Patient-Reported Outcome Measures Modestly Enhance Prediction of Readmission in Patients with Cirrhosis

Short Title: PROMs and Cirrhosis Readmissions

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Grant support: Research reported in this publication was supported, in part, by the National Institutes of Health under award numbers K23DK109202 and KL2TR002530. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Abbreviations: ADL, activity of daily living; AUROC, area under the receiver operating characteristic curve; CLDQ, chronic liver disease questionnaire; EHR, electronic health records; ED, emergency department; FSQ, functional status questionnaire; HE, hepatic encephalopathy; INR, international normalized ratio; IQR, interquartile range; MELD, Model for End Stage Liver Disease; NRI, net reclassification index; PROM, patient-reported outcome measure; SD, standard deviation.

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Disclosures: The authors declare no conflicts of interest. NC has several consulting agreements with and receives grant support from pharmaceutical companies, but they are unrelated to this paper.

Author contributions: Study concept and design: ESO, MSG, SG, NC; Acquisition of data: ESO, MSG, NC; Analysis and interpretation of data: ESO, MSG, APD, LN, KRP, SG, CX, NC; Drafting of the manuscript: ESO, MSG, NC; Critical revision of the manuscript for important intellectual content: ESO, MSG, APD, LN, KRP, SG, CX, NC; Statistical analysis: SG, CX; Obtained funding: ESO, NC; Administrative, technical, or material support: ESO, NC; Study supervision: ESO, NC.

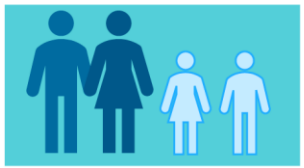
Data Transparency Statement: Data, analytic methods, and study materials may be made available to other researchers upon request.

This is the author's manuscript of the article published in final edited form as:
Orman, E. S., Ghabril, M. S., Desai, A. P., Nephew, L., Patidar, K. R., Gao, S., Xu, C., & Chalasani, N. (2021). Patient-Reported Outcome Measures Modestly Enhance Prediction of Readmission in Patients with Cirrhosis. Clinical Gastroenterology and Hepatology. https://doi.org/10.1016/j.cgh.2021.07.032

PREDICTING READMISSION

Variables:	Electronically Available	+	Clinically Available	+	Socioeconomic	+	Functional Status	+	Quality of Life
AUROCs:	0.71	→	0.72	→	0.73	→	0.73	→	0.75





Clinical Gastroenterology and Hepatology

ABSTRACT

Background & Aims: Patients with cirrhosis have high rates of hospital readmission, but prediction models are suboptimal and have not included important patient-reported outcome measures (PROMs). In a large prospective cohort, we examined the impact of PROMs on prediction of 30-day readmissions.

Methods: We performed a prospective cohort study of adults with cirrhosis admitted to a tertiary center between June 2014 and March 2020. We collected clinical information, socioeconomic status, and PROMs addressing functional status and quality of life. We used hierarchical competing risk time-to-event analysis to examine the impact of PROMs on readmission prediction.

Results: 654 patients were discharged alive, and 247 (38%) were readmitted within 30 days. Readmission was independently associated with cerebrovascular disease, ascites, prior hospital admission, admission via the emergency department, lower albumin, higher MELD, discharge with public transportation, and impaired basic activities of daily living and quality of life activity domain. Reduced readmission was associated with cancer, admission for infection, children at home, and impaired emotional function. Compared to a model including only clinical variables, addition of functional status and quality of life variables improved the area under the receiver operating characteristic curve (AUROC) from 0.72 to 0.73 and 0.75, with net reclassification indices of 0.22 and 0.18, respectively. Socioeconomic variables did not significantly improve prediction compared to clinical variables alone. Compared to a model using electronically-available variables only, no models improved prediction when examined with integrated discrimination improvement.

Conclusions: PROMs may marginally add to the prediction of 30-day readmissions for patients with cirrhosis. Poor social support and disability are associated with readmissions and may be high-yield targets for future interventions.

KEYWORDS: hepatology; hospitalization; health services

INTRODUCTION

Following hospital discharge, patients with cirrhosis have high rates of early readmission.[1] These readmissions are often preventable, expensive, and associated with additional poor outcomes, including mortality.[2,3] Existing interventions to reduce readmissions in this population are resource-intensive, with limited evidence for efficacy.[4–6] Therefore, risk stratification tools are needed so that interventions can be refined and targeted to those most likely to benefit.

Multiple models have been developed to predict readmission, with disappointing results.[2,7,8] Attempts to improve prediction have included the use of numerous variables from large datasets, inclusion of frailty and social stability, and use of novel analytic techniques.[9–12] Despite these efforts, accuracy has remained suboptimal, with c-statistics ranging from 0.6 to 0.7, and it is unclear whether prediction could be improved. Limitations of existing studies include retrospective study designs and absence of important socioeconomic variables and patient-reported outcome measures (PROMs). Notably, behavioral, physical, and psychological factors have all been associated with readmissions in other populations.[13–16] However, it is unknown whether PROMs addressing these factors can improve prediction in cirrhosis.

We therefore sought to develop a model to predict readmissions in hospitalized patients with cirrhosis and to determine the impact of socioeconomic status, functional status, and quality of life. We hypothesized that these factors would enhance prediction and improve model performance. To achieve these goals, we studied a large prospective cohort of hospitalized patients with cirrhosis in which multiple validated PROMs were collected.

METHODS

Study Design

We performed a prospective cohort study of adults (age≥18) with cirrhosis admitted to Indiana University Hospital between June 2014 and March 2020. Patients were consented during their first hospitalization during the study period for this analysis. Subsequent hospitalizations were not included. Cirrhosis was based on liver histology or clinical, laboratory, and radiologic findings. We excluded patients with organ transplants and those unable to consent. Patients unable to consent due to altered mentation could be enrolled later during the hospitalization once able to consent. Patients were followed from admission throughout the hospitalization and were assessed for outcomes at 30 days post-discharge. The Indiana University Institutional Review Board approved the study.

Outcomes

The primary outcome was unplanned 30-day readmission. Post-discharge outcomes were obtained from the local electronic health records (EHR) and the Indiana Network for Patient Care. The network is among the largest health information exchanges in the US, connecting over 110 hospitals, 18,000 practices, and 50,000 providers across Indiana. It contains data on over 16 million patients, including death certificate information.[17] Patients without a readmission identified in the EHR were contacted by phone to ensure accuracy.

Variables

Electronically-available

Potential predictors were considered in a stepwise fashion. The first set of variables were those available through EHR extraction. These variables included demographics (age, sex, race), health insurance (private, Medicare, Medicaid, other), Charlson comorbidity index,[18] prior healthcare utilization (admission in the prior 30 days, emergency department [ED] visits in the prior 6 months [per the LACE readmission index[19]]), and admission source (direct, ED, hospital transfer). We also collected cirrhosis complications (ascites, hepatic encephalopathy [HE], hepatocellular carcinoma), laboratory results at admission and discharge (creatinine, bilirubin, and INR to calculate the Model for End Stage Liver Disease [MELD[20]]; sodium; albumin; and hemoglobin), and discharge medications. Comorbidities and cirrhosis complications were obtained by chart review but were considered electronically-available because of the existence of valid diagnosis codes.[21–23]

Clinically-available

We next examined variables that cannot be automatically extracted from the EHR, but are available from a clinical history. These included marital status, alcohol use (prior 3 months), cirrhosis etiology (alcohol, hepatitis C, alcohol/hepatitis C, nonalcoholic steatohepatitis, and other), Child-Pugh,[24] liver transplant listing, reason for admission, discharge transportation (self/spouse, other family/friend, or public), and discharge location (home vs. facility). Cirrhosis etiology was not considered electronically-available due to poor validity of diagnosis codes for conditions such as nonalcoholic steatohepatitis.[25]

Socioeconomic Status

Socioeconomic status was evaluated using the MacArthur Foundation Research Network on Socioeconomic Status and Health sociodemographic questionnaire. It includes items regarding social standing, education, occupation, and income, and has been used in patients with cirrhosis.[26,27]

PROMs

PROMs collected included functional status and quality of life. Functional status was evaluated with the functional status questionnaire (FSQ) covering: basic activities of daily living (ADLs), intermediate ADLs, mental health, social/role function, social activity, and quality of interactions.[28] Each domain is scored 0-100, with pre-defined impairment thresholds. The FSQ has excellent reliability and construct and criterion validity in different settings, including hospitalized populations.[28,29] Disease-specific quality of life was examined using the chronic liver disease questionnaire (CLDQ) covering: abdominal symptoms, fatigue, systemic symptoms, activity, emotional function, and worry.[30] Each domain is scored 1-7, with higher scores corresponding to less impairment. The CLDQ has been validated in patients with decompensated cirrhosis and has been used elsewhere in cirrhosis hospitalizations.[30–32] For all questionnaires, patients were asked to reflect on the time prior to admission. All patient-reported variables were collected from the patients (no proxy responses).

Statistical Analysis

Variables were categorized as electronically-available, clinically-available, socioeconomic, and PROM. Death was considered a competing risk for time to readmission. Univariate cause-specific Cox regression models were used to identify predictors of readmission using $p<0.2$.

Variables that met the univariate threshold were selected into multivariate models by stepwise selection, retaining factors with $p<0.1$. A hierarchical model building process was used. Model 1 was built with electronically-available variables only; Model 2 added clinically-available variables to Model 1; Model 3 added socioeconomic variables to Model 2; Model 4 added functional status to Model 3; and Model 5 added quality of life to Model 4. The proportional hazards assumption was tested and found to be valid. Hazard ratios (HR) and their corresponding 95% confidence intervals (CI) were reported. Data were randomly split into 3 groups and each group was used as a validation group once with the remaining two-thirds serving as derivation data. Area under the time-dependent receiver operating characteristic curve (AUROC) at 30 days was used to evaluate discriminative ability.

We additionally evaluated improvements in prediction using the continuous net reclassification index (NRI) and integrated discrimination improvement (IDI). NRI and IDI are time-dependent in the time-to-event analysis setting. Predicted probability of 30-day readmission for each subject was obtained from the Cox models and used to calculate both statistics. To compare any two models, the one with fewer predictors was the reference model. The NRI is the sum of proportions of correctly reclassified individuals with and without readmission.[33] For a patient who was readmitted, an increase in comparator model-based predicted risk compared to the reference model was considered a correct reclassification. For a patient who was not readmitted, a decrease in comparator model-based predicted risk was considered a correct reclassification. Positive values indicated improved reclassification. IDI was calculated as the difference in discrimination slopes between two models, defined as the average predicted probability of

readmission for those who were readmitted versus those who were not. All analyses were performed in SAS v9.4.

RESULTS

Study Cohort

Of 915 patients meeting eligibility criteria who were approached, 744 were enrolled during the study period. Of these, 42 died in-hospital, 36 were discharged to hospice, 9 underwent liver transplantation, and 3 were lost to follow-up before 30 days, leaving 654 patients for analysis (**Figure 1**).

Patient Characteristics

The mean age was 57.5 years (standard deviation [SD] 10.6), 54.7% were male, and 95.3% were white. Electronically-available characteristics are shown in **Table 1**. 35.3% were admitted in the prior 30 days, a history of ascites was present in 79.8%, and HE in 70.2%. Mean MELD on admission was 18.9 (SD 6.9) and on discharge was 17.6 (SD 6.3). Patients were taking a median of 12 medications at discharge (interquartile range [IQR] 8-16). The median Charlson comorbidity index was 6 (IQR 5-8), and individual comorbidities are shown in **Supplemental Table 1**. 41.9% had diabetes, and 23.5% had chronic kidney disease. Notable clinically-available characteristics include a mean Child-Pugh score of 10 (SD 2.2), with 8.0% listed for liver transplant (**Table 2**). The most common reasons for admission were HE (21.9%), ascites/volume overload (20.5%), and abdominal pain (17.9%). 16.1% were discharged to a facility. Socioeconomic variables are shown in **Table 3**. 69.9% had a high school education or less, 50.6% were unemployed, and 27.2% had saved >6 months of expenses.

PROMs

Results of PROMs are shown in **Table 3**. The percentage with functional status impairments ranged from 34.4% (quality of interactions) to 73.4% (intermediate ADLs). Mean quality of life scores (1-7: higher=better) ranged from 2.8 (fatigue) to 4.5 (emotional function), with an overall score of 3.8 (SD 1.0).

30-Day Readmissions

Readmissions occurred in 247 (37.8%), most commonly for HE (22%), acute kidney injury/electrolyte disturbance (16%), gastrointestinal bleeding (13%), and ascites/volume overload (10%). (**Supplemental Figure**). 36% of readmissions occurred at other hospitals. 39 patients died within 30 days (6%). In univariate analysis, electronically-available factors associated with readmission included cerebrovascular disease, prior admissions and ED visits, ascites, MELD, albumin, hemoglobin, and use of an antibiotic for HE (**Table 1**). Although hepatocellular carcinoma was not associated with readmission, the presence of any cancer inclusive of hepatocellular carcinoma was associated with reduced readmission (**Supplemental Table 1**). Clinically-available variables associated with readmission included Child-Pugh, discharge transportation, and discharge to a facility (**Table 2**). No socioeconomic variables were associated with readmission. Of the PROMs, only basic ADL impairment was associated with readmission (**Table 3**).

Independent Predictors of Readmission

In multivariable analysis (**Table 4**), independent predictors of readmission included cerebrovascular disease, ascites, admission in the prior 30 days, admission via ED, lower admission albumin, higher discharge MELD, and discharge via public transportation. Cancer and

admission for infection were associated with reduced readmission risk. Of the socioeconomic variables, children in the home was associated with reduced readmission. Basic ADL impairment was associated with readmission, as was impaired CLDQ activity domain. Impaired emotional function was associated with reduced readmission risk.

Multivariable Models

Model 1, including only electronically-available variables, had an AUROC of 0.71 (validation: 0.66) (**Table 4**). Addition of clinically-available variables (Model 2) modestly improved prediction, with NRI of 0.198 (p=0.02) (**Table 5**). Model 3, adding socioeconomic status, brought the AUROC to 0.73 (validation: 0.68), and addition of functional status to create Model 4 resulted in a similar AUROC. Adding quality of life (Model 5) led to minimally improved discrimination (AUROC 0.75; validation 0.69). In comparing models, there were significant improvements in NRI with PROMs compared to Models 1 and 2, though differences between Models 3, 4, and 5 were not significant (**Table 5**). When using IDI, compared to Model 1, there was no advantage for any of the other models.

Comparison to Other Models

Other readmission models in cirrhosis have had fair-to-poor discrimination, with AUROCs 0.6-0.7 (**Supplemental Table 2**). These models include variables covering disease characteristics, demographics, medications, healthcare utilization, and comorbidities. Though some included frailty, none included details of socioeconomic status, functional status, or quality of life. Of these models, five could be applied to this study cohort, and all had AUROC <0.6. In addition to cirrhosis-specific models, the widely-used LACE index had AUROC 0.53.

DISCUSSION

In this large, prospective study, we examined the impact of socioeconomic factors and PROMs on readmission risk for patients with cirrhosis. A model based on electronically-available data had fair discrimination, and the addition of patient-reported behavioral, socioeconomic, physical, and psychological factors resulted in modest improvement in prediction. Factors associated with readmission included comorbidities, liver disease severity and complications, healthcare utilization, support at discharge and at home, functional impairment, and quality of life.

Excess readmissions often indicate poor quality of care, and for conditions including heart failure, they can prompt financial penalties for hospitals. Compared to heart failure, cirrhosis carries a greater risk of readmission, largely related to ascites and HE. Therefore, accurate readmission prediction for patients with cirrhosis is a priority. Previous models have been suboptimal, with c-statistics of 0.6-0.7. These models have also varied with regard to the types of derivation datasets, potential predictor variables, and analytic methodologies and outcome timepoints. Several have been based on administrative or electronically-available data that could generate EHR-based risk prediction.[7,9,12] To leverage the potential for an automated model, we used a sequential process in which the initial model only included electronically-available variables. This model, which included comorbidities, liver disease complications and severity, prior utilization, and acuity, performed similarly to previous models despite fewer variables. Further, the addition of clinically-available variables had minimal impact on discrimination (Model 2), suggesting limited utility for additional manual data collection.

Addition of socioeconomic and PROMs had marginal effects on prediction. Inclusion of these variables resulted in minimal changes in reclassification, with non-significant NRIs and IDIs and modest AUROC increases, similar to previously published models. The slight benefit of social factors and PROMs in predicting readmission is unsurprising; in non-liver populations, readmissions have been associated with impairments in these domains.[13–16] Lower quality of life has also been associated with increased hospitalizations and mortality in ambulatory patients with cirrhosis.[32] Whether any modest improvement with these particular measures could be further improved with other PROMs remains to be seen. Such measures, including health literacy, self-management, and caregiver burden could add value and are deserving of study.[14,34,35] Further work could also address whether the additive value of PROMs would justify the cost and effort of their collection.

Beyond prediction, this work illuminates potential targets for interventions. In multivariable analyses, readmissions were associated with public transportation at discharge and fewer children in the home. These findings, suggestive of reduced social support, are consistent with the trend toward fewer readmissions in married patients, and are consistent with prior studies showing associations between readmissions and poor social support.[14,36] Social isolation, which is common in cirrhosis, may be addressed through linkage to community resources, which should be integral to readmission interventions.[37,38] Readmissions related to poor social support may also benefit from complex, multicomponent interventions.[39] Such interventions may reduce readmissions related to disability, where patients require assistance with ADLs. Indeed, we found readmissions associated with cerebrovascular disease and impaired activity and basic ADLs. Elsewhere, interventions have been more effective in reducing readmissions when they

increase capacity for self-care, and such aspects should be emphasized when applied to cirrhosis.[39]

Despite the increased readmissions observed with impaired basic ADLs and activity, other quality of life and functional status domains were not associated with readmission. This lack of association contrasts with work showing associations with 6-month admission/mortality in ambulatory patients across all CLDQ domains.[32] These factors are likely less predictive of clinical outcomes in our sicker group of hospitalized patients who have higher MELD scores and a greater burden of complications. Comparison of these studies highlights the difficulty in predicting outcomes in hospitalized patients, who have complex clinical courses compared to stable ambulatory patients. Interestingly, greater emotional function in the CLDQ (i.e., fewer depressive symptoms) was associated with readmission. This finding contrasts with mixed results from other studies showing either a positive association between depression and readmission or no association.[40,41] Reasons for this counterintuitive result are not clear, but may relate to relative sparing of mental health as compared to physical health in both the FSQ and CLDQ. Other unexpected findings include fewer readmissions in those with cancer, which could be due to closer monitoring afforded to those seeing oncology.

This large, prospective study provides novel data on the contribution of PROMs to readmission risk. The large sample size provides the ability to examine numerous variables simultaneously, including clinical, behavioral, socioeconomic, physical, and psychological factors. Many of these factors can only be examined in a prospective study. The questionnaires used were also previously validated and could be applied elsewhere in refining readmission risk. Use of a large

health information exchange allowed us to accurately identify readmissions at other medical centers. Despite these strengths, this study was performed in a single center, limiting external validity. However, much cirrhosis care in the US is localized to similar high-volume transplant centers.[42] Although the addition of the PROMs did improve prediction when assessed with NRI (but not IDI), the absolute improvement in AUROCs was modest; the highest AUROC was still only 0.69 in validation. This finding highlights that either readmission in cirrhosis is inherently unpredictable, or study of additional variables and/or analytic methods is needed. In addition, despite favorable performance of our models compared to others, this advantage may be overestimated due to internal validation compared to the external validation of others. Another potential limitation is that PROMs were administered in the hospital and only assessed pre-hospital functional status. These measures may not reflect post-discharge impairments, particularly if patients experienced worsening symptoms. Future work should assess how post-discharge PROMs may impact readmission.

Early readmission is common for patients with cirrhosis, and development of interventions to prevent readmission is a priority. This study demonstrates the value of PROMs in enhancing prediction and in considering how to best target and implement interventions. In addition to targeting the population of high utilizers with more severe liver disease, prevention efforts must also address the negative effects of poor social support and disability. These goals may be achieved through complex, multicomponent interventions, focused on enhancing self-care and linking patients to community resources.

FIGURE LEGENDS

Figure 1. Flow of patients enrolled in the study.

REFERENCES

1. Orman ES, Ghabril M, Emmett TW, et al. Hospital Readmissions in Patients with Cirrhosis: A Systematic Review. J Hosp Med 2018;13:490-495.

2. Volk ML, Tocco RS, Bazick J, et al. Hospital readmissions among patients with decompensated cirrhosis. Am J Gastroenterol 2012;107:247-252.

3. Berman K, Tandra S, Forssell K, et al. Incidence and Predictors of 30-Day Readmission Among Patients Hospitalized for Advanced Liver Disease. Clin Gastroenterol Hepatol 2011;9:254-259.

4. Wigg AJ, McCormick R, Wundke R, et al. Efficacy of a Chronic Disease Management Model for Patients With Chronic Liver Failure. Clin Gastroenterol Hepatol 2013;11:850-858.e4.

5. Morando F, Maresio G, Piano S, et al. How to improve care in outpatients with cirrhosis and ascites: A new model of care coordination by consultant hepatologists. J Hepatol 2013;59:257-264.

6. Morales BP, Planas R, Bartoli R, et al. HEPACONTROL. A program that reduces early readmissions, mortality at 60 days, and healthcare costs in decompensated cirrhosis. Dig Liver Dis 2018;50:76-83.

7. Mumtaz K, Issak A, Porter K, et al. Validation of Risk Score in Predicting Early Readmissions in Decompensated Cirrhotic Patients: A Model Based on the Administrative Database. Hepatology 2019;70:630-639.

8. Bajaj JS, Reddy KR, Tandon P, et al. The 3-month readmission rate remains unacceptably high in a large North American cohort of patients with cirrhosis. Hepatology 2016;64:200-208.

9. Koola JD, Ho SB, Cao A, et al. Predicting 30-Day Hospital Readmission Risk in a National Cohort of Patients with Cirrhosis. Dig Dis Sci 2020;65:1003-1031.

10. Tapper EB, Finkelstein D, Mittleman MA, et al. Standard assessments of frailty are validated predictors of mortality in hospitalized patients with cirrhosis. Hepatology 2015;62:584-590.

11. Hu C, Anjur V, Saboo K, et al. Low Predictability of Readmissions and Death Using Machine Learning in Cirrhosis. Am J Gastroenterol 2021;116:336-346.

12. Singal AG, Rahimi RS, Clark C, et al. An automated model using electronic medical record data identifies patients with cirrhosis at high risk for readmission. Clin Gastroenterol Hepatol 2013;11:1335-1341.e1.

13. Calvillo–King L, Arnold D, Eubank KJ, et al. Impact of Social Factors on Risk of Readmission or Mortality in Pneumonia and Heart Failure: Systematic Review. J Gen

Intern Med 2013;28:269-282.

14. Arbaje AI, Wolff JL, Yu Q, et al. Postdischarge Environmental and Socioeconomic Factors and the Likelihood of Early Hospital Readmission Among Community-Dwelling Medicare Beneficiaries. Gerontologist 2008;48:495-504.

15. Middleton A, Graham JE, Ottenbacher KJ. Functional Status Is Associated With 30-Day Potentially Preventable Hospital Readmissions After Inpatient Rehabilitation Among Aged Medicare Fee-for-Service Beneficiaries. Arch Phys Med Rehabil 2018;99:1067-1076.

16. Rodríguez-Artalejo F, Guallar-Castillón P, Pascual CR, et al. Health-Related Quality of Life as a Predictor of Hospital Readmission and Death Among Patients With Heart Failure. Arch Intern Med 2005;165:1274-1279.

17. McDonald CJ, Overhage JM, Barnes M, et al. The Indiana Network for Patient Care: A working local health information infrastructure. Health Aff 2005;24:1214-1220.

18. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-383.

19. Van Walraven C, Dhalla IA, Bell C, et al. Derivation and validation of an index to predict early death or unplanned readmission after discharge from hospital to the community. Cmaj 2010;182:551-557.

20. Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. Hepatology 2001;33:464-470.

21. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in. Med Care 2005;43.

22. Re III V Lo, Lim JK, Goetz MB, et al. Validity of diagnostic codes and liver-related laboratory abnormalities to identify hepatic decompensation events in the Veterans Aging Cohort Study. Pharmacoepidemiol Drug Saf 2011;20:689-699.

23. Goldberg DS, Lewis JD, Halpern SD, et al. Validation of a coding algorithm to identify patients with hepatocellular carcinoma in an administrative database. Pharmacoepidemiol Drug Saf 2013;22:103-107.

24. Pugh RN, Murray-Lyon IM, Dawson JL, et al. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 1973;60:646-649.

25. Corey KE, Kartoun U, Zheng H, et al. Development and Validation of an Algorithm to Identify Nonalcoholic Fatty Liver Disease in the Electronic Medical Record. Dig Dis Sci 2016;61:913-919.

26. Singh-Manoux A, Adler NE, Marmot MG. Subjective social status: its determinants and

its association with measures of ill-health in the Whitehall II study. Soc Sci Med 2003;56:1321-1333.

27. Bajaj JS, Wade JB, Gibson DP, et al. The multi-dimensional burden of cirrhosis and hepatic encephalopathy on patients and caregivers. Am J Gastroenterol 2011;106:1646-1653.

28. Jette AM, Davies AR, Cleary PD, et al. The Functional Status Questionnaire: reliability and validity when used in primary care. J Gen Intern Med 1986;1:143-149.

29. Cleary PD, Jette AM. Reliability and validity of the Functional Status Questionnaire. Qual Life Res 2000;9:747-753.

30. Younossi ZM, Guyatt G, Kiwi M, et al. Development of a disease specific questionnaire to measure health related quality of life in patients with chronic liver disease. Gut 1999;45:295-300.

31. Younossi ZM, Boparai N, Price LL, et al. Health-related quality of life in chronic liver disease: the impact of type and severity of disease. Am J Gastroenterol 2001;96:2199-2205.

32. Kok B, Whitlock R, Ferguson T, et al. Health-Related Quality of Life: A Rapid Predictor of Hospitalization in Patients with Cirrhosis. Am J Gastroenterol 2020;115:575-583.

33. Pencina MJ, D'Agostino RBS, D'Agostino RBJ, et al. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. Stat Med 2008;27:112-157.

34. Baker DW, Gazmararian JA, Williams M V, et al. Functional health literacy and the risk of hospital admission among Medicare managed care enrollees. Am J Public Health 2002;92:1278-1283.

35. Lotus Shyu Y-I, Chen M-C, Lee H-C. Caregiver's needs as predictors of hospital readmission for the elderly in Taiwan. Soc Sci Med 2004;58:1395-1403.

36. Rodríguez-Artalejo F, Guallar-Castillón P, Herrera MC, et al. Social network as a predictor of hospital readmission and mortality among older patients with heart failure. J Card Fail 2006;12:621-627.

37. National Academies of Sciences Engineering and Medicine. Social Isolation and Loneliness in Older Adults: Opportunities for the Health Care System. Washington, DC: The National Academies Press, 2020. https://www.nap.edu/catalog/25663/social-isolation-and-loneliness-in-older-adults-opportunities-for-the.

38. Vaughn-Sandler V, Sherman C, Aronsohn A, et al. Consequences of perceived stigma among patients with cirrhosis. Dig Dis Sci 2014;59:681-686.

39. Leppin AL, Gionfriddo MR, Kessler M, et al. Preventing 30-day hospital readmissions: A

systematic review and meta-analysis of randomized trials. JAMA Intern Med 2014;174:1095-1107.

40. Cancino RS, Culpepper L, Sadikova E, et al. Dose-response relationship between depressive symptoms and hospital readmission. J Hosp Med 2014;9:358-364.

41. Albrecht JS, Gruber-Baldini AL, Hirshon JM, et al. Depressive Symptoms and Hospital Readmission in Older Adults. J Am Geriatr Soc 2014;62:495-499.

42. Mellinger JL, Richardson CR, Mathur AK, et al. Variation among United States hospitals in inpatient mortality for cirrhosis. Clin Gastroenterol Hepatol 2015;13:577-584.

43. Morales BP, Planas R, Bartoli R, et al. Early hospital readmission in decompensated cirrhosis: Incidence, impact on mortality, and predictive factors. Dig Liver Dis 2017;49:903-909.

44. Mukthinuthalapati VVPK, Akinyeye S, Fricker ZP, et al. Early predictors of outcomes of hospitalization for cirrhosis and assessment of the impact of race and ethnicity at safety-net hospitals. PLoS One 2019;14:1-15.

Table 1. Electronically-available characteristics of the cohort and their associations with 30-day readmission

Characteristic	Value	HR (95% CI)	p-value
Age (years), mean (SD)	57.5 (10.6)	1.00 (0.99-1.01)	0.72
Male sex, %	54.7	1.12 (0.87-1.44)	0.38
White race, %	95.3	0.87 (0.50-1.52)	0.63
Insurance, %			
Private	29.2	Ref	
Medicare	41.3	0.99 (0.73-1.34)	0.93
Medicaid	27.4	1.10 (0.79-1.52)	0.58
Other	2.1	0.73 (0.27-1.99)	0.53
Charlson comorbidity index, median (IQR)	6 (5-8)	1.00 (0.94-1.05)	0.87
Admission in prior 30 days, %	35.3	1.41 (1.23-1.62)	<0.001
ED visits in prior 6 months, median (IQR)	0 (0-1)	1.06 (1.01-1.10)	0.01
Admission source, %			
Direct admission	17.3	Ref	
Via ED	45.3	1.38 (0.96-1.99)	0.08
Hospital transfer	37.5	1.08 (0.74-1.59)	0.69
Ascites, %	79.8	1.75 (1.22-2.50)	0.002
Hepatic encephalopathy, %	70.2	1.25 (0.94-1.67)	0.12
Hepatocellular carcinoma, %	9.3	1.00 (0.65-1.54)	0.98
Admission laboratories			
MELD, mean (SD)	18.9 (6.9)	1.03 (1.01-1.04)	0.005
Sodium (mmol/L), mean (SD)	133 (5.8)	0.98 (0.96-1.01)	0.14
Albumin (g/dL), mean (SD)	2.9 (0.6)	0.67 (0.54-0.83)	<0.001
Hemoglobin (g/dL), mean (SD)	10.1 (2.2)	0.93 (0.88-0.98)	0.01
Discharge laboratories			
MELD, mean (SD)	17.6 (6.3)	1.04 (1.02-1.05)	<0.001
Sodium (mmol/L), mean (SD)	135 (4.3)	0.98 (0.96-1.01)	0.22
Albumin (g/dL), mean (SD)	2.9 (0.6)	0.85 (0.68-1.06)	0.15
Hemoglobin (g/dL), mean (SD)	9.3 (1.7)	0.92 (0.85-0.99)	0.02
Discharge medications, median (IQR)	12 (8-16)	1.02 (1.00-1.04)	0.11
SBP prophylaxis, %	35.1	1.10 (0.85-1.43)	0.47
Diuretics, %	63.1	0.93 (0.72-1.21)	0.60
Lactulose, %	63.4	1.28 (0.98-1.68)	0.07
HE antibiotics, %	51.4	1.39 (1.08-1.80)	0.01

Abbreviations: CI, confidence interval; ED, emergency department; HR, hazard ratio; HE, hepatic encephalopathy; IQR, interquartile range; MELD, model for end-stage liver disease; SBP, spontaneous bacterial peritonitis; SD, standard deviation

Table 2. Clinically-available characteristics of the cohort and their associations with 30-day readmission

Characteristic	Value	HR (95% CI)	p-value
Married, %	54.3	0.84 (0.65-1.08)	0.16
Recent alcohol use, %	13.1	0.89 (0.60-1.31)	0.55
Cirrhosis etiology, %			
Alcohol	30.9	Ref	
Hepatitis C	13.0	0.87 (0.57-1.33)	0.52
Alcohol/Hepatitis C	7.8	0.76 (0.45-1.31)	0.33
NASH	32.3	1.01 (0.74-1.38)	0.96
Other	16.1	1.15 (0.79-1.67)	0.46
Child-Pugh score, mean (SD)	10 (2.2)	1.13 (1.07-1.20)	<0.001
Listed for liver transplant, %	8.0	1.29 (0.84-1.96)	0.24
Reason for admission, %			
Ascites/volume overload	20.5	Ref	
Hepatic encephalopathy	21.9	1.33 (0.91-1.95)	0.14
Gastrointestinal bleeding	15.7	1.13 (0.74-1.74)	0.57
AKI/electrolyte abnormality	11.5	1.25 (0.79-1.97)	0.34
Abdominal pain	17.9	1.14 (0.75-1.72)	0.54
Infection	7.2	0.65 (0.34-1.26)	0.20
Other	5.4	0.98 (0.52-1.85)	0.95
Discharge transportation, %			
Self/spouse	40.6	Ref	
Family/friend	41.7	1.23 (0.92-1.64)	0.17
Public	17.6	1.81 (1.29-2.54)	<0.001
Discharge to facility, %	16.1	1.68 (1.24-2.28)	<0.001

Abbreviations: AKI, acute kidney injury; CI, confidence interval; HR, hazard ratio; NASH, nonalcoholic steatohepatitis; SD, standard deviation

Table 3. Socioeconomic status, functional status, and quality of life and their associations with 30-day readmission

Characteristic	Value	HR (95% CI)	p-value
Socioeconomic Status			
Education (degree earned), %			
Less than high school	12.3	Ref	
High school or equivalent	57.6	1.04 (0.69-1.57)	0.84
Any college	30.1	1.08 (0.70-1.68)	0.72
Employment, %			
Employed	20.4	Ref	
Unemployed	50.6	1.20 (0.85-1.69)	0.30
Retired	29.0	0.93 (0.63-1.38)	0.73
Adults at home, median (IQR)	2 (2-2)	0.92 (0.78-1.10)	0.36
Adults with income, median (IQR)	2 (1-2)	0.86 (0.71-1.04)	0.13
Children at home, median (IQR)	0 (0-0)	0.81 (0.65-1.03)	0.08
>6 months' expenses saved, %	27.2	0.76 (0.55-1.06)	0.11
Functional Status			
Impaired basic ADLs, %	49.9	1.37 (1.07-1.77)	0.01
Impaired intermediate ADLs, %	73.4	1.15 (0.86-1.54)	0.35
Impaired mental health, %	41.6	1.22 (0.95-1.58)	0.12
Impaired social/role function, %	64.7	0.88 (0.47-1.65)	0.69
Impaired social activity, %	59.6	1.09 (0.84-1.41)	0.53
Impaired quality of interactions, %	34.4	1.04 (0.80-1.36)	0.76
Quality of Life			
Abdominal symptoms, mean (SD)	3.5 (1.4)	0.96 (0.88-1.05)	0.41
Fatigue, mean (SD)	2.8 (1.3)	0.96 (0.87-1.06)	0.44
Systemic symptoms, mean (SD)	3.8 (1.2)	0.98 (0.89-1.09)	0.73
Activity, mean (SD)	3.7 (1.3)	0.94 (0.86-1.03)	0.20
Emotional function, mean (SD)	4.5 (1.2)	1.07 (0.96-1.19)	0.24
Worry, mean (SD)	4.3 (1.4)	0.95 (0.87-1.04)	0.28
Overall, mean (SD)	3.8 (1.0)	0.97 (0.85-1.10)	0.62

Abbreviations: ADL, activity of daily living; CI, confidence interval; HR, hazard ratio; IQR, interquartile range; SD, standard deviation

Table 4. Multivariable models to predict 30-day readmission

	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)	Model 5 HR (95% CI)
Electronically-available					
Cerebrovascular disease	1.68 (0.97-2.91)	1.83 (1.05-3.17)	1.73 (0.95-3.15)	1.67 (0.92-3.04)	1.51 (0.82-2.78)
Cancer	0.57 (0.33-1.00)	0.59 (0.34-1.04)	0.54 (0.30-0.97)	0.53 (0.30-0.96)	0.55 (0.31-0.99)
Ascites	1.61 (1.10-2.35)	1.53 (1.04-2.27)	1.59 (1.05-2.40)	1.54 (1.02-2.32)	1.57 (1.04-2.36)
Admission in prior 30 days	1.87 (1.44-2.42)	1.86 (1.43-2.43)	1.94 (1.47-2.56)	1.96 (1.48-2.59)	1.96 (1.48-2.59)
Admission via ED	1.47 (1.14-1.91)	1.49 (1.15-1.95)	1.64 (1.24-2.16)	1.64 (1.24-2.16)	1.56 (1.18-2.06)
Admission albumin	0.71 (0.57-0.88)	0.70 (0.56-0.88)	0.67 (0.53-0.86)	0.69 (0.54-0.88)	0.70 (0.55-0.89)
Discharge MELD	1.02 (1.00-1.04)	1.02 (1.00-1.04)	1.02 (1.00-1.05)	1.02 (1.00-1.05)	1.03 (1.00-1.05)
Clinically-available					
Admission for infection		0.59 (0.32-1.10)	0.44 (0.21-0.89)	0.43 (0.21-0.87)	0.39 (0.19-0.81)
Discharge with public transportation		1.45 (1.06-1.99)	1.31 (0.94-1.84)	1.20 (0.85-1.71)	1.17 (0.82-1.68)
Socioeconomic Status					
Children at home			0.81 (0.64-1.04)	0.79 (0.61-1.02)	0.75 (0.58-0.97)
Functional Status					
Impaired basic ADLs				1.26 (0.94-1.68)	1.32 (0.97-1.81)
Quality of Life					
Activity (top quartile referent)					
Bottom quartile					1.57 (1.01-2.46)
Second quartile					1.21 (0.80-1.83)
Third quartile					1.34 (0.91-2.00)
Emotional function (top quartile referent)					
Bottom quartile					0.54 (0.35-0.85)
Second quartile					0.70 (0.47-1.06)
Third quartile					0.56 (0.38-0.84)
AUROC (30-day)					
Derivation	0.71 (0.67-0.75)	0.72 (0.68-0.77)	0.73 (0.68-0.77)	0.73 (0.69-0.77)	0.75 (0.71-0.79)
Validation	0.66 (0.61-0.70)	0.68 (0.63-0.72)	0.68 (0.64-0.73)	0.69 (0.64-0.73)	0.69 (0.65-0.74)

Model 1: electronically-available variables only; Model 2: Model 1 + clinically-available variables; Model 3: Model 2 + socioeconomic variables; Model 4: Model 3 + functional status variables; Model 5: Model 4 + quality of life variables

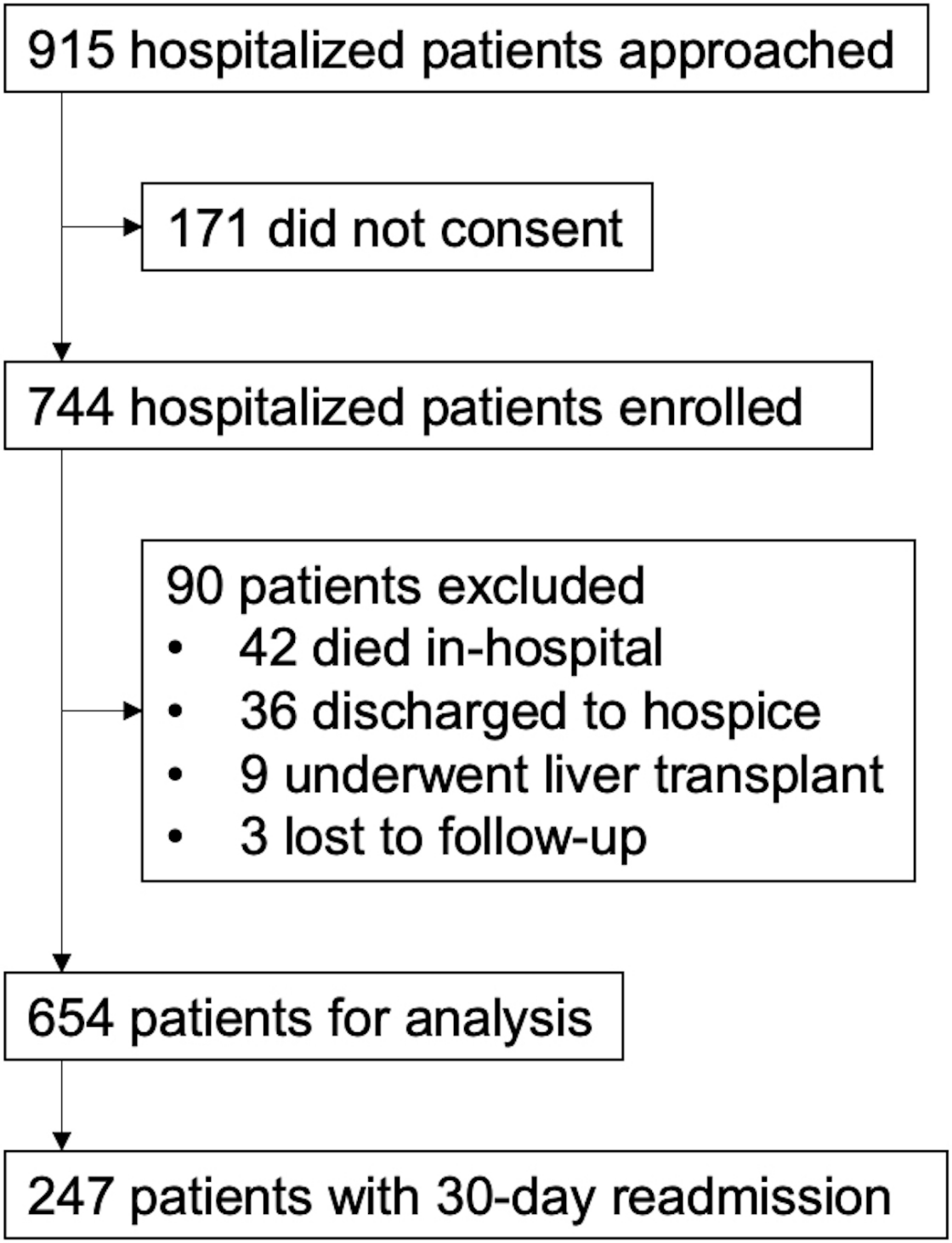
Abbreviations: ADL, activity of daily living; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; ED, emergency department; HR, hazard ratio; MELD, model for end-stage liver disease

Table 5. Comparison of readmission models based on the net reclassification index and integrated discrimination improvement

Reference	Comparator	NRI	p-value	IDI	p-value
Model 1	Model 2	0.198	0.02	0.015	0.87
	Model 3	0.264	0.003	0.020	0.85
	Model 4	0.228	0.01	0.023	0.85
	Model 5	0.236	0.007	0.036	0.83
Model 2	Model 3	0.095	0.28	0.005	0.93
	Model 4	0.218	0.01	0.008	0.92
	Model 5	0.181	0.04	0.021	0.88
Model 3	Model 4	0.160	0.07	0.003	0.96
	Model 5	0.135	0.13	0.016	0.90
Model 4	Model 5	0.167	0.06	0.013	0.91

Model 1: electronically-available variables only; Model 2: Model 1 + clinically-available variables; Model 3: Model 2 + socioeconomic variables; Model 4: Model 3 + functional status variables; Model 5: Model 4 + quality of life variables

Abbreviations: IDI; integrated discrimination improvement; NRI, net reclassification index


915 hospitalized patients approached
171 did not consent
744 hospitalized patients enrolled
90 patients excluded
• 42 died in-hospital
• 36 discharged to hospice
• 9 underwent liver transplant
• 3 lost to follow-up
654 patients for analysis
247 patients with 30-day readmission

What You Need to Know

Background:

Patients with cirrhosis have high rates of hospital readmission, but models to predict readmission are suboptimal and have not included important patient-reported outcome measures.

Findings:

Consideration of patient-reported outcome measures including functional status and quality of life may marginally improve the prediction of 30-day readmission. Poor social support and disability are associated with readmissions.

Implications for patient care:

Routine collection of patient-reported outcome measures may not add much value in predicting readmissions, but interventions to reduce readmission should address poor social support and patient disability.