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Incidence and Predictors of 30-Day Readmission Among Patients Hospitalized for Advanced Liver Disease

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Abstract

BACKGROUND & AIMS—The rate of readmission to the hospital 30 days after discharge (30-day readmission rate) is used as a quality measure for hospitalized patients, but it has not been studied adequately for patients with advanced liver disease. We investigated the incidence and factors that predict this rate and its relationship with mortality at 90 days.

METHODS—We analyzed data from patients with advanced liver disease who were hospitalized to an inpatient hepatology service at 2 large academic medical centers in 2008. Patients with elective admission and recipients of liver transplants were not included. During the study period, there were 447 patients and a total of 554 eligible admissions. Multivariate analyses were performed to identify variables associated with 30-day readmission and to examine its relationship with mortality at 90 days.

RESULTS—The 30-day readmission rate was 20%. After adjusting for multiple covariates, readmission within 30 days was associated independently with model for end-stage liver disease scores at discharge (odds ratio [OR], 1.06; 95% confidence interval [CI], 1.02–1.09; $P = .002$), the presence of diabetes (OR, 1.78; 95% CI, 1.07–2.95; $P = .027$), and male sex (OR, 1.73; 95% CI, 1.03–2.89; $P = .038$). After adjusting for age, sex, and model for end-stage liver disease score at discharge, the 90-day mortality rate was significantly higher among patients who were readmitted to the hospital within 30 days than those who were not (26.8% vs 9.8%; OR, 2.6; 95% CI, 1.36 – 5.02; $P = .004$).

CONCLUSIONS—Patients with advanced liver disease frequently are readmitted to the hospital within 30 days after discharge; these patients have a higher 90-day mortality rate than those who are not readmitted in 30 days. These data might be used to develop strategies to reduce early readmission of hospitalized patients with cirrhosis.

Keywords

Liver Disorders; Liver Cancer; Transplantation; Cirrhosis

Thirty-day hospital readmission rates frequently are used as a quality measure for hospitalized patients because readmissions have negative consequences on both patients and

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Conflicts of interest

The authors disclose no conflicts.

the health care system.¹⁻³ Patients suffer from hospital readmissions directly with either a recurrence of an initial illness or a complication from an initial hospital stay. In addition, an illness requiring readmission may provoke anxiety for patients and undermine their confidence in their providers and the medical system. Readmissions place a burden on the health care system in terms of cost and the need to duplicate much of the hospital care including initial assessments, repeat emergency room visits, and facility expenses.⁴ Certainly, all complications, relapses, and failures of outpatient care cannot be predicted and certain progressive disease states inevitably will lead to frequent hospital admissions. Presumably, however, a proportion of 30-day hospital readmissions could be prevented before discharge. Although there is an increasing awareness of the negative impact of early hospital readmissions, there is an increasing attention to reduce costs by shortening lengths of stay. To help clinicians with this dilemma, studies have attempted to identify risk factors for readmission before discharge among patients admitted for congestive heart failure, chronic obstructive pulmonary disease, and pneumonia; however, data in patients with cirrhosis is lacking.⁵⁻⁹

Patients with cirrhosis are emblematic of those with progressive disease states that may lead to frequent hospital readmission. The 30-day hospital readmission rate in patients with cirrhosis has not been well described. Planas et al,¹⁰ noted 1-year readmission rates of 74% and 45% for patients admitted for hepatic encephalopathy and ascites, respectively. In a study evaluating the benefits of a gastroenterology consult, Bini et al,¹¹ described 30-day readmission rates in a Veteran's Affairs population with cirrhosis of approximately 20%. In 2004, the estimated annual direct cost of liver disease in the United States was \$2.5 billion, with an additional \$10 billion of indirect costs.¹² With 1.2 million hospitalizations in 2004 related to liver disease, there are huge economic costs attributable to hospital admissions in patients with advanced liver disease. Therefore, there may be significant benefit in identifying risk factors that predict 30-day hospital readmission in patients with advanced liver disease.

We conducted a study to investigate the incidence and predictors of the 30-day readmission rate of hospitalized patients with advanced liver disease. We also examined the relationship between 30-day readmission and mortality at 90 days.

Methods

This retrospective study was conducted at Indiana University Hospital in Indianapolis, Indiana, and the University of Colorado Hospital (UCH) in Aurora, Colorado, after the approval of the respective Institutional Review Boards. Data were compiled, and statistical analysis was performed at Indiana University. Both hospitals serve as tertiary care referral centers with large, established hepatology practices and dedicated in-patient hepatology services. The hepatology service at UCH serves patients who are followed up in their hepatology clinics as well as patients who are undergoing evaluation for liver transplantation. The Indiana University hepatology service cares for a similar population, however, they also will admit patients with a primary liver-related diagnosis who are not followed up in clinic and are not undergoing transplant evaluation. Medical records were reviewed for all admissions to either hospital during 2008 that were discharged from the hepatology services. This allowed capturing of intensive care unit admissions that subsequently were transferred to the hepatology service during the same hospitalization. The medical records were reviewed for readmission to the same hospital within 30 days. Relevant demographic, clinical, and laboratory values were collected. Admissions were excluded if patients previously had undergone liver transplantation, left against medical advice, or died during the initial hospital stay. Admissions under observation status were not included. Readmissions within 30 days explicitly for transplantation surgery as well as

planned readmissions were excluded. Each admission was considered separately for patients with multiple admissions in 2008 as long as there were more than 30 days between hospitalizations.

Data collected regarding the initial hospital stay included demographic data, listing status for liver transplantation, alcohol use history, etiology of liver disease, presence of other adults in the home, Child–Pugh–Turcotte (CPT) score, history of hepatocellular carcinoma or a history of an extrahepatic cancer (EHC), etiology of cirrhosis, length of hospital stay, comorbid states, laboratory values (admission and discharge), presence of a dietician consultation, and reason for initial admission.

The etiology of cirrhosis was ascertained by chart diagnosis. Patients with hepatitis C virus and/or alcohol-related liver disease were grouped together, as were patients with nonalcoholic steatohepatitis (NASH) or cryptogenic liver disease. All other etiologies of liver disease, including cholestatic liver disease, hemochromatosis, autoimmune hepatitis, and acute hepatitis were condensed into a final group for analytic purposes.

The indication for the index admission was grouped into 5 categories as follows: hepatic encephalopathy (HE), volume overload or renal failure, infection including spontaneous bacterial peritonitis, portal hypertensive bleeding (gastropathy or variceal), and other diagnoses. For admissions with more than one of the earlier-described diagnoses, the primary reason for admission was established based on the following rules, which were determined a priori.¹⁰ For patients presenting with HE and renal failure, infection, or portal hypertensive bleed, HE was considered the secondary diagnosis. Similarly, admissions for portal hypertensive bleeding and infection were considered primarily related to the bleed. Volume overload (ascites, edema, or hydrothorax) was considered the primary reason for admission if this was the sole reason for admission and infection was not present.

Mortality within 90 days of discharge was analyzed for all patients who survived the initial hospital stay excluding those placed into hospice care at time of discharge. Because of the high long-term mortality rate for patients with decompensated cirrhosis, we chose to evaluate medium-term mortality at 90 days. Mortality data for patients admitted to Indiana University Hospital were ascertained by Indiana death records. Mortality data for patients admitted to UCH were determined by clinical records (92% of admissions with available vital status).

Descriptive statistics of patients' characteristics were calculated by readmission status to compare features of admissions with and without subsequent 30-day readmission. Univariate and multivariate analysis were used to evaluate the association between the readmission event and various patient characteristics collected at time of discharge. Multivariate logistic regression with generalized estimating equation models was used to allow analysis of data in patients with multiple admissions. Thirteen variables with a *P* value of less than .1 in the univariate logistic regression were selected for model building. Forward stepwise procedure was used to select the final multivariate model from the interested generic and discharge variables. Variables with an odds ratio larger than 1 are risk factors for readmission, whereas factors with an odds ratio less than 1 would be protective against readmission. Univariate and multivariate logistic regression models also were used to evaluate the association between 90-day mortality rate and readmission.

Results

There were 447 patients with a total of 554 admissions eligible for the analysis. Of these, there were 112 readmissions within 30 days, yielding a rate of 20%. The readmission rates were 20% at both centers. Selected patient characteristics for the index hospital admissions

are listed in Table 1. Forty-three percent were women, 83% were Caucasian, and their mean age was 53.6 ± 12.3 years. The mean model for end-stage liver disease (MELD) score was 18.6 ± 6.9 , and 30% of patients were listed for transplantation.

Univariate Analyses

Univariate comparisons of continuous and categorical variables between index admissions with and without 30-day readmission are shown in Tables 2 and 3. Among the categorical variables, sex, presence of other adults in the home, etiology of liver disease, indication for index admission, chronic kidney disease, diabetes mellitus, and alcohol history were associated with 30-day readmission (Table 2). Older age at admission had an association of borderline statistical significance with 30-day readmission ($P = .052$). Discharge MELD score as a categorical variable (≤ 15 , >15 to ≤ 20 , >20 to ≤ 30 , and >30) was associated with 30-day readmission rate and this relationship nearly approached statistical significance ($P = .05$) (Figure 1). No significant association existed with many other comorbidities or length of stay for the index hospitalization. Among continuous variables, discharge platelet count ($P = .007$), discharge MELD score ($P = .001$), and discharge creatinine level ($P = .02$) were associated univariately with 30-day readmission (Table 3). However, no statistically significant association with hospital readmission was seen with discharge absolute neutrophil count, white blood cell count, albumin level, bilirubin level, alanine aminotransaminase level, aspartate aminotransaminase level, alkaline phosphatase level, or CPT score (Table 3).

Multivariate Analyses

Eleven clinically relevant variables with P values less than .1 in the univariate logistic regression analyses were selected as candidates for the multivariate model building. These factors were discharge MELD score, discharge platelet count, discharge WBC count, age, sex, etiology of liver disease, alcohol history, living alone, history of diabetes mellitus, history of venous thrombosis, and indication for index hospitalization. Forward stepwise procedure with a cut-off P value of .15 was used to select the final multivariate logistic model. The results of the multivariate analyses are shown in Table 4. Discharge MELD score (odds ratio [OR], 1.06; 95% confidence interval [CI], 1.02–1.09; P value = .002), the presence of diabetes (OR, 1.78; 95% CI, 1.07–2.95; $P = .027$), and male sex (OR, 1.73; 95% CI, 1.03–2.89; $P = .038$) were associated independently with readmission within 30 days. For each unit increase in the discharge MELD score, the odds of readmission within 30 days increased by 6%. Subjects with diabetes had 78% higher odds of 30-day readmission compared with subjects without diabetes. Male patients had 73% higher odds of 30-day readmission compared with females.

Ninety-Day Mortality

After excluding patients placed in hospice care or who died during the index hospital stay, the 90-day mortality rate in patients with 30-day readmission was 26.8%, and was significantly higher than those without 30-day readmission (9.8%) (OR, 3.39; 95% CI, 2.03–5.66; $P < .001$). Older age and higher MELD scores also were associated with an increased risk of 90-day mortality (OR, 1.05; 95% CI, 1.02–1.07; $P < .001$; and OR, 1.08; 95% CI, 1.02–1.15; $P = .013$, respectively). Sex was not associated with 90-day mortality ($P = .53$). The results of the multivariate analysis for the 90-day mortality rate are presented in Table 5. After adjusting for age, sex, and discharge MELD score, patients with a 30-day readmission had significantly higher 90-day mortality (OR, 2.6; 95% CI, 1.36–5.02; $P = .004$). Age and discharge MELD score also were associated independently with an increased 90-day mortality (OR, 1.05; 95% CI, 1.02–1.08; $P < .001$; and OR, 1.08; 95% CI, 1.02–1.13; $P = .006$, respectively).

Discussion

This study was notable for several reasons. In a large cohort of patients with advanced liver disease we defined a 30-day readmission rate of 20%. Despite being a tertiary referral center, this is very similar to the overall rate described in a Veteran's Affairs population.¹¹ This speaks to the morbidity of liver disease and suggests that there is potential room for improvement. Our study describes independent predictors of 30-day hospital readmission, namely MELD score, sex, and diabetes. Finally, our results indicate high short-term mortality in patients readmitted within 30 days of discharge that cannot be attributed to MELD score and age alone.

In our population, the presence of diabetes carried a greater than 75% increased odds of readmission. Patients with diabetes have an increased risk of infections, a higher propensity toward renal impairment, and multiple other disease-related illnesses.^{13–16} Prior studies among patients with heart failure, cardiac surgery, general medicine, and intensive care also have found an increased risk of readmissions in diabetic patients.^{17–20} One may reasonably attribute the risk of readmission in diabetic patients to a composite effect of diabetes-related complications.

This study shows yet another predictive role of the MELD score.^{21–23} Incorporating function of 2 organs (renal and hepatic), the MELD score has been shown to be a robust predictor of multiple outcomes in patients with cirrhosis. In addition to improving the selection process for both transplant and non-transplant surgery, MELD has been used to gauge survival in cirrhotic patients with sepsis, variceal bleeding, fulminate hepatic failure, and alcoholic hepatitis.^{23–25} Admissions for which the patient's discharge MELD score was 15 or less had a 16% risk of readmission, compared with 21% when the discharge MELD score was 15 to 20 and 28% for a discharge MELD of 20 to 30. Interestingly, CPT score did not predict 30-day readmission.

Admissions for women were 42% less likely to be followed by a readmission within 30 days of discharge. Although this has been shown previously in some noncirrhotic populations, the source of the protective benefit is not clear.^{26,27} The difference is not explained with multiple clinical variables and may be explained by psychosocial differences in the manner women seek care and physicians provide care to women.

Several interesting findings on univariate analysis that did not maintain significance after multivariate analysis are worth noting. Admissions for patients with NASH/cryptogenic liver disease had the highest risk of 30-day readmission at 27.8% compared with admissions for patients with hepatitis C virus and alcohol-related liver disease with an 18.1% readmission rate ($P = .018$). We suspect this is related to the presence of comorbid states seen in NASH patients, principally diabetes. Admissions for HE or volume overload/renal failure were associated with readmission rates of 29% and 26%, respectively, compared with 14% for admissions for diagnoses unrelated to hepatic decompensation ($P = .004$ and $.006$, respectively). Anecdotally, we expect to see high rates of readmission for patients with difficult-to-control HE or volume status, although in multivariate analysis the MELD score appears to be a better predictor for readmission. The findings that ongoing alcohol use and living alone decreased the risk of readmission are interesting. We could hypothesize as to effects of various social environments, yet these factors did not prove prophetic after adjusting for other clinical variables.

Although the risk factors for 30-day readmission are either difficult to modify or not modifiable, they do allow for identification of patients who may benefit from medical intervention. Additional attention should be directed toward these patients in the form of careful discharge planning and closer follow-up evaluation. Recent data have shown that

changes in postdischarge care yield a positive impact on readmission rates in other conditions.^{6,28} In a similar fashion, interventions in discharge planning for patients with liver disease may best be directed toward those with diabetes and/or an increased MELD score.

Our study illustrates the high short-term mortality among hospitalized patients with liver disease with an overall 90-day mortality rate of 13%. This underlines the severity of illness in these patients and helps explain the high rate of readmissions. Moreover, the 90-day mortality for patients who were readmitted was 26.8% compared with 9.8% in those without readmission. In patients with advanced liver disease, a hospital readmission within 30 days serves as a poor prognosticator that should be considered in clinical practice. If these patients are being considered for liver transplantation, their evaluation should be expedited and closer follow-up evaluation may be warranted. Conversely, if a patient is not a transplant candidate, end-of-life discussions regarding palliative care options and goals of treatment should be discussed.

There were several limitations to our study that should be addressed. Our study carries the limitations of a retrospective study design including potential for misclassification and incomplete data. This may have affected our ability to appropriately categorize diagnoses; however, the majority of the variables studied were based on objective data such as laboratory data and demographics. Because we did not capture hospital records outside of the 2 hospitals studied, it is likely that some patients were readmitted within 30 days to another facility. Although a clear limitation, this probably accounts for a small percentage of the readmissions because patients with advanced liver disease tend to funnel into and stay at tertiary care centers. One would expect that patients with complicated medical histories would attempt centralized care at a familiar hospital. We accept that sicker patients with higher MELD scores preferentially may be readmitted to our tertiary care centers as opposed to less severely ill patients who may be less discriminating in their choice of hospitals.

In summary, this study identified a high rate of 30-day readmission in patients with advanced liver disease. The MELD score, diabetes, and male sex are independent predictors of readmission and our data are potentially useful to guide future interventions aimed at reducing 30-day hospital readmission. In addition, patients readmitted within 30 days have a very high risk of short-term mortality independent of MELD score. This highlights the poor prognosis in these patients and suggests that patient–physician discussions are in order to direct either very aggressive or palliative care.

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Abbreviations used in this paper

CI	confidence interval
CPT	Child–Pugh–Turcotte
HE	hepatic encephalopathy
MELD	Model for End-Stage Liver Disease
NASH	nonalcoholic steatohepatitis
OR	odds ratio

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Figure 1.

Thirty-day readmission rate (%) based on discharge MELD score categories: ≤15, >15 and ≤20, >20 and ≤30, and >30. The number of patients in each category is denoted in *parentheses*. The odds of 30-day readmission increased with each category of MELD score with a rate of 16%, 21%, 27%, and 29% for MELD scores of ≤15, >15 and ≤20, >20 and ≤30, and >30, respectively (overall $P = .05$).

Table 1

Selected Clinical Characteristics of the Study Cohort (n = 447)

Mean age ($\pm$ SD), y	53.6 $\pm$ 12.3
Female	43%
Caucasian	83%
On the transplant waiting list	23%
Mean admission MELD score ($\pm$ SD)	18.6 $\pm$ 6.9
Etiology of liver disease	
HCV or alcohol	49%
NASH or cryptogenic	20%
All others	31%
30-day readmission rate	20%

HCV, hepatitis C virus.

Table 2

Univariate Relationship Between Categorical Variables Obtained During Index Hospitalization and 30-Day Readmission

Variable	30-Day readmission rate, %	Odd ratio (95% CI)	P value	Overall P value
Etiology of liver disease				.044
HCV and/or ALD	18.2	1		
NASH or cryptogenic	29	1.9 (1.12–3.24)	.018	
Other etiologies	19.0	1.06 (0.63–1.78)	.834	
Male sex	23.4	1.6 (1.02–2.52)	.041	
Caucasian	20.1	0.98 (0.55–1.74)	.948	
Indication for admission				.013
HE	29	2.51 (1.34–4.72)	.004	
Volume overload or renal failure	26.5	2.33 (1.27–4.27)	.006	
Infections	18.8	1.41 (0.76–2.63)	.275	
Portal hypertensive bleed	15.4	1.12 (0.5–2.5)	.778	
Others	13.8	1		
Alcohol use				.037
No significant history	22	1		
Prior significant history	21.5	0.95 (0.59–1.51)	.824	
Ongoing alcohol use	9	0.35 (0.16–0.79)	.012	
Other adults in home				.002
Yes	24	1		
No	12	0.45 (0.24–0.85)	.014	
Unknown	8	0.27 (0.11–0.67)	.005	
MELD score at discharge				.050
≤15	16	0.47 (0.13–1.68)	.244	
>15 to ≤20	21.4	0.7 (0.19–2.5)	.580	
>20 to ≤30	27.9	0.98 (0.27–3.55)	.973	
>30	28.6	1		
Hepatocellular carcinoma				.692
No history	20	1		
Ablated or resected	30	1.6 (0.43–5.95)	.48	
Current	17	0.81 (0.34–1.94)	.643	
History of extrahepatic cancer	31	1.96 (0.87–4.42)	.102	
Prior TIPS placement	25	1.34 (0.76–3.35)	.316	
Diabetes	26	1.74 (1.12–2.7)	.013	
Chronic kidney disease	30	2.08 (1.2–3.34)	.003	
Coronary artery disease	20	0.92 (0.47–1.83)	.819	
Congestive heart failure	9	0.36 (0.09–1.46)	.155	
Arrhythmia	21	0.9 (0.28–2.85)	.857	
Hypertension	20.5	0.99 (0.62–1.59)	.981	
Psychiatric disorder	16	0.69 (0.4–1.19)	.184	

Variable	30-Day readmission rate, %	Odds ratio (95% CI)	P value	Overall P value
Cerebral vascular accident	12.5	0.54 (0.13–2.24)	.394	
Inflammatory bowel disease	14	0.6 (0.22–1.64)	.317	
Thyroid disease	27	1.57 (0.91–2.73)	.108	
Venous thromboembolism	40	2.58 (0.96–6.9)	.059	
COPD	16	0.72 (0.28–1.84)	.487	
Asthma	27	1.27 (0.28–5.82)	.755	

ALD, alcohol-related liver disease; COPD, chronic obstructive pulmonary disease; HCV, hepatitis C virus; TIPS, transjugular intrahepatic portosystemic shunt.

Table 3

Univariate Relationship Between Continuous Variables Obtained at Discharge From the Index Hospitalization and 30-Day Readmission

Variable	30-Day readmission, mean (SD)	No 30-day readmission, mean (SD)	Odds ratio (95% CI)	P value
Patient age, y	55.4 (11.5)	52.9 (12.3)	1.02 (1–1.04)	.052
Length of stay, d	5.8 (4.5)	5.9 (5.8)	1.00 (0.97–1.03)	.970
WBC, $\times 10^3$ per mm ³	5.4 (3.2)	6.1 (3.7)	0.94 (0.88–1.01)	.093
ANC, $\times 10^3$ per mm ³	4.0 (3.1)	4.2 (3.0)	0.99 (0.91–1.08)	.791
Platelets, $\times 10^3$ per mm ³	90.5 (62.6)	118.5 (91.0)	0.99 (0.99–1.00)	.007
INR	1.8 (0.5)	1.7 (0.6)	1.23 (0.87–1.74)	.247
Creatinine level, mg/dL	1.5 (1.5)	1.3 (1.1)	1.17 (1.03–1.34)	.019
Bilirubin level, mg/dL	5.7 (8.2)	4.5 (5.9)	1.03 (1.00–1.06)	.075
AST level, U/L	69.6 (103.7)	74.8 (127.1)	1.00 (1.00–1.00)	.691
ALT level, U/L	44.5 (73.5)	90.5 (263.9)	1.00 (1.00–1.00)	.073
Alkaline phosphatase level, U/L	135.8 (129.6)	137 (128.0)	1.00 (1.00–1.00)	.832
Albumin level, g/dL	2.8 (1.0)	2.9 (2.4)	0.99 (0.92–1.06)	.711
CPT score	9.1 (3.1)	8.5 (3.0)	1.07 (0.98–1.17)	.159
MELD score	20.4 (8.5)	17.8 (6.4)	1.06 (1.02–1.09)	.001

ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; INR, international normalized ratio for prothrombin time; WBC, white blood cell count.

Table 4

Significant Independent Predictors of 30-Day Hospital Readmission: Results of the Multivariate Analyses

Predictor	Odds ratio (95% CI)	P value
Discharge MELD score	1.06 (1.02–1.09)	.002
Presence of diabetes	1.78 (1.07–2.95)	.027
Male sex	1.73 (1.03–2.89)	.038

Table 5

Independent Predictors of 90-Day Mortality: Results of the Multivariate Analyses

Predictor	Odds ratio (95% CI)	P value
Age	1.05 (1.02–1.08)	<.001
Discharge MELD score	1.08 (1.02–1.13)	.006
30-day hospital readmission	2.61 (1.36–5.02)	.004
Male sex	1.71 (0.83–3.54)	.146