Vaz Karl (Orcid ID: 0000-0002-6427-6140)

Rate of early hospital readmission amongst cirrhotic patients is high in Australia: experience from a single liver transplant centre

Karl Vaz[1] (Gastroenterologist)
Katrina Tan[1] (House Medical Officer)
Melissa Chew[1] (House Medical Officer)
Jordan Crawford[1] (House Medical Officer)
Ronald Ma[2] (Clinical Costing Analyst)
Josephine Grace[1,3] (Director of Gastroenterology)
Paul Gow[1,3] (Deputy Director of Gastroenterology)
Marie Sinclair[1,3] (Gastroenterologist)
Adam Testro[1,3] (Gastroenterologist)

Affiliations

[1]Victorian Liver Transplant Unit, Austin Health, Heidelberg, Victoria, Australia

[2]Clinical Costing, Austin Health, Heidelberg, Victoria, Australia

[3]The University of Melbourne, Parkville, Victoria, Australia

Corresponding Author

Dr Karl Vaz, Victorian Liver Transplant Unit, Austin Health, 145 Studley Rd, Heidelberg, Victoria 3084, Australia. Email – karl.vaz@austin.org.au; Phone – +61 3 9496 2000

Short Title

30-day cirrhotic readmission in Australia.

Acknowledgments

There are no relevant acknowledgments.

Data Availability

Request for unidentified data may be made to the corresponding author and subject to approval by the corresponding author.

Consent to Publish (Ethics)

This study was approved by the Austin Health Ethics Committee (project 20/63).

Author Contribution

KV, JG, PG, MS and AT conceived the study plan. KV, KT, MC, JC and RM were involved in data collection. KV and RM undertook data analysis. KV drafted the manuscript and all authors contributed to editing the manuscript and approve the final version.

Conflict of Interest

The authors declare there are no conflicts of interest.

Funding

This research project received no funding.

Abstract

Background and Aims: The 30-day hospital readmission rate in cirrhotic patients has been demonstrated to be up to 40% in international studies, but is not well studied in Australia. The aim of this study was to report on the rate and cause of 30-day hospital readmission from a single liver-transplant referral centre, including a cost analysis of readmissions.

Methods: Retrospective study of consecutive cirrhotic patients admitted to a liver transplant centre in Victoria, Australia between 1st January 2019 and 31st December 2019. Cases were identified through International Classification of Diseases version 10 coding for cirrhosis and its complications. Baseline demographic data, liver-related complications and unrelated extra-hepatic comorbidities, laboratory values, and prognostic scores were collected from the electronic medical record.

Results: 179 patients (63% male, median age at index admission 59 years old) who were admitted a total of 427 times during the study period were included in the final analysis. 30-day hospital readmission rate was 46%, with the majority of readmissions due to fluid overload (29%), miscellaneous reasons (27%) and infection (20%). One-fifth of readmissions were considered preventable. History of variceal haemorrhage was found to be an independent predictor of 30-day hospital readmission. Annual cost of readmission is over 2.7 million dollars and median cost of hospital readmission was about $9,000.

Conclusions: The 30-day hospital readmission rate of 46% is higher than previously reported and almost half due to either fluid overload or infection.

Key Words

Cirrhosis, hospital readmission, cost analysis, preventable readmission.

Word Count

Abstract – 234

Manuscript – 2900

Introduction

The transition from compensated to decompensated cirrhosis is an important landmark in the natural history of the disease as it is associated with increased mortality [1]. It heralds a phase of disease that leads to greater healthcare utilisation and expenditure [2], with decompensated patients more likely to be symptomatic, particularly from fluid overload, encephalopathy, gastrointestinal (GI) bleeding, and infection.

Literature primarily stemming from North American cohorts report 30-day readmission rates of up to 40% [3-5]. Hepatic encephalopathy (HE) and metabolic derangements have been demonstrated to be the leading causes of readmission [6], and predictors of readmission include Model for End Stage Liver Disease (MELD) score, number of cirrhotic complications and extrahepatic comorbidities, and polypharmacy [3-6].

Hospitalisation rates for cirrhosis are increasing in Australia [7] and abroad [8] and are expected to rise further with the ballooning prevalence of non-alcoholic fatty liver disease (NAFLD). Furthermore, the COVID-19 pandemic highlighted the importance of reducing unnecessary admissions, as a premium was placed on vacant hospital beds. To date, the burden of unanticipated early hospital readmissions in a cirrhotic population in Australia remains largely unknown.

We aimed to report on the rate of 30-day hospital readmission, to examine the principal causes of readmissions, and identify factors predicting readmission in a single liver-transplant centre in Australia. We also sought to estimate the direct cost of hospital readmission in cirrhotic patients.

Methods

Study Population

Consecutive adult patients with cirrhosis as per standard clinical, radiologic and/or histologic definition admitted to a single liver transplant centre in Victoria, Australia between 1st January 2019 and 31st December 2019 were considered for inclusion into the study. The primary catchment for this health service is 343,000 people covering three local government areas, whilst the state-wide service of the liver transplant unit has a catchment of 6 million people in Victoria, southern New South Wales and Tasmania. Admissions were identified according to International Classification of Diseases (ICD)-10 coding for liver cirrhosis and its complications (portal hypertension, hepatorenal syndrome, variceal bleeding, hepatocellular carcinoma, ascites, and hepatic encephalopathy) (Supplementary Table 1). Patients who were readmitted in January 2019 with a preceding index admission in the 30 days prior in December 2018, and patients admitted in December 2019 with a readmission in the following 30 days in January 2020 were included in order to capture all admissions in 2019. Patients with multiple single admissions or multiple readmissions were only counted once in the analysis.

Only unanticipated hospitalisations referred from the emergency department, outpatient clinic, or transfer directly from another hospital were included. Elective admissions and

admissions resulting in discharge to another hospital, palliative care ward or hospice, or resulting in liver transplantation or death were excluded.

Data Collection

Retrospective review of electronic medical records was undertaken for patients meeting the inclusion and exclusion criteria and, for all admissions, data was collected on patient demographics, comorbidities (composite score per the Charlson Comorbidity Index [CCI] [9]), cause of liver disease, liver transplant waitlist status, prior complications of liver disease (ascites, acute kidney injury [AKI] and/or hepatorenal syndrome [HRS], HE, variceal haemorrhage [VH], hepatocellular carcinoma), principal reason for admission, hospital length of stay, discharge medications, discharge summary completion within 48 hours of discharge, discharge biochemistry, admission and discharge liver prognostic scores, and 90-day mortality. Furthermore, patients readmitted within 30-days of discharge had additional information collected on principal reason for readmission, time to readmission, and hospital length of stay.

Principal diagnosis was dichotomized as liver-related and not liver-related, or categorized as fluid overload (ascites, hepatic hydrothorax and/or peripheral oedema), AKI-HRS, infection, GI bleeding, HE, and miscellaneous (all other diagnoses). Readmissions were considered potentially preventable by a single gastroenterologist if deemed physician-directed pharmacological or non-pharmacological management (eg. Diuretic titration, elective paracentesis) could have avoided the need for readmission.

Healthcare cost analysis was conducted by a single clinical costing analyst and expressed in Australian dollars.

Statistical Analysis

Data is expressed as median with interquartile range (IQR) or number (%) as it followed non-Gaussian distribution after normality testing. Mann-Whitney-U and Fisher's exact tests were used for continuous and categorical variables, respectively, comparing those readmitted versus those not readmitted within 30-days of index admission. Kruskal-Wallis test was used to compare cost between groups. Univariate and multivariate logistic regression analyses were used to assess predictors of readmission. Those variables with a p-value <0.10 on univariate analysis were included in the multivariate model, along with age and gender. Two-sided p-value <0.05 was considered significant. Statistical analysis was conducted using GraphPad Prism 9 version 9.2.0 (San Diego, California, USA).

This study was approved by the Austin Health Ethics Committee (project 20/63).

Results

Patient Baseline Demographics

In total, 694 admissions were identified during the study period, with 427 meeting the inclusion and exclusion criteria (Figure 1.). These occurred in 179 patients, with 82 (46%) readmitted within 30-days of index admission ('readmitted' group) and 97 (54%) in the 'not readmitted' group. All subsequent results pertain to these dichotomized groups.

The majority of patients were male (n=113, 63%) with median age 59 years old (IQR 48 – 65) at index admission. Most common aetiology was alcohol-related liver disease

(n=76, 42%), with fewer with NAFLD (n=27, 15%), viral hepatitis (n=24, 13%; hepatitis C virus [HCV] n=16, hepatitis B virus [HBV] n=8) or coexistent alcohol-related liver disease and viral hepatitis (n=20, 11%; HCV n=18, HBV n=2) (Table 1.).

Over three-quarters were principally admitted for liver-related reasons (Figure 2.) with a significant difference between the 'readmitted' and 'not readmitted' groups (84% vs 71%, p=0.049). Foremost indications for index admission were miscellaneous (n=58, 32%; Supplementary Table 2.), followed by HE, infection and fluid overload (each n=31, 17%) (Figure 2.). A greater proportion of NAFLD patients were admitted for non-liver related reasons compared to other aetiologies, however, this was not statistically significant (33% vs 21%, p=0.21).

Readmission

Median time to readmission was 11 days (IQR 5 – 18) and median readmission hospital length of stay was 5 days (IQR 3 – 9). Principal reason for readmission was most commonly for fluid overload (n=24, 29%), followed by miscellaneous reasons (n=22, 27%; Supplementary Table 3.) and infection (n=16, 20%) (Figure 3.). SBP accounted for 44% (n=7) of infections.

One-fifth (n=16) of readmissions were adjudicated to be potentially preventable. In those primarily readmitted for ascites (n=23, 28%), 12 (52%) were potentially preventable as outpatient arrangements for paracentesis were not made upon discharge. In those not potentially preventable (n=11, 48%), this was due to timely arrangements for early paracentesis or outpatient clinic being scheduled pre-discharge (n=6), ascites not being an active issue during index admission (n=4), and non-adherence with

scheduled follow-up (n=1). Two of the seven (29%) patients re-admitted with SBP were potentially preventable as they had not been discharged on SBP prophylaxis at index admission, with three of the remaining patients already on prophylaxis at the time of readmission, and two not meeting accepted guidelines for primary prophylaxis [10-11]. The final two potentially preventable readmissions were in patients who were readmitted with GI bleeding and had not been scheduled for repeat gastroscopy within the intended timeframe upon discharge from index admission. No readmission for HE was adjudicated as potentially preventable, given patients were already on prophylactic therapy (n=7) or were readmitted with an index episode of overt HE (n=2).

Factors Associated with 30-day Hospital Readmission

Demographic details, admission and discharge characteristics, liver-related complications and prognostic scores, and comorbidities separated according to incidence of 30-day readmission are demonstrated in Table 1.

A greater proportion in the 'readmitted' group had a history of ascites (83% vs 60%, p <0.01), VH (28% vs 12%, p=0.01) and hyponatremia (56% vs 35%, p <0.01), despite no differences in admission prognostic scores or in proportion waitlisted for liver transplantation (Table 1.). Cumulative comorbid illness was the same between the groups (CCI 5, p=0.42), as was index hospital length of stay (5 days, p=0.77).

There was no between-group statistical difference for principal reason for index admission (data not shown). Subjects in the 'readmitted' group had higher discharge prognostic scores at index admission (MELD score 17 vs 14, p <0.01; Child-Pugh score 9 vs 8, p <0.01), were discharged on a greater number of medications (9 vs 8, p <0.01),

and had a greater proportion discharged on SBP prophylaxis (41% vs 17%, p <0.01). Ninety-day mortality rate was higher in the 'readmitted' group (9.8% vs 6.2%) but was not statistically significant (p=0.41).

The only significant difference in the aetiology of liver disease between the 'readmitted' and 'not readmitted' groups was a greater proportion of patients with coexistent alcohol-related liver disease and viral hepatitis in the latter (4.9% vs 16%, p=0.02; Table 1.).

On univariate logistic regression analysis, number of previous cirrhotic complications at the time of index admission; history of ascites, HE, VH, and hyponatremia; number of discharge medications, discharge on SBP prophylaxis and discharge on lactulose; and admission and discharge Child-Pugh score, and discharge MELD score were identified as factors associated with 30-day readmission to hospital (Table 2.). Only a history of VH (odds ratio [OR] 3.08, 95% confidence interval [CI] 1.08 – 9.28, p=0.04) remained significant on the multivariate model (Table 2.).

Cost Analysis

The median cost of index admission was $10,266 (IQR 6,082 – 18,301) for the 'readmitted' group and $10,045 (IQR 6,935 – 19,488) for the 'not readmitted' group.

The annual total cost of 30-day readmissions was $2,767,336, with the cost of potentially preventable admissions $532,270 (19%), and the median cost of readmission $8,817 (IQR 5,814 – 21,028). Median cost of readmission was highest for those with autoimmune liver disease ($11,439) and alcohol-related liver disease

($10,412) compared to other aetiologies of liver disease (mixed alcohol-related and viral liver disease $9,161; NAFLD $7,783; viral $7,495; and miscellaneous $6,511), and for those readmitted due to GI bleeding ($18,993) compared to other reasons (infection $9,450; HE $8,817; miscellaneous $8,677; fluid overload $7,218; AKI-HRS $4,102), however this did not reach statistical significance for either (p=0.84 and p=0.08, respectively). There was no difference in cost between non-liver related admissions and liver-related admissions ($11,471 vs $8,200, p=0.48).

Discussion

In this retrospective cohort study conducted in a single liver transplant centre in Australia over 12-months, we found the 30-day hospital readmission rate in cirrhotic patients was high at 46%. Fluid overload and infection accounted for 49% of all 30-day readmissions, and one-fifth of readmissions were considered potentially preventable.

In comparison to other single- and multi-centre studies [3-5, 12-16], our 30-day readmission rate is notably higher than prior reports (Table 3.). Most published data primarily exist from North American cohorts, likely related to the Affordable Care Act mandating the reporting of 30-day readmission rates for common medical conditions [17]. Tapper et al. report of 12.9% is the lowest in the literature [5], whilst Fagan et al. finding from a single Australian institution of 42% in cirrhotic patients admitted with ascites is the previous highest [18]. It is difficult to directly compare the current study with that of Fagan et al., as their cohort only included readmission in those cirrhotics initially admitted with ascites [18], whilst the current study includes cirrhotics admitted for any reason. A 2018 systematic review including 26 studies of 180,000 patients reported a pooled rate of 26% [19].

The heterogeneity in methodology for case ascertainment and population studied, related to differing inclusion and exclusion criteria, are the likely attributable factors for the variance in our reported 30-day readmission rate and those reported previously. Compared to other studies, our report did not exclude patients with compensated disease [4, 13, 15-16, 18], hepatocellular carcinoma [16] or who underwent liver transplantation during the study period [5, 14], as well as incorporating a greater number of ICD codes for complications of liver disease (22 vs 3-16) [4-5, 12-13, 15-16].

Furthermore, it is likely that the severity of liver disease in our study cohort was greater than those in existing literature, with higher median MELD score compared to Volk et al. cohort (17 vs 14) [4] and a greater proportion of Child-Pugh B or C patients compared with Sood & Wong's study population (85% vs 52%) (Table 3.) [14]. It is also one of a few studies that have included patients being assessed and waitlisted for liver transplantation [3-4, 13, 18] and typically was an older demographic of patients (Table 3.), again suggesting inclusion of a sicker patient group. Although these factors together may have led to a greater than previously reported readmission rate, given the differences in study methodology, it is difficult to tease out institutional factors that may lead to the regional disparity in 30-day readmission rate.

Fewer studies have reported on reason for hospital readmission, with only 12 out of the 26 studies included in the 2018 systematic review assessing this metric [19]. Our study's finding of fluid overload and infection being the most common reasons for early readmission is consistent with the larger studies that have reported this outcome [5,13].

These findings are expected given ascites is the most common decompensating event [1], and the increasing recognition of cirrhosis as an immunosuppressive condition [20].

Our finding of prior VH as a predictor for 30-day hospital readmission has only been reported once before in the literature [15]. Other cirrhotic complications, particularly ascites and HE, have previously been identified as predictors for early readmission [5, 12, 14, 15]. Each of these sequelae define a decompensated state, with portal hypertension progressively worsening during the natural history of the disease, and accumulation of complications defining the various stages of cirrhosis, each associated with a stepwise increase in mortality [1]. Our finding that prior VH is a predictor of early readmission reaffirms that it is just another surrogate marker for advanced disease state with more severe portal hypertension. No traditional prognostic score of liver disease includes prior VH, and although the Child-Pugh score includes clinical markers of portal hypertension, hepatic venous pressure gradient measurement is not included in any commonly adopted prognostic score. This may reduce the sensitivity of these prognostic scores in determining the most severe cases of portal hypertension, and a reason for why these prognostic scores were not found to be independent markers of early readmission in this study. Further studies will be required to confirm past VH as a predictor for 30-day readmission amongst cirrhotics, and if this relationship is solely due to more advanced liver disease, or other, currently unidentified factors.

Volk et al. considered 22% of 30-day readmissions in their institution to be "possibly preventable", with one of the major reasons noted to be "failure to plan ahead for paracentesis" [4], whilst Le and colleagues identified early paracentesis as a significant factor associated with reduced 30-day readmission in patients admitted with cirrhotic

ascites [21]. The implementation of a pre-discharge paper checklist assessing appropriate medication prescription for HE, SBP prophylaxis, portal vein thrombosis and VH led to a 40% reduction in 30-day readmission rate when compared to historical controls in a tertiary referral institution in Boston [22]. Contrary to this, a randomized controlled pilot study from Australia assessing the utility of a multifaceted chronic disease management plan for decompensated cirrhotic patients post-discharge did not show any difference in the liver-related readmission rate [23]. Given one-fifth of readmissions in our study were potentially preventable, there is a need for further prospective studies of novel models of care [22, 24-25] to reduce early readmission in this vulnerable cohort.

This is the first time the financial burden of early readmission in cirrhotic patients has been quantified in an Australian context. We found the total annual total cost of readmission to near 3 million dollars and the median cost of readmission to be just under $9,000. In the North American studies, Volk et al. demonstrated a mean cost of 30-day readmission over 20,000 US dollars (USD) [4], Chirapongsathorn and colleagues reported the 12-month post-index hospitalisation cost to be about 12,000 USD greater in patients readmitted within 30-days compared to those who were not readmitted within 30-days [13], and Okafor et al. noted about a 3,500 USD greater mean hospital cost if patients were readmitted to a different rather than the same institution [16]. In Chirapongsathorn et al. study, the authors estimated the US national readmission cost to be 4.45 billion USD annually [13]. More studies reporting the direct healthcare cost of unexpected readmissions in cirrhotic patients are necessary in Australia to allow us to better measure the economic impact of future interventions aimed at reducing readmission.

Whilst there are a few limitations inherent to retrospective study design, we have been able to report the 30-day readmission rate and reason in a well-defined cohort of cirrhotic patients hospitalized and readmitted to a tertiary liver-transplant referral centre in Australia. Strengths of our study include the large number of subjects included through a validated coding system for case ascertainment, the reporting on cause of readmission with its relevance to healthcare utilisation, and adjudicating on preventable readmissions that allows for the construct of region-specific prospective interventional studies. Limitations of our study include the potential for missed cases through retrospective case ascertainment, single-centre data collection that prevents knowledge of patients who may have been readmitted to other institutions within 30-days of discharge from our centre, and the bias toward a sicker population of patients included in the study.

In conclusion, this study reports on high 30-day hospital readmission rate amongst cirrhotic patients in a single liver transplant centre in Australia, with one-fifth of readmissions adjudicated as potentially preventable with high associated cost. There is a paucity of literature regarding interventions to reduce readmissions in this vulnerable cohort, and future studies should include cost-benefit analyses given the high costs of medical care for patients with cirrhosis.

References

1. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol*. 2006;44(1):217-231.
2. Ge PS, Runyon BA. Treatment of patients with cirrhosis. *N Engl J Med*. 2016;375(8):67-77.
3. Berman K, Tandra S, Forssell K, Vuppalanchi R, Burton Jr JR, Nguyen J, et al. Incidence and predictors of 30-day readmission among patients hospitalized for advanced liver disease. *Clin Gastroenterol Hepatol*. 2011;9(3):254-259.
4. Volk ML, Tocco RS, Bazick J, Rakoski MO, Lok AS. Hospital re-admissions among patients with decompensated cirrhosis. *Am J Gastroenterol*. 2012;107(2):247-252.
5. Tapper EB, Halbert B, Mellinger J. Rates of and reasons for hospital readmissions in patients with cirrhosis: A multistate population-based cohort study. *Clin Gastroenterol Hepatol*. 2016;14(8):1181-1188.
6. Bajaj JS, Rajender Reddy K, Tandon P, Wong F, Kamath PS, Garcia-Tsao G, et al. The 3-month readmission rate remains unacceptably high in a large North American cohort of patients with cirrhosis. *Hepatology*. 2016;64(1):200-208.
7. Powell EE, Skoien R, Rahman T, Clark PJ, O'Beirne J, Hartel G, et al. Increasing hospitalization rates for cirrhosis: Overrepresentation of disadvantaged Australians. *EClinicalMedicine*. 2019;11:44-53.
8. Hirode G, Saab S, Wong RJ. Trends in the burden of chronic liver disease among hospitalized US adults. *JAMA Netw Open*. 2020;3(4):e201997.

9. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
10. European Association for the Study of Liver Disease. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *J Hepatol*. 2010;53(3):397-417.
11. Biggins SW, Angeli P, Garcia-Tsao G, Gines P, Ling SC, Nadim MK, et al. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;74:1014.
12. Garg SK, Goyal H, Obaitan I, Shah PA, Sarvepalli S, Jophlin LL, et al. Incidence and predictors of 30-day hospital readmissions for liver cirrhosis: insights from United States National Readmissions Database. *Ann Transl Med*. 2021;9(13):1052.
13. Chirapongsathorn S, Kirttanawong C, Enders FT, Pendegraft R, Mara KC, Borah BJ, et al. Incidence and cost analysis of hospital admission and 30-day readmission among patients with cirrhosis. *Hepatol Commun*. 2018;2(2):188-198.
14. Sood KT, Wong RJ. Hepatic encephalopathy is a strong predictor of early hospital readmission among cirrhosis patients. *J Clin Exp Hepatol*. 2019;9(4):484-490.

15. Brahmania M, Wiskar K, Walley KR, Celi LA, Rush B. Lower household income is associated with an increased risk of hospital readmission in patients with decompensated cirrhosis. *J Gastroenterol Hepatol*. 2021;36(4):1088-1094.

16. Okafor PN, Knadi AK, Okoli O, Huang AE, Nwaiwu O. Same- vs different-hospital readmissions in patients with cirrhosis after hospital discharge. *Am J Gastroenterol*. 2019;114(3):464-471.

17. Centers for Medicare and Medicaid Services. Hospital Readmissions Reduction Program (HRRP). https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program. Accessed 21 Nov 2021.

18. Fagan KJ, Zhao EY, Horsfall LU, Ruffin BJ, Kruger MS, McPhail SM, et al. Burden of decompensated cirrhosis and ascites on hospital services in a tertiary care facility: time for change? *Intern Med J*. 2014;44(9):865-872.

19. Orman ES, Ghabril M, Emmett TW, Chalasani N. Hospital readmissions in patients with cirrhosis: a systematic review. *J Hosp Med*. 2018;13(7):490-495.

20. Bajaj JS, Kamath PS, Reddy KR. The evolving challenge of infections in cirrhosis. *N Engl J Med*. 2021;384(24):2317-2330.

21. Le S, Spelman T, Chong CP, Ha P, Sahhar L, Lim J, et al. Could adherence to quality of care indicators for hospitalized patients with cirrhosis-related ascites improve clinical outcomes? *Am J Gastroenterol*. 2016;111(1):87-92.

22. Tapper EB, Finkelstein D, Mittleman MA, Piatkowski G, Chang M, Lai M. A quality improvement initiative decreases 30-day readmission rates for patients with cirrhosis: a prospective trial. *Clin Gastroenterol Hepatol*. 2016;14(5):753-759.

23. Wigg AJ, McCormick R, Wundke R, Woodman RJ. Efficacy of a chronic disease management model for patients with chronic liver failure. *Clin Gastroenterol Hepatol*. 2013;11(7):850-8.e1-4.

24. Wundke R, McCormick R, Narayana S, Sorensen L, Wigg A. The chronic liver disease nurse role in Australia: Describing 10 years of a new role in cirrhosis management. *Gastroenterol Nurs*. 2020;43(1):E9-E15.

25. Fabrellas N, Carol M, Palacio E, Aban M, Lanzillotti T, Nicolao G, et al. Nursing care of patients with cirrhosis: The LiverHope Nursing Project. *Hepatology*. 2020;71(3):1106-1116.

Figures Legends

Figure 1. Study flow diagram

Figure 2. Reason for index admission according to a) specific reason and b) dichotomization according to liver-related or non-liver related reason

Figure 3. Reason for hospital readmission

Table 1. Baseline demographics, comorbidities and liver-related complications, index admission indices and mortality according to 30-day readmission status

Characteristic	Whole group (n=179)	Readmitted (n=82)	Not readmitted (n=97)	*P* value
Demographics				
Age, years	59 (48 – 65)	60 (47 - 67)	58 (48 – 64)	0.65
Female gender, n (%)	66 (37%)	31 (38%)	35 (36%)	0.88
Active on liver transplant waitlist, n (%)	20 (11%)	9 (11%)	11 (11%)	1
CCI	5 (4 – 7)	5 (4 – 7)	5 (4 – 7)	0.42
Aetiology of liver disease				
Alcohol related, n (%)	76 (42%)	39 (48%)	37 (38%)	0.23
NAFLD, n (%)	27 (15%)	11 (13%)	16 (16%)	0.68
Viral, n (%)	24 (13%)	13 (16%)	11 (11%)	0.39
Mixed alcohol-related and viral, n (%)	20 (11%)	4 (4.9%)	16 (16%)	0.02*
Autoimmune, n (%)	21 (12%)	10 (12%)	11 (11%)	1
Miscellaneous, n (%)	11 (6.1%)	5 (6.1%)	6 (6.2%)	1
Liver-related complications				
Ascites, n (%)	126 (70%)	68 (83%)	58 (60%)	<0.01*
AKI-HRS, n (%)	65 (36%)	34 (41%)	31 (32%)	0.21
HE, n (%)	93 (52%)	49 (60%)	44 (45%)	0.07
VH, n (%)	35 (20%)	23 (28%)	12 (12%)	0.01*
HCC, n (%)	38 (21%)	14 (17%)	24 (25%)	0.27
PVT, n (%)	26 (15%)	15 (18%)	11 (11%)	0.21
Hyponatremia, (%)	80 (45%)	46 (56%)	34 (35%)	<0.01*
Index admission indices				
Admission MELD	17 (13 – 21)	18 (14 – 22)	16 (12 – 21)	0.13
Admission CP	9 (7 – 11)	9 (8 – 11)	9 (7 – 10)	0.01*
Admission CP-B/C, n (%)	153 (85%)	75 (91%)	78 (80%)	0.05
Number of discharge medications	9 (6 – 11)	9 (7 - 12)	8 (5 - 10)	<0.01*
NSBB, n (%)†	20 (11%)	9 (11%)	11 (11%)	1
Lactulose, n (%)†	112 (63%)	57 (70%)	55 (57%)	0.09
SBP prophylaxis, n (%)†	51 (28%)	34 (41%)	17 (17%)	<0.01*
PPI, n (%)†	118 (66%)	54 (66%)	64 (66%)	1
DC summary <48hrs, n (%)	95 (53%)	47 (57%)	48 (49%)	0.37
DC MELD	15 (12 – 19)	17 (13 – 21)	14 (11 – 18)	<0.01*
DC CP	8 (7 – 10)	9 (7 – 10)	8 (7 – 9)	<0.01*

DC CP-B/C, n (%)	150 (84%)	75 (91%)	75 (77%)	<0.01*
Length of stay, days	5 (3 – 10)	5 (3 – 10)	5 (3 – 9)	0.77
90-day mortality, n (%)	14 (7.8%)	8 (9.8%)	6 (6.2%)	0.41

Results given as median (IQR); IQR = interquartile range
†On discharge from index admission
CCI = Charlson comorbidity index; NAFLD = non-alcoholic fatty liver disease; AKI-HRS = acute kidney injury-hepatorenal syndrome; HE = hepatic encephalopathy; VH = variceal haemorrhage; HCC = hepatocellular carcinoma; PVT = portal venous thrombosis; MELD = Model for End-stage Liver Disease; CP = Child-Pugh; NSBB = non-selective beta-blocker; SBP = spontaneous bacterial peritonitis; PPI = proton pump inhibitor; DC = discharge

Table 2. Univariate and multivariate logistic regression of demographic features, comorbidities and liver-related complications, and index admission indices

	Univariate		Multivariate	
	Odds ratio (95% confidence interval)	*P* value	Odds ratio (95% confidence interval)	*P* value
Variables				
Age	1.00 (0.98 – 1.02)	0.92	1.01 (0.98 – 1.03)	0.71
Female gender	1.07 (0.58 – 1.98)	0.81	1.06 (0.52 – 2.13)	0.88
Waitlisted†	0.96 (0.37 – 2.46)	0.94		
CCI	1.05 (0.91 – 1.21)	0.54		
Number of cirrhosis complications	1.60 (1.21 – 2.16)	<0.01*	0.81 (0.45 – 1.45)	0.48
Ascites	3.27 (1.65 – 6.78)	<0.01*	1.78 (0.63 – 5.09)	0.28
AKI-HRS	1.51 (0.82 – 2.79)	0.19		
HE	1.79 (0.99 – 3.26)	0.06	1.28 (0.49 – 3.32)	0.61
VH	2.76 (1.30 – 6.15)	<0.01*	3.08 (1.08 – 9.28)	0.04*
HCC	0.63 (0.29 – 1.30)	0.21		
PVT	1.75 (0.76 – 4.15)	0.19		
Hyponatremia	2.37 (1.30 – 4.36)	<0.01*	1.70 (0.80 – 3.61)	0.17
Admission MELD	1.02 (0.98 – 1.07)	0.32		
Admission CP	1.22 (1.05 – 1.41)	<0.01*	0.99 (0.74 – 1.32)	0.95
Number of discharge medications	1.14 (1.05 – 1.24)	<0.01*	1.10 (0.99 – 1.24)	0.08
NSBB‡	0.96 (0.37 – 2.46)	0.94		
Lactulose‡	1.74 (0.94 – 3.26)	0.08	0.63 (0.26 – 1.50)	0.30
SBP prophylaxis‡	3.33 (1.70 – 6.72)	<0.001*	2.13 (0.98 – 4.72)	0.06
PPI‡	0.99 (0.53 – 1.86)	0.99		
DC summary <48hrs	1.37 (0.76 – 2.49)	0.30		
DC MELD	1.07 (1.01 – 1.13)	0.02*	1.02 (0.94 – 1.11)	0.66
DC CP	1.26 (1.07 – 1.49)	<0.01*	1.11 (0.80 – 1.54)	0.53
Length of stay	0.99 (0.97 – 1.02)	0.64		

†Waitlisted for liver transplant

‡On discharge from index admission

CCI = Charlson comorbidity index; AKI-HRS = acute kidney injury-hepatorenal syndrome; HE = hepatic encephalopathy; VH = variceal haemorrhage; HCC = hepatocellular carcinoma; PVT = portal venous thrombosis; MELD = Model for End-stage Liver disease; CP = Child-Pugh; NSBB = non-selective beta-blocker; SBP = spontaneous bacterial peritonitis; PPI = proton pump inhibitor; DC = discharge

Table 3. Literature review of studies reporting on rate of 30-day readmission in cirrhotic patients

Study	Number of patients	Methodology	Study population	30-day readmission rate
Berman *et al.* 2011 [3]	447	Two hospitals in US (one LT referral centre) 1-year study period Unclear methodology case ascertainment Exclusions – admission resulting in LT, discharge against medical advice, elective admissions	Mean age 54 yo, female 43% Cause CLD – HCV/ETOH 49%; NAFLD/cryptogenic 20%, other 31% Median MELD 19 23% LT waitlisted	**20%**
Volk *et al*. 2012 [4]	402	Single LT referral centre in US 3-year study period Case ascertainment through ICD-9 coding Exclusions – admissions resulting in discharge to hospice or LT	Decompensated cirrhosis only Median age 54 yo, female 43% Median MELD 15 16% LT waitlisted Median CCI 5	**37%**
Tapper *et al.* 2016 [5]	119,722	Healthcare Cost and Utilisation Project encompassing state inpatient databases from 6 US states 1-year study period Case ascertainment through ICD-9 coding Exclusions – admissions resulting in death or discharge to hospice or another facility; any LT during study period	Mean age 61 yo, female 45% Cause CLD – ETOH 35%, viral 24% (HCV 21%, HBV 3%), other 41% 67% Quan modified Deyo-Charlson Index 1-2	**13%**
Garg *et al.* 2021 [12]	303,346	Nationwide Readmission Database in US 5-year study period Case ascertainment through ICD-9 coding No stipulated exclusions	64% between 45-64 yo, female 36% Cause CLD – ETOH 62%, non-ETOH 36%, biliary 2%	**31%**
Chirapongsathorn *et al.* 2018 [13]	2,048	Two LT referral centres in US 4-year study period Case ascertainment through ICD-9 coding Exclusions – elective admissions; admission resulting in death; LT before or during study period; patients denying access to health record for research purposes	Decompensated cirrhosis only Median age 60 yo, female 41% Cause CLD – ETOH 31%, NAFLD 28%, viral 18%, autoimmune 7%, other 16%	**32%**

Sood & Wong. 2019 [14]	230	Single non-LT hospital in US 2.5-year study period Case ascertainment through review of hospital encounters at institution for all cirrhotic patients seen in outpatient clinic during study period No stipulated exclusions	Mean age 57 yo, female 37% Cause CLD – ETOH 34%, viral 43% (HCV 27%, HBV 16%), HCV/ETOH 9%, NAFLD 8%, other 5% 52% CP-B/C	**31%**
Brahmania *et al.* 2021 [15]	82,598	Nationwide Readmission Database in US 3-year study period Case ascertainment through ICD-9 coding Exclusions – LT during study period; death within 6-months of index discharge	Decompensated cirrhosis only Mean age 56 yo, female 35% Cause CLD – ETOH 51%, viral 68%	**31%**
Okafor *et al.* 2019 [16]	50,841	Nationwide Readmission Database in US 1-year study period Case ascertainment through ICD-9 coding Exclusions – readmission for non-cirrhosis related indications; HCC; LT during study period; discharge to hospice care during study period	Decompensated cirrhosis only Median age 57 yo, female 41%	**29%**
Fagan *et al.* 2014 [18]	41	Single LT centre in Australia 1-year study period Case ascertainment through review of ascitic fluid sample record on statewide pathology database No stipulated exclusions	Cirrhotic with ascites only Mean age 54 yo, female 22% Cause CLD – ETOH 44%, viral 34%, other 22% Median MELD 17, median CP 10 Median CCI 4	**42%**
Current study	179	Single LT centre in Australia 1-year study period Case ascertainment through ICD-10 coding Exclusions – elective admissions; admissions resulting in discharge to external facility, hospice or palliative care centre, admissions resulting in LT or death	Median age 59 yo, female 37% Cause CLD – ETOH 42%, NAFLD 15%, viral 13%, viral/ETOH 11%, autoimmune 12%, miscellaneous 6% Median MELD 17, median CP 9, CP-B/C 85% 11% LT waitlisted Median CCI 5	**46%**

US – United States; LT – liver transplant; CLD – chronic liver disease; HCV – hepatitis C virus; ETOH – alcohol-related liver disease; NAFLD – non-alcoholic fatty liver disease; MELD – Median for End-stage Liver Disease score; ICD – International Classification of Diseases; CCI – Charlson comorbidity index; HBV – hepatitis B virus, CP – Child-Pugh

Supplementary Table 1. ICD-10 codes utilised to capture admissions

ICD-10 code	ICD-10 code descriptor
K70.0	Alcoholic fatty liver
K70.1	Alcoholic hepatitis
K70.2	Alcoholic fibrosis and sclerosis of liver
K70.3	Alcoholic cirrhosis of liver
K70.4	Alcoholic hepatic failure
K70.9	Alcoholic liver disease, unspecified
K72.1	Chronic hepatic failure
K72.9	Hepatic failure, unspecified
K74.0	Hepatic fibrosis
K74.1	Hepatic sclerosis
K74.2	Hepatic fibrosis with hepatic sclerosis
K74.3	Primary biliary cirrhosis
K74.4	Secondary biliary cirrhosis
K74.5	Biliary cirrhosis, unspecified
K74.6	Other and unspecified cirrhosis of liver
K76.6	Portal hypertension
K76.7	Hepatorenal syndrome
I81	Portal vein thrombosis
I85.9	Oesophageal varices without bleeding
I86.4	Gastric varices
I98.3	Oesophageal varices with bleeding in disease classified elsewhere
C22.0	Malignant neoplasm: Liver cell carcinoma
R18	Ascites

Supplementary Table 2. Miscellaneous reasons for index admission

Diagnosis	Number of patients
Post-TACE syndrome	8
Alcoholic hepatitis	7
Coagulopathic with non-GI bleeding	5
Fall	5
Symptomatic anaemia	4
Strangulated umbilical hernia	4
Abdominal pain, unspecified	2
Choledocholithiasis	2
Alcohol withdrawal	2
Autoimmune hepatitis flare	2
Malnutrition	2
Hepatitis B flare	1

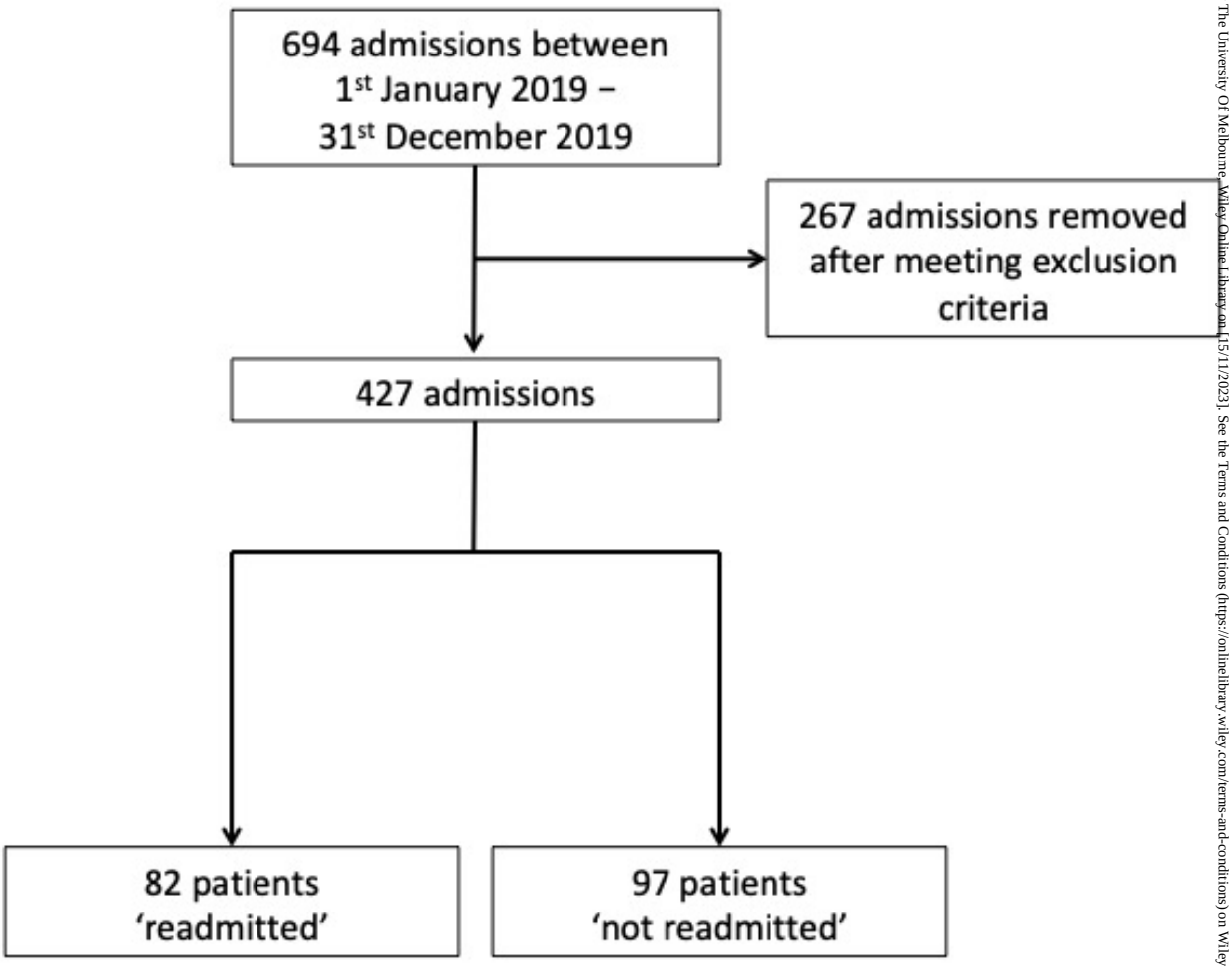
Alcoholic pancreatitis	1
Occluded PTC	1
TIPS dysfunction	1
End-stage renal failure	1
Exacerbation of COPD	1
Functional decline	1
Haemoperitoneum following ascitic tap	1
Hypoglycaemia	1
Gallstone pancreatitis	1
Jaundice	1
PEG dislodgement	1
Migrated biliary stent	1
Rapid atrial fibrillation	1
Chest pain	1

TACE – transarterial chemoembolization; GI – gastrointestinal; PTC – percutaneous transhepatic cholangiogram; TIPS – transjugular intrahepatic portosystemic shunt; COPD – chronic obstructive pulmonary disorder; PEG – percutaneous endoscopic gastrostomy

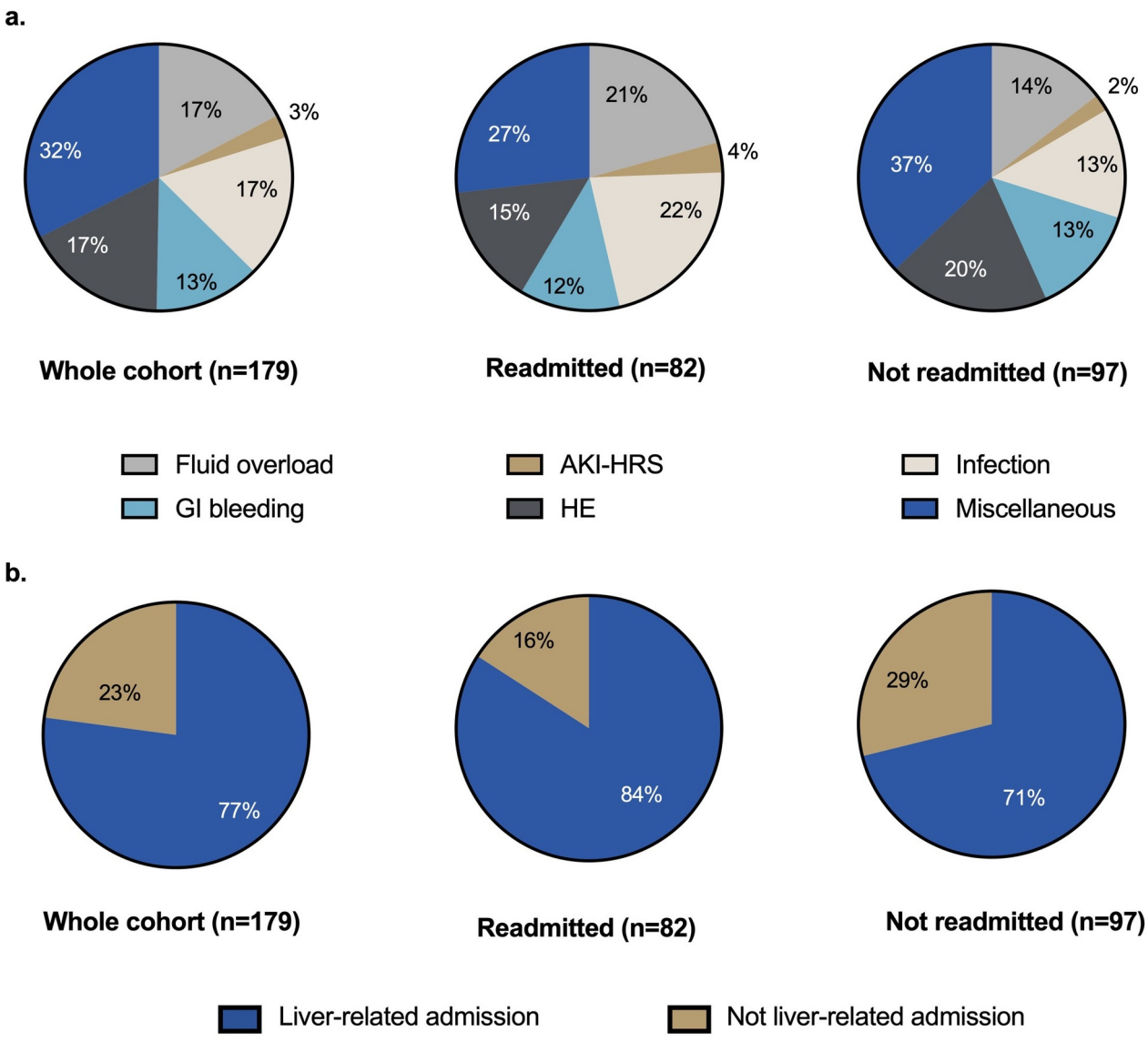
Supplementary Table 3. Miscellaneous reasons for 30-day readmission

Diagnosis	Number of patients
Abdominal pain	2
Acutely decompensated heart failure	2
Constipation	2
Broken tooth	1
Flare of chronic neuropathic leg pain	1
DVT	1
Fall	1
Gastritis	1
Gastroparesis	1
Seizures	1
Hyperkalemia	1
Hypoglycaemia	1
Jaundice	1
Post-TACE syndrome	1
Pruritus	1
PVT	1
Stroke	1
Symptomatic anaemia	1
Draining umbilical drain	1

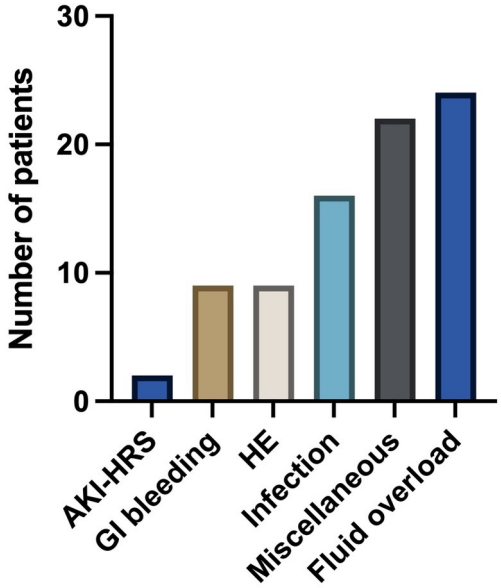
DVT – deep vein thrombosis; TACE – transarterial chemoembolization; PVT – portal vein thrombosis



IMJ_15932_Figure 1..tiff



IMJ_15932_Figure 3. copy.jpg



IMJ_15932_Figure 4. copy.jpg