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Infection-Related Readmissions Are Rising among Patients with Hepatorenal Syndrome: A Nationwide Analysis

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Brief Report

Infection-Related Readmissions Are Rising among Patients with Hepatorenal Syndrome: A Nationwide Analysis

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Abstract: Hepatorenal syndrome (HRS) is a unique form of renal dysfunction that results from circulatory hemodynamic dysfunction in advanced liver disease. We aimed to determine longitudinal trends in both all-cause and cause-specific readmissions for HRS in the United States. Using the National Readmission Database (2010–2018), we identified adult HRS patients during index admission via ICD codes. Fisher's exact test and Cox regression analysis were used to compare proportions and compute adjusted *p*-values, respectively. Regression models were adjusted for gender, age, the Charlson comorbidity index, median household income, and hospital factors. A total of 169,522 HRS patients were included in the analysis (overall mean age 58.97 years). The incidence of HRS hospitalization increased from 5.30% in 2010 to 5.84% in 2018 ($p < 0.01$). Over the same duration, all-cause readmission at 30 days showed an overall increasing trend from 19.81% to 19.99% (trend $p < 0.01$). HRS-specific readmission at 30 days following an index hospitalization ranged from 13.60 to 15.98, with an overall increasing trend in the study period (2010–2018). While cirrhosis, hepatic failure, and infection were uniformly the three most common causes of readmission throughout the study period, cirrhosis and infection showed an upward trend. Rising readmissions, especially with hepatic failure and infection, in HRS patients signal a need for national strategies to manage and prevent HRS towards reducing its healthcare burden.

Keywords: hepatorenal syndrome; thirty-day readmissions; infections; spontaneous bacterial peritonitis

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1. Introduction

Hepatorenal syndrome (HRS) is characterized by a reduction in renal blood flow and glomerular filtration rate in patients with liver cirrhosis, ultimately leading to a progressive but potentially reversible deterioration in kidney function [1]. It results from liver injury that leads to a cascade of events, including splanchnic vasodilation triggered by the release of vasodilators and activation of both the renin–angiotensin–aldosterone system and renal vasoconstriction, resulting in functional renal dysfunction [2]. The incidence of HRS ranges from 18% to 47%, depending on the diagnostic criteria used [3]. When developed, HRS confers higher mortality rates ranging from 32 to 80% [4,5].

Patients with HRS have a higher risk of developing complications, such as infections, hepatic encephalopathy, and variceal bleeding [3]. They exhibit immune dysfunction, rendering them particularly susceptible to infections [6]. Furthermore, HRS is an independent predictor of readmission, length of hospital stays, and healthcare costs [7]. The economic burden of HRS is significant and is expected to rise globally as the prevalence of HRS continues to increase [8]. Moreover, advancements in therapeutic strategies, including the use of vasoconstrictors like terlipressin and albumin, have shown promise in managing

HRS, yet their accessibility and efficacy vary across different healthcare settings. Integrating care pathways that encompass comprehensive management of both liver and renal problems could potentially mitigate the adverse effects of HRS and enhance patient survival rates. Standardized treatment protocols and the exploration of novel therapeutic agents are necessary to achieve more consistent outcomes for hepatorenal syndrome (HRS). Despite the substantial impact of HRS on patient outcomes and healthcare resource utilization, there is a paucity of longitudinal data on readmission trends following HRS. Addressing this knowledge gap is essential for healthcare providers and policymakers to develop targeted interventions aimed at reducing readmission rates and improving overall patient care. Therefore, the objective of this study was to conduct a longitudinal assessment of HRS readmissions in the USA. This study aims to provide a comprehensive analysis of readmission patterns, including both all-cause and HRS-specific readmissions, as well as the underlying causes of these readmissions.

2. Materials and Methods

2.1. Data Source

We conducted a retrospective survey using the National Readmission Database (NRD) from 2010 through 2018 following the STROBE reporting guideline. The surveyed database consists of a stratified sample of 20% of all hospital stays in the United States of America (USA). It consists of weighted observations (weight = total number of discharges from all acute care hospitals in the USA divided by the number of discharges included in the 20% sample) from hospitals across the United States, clustered into strata to produce national estimates. A total of 35 million stays were recorded in 30 states in the USA in 2018, accounting for 60.4% of all hospitalizations and 61.8% of the total US population [9]. In addition, patients admitted to any hospital can be tracked via patient linkage numbers within the NRD. All research was conducted in accordance with both the Declarations of Helsinki and Istanbul.

2.2. Study Population

Using the International Classification of Diseases (ICD), Ninth Revision, and ICD, Tenth Revision codes for the corresponding years, we sampled adult patients ($\geq$18 years old) with cirrhosis. Patients under the age of 18 were excluded from this study. We eliminated patients discharged in December to obtain a 30-day period to track readmissions post-discharge when evaluating readmission trends. Finally, patients who died during the index hospitalization were excluded.

2.3. Statistical Analysis

Analyses were conducted using Stata (version 14.2). NRD is founded on an intricate sampling design that includes stratification, clustering, and weighting. Using this software, unbiased results with p values that are nationally representative can be generated. The weighting of patient-level observations was applied to procure estimates for the entire United States population of hospitalized patients with HRS for the data studied. We followed Healthcare Cost and Utilization Project recommendations to use revised trend weights to obtain proportionate estimates. Proportions were compared using the Fisher exact test for categorical variables, and continuous variables were compared using Student's t-test. The linear trend for hospitalization and readmission across years was tested using the Mantel–Haenszel linear trend test. The variables adjusted for in the regression models were gender, age, Charlson comorbidity index score, median household income for patients' ZIP codes, hospital location, hospital size, and teaching status. The p values were all two-sided, and statistical significance was determined by 0.05 as the threshold.

3. Results

3.1. Baseline Characteristics

A total of 2,987,156 patients were included in the analysis, and 169,522 (6.57%) had an associated HRS diagnosis (Table 1). Noteworthy temporal shifts were observed during the study duration: the mean age at diagnosis increased over the study period from 58.09 years to 59.16 years ($p < 0.01$). Furthermore, there was a discernible upward trend in the proportion of female patients diagnosed with HRS, which rose from 36.92% to 38.15% ($p < 0.01$). The majority of the patients were insured by Medicare. The comorbidity burden marked by the Charlson comorbidity index (CCI) (score ≥ 4) increased in HRS patients ($p < 0.01$). Although certain other demographic and clinical attributes demonstrated numerical variances, their clinical significance remained negligible.

Table 1. Baseline characteristics.

Variables	Year					
	2010	**2012**	**2014**	**2016**	**2018**	***p*-Value**
No. of hospitalization	25,291	28,294	34,262	39,414	42,261	
Sex, %						<0.001
Male	63.08	64.40	63.03	61.43	61.85	
Female	36.92	35.60	36.97	38.57	38.15	
Age, mean, y	58.09	58.39	59.01	59.09	59.16	<0.001
Insurance type, %						<0.001
Medicare	40.71	41.66	44.43	44.84	46.11	
Medicaid	22.12	23.69	23.74	25.50	24.51	
Private	31.22	29.48	27.96	27.38	25.42	
Uninsured	5.95	5.17	4.18	3.28	3.97	
Household income quartile, %						0.001
1st	30.66	31.13	27.65	30.81	29.49	
2nd	25.22	25.13	28.56	26.89	29.72	
3rd	24.08	23.54	24.12	24.80	23.80	
4th	20.04	20.20	19.67	17.50	16.99	
Charlson comorbidity index score, %						<0.001
<4	30.46	29.19	25.83	21.19	20.53	
≥4	69.54	70.81	74.17	78.81	79.47	
Hospital size, %						<0.001
Small	8.22	8.63	11.70	11.33	13.26	
Medium	18.55	20.73	23.54	25.23	23.77	
Large	73.23	70.64	64.76	63.45	62.97	
Hospital teaching status, %						<0.001
Metropolitan non-teaching	33.97	31.47	20.87	21.39	16.73	
Metropolitan teaching	58.40	60.16	73.17	73.12	77.79	
Non-metropolitan	7.63	8.37	5.97	5.48	5.48	

3.2. Hospitalization and 30-Day Readmission

The incidence of HRS hospitalization in cirrhosis demonstrated a statistically significant increase from 5.30% in 2010 to 5.84% in 2018 ($p < 0.01$) (Figure 1). In addition, 13.27% had a coexistent diagnosis of infection during the index admission. Over the same duration,

the all-cause readmission at 30 days showed an overall increasing trend from 19.81% to 19.99% (trend $p < 0.01$). HRS-specific readmission at 30 days following an index hospitalization ranged from 13.60 to 15.98, with an overall increasing trend in the study period (2010–2018). Cirrhosis, hepatic failure, and infection were consistently among the top three reasons for readmission throughout the study period (Figure 2). Infection-specific readmission increased from 6.25% in 2010 to 12.12% in 2018 (trend $p < 0.01$). The infection-related billing codes upon readmission included 038.9 (unspecified septicemia) and 567.23 (spontaneous bacterial peritonitis) for ICD-9 as well as A41.9 (sepsis, unspecified organism) and K65.2 (spontaneous bacterial peritonitis) for ICD-10.

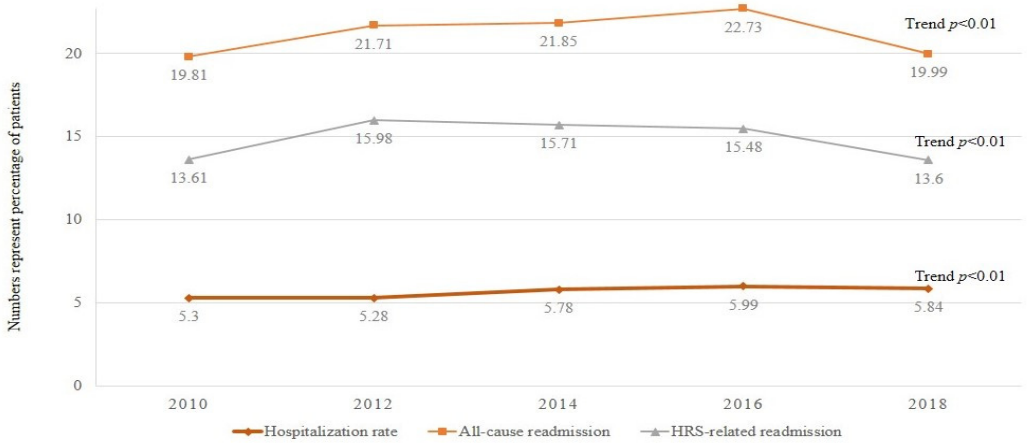

Figure 1. Hospitalization and 30-day readmission rate.

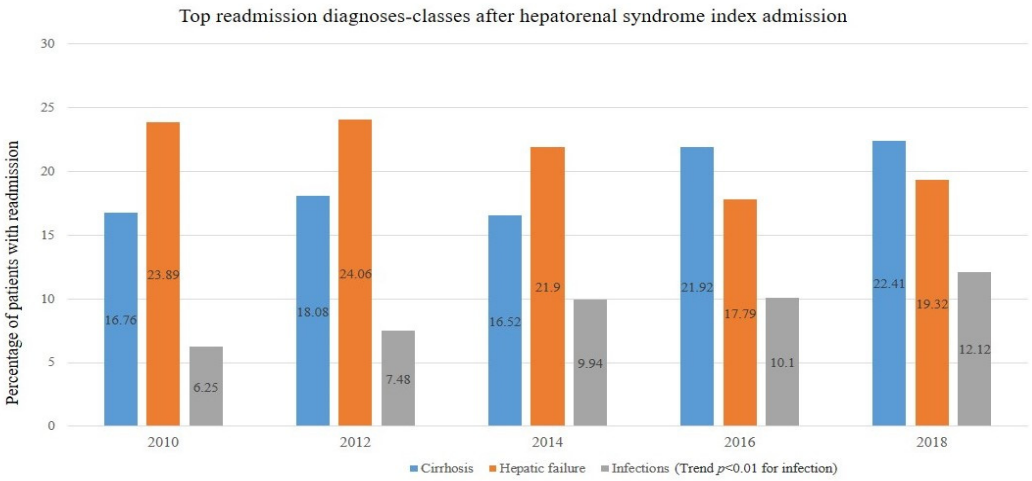

Figure 2. Causes of readmission.

4. Discussion

HRS is a characteristic manifestation of severe liver injury and advanced cirrhosis, and its prevalence is increasing accordingly [8]. The current study reveals an increasing trend in HRS hospitalization and all-cause readmission at 30 days from 2010 to 2018 in cirrhosis patients. Although the absolute increase is minimal, the overall increasing trend over an extended study period raises concerns. This trend is a consequence of the rising prevalence of both cirrhosis and decompensated liver disease globally [10]. The 30-day readmission rate after cirrhosis remains high, ranging from 17 to 50%, while limited published data are available regarding early readmission after HRS [11–13]. Using a nationally representative patient cohort consisting of an inpatient population, this study demonstrates that the 30-day readmission rate after HRS ranges from 13.60% to 15.98%. HRS-specific readmission displays an initial increase followed by a decrease during the

latter portion of the study, with an overall upward slope of the trend curve observed throughout the duration of the study. This fluctuation may be attributed to variations in hospital practices, patient management strategies, and the implementation of new treatment protocols during the study period. Understanding the factors contributing to this decrease presents difficulties, highlighting the need for additional demographic investigations to ascertain if these declining trends persist.

By virtue of its immune dysregulation, cirrhosis poses a significant risk of infection in patients [6]. Bacterial infections can lead to the development of HRS, and our study showed that 13.27% of HRS patients had a coexistent diagnosis of infection [14]. The intricate interplay between cirrhosis, infection, and HRS underscores the multifactorial nature of patient management in this cohort. The rising prevalence of cirrhosis globally contributes to the escalating burden of HRS, necessitating a proactive approach to address this concerning trend. Furthermore, the observed temporal shifts in patient demographics highlight the evolving landscape of HRS epidemiology, warranting continued surveillance and tailored interventions. Infections are also a frequent cause of readmission in cirrhosis patients; however, there is limited published literature on readmissions specifically related to HRS [7,15]. Our study revealed that infection is a significant contributor to the readmission rates observed in patients with HRS, besides cirrhosis and its complications. The frequency of infection-related readmissions was found to be on a steady rise. The utilization of ICD codes within databases and the non-specificity of readmission diagnosis codes posed a challenge in the evaluation of various infection-related readmission causes. Nevertheless, our analysis revealed that spontaneous bacterial peritonitis (SBP) is a noteworthy infection-related readmission culprit. The disproportionate burden of infection-related readmissions emphasizes the critical role of infection prevention measures in reducing healthcare utilization and improving patient outcomes. The clinical implications of these findings suggest that more rigorous screening and early intervention protocols for infections in HRS patients could be beneficial. This highlights the urgent need for healthcare providers to take steps to reduce the incidence of infection in patients with HRS in order to mitigate the need for readmission and improve patient outcomes.

While evidence supporting antibiotics' utility in the primary prevention of SBP is not robust, most studies demonstrate significant overall mortality benefits; nonetheless, their ability to prevent future SBP episodes remains uncertain [16–18]. Accordingly, the American Association for the Study of Liver Diseases (AASLD) recommends SBP prophylaxis in high-risk patients with low ascitic protein (<1.5 g/dL) and additional risk factors (renal dysfunction, hyponatremia, and Child–Turcotte–Pugh score > 9) [19]. Prophylactic measures not only reduce the incidence of SBP but also diminish the subsequent healthcare burden associated with recurrent hospitalizations. In addition, as reported in our study, the rising incidence of readmissions in HRS patients is concerning and stresses the need to investigate guidelines adherence across the states.

The limitations of our study include the reliance on ICD codes and the inability to gather information about laboratory values to assess the severity of liver disease. Similarly, the overlapping diagnosis of AKI and hepatorenal syndrome in cirrhosis poses challenges in assessment. Although the risk of miscoding exists, the NIS database operates at the level of patient discharge and assigns final diagnosis codes based on completed hospitalizations. Moreover, due to the unavailability of distinct ICD codes for HRS types 1 and 2, it was not possible to ascertain readmission rates based on HRS subtype. This study's data only encompassed observations up to 2018. Future studies should aim to include more recent data to evaluate whether these trends have continued or changed in subsequent years, thereby providing a more comprehensive understanding of the trends observed in our study as additional data becomes available. Nonetheless, to the best of our knowledge, this is the first study that describes the longitudinal readmission trends in HRS. Patient linkage numbers within the NRD allowed for the tracking of the same patients across hospitals after index admission; hence, the readmission rates obtained are very reliable. The unavailability of medication-related data precluded the identification of antibiotic

prophylaxis use by HRS patients against SBP (primary or secondary). Addressing these limitations in future research could provide more nuanced insights into the management and outcomes of HRS patients.

In conclusion, our study sheds light on the evolving landscape of HRS epidemiology and readmission trends, highlighting the imperative for targeted interventions to mitigate the burden of HRS and its complications. The observed trend of increasing HRS hospitalizations underscores the escalating burden of liver disease globally [20]. This trend, coupled with the persistently high 30-day readmission rates, emphasizes the critical role of healthcare providers in ensuring comprehensive care delivery and monitoring for complications. Moreover, the association between bacterial infections and HRS exacerbates the clinical complexity of managing these patients. With over 13% of HRS cases demonstrating a concurrent infection diagnosis, the need for vigilant infection prevention measures becomes paramount. The steady rise in infection-related readmissions further emphasizes the urgency for targeted interventions, such as antibiotic prophylaxis and adherence to evidence-based guidelines. The identification of spontaneous bacterial peritonitis (SBP) as a predominant cause of infection-related readmissions underscores the importance of early recognition and treatment of this potentially life-threatening complication. Implementation of prophylactic measures, as recommended by the American Association for the Study of Liver Diseases (AASLD), becomes imperative in high-risk HRS patients to mitigate the risk of SBP and subsequent readmissions. Furthermore, the findings of our preliminary study lay the groundwork for subsequent research, offering direction on evaluating the preventive potential of antibiotic prophylaxis in HRS patients while conducting cost-benefit analyses regarding SBP prevention through meticulously planned randomized controlled trials in the future. By continuing to refine and expand upon these initial findings, future studies can significantly contribute to improving patient outcomes and reducing the healthcare burden associated with HRS and its complications.

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Institutional Review Board Statement: This statement outlines the ethical considerations and practices followed in conducting this observational study that utilized deidentified data, without any involvement in animal or human experimentation. This study adhered to principles of ethical research conduct, data protection, and privacy preservation. The data used in this observational study were obtained from a public database and were thoroughly deidentified in accordance with best practices and applicable data protection regulations. No personally identifiable information (PII) or sensitive data were included in the dataset.

Informed Consent Statement: Since this study did not involve direct interactions with human participants or the collection of personal data, obtaining informed consent was not applicable.

Data Availability Statement: The abstract of this manuscript was presented at Digestive Disease Week, Chicago Meeting in 2023.

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References

1. Angeli, P.; Garcia-Tsao, G.; Nadim, M.K.; Parikh, C.R. News in pathophysiology, definition and classification of hepatorenal syndrome: A step beyond the International Club of Ascites (ICA) consensus document. *J. Hepatol.* **2019**, *71*, 811–822. [CrossRef] [PubMed]
2. Flamm, S.L.; Brown, K.; Wadei, H.M.; Brown, R.S., Jr.; Kugelmas, M.; Samaniego-Picota, M.; Burra, P.; Poordad, F.; Saab, S. The Current Management of Hepatorenal Syndrome-Acute Kidney Injury in the United States and the Potential of Terlipressin. *Liver Transpl.* **2021**, *27*, 1191–1202. [CrossRef] [PubMed]

3. Jung, C.Y.; Chang, J.W. Hepatorenal Syndrome: Current Concepts and Future Perspectives. *Clin. Mol. Hepatol.* **2023**, *29*, 891–908. [CrossRef] [PubMed]
4. Ginès, A.; Escorsell, A.; Ginès, P.; Saló, J.; Jiménez, W.; Inglada, L.; Navasa, M.; Clària, J.; Rimola, A.; Arroyo, V.; et al. Incidence, predictive factors, and prognosis of the hepatorenal syndrome in cirrhosis with ascites. *Gastroenterology* **1993**, *105*, 229–236. [CrossRef] [PubMed]
5. Kaewput, W.; Thongprayoon, C.; Dumancas, C.Y.; Kanduri, S.R.; Kovvuru, K.; Kaewput, C.; Pattharanitima, P.; Petnak, T.; Lertjitbanjong, P.; Boonpheng, B.; et al. In-hospital mortality of hepatorenal syndrome in the United States: Nationwide inpatient sample. *World J. Gastroenterol.* **2021**, *27*, 7831–7843. [CrossRef] [PubMed]
6. Albillos, A.; Lario, M.; Álvarez-Mon, M. Cirrhosis-associated immune dysfunction: Distinctive features and clinical relevance. *J. Hepatol.* **2014**, *61*, 1385–1396. [CrossRef] [PubMed]
7. Chirapongsathorn, S.; Poovorawan, K.; Soonthornworasiri, N.; Pan-Ngum, W.; Phaosawasdi, K.; Treeprasertsuk, S. Thirty-Day Readmission and Cost Analysis in Patients with Cirrhosis: A Nationwide Population-Based Data. *Hepatol. Commun.* **2020**, *4*, 453–460. [CrossRef] [PubMed]
8. Singh, J.; Dahiya, D.S.; Kichloo, A.; Singh, G.; Khoshbin, K.; Shaka, H. Hepatorenal syndrome: A Nationwide Trend Analysis from 2008 to 2018. *Ann. Med.* **2021**, *53*, 2018–2024. [CrossRef] [PubMed]
9. Healthcare Cost & Utilization Project. HCUP Databases. Rockville, MD. September 2022. Available online: https://hcup-us.ahrq.gov/nisoverview.jsp (accessed on 29 May 2023).
10. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol. Hepatol.* **2020**, *5*, 245–266. [CrossRef] [PubMed]
11. Keller, J.J.; Offerhaus, G.J.; Hylind, L.M.; Giardiello, F.M. Rectal epithelial apoptosis does not predict response to sulindac treatment or polyp development in presymptomatic familial adenomatous polyposis patients. *Cancer Epidemiol. Biomarkers Prev.* **2002**, *11*, 670–671. [PubMed]
12. Garg, S.K.; Goyal, H.; Obaitan, I.; Shah, P.A.; Sarvepalli, S.; Jophlin, L.L.; Singh, D.; Asrani, S.; Kamath, P.S.; Leise, M.D. Incidence and predictors of 30-day hospital readmissions for liver cirrhosis: Insights from the United States National Readmissions Database. *Ann. Transl. Med.* **2021**, *9*, 1052. [CrossRef] [PubMed]
13. Scaglione, S.J.; Metcalfe, L.; Kliethermes, S.; Vasilyev, I.; Tsang, R.; Caines, A.; Mumtaz, S.; Goyal, V.; Khalid, A.; Shoham, D.; et al. Early Hospital Readmissions and Mortality in Patients with Decompensated Cirrhosis Enrolled in a Large National Health Insurance Administrative Database. *J. Clin. Gastroenterol.* **2017**, *51*, 839–844. [CrossRef] [PubMed]
14. Barreto, R.; Fagundes, C.; Guevara, M.; Solà, E.; Pereira, G.; Rodríguez, E.; Graupera, I.; Martín-Llahí, M.; Ariza, X.; Cárdenas, A.; et al. Type-1 hepatorenal syndrome associated with infections in cirrhosis: Natural history, outcome of kidney function, and survival. *Hepatology* **2014**, *59*, 1505–1513. [CrossRef] [PubMed]
15. Umapathy, C.; Loganathan, P.; Dodoo, C.; Gajendran, M. Predictors for Early Readmission in Cirrhosis in the United States—A Nationwide Population-based Study. *Am. J. Gastroenterol.* **2018**, *113*, S460–S461. [CrossRef]
16. Saab, S.; Hernandez, J.C.; Chi, A.C.; Tong, M.J. Oral antibiotic prophylaxis reduces spontaneous bacterial peritonitis occurrence and improves short-term survival in cirrhosis: A meta-analysis. *Am. J. Gastroenterol.* **2009**, *104*, 993–1001, quiz 1002. [CrossRef] [PubMed]
17. Komolafe, O.; Roberts, D.; Freeman, S.C.; Wilson, P.; Sutton, A.J.; Cooper, N.J.; Pavlov, C.S.; Milne, E.J.; Hawkins, N.; Cowlin, M.; et al. Antibiotic prophylaxis to prevent spontaneous bacterial peritonitis in people with liver cirrhosis: A network meta-analysis. *Cochrane Database Syst. Rev.* **2020**, *1*, Cd013125. [CrossRef] [PubMed]
18. Bajaj, J.S.; Tandon, P.; O'Leary, J.G.; Wong, F.; Biggins, S.W.; Garcia-Tsao, G.; Kamath, P.S.; Maliakkal, B.; Fallon, M.B.; Lai, J.C.; et al. Outcomes in Patients with Cirrhosis on Primary Compared to Secondary Prophylaxis for Spontaneous Bacterial Peritonitis. *Am. J. Gastroenterol.* **2019**, *114*, 599–606. [CrossRef]
19. Biggins, S.W.; Angeli, P.; Garcia-Tsao, G.; Ginès, P.; Ling, S.C.; Nadim, M.K.; Wong, F.; Kim, W.R. 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*, 1014–1048. [CrossRef] [PubMed]
20. Tapper, E.B.; 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*, 1181–1188.e2. [CrossRef] [PubMed]