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Hospital Readmissions in Patients with Cirrhosis: A Systematic Review

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Abstract

BACKGROUND—Hospital readmission is a significant problem for patients with complex chronic illnesses such as liver cirrhosis.

PURPOSE—We aimed to describe the range of readmission risk in patients with cirrhosis and the impact of the model for end-stage liver disease (MELD) score.

DATA SOURCES—We conducted a systematic review of studies identified in Ovid MEDLINE, PubMed, EMBASE, CINAHL, the Cochrane Library, Scopus, Google Scholar, and ClinicalTrials.gov from 2000 to May 2017.

STUDY SELECTION—We examined studies that reported early readmissions (up to 90 days) in patients with cirrhosis. Studies were excluded if they did not examine the association between readmission and at least 1 variable or intervention.

DATA EXTRACTION—Two reviewers independently extracted data on study design, setting, population, interventions, comparisons, and detailed information on readmissions.

DATA SYNTHESIS—Of the 1363 records reviewed, 26 studies met the inclusion and exclusion criteria. Of these studies, 21 were retrospective, and there was significant variation in the inclusion and exclusion criteria. The pooled estimate of 30-day readmissions was 26% (95% confidence interval [CI], 22%–30%). Few studies examined readmission preventability or the relationship between readmissions and social determinants of health. Reasons for readmission were highly variable. An increased MELD score was associated with readmissions in most studies. Readmission was associated with increased mortality.

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CONCLUSION—Hospital readmissions frequently occur in patients with cirrhosis and are associated with liver disease severity. The impact of functional and social factors on readmissions is unclear.

Cirrhosis is a morbid condition characterized by complications such as ascites, gastrointestinal bleeding, and hepatic encephalopathy. These complications frequently require hospitalization, which is a substantial burden to the healthcare system. In 2012, liver disease was responsible for nearly 250,000 admissions across the United States, costing $3 billion.[1] Despite this substantial resource utilization, outcomes remain poor, with an inpatient mortality of 6%. For those that survive, many experience hospital readmission.

More generally, early readmission reflects poor quality of care in the US. In 2004, 30-day readmissions occurred in nearly 20% of Medicare beneficiaries and costed over $17 billion.[2] In response to this problem, the Affordable Care Act established the Hospital Readmissions Reduction Program (HRRP), which reduces Centers for Medicare & Medicaid Services (CMS) payments to hospitals with excess 30-day readmissions for high-risk conditions, including pneumonia and heart failure.[3] Heart failure, in particular, has been the subject of numerous studies detailing risk factors and interventions to predict and prevent readmission. [4–6] Based on this extensive evidence, guidelines recommend disease management programs to reduce readmissions in this population.[7] In contrast, readmission in the cirrhosis population has received limited attention.

We therefore conducted a systematic review aiming to examine the range of readmission risk noted in the literature, with a focus on the model for end-stage liver disease (MELD) score as a risk factor for readmission.

METHODS

Search Strategy

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for conducting and reporting systematic reviews.[8] A literature search was performed by a medical librarian using the following databases: Ovid MEDLINE, PubMed, EMBASE, CINAHL, the full Cochrane Library, Scopus, Google Scholar, and ClinicalTrials.gov. All the databases were searched from 2000 to May 2017. We did not include older reports because the review focused on contemporary care; earlier studies may not reflect current cirrhosis management. To ensure literature saturation, included articles' reference lists were reviewed.

Search strategies were developed by combining database-specific subject headings and keywords for readmissions with those for cirrhosis or its complications (Supplementary Material). Google Scholar and ClinicalTrials.gov were searched using keywords only. All results were limited to the English language and those published in 2000 or later, but no other limits were applied.

Identified records were reviewed based on strict criteria. We excluded case reports, case series, reviews, editorials, letters, and meeting abstracts without final peer-reviewed publication. We also excluded studies of pediatric populations (age < 18 years), patients

without cirrhosis, and patients with liver transplants. We excluded studies in which patients were not hospitalized at study onset and those where the index admission was for an elective procedure. Because our interest was to identify factors associated with early readmission, we excluded studies that did not report readmissions within 90 days or those with a mean or median follow-up of less than 30 days. We also excluded studies that did not examine the association between readmission and at least 1 independent variable or intervention. Duplicate reports of a common sample were excluded unless the duplicate provided additional information, and such reports were examined together in our synthesis.

Two authors identified potentially eligible records by independently screening titles and abstracts. At this stage, records that did not meet the eligibility criteria were excluded, and the reasons for exclusion were not recorded. Records with disagreement were retained for full-text review. After this initial exclusion of records, the remaining full-text records were reviewed independently. For this full-text review, we recorded exclusion reasons and disagreements were resolved through discussion.

Data Collection

Data were abstracted from each study by 2 authors independently and recorded in a REDCap database.[9] Discrepancies were resolved through discussion. We recorded study characteristics, including study design, setting, population (including the inclusion/exclusion criteria, sample size, and patient and hospitalization characteristics), interventions, and comparisons. To facilitate comparisons across studies, we employed validated methods to approximate means and standard deviations (SD).[10] We recorded detailed information on outcomes including readmissions, preventability, independent variables, and mortality. Studies that focused on a single independent factor or intervention were classified as "focused," while those that examined multiple factors were classified as "broad." We used the Newcastle–Ottawa Scale to assess the risk of bias in each study.[11] This instrument uses a 9-point scale to gauge methodological quality based on selection, group comparability, and exposure/outcome assessment.

Statistical Analysis

Analyses were performed using Stata 13.1 (StataCorp LP, College Station, Texas). We determined the pooled proportion of patients with 30-day readmission using a random-effects model, with the Freeman–Tukey double-arcsine transformation for meta-analysis of proportions.[12] We investigated the heterogeneity by stratifying analyses according to prespecified study characteristics, including "broad" versus "focused." However, the readmission risk was not different in the stratified analysis; therefore, we chose to pool the findings. For point estimates, 95% confidence intervals (CIs) were calculated, and a P-value < .05 was considered statistically significant.

RESULTS

Search Results

The initial search yielded 1363 records, of which 173 full-text articles were assessed for eligibility. Twenty-seven articles representing 26 studies of 180,049 patients were included (Figure 1).[13–39]

Study Characteristics

Two studies were performed in Australia, 4 in Europe, and the remainder in North America. Twenty one of the 26 studies were retrospective cohort studies (Table 1). Twenty studies were single-center studies (of which half were performed at transplant centers), and 4 of the 6 multicenter studies were based on administrative data with large samples (173,254 patients). The inclusion/exclusion criteria varied widely (Supplementary Material). Some studies only included patients admitted for specific cirrhosis complications, while others included those admitted for any reason. Two studies excluded patients admitted in the prior 30 days, and 6 excluded patients discharged to hospice. The mean risk of bias score was 7.5 (SD 1.3) out of a possible 9 points, with most lacking an adequate description of follow-up and several lacking adjustment for confounders.

The mean age of patients ranged from 53 to 65 years, and males comprised 56%–78% (except for 4 Veterans Affairs studies). The mean MELD score ranged from 12 to 23. Hepatitis C accounted for 14%–100% of cirrhosis, alcohol accounted for 25%–67%, and nonalcoholic fatty liver disease accounted for 0%–20%. Hepatocellular carcinoma was present in 6%–30% of the patients. Reasons for the index admission varied widely and were dependent on the inclusion/exclusion criteria.

Outcomes

Thirty-day readmissions ranged from 10% to 50%, with a pooled estimate of 26% (95% CI, 22%–30%; Figure 2). Five studies reported 90-day readmissions, ranging from 21% to 71%. [29,31,33,35,36] Only 4 of the 20 single-center studies captured readmissions at centers aside from the index admission hospital. Two studies assessed readmission preventability: 1 through independent chart review by 2 physicians (22% preventable), the other based on the judgement of 1 physician (37%).[16,26] Reasons for readmission were reported in 12 studies and were highly variable: hepatic encephalopathy in 6%–100%, ascites/volume overload in 2%–38%, and decompensated liver disease (without further elaboration) in 25%–100%. The studies that focused on single risk factors or interventions reported a wide range of possible readmission risk factors, ranging from biomarkers to clinical processes of care. Although multiple putative risk factors were reported, few conclusions can be drawn due to the heterogeneity in the findings. In 5 studies, 90-day mortality was reported and ranged from 10.3% to 18.6%. The relationship between readmission and subsequent mortality was examined in 5 studies, and all were statistically significant.[14,16,20,33,38]

Readmission and MELD

The MELD score was examined in numerous studies as a risk factor for readmissions and was found to be significantly associated with readmission in most studies (Table 2). Notably,

even small differences in the MELD score are associated with a higher risk for readmission, though no cutoff point can be discerned. In addition, this association is seen regardless whether the MELD score is assessed at index admission or discharge. Several studies did not report the absolute differences in the MELD score listed in Table 2, but did find associations between increased MELD score and readmission in adjusted models.[16,20,27,34] One study found that a higher MELD score was associated with decreased readmissions over 6 months, but this study did not account for the competing risk of death.[37]

DISCUSSION

Hospital readmission is a costly and common problem in the US.[2] In addition to the negative impact that readmissions have on patients' lives,[40] readmissions are increasingly being used to measure quality. Unplanned 30-day readmissions are posted publicly, and excess readmissions for high-risk conditions are penalized through HRRP.[3] Although HRRP does not currently include cirrhosis, the program has expanded to include several conditions that were not included in the initial iteration. Whether cirrhosis will be included in future iterations remains to be seen; however, increasing scrutiny is likely to continue. Of specific populations at risk, patients with cirrhosis are particularly vulnerable due to several features. Ascites management often requires hospitalization due to diuretic titration and poor access to paracentesis, and hepatic encephalopathy treatment requires complex lactulose titration.[16] Other features of cirrhosis, such as gastrointestinal bleeding, infections, and renal failure, also place patients at risk of poor outcomes. The resulting readmission burden is high, with a pooled 30-day readmission rate of 26%. Other associated outcomes are also poor, with a consistent relationship between readmission and subsequent mortality.

We found striking heterogeneity in various aspects. First, the inclusion/exclusion criteria varied widely, both cirrhosis-specific (eg, spontaneous bacterial peritonitis) and more general (patients admitted within the prior 30 days). Some of these criteria may bias readmission estimates; the risk of readmission may be reduced in those on hospice, as patients forgo curative therapy. Additionally, an established risk factor for readmission is prior hospitalization[41]; excluding patients with prior admissions prohibits analysis of this variable. Another aspect is the capture of readmissions: readmissions outside of the index hospital were not included in most studies. In those that did include outside readmissions, the burden was sizeable: 17% in 1 single-center study and 23% in a multistate administrative database.[16,36] These outside readmissions must be included in future studies; they are as important as same-center readmissions both to patients and CMS.[3] Despite this heterogeneity, the studies scored relatively high on the Newcastle–Ottawa risk of bias scale, with the only common deficiency being an inadequate description of follow-up.

Building on the findings of this review, an important step will be the design of interventions to reduce readmissions. Such interventions require a full understanding of this population's characteristics and needs. Critically, we found a lack of data on social determinants of health. Impairments in these factors are well-established contributors to readmission risk in other populations,[4,40] and are highly prevalent in cirrhosis.[42] Indeed, CMS has focused resources toward social determinants of health in the effort to reduce utilization and improve outcomes. This lack of data on social determinants of health, as well as other understudied

factors, represents an important opportunity for future research efforts to better define the modifiable features that could be targeted in the future to prevent readmissions. Such research is urgently needed and will likely require prospective studies to gather these important factors. Notably, most studies in this systematic review were retrospective and therefore unable to examine many of these understudied factors. Another important aspect that has received little attention is readmission preventability: only 2 studies assessed preventability, both through unstructured chart review. Preventability assessments in noncirrhotic populations have used wide-ranging methodologies, yielding inconsistent results.[43] This variability prompted recommendations that preventability should be assessed by multiple reviewers guided by explicit parameters.[43] Such detailed attention to preventability is urgently needed to better inform interventions.

In contrast to the lack of data on social factors, we found that the MELD score was examined in most studies and was frequently associated with readmission. Despite this consistent association, differences in the MELD scores between studies limit inferences into specific cutoff values that could identify the highest risk patients. Because of its existing widespread clinical use, the MELD score may prove to be important in readmission risk stratification. Efforts to develop a useful model including the MELD score are needed to target interventions to the highest risk patients.

This review has several limitations. Although we used a broad search strategy to capture studies, some may not have been included due to our selection criteria. For instance, 1 retrospective paper described factors associated with high admission density during 1 year but did not specifically report the frequency of early readmissions.[44] Similarly, a randomized trial of a disease management program did not specifically examine early readmissions.[45] Another quasi-experimental study of a quality improvement initiative was not included because a large proportion of their subjects was post liver transplant.[46] However, the inclusion of these papers is unlikely to change our conclusions; the retrospective study identified factors similar to those in the included studies, and the quasi-experimental study overlapped with the included study that assessed frailty.[27] Another potential limitation is the exclusion of studies published in abstract form only. Such studies may be important, as the field of cirrhosis readmissions is relatively young. However, including only full-paper publications ensures the inclusion of only higher quality studies scrutinized during the peer-review process. Similarly, newer published studies may have been missed due to the abundant interest in this topic and ongoing research. Lastly, the significant heterogeneity of the studies limits conclusions that can be made regarding the pooled readmission rates.

In summary, we found that patients with cirrhosis experience a high incidence of hospital readmissions. Several processes of care may be associated with readmissions, suggesting room for improvement in caring for this population and reducing readmissions. However, we identified several gaps in the literature, which does not adequately describe social factors and is lacking details on readmission preventability assessment. Future studies should attempt to address these issues so that interventions can be targeted to the highest risk patients and designed to best meet the needs of patients with cirrhosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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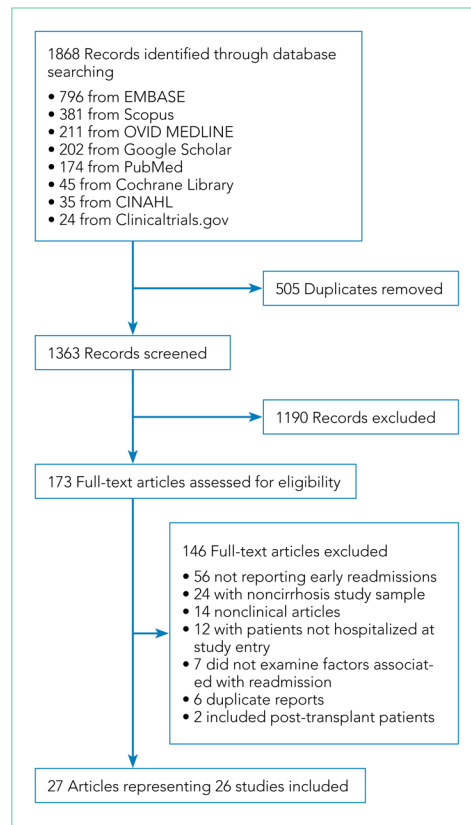
FIG 1.
Study flow.
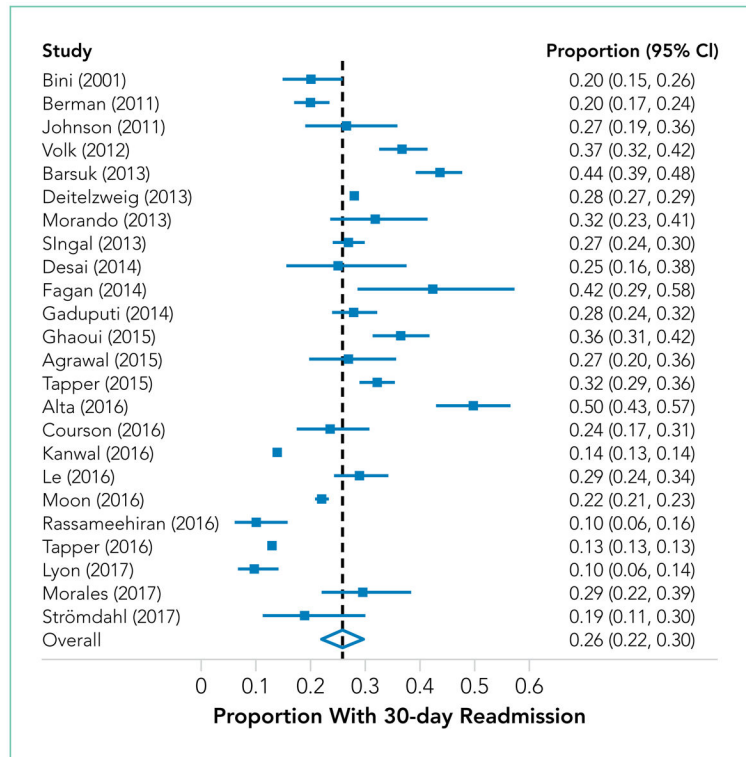
FIG 2.
Forest plot of the proportion of patients with cirrhosis with a 30-day hospital readmission.

TABLE 1

Study Characteristics

Study	Study Design	Sample Size	Age (mean)	Males (%)	MELD (mean)	30-day Readmissions, 95% CI (%)
Bini 2001[13]	Prospective cohort	197	57	97	NR	20 (15–26)
Berman 2011[14]	Retrospective cohort	554	54	57	19	20 (17–24)
Johnson 2011[15]	Quasi-experimental	99	54	67	NR	27 (19–36)
Volk 2012[16]	Retrospective cohort	402	54	57	19	37 (32–42)
Barsuk 2013[17]	Retrospective cohort	502	57	60	23	44 (39–48)
Deitelzweig 2013[18]	Retrospective cohort	21,864	55	64	NR	28 (27–29)
Morando 2013[19]	Quasi-experimental	100	60	58	16	32 (23–41)
Singal 2013[20]	Retrospective cohort	836	53	68	15	27 (24–30)
Desai 2014[21]	Quasi-experimental	56	57	63	22	25 (16–38)
Fagan 2014[22]	Retrospective cohort	41	54	78	17	42 (29–58)
Gaduputi 2014[23]	Retrospective cohort	447	60	66	12	28 (24–32)
Ghaoui 2014/2015[24, 25]	Quasi-experimental	303	54	60	16	36 (31–42)
Agrawal 2015[26]	Retrospective cohort	111	59	98	14	27 (20–36)
Tapper 2015[27]	Retrospective cohort	734	57	62	18	32 (29–36)
Atla 2016[28]	Retrospective cohort	189	54	69	12	50 (43–57)
Bajaj 2016[29]	Prospective cohort	1013	57	64	18	NR
Courson 2016[30]	Retrospective cohort	149	59	60	20	24 (17–31)
Graupera 2016[31]	Prospective cohort	218	60	65	16	NR
Kanwal 2016[32]	Retrospective cohort	25,217	62	97	NR	14 (13–14)
Le 2016[33]	Retrospective cohort	302	57	69	15	29 (24–34)
Moon 2016[34]	Retrospective cohort	6451	61	97	12	22 (21–23)
Rassameehiran 2016[35]	Retrospective cohort	140	56	62	18	10 (6–16)
Tapper 2016[36]	Retrospective cohort	119,722	61	56	NR	13 (13–13)
Lyon 2017[37]	Retrospective cohort	226	57	62	21	10 (6–14)
Morales 2017[38]	Retrospective cohort	112	65	57	15	30 (22–39)

Study	Study Design	Sample Size	Age (mean)	Males (%)	MELD (mean)	30-day Readmissions, 95% CI (%)
Strömdahl 2017[39]	Retrospective cohort	64	58	74	NR	19 (11–30)

Abbreviations: CI, confidence index; MELD, Model for End-Stage Liver Disease; NR, not reported.

TABLE 2

Comparison of MELD Scores According to Readmission Status

Study	Outcome	Index Admission MELD Score			Index Discharge MELD sScore		
		Not Readmitted	Readmitted	*P* Value	Not Readmitted	Readmitted	*P* Value
Berman 2011[14]	30-day readmission	NR	NR		17.8 (6.4)	20.4 (8.5)	.001
Fagan 2014[22]	30-day readmission	14.5 (6.0)	18.9 (7.7)	.03	NR	NR	
Agrawal 2015[26]	30-day readmission	NR	NR		13.4 (4.5)	14.8 (4.6)	NS
Atla 2016[28]	30-day readmission	9.8 (3.2)	13.1 (6.7)	.001	NR	NR	
Bajaj 2016[29]	90-day readmission	17.2 (6.6)	19.0 (6.6)	.0001	16.3 (6.6)	18.7 (6.5)	.0001
Graupera 2016[31]	90-day readmission	15 (7)	18 (7)	.003	NR	NR	
Rassameehiran 2016[35]	90-day readmission	16.7 (7.0)	17.8 (6.4)	.41	NR	NR	
Morales 2017[38],[a]	30-day readmission	NR	NR		13.8 (4.6)	16.9 (5.0)	.002

[a] The study by Morales et al. examined the discharge MELD-sodium score in relation to 30-day readmission.

NR; not reported.