMed: 16697729]
13. Kim WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, Edwards E, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. New England Journal of Medicine. 2008; 359:1018–1026. [PubMed: 18768945]
14. Kruse JA, Thill-Baharozian MC, Carlson RW. Comparison of clinical assessment with APACHE II for predicting mortality risk in patients admitted to a medical intensive care unit. Jama. 1988; 260:1739–1742. [PubMed: 3137374]
15. Carey EJ, Steidley DE, Aqel BA, Byrne TJ, Mekeel KL, Rakela J, Vargas HE, et al. Six-minute walk distance predicts mortality in liver transplant candidates. Liver Transplantation. 2010; 16:1373–1378. [PubMed: 21117246]
16. Bergstrom N, Braden B, Kemp M, Champagne M, Ruby E. Predicting pressure ulcer risk: a multisite study of the predictive validity of the Braden Scale. Nursing research. 1998; 47:261–269. [PubMed: 9766454]
17. Morse, JM. Preventing patient falls. Sage publications; London: 1997.
18. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Preventive medicine. 2007; 45:247–251. [PubMed: 17950122]
19. Hauser TH, Ho KK. Accuracy of on-line databases in determining vital status. J Clin Epidemiol. 2001; 54:1267–1270. [PubMed: 11750196]
20. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. Journal of hepatology. 2006; 44:217–231. [PubMed: 16298014]
21. Ripoll C, Bari K, Garcia-Tsao G. Serum Albumin Can Identify Patients With Compensated Cirrhosis With a Good Prognosis. Journal of clinical gastroenterology. 2014
22. Arvaniti V, D'Amico G, Fede G, Manousou P, Tsochatzis E, Pleguezuelo M, Burroughs AK. Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis. Gastroenterology. 2010; 139:1246–1256. e1245. [PubMed: 20558165]
23. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol. 1992; 45:613–619. [PubMed: 1607900]
24. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988:837–845. [PubMed: 3203132]

25. Harrell F, Lee KL, Mark DB. Tutorial in biostatistics multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Statistics in medicine. 1996; 15:361–387. [PubMed: 8668867]
26. Zhang Z, Chen R, Zhou Z, Peng C, Zhou G. Prognostic Evaluation of Patients Undergoing Living-Donor Liver Transplant By APACHE II and MELD Scores. Experimental and clinical transplantation: official journal of the Middle East Society for Organ Transplantation. 2014
27. Gobbens RJ, van Assen MA. The Prediction of ADL and IADL Disability Using Six Physical Indicators of Frailty: A Longitudinal Study in the Netherlands. Current gerontology and geriatrics research. 2014; 2014
28. Montano–Loza AJ, Meza–Junco J, Prado CM, Lieffers JR, Baracos VE, Bain VG, Sawyer MB. Muscle wasting is associated with mortality in patients with cirrhosis. Clinical Gastroenterology and Hepatology. 2012; 10:166–173. e161. [PubMed: 21893129]
29. Periyalwar P, Dasarathy S. Malnutrition in cirrhosis: contribution and consequences of sarcopenia on metabolic and clinical responses. Clinics in liver disease. 2012; 16:95–131. [PubMed: 22321468]
30. Singal AG, Rahimi RS, Clark C, Ma Y, Cuthbert JA, Rockey DC, Amarasingham R. An automated model using electronic medical record data identifies patients with cirrhosis at high risk for readmission. Clin Gastroenterol Hepatol. 2013; 11:1335–1341. e1331. [PubMed: 23591286]

Abbreviations

ADL	activities of daily living
CI	confidence interval
HR	hazard ratio
INR	international normalized ratio
LOS	length of stay
MELD	Model for Endstage Liver Disease
OR	odds ratio

Table 1

Demographics and Clinical Variables

Number of unique patients (N)	734
Age - average years (SD)	57.3 (11.5)
Males - n (%)	453 (62%)
Number of admissions (n)	1358
1 admission - n (%)	462 (63%)
2-4 admissions - n (%)	225 (31%)
5+ admissions - n (%)	47 (6%)
Patient Characteristics at Each Admission	
MELD - average (SD)	17.9 (7.5)
Admission Sodium - median meq/L (IQR)	136 (131 - 139)
Admission Bilirubin - median mg/dL (IQR)	5.1 (0.9 - 5.5)
Admission INR - median (IQR)	1.4 (1.2 - 1.8)
Admission Platelet Count - median (IQR)	114 (75 - 174)
Charlson Comobidity Index - median (IQR)	4 (2 - 6)
Length of stay - median days (IQR)	4 (2 - 8)
Discharge to rehabillitation - n (%)	199 (14.7)
30-day readmssion - n (%)	436 (32.1)
90-day mortality - n (%)	230 (16.9)
Active Problems During Hospitalization	
Overt Hepatic Encephalopathy	613 (45.1%)
Ascites - n (%)	565 (41.6%)
Gastrointestinal Bleeding - n (%)	385 (28.4%)
Hepatocellular Carcinoma - n (%)	138 (10.2%)
Spontaneous bacterial peritonitis - n (%)	102 (7.5%)
Acute alcoholic hepatitis	95 (7.0%)

IQR = Interquartile range; MELD = Model for Endstage Liver Disease, SD = Standard deviation

Table 2

Univariate and Multivariable Models of Associations between Patient Characteristics and Clinical Outcomes

	90 Day Mortality		Discharge to a Rehabilitation Hospital		Time to Discharge (days)	
	Unadjusted OR (95% CI)	**Adjusted OR (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)**
Female (compared to male)	0.9 (0.62 – 1.31)	0.93 (0.59 – 1.46)	1.02 (0.67 – 1.56)	0.76 (0.46 - 1.25)	0.85 (0.76 - 0.96)	0.83 (0.74 - 0.94)
Age (per year)	1.03 (1.01 - 1.04)	1.04 (1.02 - 1.06)	1.02 (1.00 - 1.04)	1.01 (0.98 - 1.03)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)
Charlson (per point)	1.25 (1.18 - 1.33)	1.11 (1.02 - 1.20)	1.19 (1.12 - 1.27)	1.08 (0.98 - 1.19)	0.94 (0.92 - 0.96)	0.97 (0.95 - 1.00)
MELD (per point)	1.10 (1.08 - 1.13)	1.09 (1.06 - 1.12)	1.07 (1.04 - 1.10)	1.04 (1.0 - 1.08)	0.96 (0.95 - 0.96)	0.97 (0.96 - 0.98)
Admission Sodium (per meq/L)	0.92 (0.89 - 0.95)	0.96 (0.93 - 0.99)	0.95 (0.93 - 0.98)	0.96 (0.93 - 1.00)	1.04 (1.03 - 1.05)	1.02 (1.01 - 1.03)
ADL score (compared to a score of 15)						
12 to 14	1.88 (1.15 - 3.08)	1.13 (0.64 - 2.00)	2.52 (1.50 - 4.25)	1.43 (0.78 - 2.65)	0.84 (0.71 - 1.01)	0.93 (0.76 - 1.14)
< 12	3.84 (2.60 - 5.67)	1.83 (1.05 - 3.20)	11.7 (7.29 - 18.6)	3.78 (1.97 - 7.29)	0.69 (0.59 - 0.82)	0.87 (0.70 - 1.09)
Braden Score (compared to a score of 19-23)						
16 to 18	2.71 (1.88 - 3.90)	1.62 (1.03 - 2.56)	5.92 (4.01 - 8.74)	2.41 (1.47 - 3.96)	0.74 (0.63 - 0.87)	0.85 (0.71 - 1.03)
< 16	3.40 (1.90 - 6.07)	1.85 (0.83 - 4.12)	24.4 (12.4 - 47.8)	6.23 (2.53 - 15.4)	0.56 (0.42 - 0.76)	0.63 (0.44 - 0.91)
Morse Fall Risk Score (per point)	1.01 (1.01 - 1.02)		1.03 (1.03 - 1.03)	1.02 (1.00 - 1.03)	1.00 (0.99 - 1.00)	1.0 (1.0 - 1.0)

HR=Hazard Ratio; OR=Odds Ratio; 95% CI=95% Confidence Interval

All adjusted results include adjustments for active cirrhotic decompensation, hepatocellular carcinoma, and infection

Table 3
Measures of Outcome Prediction by Models With and Without Frailty Measures

	Model 1 (Full Model)	Model 2	Model 3
	Area Under the Receiver Operating Curve (95% Confidence Interval)		
90 day mortality	0.83 (0.80 - 0.86)	0.81 (0.78 - 0.84)	0.80 (0.77 - 0.84)
Discharge to a rehabilitation facility	0.85 (0.82 - 0.88)	0.73 (0.70 - 0.77)	0.72 (0.68 - 0.76)
30 day readmission	0.69 (0.66 - 0.72)	0.69 (0.66 - 0.72)	0.69 (0.65 - 0.72)

For 90 Day Mortality: Model 1 includes Charlson, Braden and ADL scores and the variables described in Model 3. Model 2 includes Charlson and Model 3's variables but excludes Braden and ADL; Model 3 includes Sex, Age, MELD, Sodium, Cirrhotic Decompensation, Infection, Hepatocellular Carcinoma, Provider, Quality Improvement Intervention Phase, and prior admission in the Past 30 days (excludes Braden, ADL, and Charlson).

For Discharge to a rehabilitation facility: Model 2 includes Sex, Age, MELD, Sodium, and Charlson (excludes Braden, ADL, Morse Fall); Model 3 is described above

For 30 Day Readmission: Model 2 includes Sex, Age, MELD, Sodium, and Charlson (excludes Braden); Model 3 is described above

Table 4

Results of the Model Validation

	Prediction Model		Validation Model
Measure	**C-Statistic (95% CI)**	**Concordance Rate**	**C-Statistic (95% CI)**
90 day mortality	0.83 (0.80 - 0.86)	0.83	0.77 (0.71 - 0.83)
Discharge to a rehabilitation facility	0.85 (0.82 - 0.88)	0.85	0.76 (0.69 - 0.83)
30 day readmission	0.70 (0.66 - 0.75)	0.69	0.69 (0.65 - 0.74)

Note: Concordance rate reflects the proportion of cases in which the observed outcome and the outcome predicted by the model (derived in the prediction data set) were concordant