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Early Paracentesis is Associated with Better Prognosis Compared to Late or No-paracentesis in Hospitalized Veterans with Cirrhosis and Ascites

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Abstract

Background and Aims: Guidelines recommend that all hospitalized patients with cirrhosis and ascites receive an early (<24 hours from admission) paracentesis. However, national data are not available regarding compliance with and consequences of this quality metric.

Methods: We utilized the national Veterans Administration Corporate Data Warehouse and validated International Classification of Disease codes to evaluate the rate and subsequent outcomes of early, late and no paracentesis for patients with cirrhosis and ascites during their first inpatient admission between 2016–2019.

Results: Of 10,237 patients admitted with a diagnosis of cirrhosis with ascites, 14.3% received an early paracentesis, 7.3% received a late paracentesis, and 78.4% never received a paracentesis. In multivariable modeling, compared to an early paracentesis: both a late paracentesis and no-paracentesis were significantly associated with increased odds of acute kidney injury (AKI) development [OR 2.16 (95% CI 1.59–2.94) and 1.34 (1.09–1.66) respectively); intensive care

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unit (ICU) transfer [OR=2.43 (1.71–3.47) and 2.01 (1.53–2.69), respectively] and inpatient death [OR=1.54 (1.03–2.29) and 1.42 (1.05–1.93), respectively].

Conclusion: Nationally, only 14.3% of admitted Veterans with cirrhosis and ascites received the AASLD guideline recommended diagnostic paracentesis within 24 hours of admission. Failure to complete early paracentesis was associated with higher odds of AKI, ICU transfer, and inpatient mortality. Universal and site-specific barriers to this quality metric should be evaluated and addressed to improve patient outcomes.

Keywords

Cirrhosis; ascites; paracentesis; Acute-on-chronic liver failure; acute kidney injury

Introduction:

Patients with cirrhosis are prone to infections that can lead to organ failure and death, especially if the diagnosis is delayed(1–6). One of the most clinically significant and prevalent infections that is prone to diagnostic delay is spontaneous bacterial peritonitis (SBP). Untreated SBP is associated with acute kidney injury (AKI), sepsis and death(4). An early and accurate diagnosis requires prompt paracentesis, which is always indicated in non-electively hospitalized patients with cirrhosis and clinically apparent ascites(4, 7). There are several perceived logistic barriers to prompt paracentesis. Some of these perceived or real barriers include: a lack of awareness that prompt paracenteses are needed in all admitted patients with cirrhosis and ascites, an incorrect assumption that all patients with SBP have symptoms, and logistical issues, such as a lack of trained personnel available to perform paracentesis, especially on nights and weekends (8). Internal medicine residents are no longer required to be proficient in paracentesis by the American Board of Internal Medicine, leaving much of the responsibility for paracentesis to interventional radiologists(8).

Variation in cirrhosis care within the Veterans Health System (VHA) is tracked and addressed through various quality programs (9). These variances include differing levels of expertise among personnel and resources available to undertake cirrhosis care(10). VHA's national health care system provides a unique opportunity to assess quality metrics and evaluate outcomes in cirrhosis and SBP(11). We hypothesized that Veterans with cirrhosis and ascites who were hospitalized and received a paracentesis within 24 hours of admission would have a better prognosis, including improved survival and renal outcomes, than those who either did not receive a paracentesis or those who receive a paracentesis >24 hours after admission.

Methods:

Data Collection:

Using VHA corporate data warehouse (CDW) and validated International Classification of Disease (ICD-10) codes, we extracted information about the first VA inpatient admission between 2016–2019, where the primary admission diagnosis code was "cirrhosis with ascites" (either one of K70.11, K70.31, K71.51,or K65.2% OR K70.30, K70.4%, K71.7%, K72.1%, K72.9%, K74.6%, K76.6%, K76.7%, K76.8%, I85%, K65.2% with

secondary ICD-10 Code of R.18%)(11, 12). Within each patient's hospitalization period, we collected information regarding the ascites paracentesis procedure using Current Procedural Terminology (CPT) procedure codes (49080–49084).We defined three groups based on their ascites paracentesis, those who received a paracentesis within 1 day of admission (reference group, early paracentesis based on AASLD guidance(4)), those who did not receive the procedure until later in their hospital stay (>1 day after admission, late-paracentesis), and those who did not receive any paracentesis at all (no-paracentesis) during their index hospitalization.

We collected serum creatinine up to 1 year before the hospital admission and throughout the patients' hospital course. Baseline serum creatinine value was defined based on the average value of the previous 3 months and baseline eGFR and CKD stage was defined based on CKD-EPI 2021 equation(13). Any patient with prior history of dialysis, renal transplant, or baseline eGFR < 15 was categorized as prior end-stage renal disease. We have collected serial serum creatinine throughout out the hospitalization and defined acute kidney injury (AKI) stages based on KDIGO-AKI (Kidney Disease Improving Global Outcomes) guidelines(14). We also divided the VA facilities by levels assigned by the VHA into complexity levels of 1, 2 and 3. Levels 2 and 3 were compared level 1, which is the highest complexity, based on the services offered, specialty care availability, and research funding (15).

Additional demographic characteristics and clinical covariates were collected from the VHA CDW. Information relating to patient's age at the time of admission, sex, admission Model for End-Stage Liver Disease-Na (MELD-Na) score, etiology of cirrhosis (viral, alcohol-related, or not specified), serum albumin, white blood cell count (WBC), prior SBP history, prior hepatic encephalopathy (HE) medications, prior AKI, prior diabetes, and Charleston Comorbidity Index (CCI) were collected per previously published definitions (11). Variceal bleeding, SBP infection and other infections (urinary, respiratory, *C.difficile*, and others) were also recorded. Etiology of cirrhosis was collected from the period of 6 months pre-admission up to 30 days post-admission. We also captured weekend versus weekday admissions. We obtained outpatient prescription data with a 90-day pre-admission lookback period. Medications that were investigated included beta-blockers (i.e., selective and carvedilol, nadolol, and propranolol), proton pump inhibitors (PPI), HMG-CoA reductase inhibitors (statins), rifaximin, lactulose, diuretics, fluroquinolones, and trimethoprim-sulfamethoxazole (TMP-SMX). We assessed the associations between paracentesis timing and ICU transfer, inpatient AKI diagnosis, inpatient transplantation and mortality, and 30-day post-discharge transplantation and mortality.

This protocol was approved by the Richmond VA Institutional Review Board, which included a waiver of informed consent.

Statistical Analysis

Cohort Characteristics—Demographic and clinical data from the cohort of patients with cirrhosis and ascites were summarized, and groups were compared (early paracentesis (±1 day) vs. late paracentesis (>1 day) vs. no paracentesis). White blood cell count was natural-log transformed, as this variable was highly skewed. Length of stay (LOS) was

analyzed using the median with IQR since it was not normally distributed. Continuous variables (except for LOS) are expressed as mean ± standard deviation (SD). Categorical variables were presented as raw values and percentages of the total. Equal variance one-way ANOVA, Kruskal-Wallis test, chi-squared test, or Fisher's exact test were used to examine differences between groups, as appropriate. Statistical significance was defined as a $p < 0.05$. Missing values in the demographic and clinical data were omitted from comparisons.

Outcomes and Multivariable Analysis—Logistic regression models for the outcomes (ICU transfer rate, inpatient death rate, death rate within 30 days post-discharge, liver transplant rate while admitted, liver transplant rate within 30 days post-discharge, and Inpatient AKI diagnosis) were fit. Adjusted odds ratios were controlled for all risk factors or demographics that were statistically significantly different between the groups in the uncontrolled analyses (shown in bold in Table 1). We presented the unadjusted and adjusted estimated effect of paracentesis timing on the outcomes of interest, modeling paracentesis within 24 hours of admission as the reference group. We used likelihood ratio tests to assess the overall group effect of late/no paracentesis versus early paracentesis. Liver transplant rates, both during inpatient admission and 30 days post-discharge, were rare (<1% occurrence among entire cohort). Thus, multivariable models were not considered for these two outcomes. Additionally, we did not consider multivariable models for length of stay; this variable is highly dependent on many external factors that we did not have access to as part of this study.

Results:

Clinical Covariates and Risk Factors

From 2016–2019, 10,237 patients had an inpatient stay for cirrhosis with ascites. Among these, 8021 (78.4%) did not receive a paracentesis, 1462 (14.3%) received a paracentesis within 1 day of admission, and 754 (7.3%) received a paracentesis after the first day of admission (Table 1).

The groups differed significantly in mean MELD-Na score (p=0.026), WBC counts (p<0.001), and serum albumin levels (p<0.001). Patients receiving late paracentesis were more likely to have a non-alcohol etiology for cirrhosis than no/early paracentesis (77.7% alcohol vs. 82.3%/81.5%, p=0.011). In our cohort, 5668 (55.4%) patients were seen in complexity level 1a, 2399 (23.4%) in complexity level 1b, 1506 (14.7%) in complexity level 1c, 461 (4.5%) in complexity level 2 and 203 (2.0%) patients in complexity level 3 sites. There was a significantly higher rate of paracentesis completed in complexity level 1 hospitals versus complexity 2/3 sites (p<0.001). There were no significant differences in the early vs late paracentesis (p=0.240) based on complexity level, but complexity level 1 was lower in no-paracentesis vs early paracentesis (p<0.001). Paracentesis groups differed in prior SBP (p<0.001), fluoroquinolone (p=0.022), rifaximin (p=0.012), lactulose (p<0.001), PPI (p=0.006), and diuretics (<0.001). Specifically, early paracentesis patients had higher rates of prior SBP and were more likely to be prescribed lactulose/fluroquinolones/diuretics versus other patients. Rates of rifaximin and PPI were similar in early/no paracentesis groups, but lower in the late paracentesis group. Additionally, patients receiving early

paracentesis were less likely to be admitted over the weekend compared to other patients (p<0.001).

Rate of SBP development was highest in late paracentesis patients followed by early and 5% of those without paracentesis were diagnosed with presumed SBP. Similarly, other infections such as *C.difficile*, urinary tract infections and others were highest in the late-paracentesis patients. Variceal bleeding and pneumonia were lowest in early paracentesis patients and equivalent across the other groups. There were no significant differences in age, gender, CCI, CKD score, presence of diabetes, admission AKI, TMP-SMX SBP prophylaxis, and selective/non-selective selective β-blocker use between the groups (Table 1).

Outcomes

Among our cohort, the median length of stay (LOS) was 3 days (IQR: 2–7 days). The groups differed significantly in terms of LOS (p<0.001), with the late- paracentesis group staying longest. Ten percent (n=1009) patients died during hospitalization, and 1311 (12.8%) died within 30 days of discharge. ICU transfers occurred during the hospital stays of 978 (9.6%) patients, 22 (0.2%) received liver transplant (LT) while hospitalized, and 17 (0.2%) received LT within 30 days of discharge. 2595 (25.3%) patients were readmitted to a VA hospital within 30 days for any reason; readmission was lowest in the early paracentesis group (p=0.002).

Death during hospitalization and at 30 days post discharge, AKI development, and ICU transfer rates (all p<0.001) were significantly different between the groups. There were no significant differences in inpatient or 30-day liver transplant rates between the groups, although the number of patients transplanted was small (<1.0%). LOS was the highest in late paracentesis group, compared to both other groups.

Unadjusted Analysis

Unadjusted logistic regression models showed that, compared to the early paracentesis (reference) group, patients who received a late paracentesis had 2.25 times higher odds of inpatient death, 1.41 times higher odds of 30-day death, 3.73 times higher odds of ICU transfer and 2.17 higher odds of Inpatient AKI diagnosis. Compared to the early paracentesis group, patients who received no paracentesis had significantly greater odds of inpatient death and ICU transfer (Table 2).

Multivariable Analysis

Adjusted odds ratios controlled for MELD-Na, serum albumin, log-WBC, etiology of cirrhosis, prior SBP, prior HE, in-hospital variceal bleed, infections at discharge, SBP at discharge, weekend admission, hospital complexity, and admission use of fluroquinolones, lactulose, rifaximin, diuretics, and PPIs. The AKI estimates were also adjusted for the presence of a CKD diagnosis, in addition to variables mentioned. Specific p-values are in Table 3.

Inpatient death was more likely in patients who received a late paracentesis (OR:1.54, 95% CI: 1.03, 2.29) or no paracentesis (OR: 1.42, 95% CI: 1.05, 1.93) compared to

those who had a timely paracentesis. High MELD-Na, high admission WBC, higher site complexity, variceal bleed, SBP diagnosis, lower albumin, and admission PPI and diuretic use were also associated with inpatient death, along with etiologies other than alcohol. Both a late (OR: 2.43, 95% CI: 1.71, 3.47) or no-paracentesis (OR: 2.01, 95% CI: 1.53, 2.69) compared to an early paracentesis significantly increased the odds of ICU transfer, along with a higher MELD-Na, cirrhosis etiology other than alcohol, admission WBC, higher site complexity, variceal bleed, other infections, SBP infection, and lower rate of admission rifaximin, diuretic, and PPI use. AKI development was associated with late paracentesis (OR: 2.16, 95% CI: 1.59, 2.94), and no-paracentesis (OR: 1.34, 95% CI: 1.09, 1.66), compared to a timely paracentesis after controlling for other factors associated with this outcome. Additional variables associated with AKI development were higher MELD-Na, non-alcoholic etiology of cirrhosis, prior CKD, admission WBC, higher site complexity, other infections, SBP infection, and lower admission lactulose and rifaximin use. Death at 30-days was linked with a late paracentesis (OR: 1.38, 95% CI: 1.01, 1.87) compared to a timely paracentesis, along with a higher admission MELD-Na and WBC, higher site complexity, and etiology other than alcohol.

Discussion

This large, national cohort study identified the frequency of paracentesis in patients with cirrhosis who were hospitalized with a diagnosis of ascites. Despite frequent SBP in this population and guidelines recommending “a diagnostic paracentesis…be performed as soon as a patient with cirrhosis and ascites is hospitalized…for any reason”(4), less than one quarter of this cohort received a paracentesis (1, 2, 7, 16). Timely (vs. late) paracentesis was associated with approximately twice the risk of ICU admission, AKI, and mortality. The rates of SBP infection, variceal bleeding, and most other infections were highest in the late paracentesis group.

A timely diagnosis of infections, such as SBP, is the key to prevent AKI, organ failure, and death in patients with cirrhosis(4, 6, 7, 17). However, due to a lack of awareness and perceived or real logistical issues, there is often a reticence to perform this invasive but safe procedure(4). As shown in our experience, which confirms and extends prior studies into the national VA context, there is a high cost to not performing early paracentesis(17). We found the lowest risk of ICU transfer, AKI development, and inpatient mortality associated with a timely paracentesis, intermediate risk in those with no paracentesis, and highest risk in those with a late paracentesis, independent of usual clinical severity markers. While the specific reasons for these differences are unclear, it is likely that a timely diagnosis and treatment of SBP or exclusion of SBP resulted in appropriate therapy to prevent AKI, need for ICU and inpatient mortality. A prior study analyzing selected inpatient databases has shown that high-risk features including AKI and HE resulted in a higher rate of early paracentesis(17). Moreover, the authors found that early paracentesis was associated with better outcomes compared to those who did not undergo this procedure early. Our study extends these results into a national cohort and, importantly, assesses the impacts of late or no paracentesis versus early paracentesis.

Some of these outcomes could be related to clinician perception of risk for SBP and therefore need for a diagnostic paracentesis. While we could not specifically determine the clinical presentations and the main reasons(s) for admission, patients who received an early paracentesis were more likely to have prior SBP and be on SBP prophylaxis, diuretics and lactulose compared to the other groups. These point towards a higher pre-paracentesis probability of SBP in this population, which could have prompted this procedure. Despite the clinical differences between the early paracentesis and no-paracentesis patients, we found a similar WBC count, MELD score, albumin levels, and rifaximin use across early and no-paracentesis patients. Importantly, co-morbid conditions, Prior AKI, demographics, beta-blocker use nor use of TMP-SMX were significantly different. However, a clinical assessment is not adequate to rule out SBP, which can be asymptomatic and therefore requires a paracentesis in all admitted patients with cirrhosis and ascites(4, 7, 18). These results further validate the approach suggested in AASLD and other guidelines to provide paracentesis to all patients admitted non-electively within 24 hours, regardless of labs, symptoms, and appearance.

The group that received a late paracentesis was also a high-risk group. This group had the highest MELD-Na scores, WBC scores, and lowest admission albumin, as well as highest PPI use, SBP history and alcohol-related liver disease rates (19). These factors are a mix of data that would decrease the chances of SBP (lower medications associated with SBP, alcohol-related etiology, and prior complications) versus those that require exclusion of an infection (worse liver disease severity). It is unclear why these patients did not receive paracentesis. However, it is possible that competing medical issues, related to their more severe disease, resulted in delays. Regardless of the reason for delay, this group had the highest rates of SBP and other infections, which were, in turn, independently associated with death. Late paracentesis in this vulnerable group may have led to a missed infection, resulting in a longer LOS, greater development of AKI, ICU requirement, and death. It is also possible that this group was sicker at baseline, predisposing to negative outcomes. However, even after controlling for baseline differences, early paracentesis was associated with better outcomes. Late paracentesis can also occur when patients have insufficient volume of ascites to complete a paracentesis, or when they present with other diagnoses that require empiric antibiotics, such as variceal bleeding. There is also a possibility that the late paracentesis was triggered because of concern for a multidrug resistant or nosocomial SBP, both of which are associated with poor outcomes(20, 21). While it is possible that the SBP could have been acquired during the hospital, the higher admission MELD-Na and WBC and lower albumin at admission in the late-paracentesis group argues against nosocomial SBP being the predominant reason for a late paracentesis.

The multi-variable analysis identified factors associated with poor prognosis (i.e., high MELD-Na and WBC count, lower albumin, and etiologies other than alcohol). Alcohol-related cirrhosis has been previously associated with higher rates of infections, while there is emerging evidence that rifaximin could be protective against SBP(22). However, some aspects, such as admission PPI, lactulose, and diuretic use being associated with a lower rate of ICU and death contradict prior publications, suggesting that differences in outcomes may be more related to the timing of paracentesis. The group with the worst outcomes (i.e., the late-paracentesis patients) had the lowest PPI, lactulose, and diuretic use. This once again

highlights the need to adhere to guideline recommended early paracentesis in all admitted patients with cirrhosis and ascites(4, 7).

There are several potential provider-, system-, and patient-related barriers to early paracentesis. The main provider-related reason is likely inadequate recognition that *all* non-elective admitted patients with cirrhosis require paracentesis within 24 hours of admission to exclude SBP, which is often asymptomatic(4, 7). This is difficult to gauge objectively, but sites with greater complexity are likely to have more GI/hepatology expertise, interventional radiology presence, greater exposure to patients with cirrhosis, and greater coverage resources. The latter also are part of system-related barriers, which we studied by involving the facility complexity scores and a significantly lower early paracentesis proportion in patients admitted over the weekend. Weekend drop in paracenteses were found in a prior study using the Nationwide Inpatient Sample, which does not include VHA data and allows for multiple admissions per person to be counted as separate events; these data extend these findings onto the VA population(23). The results showed that although there were differences in the rate of paracentesis overall, this was primarily driven by differences in no-paracentesis vs early paracentesis in those with lower resources. However, all negative outcomes were greater in level 1 complexity centers despite the higher rate early paracentesis. This could be due to a higher number of sicker patients being cared for at facilities with greater access to specialists and ICU beds. In addition, the low reimbursement rate for paracentesis further diminished the enthusiasm to perform this necessary but often time-consuming procedure when it is for therapeutic reasons, which should not have affected our study but is a system-issue outside the VA. Patient-related barriers could include obesity or prior surgery resulting in no adequate or safe location to perform the paracentesis or lack of patient consent. Future studies should evaluate the barriers to guideline implementation and explore potential corrective strategies.

The current study across the national VA system is one of the largest experiences of the prevalence and timing of paracentesis in admitted patients with cirrhosis and ascites, which has the possibility to improve outcomes. This situation has been exacerbated by procedure training including paracentesis in internal medicine residency becoming optional(8). This has resulted in paracentesis often requiring support from emergency room staff, internal medicine attendings or interventional radiologists, which has the potential to delay necessary procedures and appropriate therapy. This change in training requirements will only further encourage inappropriate empiric antibiotic stewardship, exacerbate the ever-increasing rate of multidrug resistant infections, and increase the risk of acute-on chronic liver failure(5, 20, 24, 25).

Given that CDW abstraction was based on ICD and CPT codes, there were several potential limitations of these analyses. Because we do not have granular information regarding clinical presentation, it is not possible to assess the necessity of paracentesis for all patients. Thus, it is possible that the admission diagnoses in some patients may reflect ascites that is already controlled with diuretics, or “untappable”, small-volume ascites. However, these findings still support earlier paracentesis where possible. Other limitations of this study include the inability to assess data over the admission, including daily inpatient doses of antibiotic and albumin use and reason(s) for these medications, specific reason

for admission. Likewise, the CDW does not include the causes of death. Using medical record data, we could not evaluate the reasons why some patients received a paracentesis versus not, which is an important potential area of future study. Nevertheless, AASLD guidelines recommend that every patient admitted with cirrhosis and ascites receive at least a diagnostic paracentesis(4, 7). Clearly there is a need to intervene to improve adherence to such guidelines.

In conclusion, we found that only 14.3% of admitted Veterans with an admission diagnosis of cirrhosis with ascites received an early paracentesis and less than a quarter of admitted patients with an admission diagnosis of cirrhosis with ascites ever received a paracentesis during their index hospitalization. Not receiving a timely paracentesis was associated with a higher risk of acute kidney injury, need for intensive care and inpatient mortality independent of other risk factors such as cirrhosis severity, variceal bleeding, other infections, prior complications, and admission medications. Efforts to increase paracentesis timeliness, including over the weekends, are necessary and have the potential to improve outcomes for Veterans with cirrhosis and ascites.

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List of abbreviations:

SBP	spontaneous bacterial peritonitis
CDW	Corporate Data Warehouse
ICD	International Classification of Disease
AKI	acute kidney injury
CKD	chronic kidney disease
ICU	intensive care unit
HE	hepatic encephalopathy
CPT	Current Procedural Terminology
KDIGO	Kidney Disease Improving Global Outcomes
VHA	Veterans Health System
MELD-Na	Model for End-Stage Liver Disease-Na
CCI	Charlson Comorbidity index
LOS	length of stay
LT	liver transplantation
PPI	proton pump inhibitors

TMP-SMX	trimethoprim-sulfamethoxazole
WBC	white blood cell count

References:

1. Bajaj JS, Kamath PS, Reddy KR. The Evolving Challenge of Infections in Cirrhosis. N Engl J Med 2021;384(24):2317–30. [PubMed: 34133861]
2. Bajaj JS, O'Leary JG, Reddy KR, Wong F, Biggins SW, Patton H, et al. Survival in infection-related acute-on-chronic liver failure is defined by extrahepatic organ failures. Hepatology 2014;60(1):250–6. [PubMed: 24677131]
3. Bajaj JS, Wong F, Kamath PS, Lai JC, O'Leary JG. Acute-on-Chronic Liver Failure. Am J Gastroenterol 2022;117(6):831–4. [PubMed: 35333779]
4. 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(2):1014–48. [PubMed: 33942342]
5. Piano S, Singh V, Caraceni P, Maiwall R, Alessandria C, Fernandez J, et al. Epidemiology and Effects of Bacterial Infections in Patients With Cirrhosis Worldwide. Gastroenterology 2019;156(5):1368–80 e10. [PubMed: 30552895]
6. Seymour CW, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, et al. Time to Treatment and Mortality during Mandated Emergency Care for Sepsis. N Engl J Med 2017;376(23):2235–44. [PubMed: 28528569]
7. Bajaj JS, O'Leary JG, Lai JC, Wong F, Long MD, Wong RJ, et al. Acute-on-Chronic Liver Failure Clinical Guidelines. Am J Gastroenterol 2022;117(2):225–52. [PubMed: 35006099]
8. https://blog.abim.org/wp-content/uploads/2019/03/Evolution-of-Procedural-Requirements-for-IM-1.pdf. [cited; Available from:
9. Serper M, Taddei TH, Mehta R, D'Addeo K, Dai F, Aytaman A, et al. Association of Provider Specialty and Multidisciplinary Care With Hepatocellular Carcinoma Treatment and Mortality. Gastroenterology 2017;152(8):1954–64. [PubMed: 28283421]
10. Serper M, Kaplan DE, Shults J, Reese PP, Beste LA, Taddei TH, et al. Quality Measures, All-Cause Mortality, and Health Care Use in a National Cohort of Veterans With Cirrhosis. Hepatology 2019;70(6):2062–74. [PubMed: 31107967]
11. Badal B, Silvey S, Dragilev L, O'Leary JG, Morgan TR, Cheung R, et al. Primary Prophylaxis for Spontaneous Bacterial Peritonitis is Linked to Antibiotic Resistance in the Veterans Health Administration. Hepatology 2023.
12. Mapakshi S, Kramer JR, Richardson P, El-Serag HB, Kanwal F. Positive Predictive Value of International Classification of Diseases, 10th Revision, Codes for Cirrhosis and Its Related Complications. Clin Gastroenterol Hepatol 2018;16(10):1677–8. [PubMed: 29410051]
13. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race. N Engl J Med 2021;385(19):1737–49. [PubMed: 34554658]
14. Angeli P, Gines P, Wong F, Bernardi M, Boyer TD, Gerbes A, et al. Diagnosis and management of acute kidney injury in patients with cirrhosis: revised consensus recommendations of the International Club of Ascites. J Hepatol 2015;62(4):968–74. [PubMed: 25638527]
15. Nature of Veterans Health Administration Facilities Management (Engineering) Tasks and Staffing. Facilities Staffing Requirements for the Veterans Health Administration-Resource Planning and Methodology for the Future: National Academies Press (US); 2019.
16. Arvaniti V, D'Amico G, Fede G, Manousou P, Tsochatzis E, Pleguezuelo M, et al. Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis. Gastroenterology 2010;139(4):1246–56, 56 e1–5. [PubMed: 20558165]
17. Rosenblatt R, Tafesh Z, Shen N, Cohen-Mekelburg S, Kumar S, Lucero C, et al. Early Paracentesis in High-Risk Hospitalized Patients: Time for a New Quality Indicator. Am J Gastroenterol 2019;114(12):1863–9. [PubMed: 31688022]

18. Chinnock B, Afarian H, Minnigan H, Butler J, Hendey GW. Physician clinical impression does not rule out spontaneous bacterial peritonitis in patients undergoing emergency department paracentesis. Ann Emerg Med 2008;52(3):268–73. [PubMed: 18433932]

19. O'Leary JG, Reddy KR, Wong F, Kamath PS, Patton HM, Biggins SW, et al. Long-term use of antibiotics and proton pump inhibitors predict development of infections in patients with cirrhosis. Clin Gastroenterol Hepatol 2015;13(4):753–9 e1–2. [PubMed: 25130937]

20. Bajaj JS, O'Leary JG, Tandon P, Wong F, Garcia-Tsao G, Kamath PS, et al. Nosocomial Infections Are Frequent and Negatively Impact Outcomes in Hospitalized Patients With Cirrhosis. Am J Gastroenterol 2019;114(7):1091–100. [PubMed: 31180922]

21. Piano S, Fasolato S, Salinas F, Romano A, Tonon M, Morando F, et al. The empirical antibiotic treatment of nosocomial spontaneous bacterial peritonitis: Results of a randomized, controlled clinical trial. Hepatology 2016;63(4):1299–309. [PubMed: 26084406]

22. Goel A, Rahim U, Nguyen LH, Stave C, Nguyen MH. Systematic review with meta-analysis: rifaximin for the prophylaxis of spontaneous bacterial peritonitis. Aliment Pharmacol Ther 2017;46(11–12):1029–36. [PubMed: 28994123]

23. Gupta K, Khan A, Goyal H, Cal N, Hans B, Martins T, et al. Weekend admissions with ascites are associated with delayed paracentesis: A nationwide analysis of the 'weekend effect'. Annals of hepatology 2020;19(5):523–9. [PubMed: 32540327]

24. Wong F, Piano S, Singh V, Bartoletti M, Maiwall R, Alessandria C, et al. Clinical features and evolution of bacterial infection-related acute-on-chronic liver failure. J Hepatol 2021;74(2):330–9. [PubMed: 32781201]

25. Fernandez J, Prado V, Trebicka J, Amoros A, Gustot T, Wiest R, et al. Multidrug-resistant bacterial infections in patients with decompensated cirrhosis and with acute-on-chronic liver failure in Europe. J Hepatol 2019;70(3):398–411. [PubMed: 30391380]

Table 1.

Cohort characteristics of admitted patients with cirrhosis and ascites (n=10,237)

	No Paracentesis (n = 8021)	**paracentesis ± 1 Day (n = 1462)**	**Paracentesis >1 Day (n = 754)**	***p*-value**
Age	63.03 (9.49)	63.46 (9.11)	63.24 (8.99)	0.256
Male Gender	7665 (95.6%)	1410 (96.4%)	713 (94.6%)	0.523
Weekend Admission	2619 (25.8%)	316 (21.6%)	326 (43.2%)	**<0.001**
Hospital Complexity (1: high vs 2+3: low)	1: 7453 (92.9%) 2+3: 568 (7.1%)	1: 1404 (96.0%) 2+3: 58 (4.0%)	1: 716 (95.0%) 2+3: 38 (5.0%)	**<0.001**
Diabetes	2862 (35.7%)	543 (37.1%)	273 (36.2%)	0.557
CCI	4.98 (2.92)	5.09 (2.96)	5.06 (2.93)	0.362
WBC (natural-log transform)	1.86 (0.57)	1.87 (0.55)	2.02 (0.58)	**<0.001**
Cirrhosis characteristics				
Admission MELD-Na	12.80 (9.04)	13.06 (8.76)	13.87 (8.59)	**0.026**
Alcohol etiology	6603 (82.3%)	1192 (81.5%)	586 (77.7%)	**0.011**
Admission Albumin	2.60 (1.05)	2.60 (0.61)	2.42 (0.62)	**<0.001**
Prior SBP	431 (5.4%)	132 (9.0%)	24 (3.2%)	**<0.001**
Prior HE	174 (2.2%)	24 (1.6%)	6 (<1.0%)	**0.020**
Prior CKD	1640 (20.4%)	339 (23.2%)	167 (22.1%)	0.078
Prior AKI	3806 (47.5%)	684 (46.8%)	330 (43.8%)	0.200
Inpatient events				
SBP infection	426 (5.3%)	132 (9.0%)	88 (11.7%)	**<0.001**
C. Difficile	176 (2.2%)	29 (2.0%)	34 (4.5%)	**<0.001**
Pneumonia	466 (5.8%)	55 (3.8%)	51 (6.8%)	**0.003**
Urinary Infection	508 (6.3%)	50 (3.1%)	81 (10.7%)	**<0.001**
Other Infections	461 (5.7%)	64 (4.4%)	77 (10.2%)	**<0.001**
Variceal bleeding	459 (5.7%)	54 (3.7%)	44 (5.8%)	**0.006**
Admission Meds				
Bactrim (TMP-SMX)	221 (2.8%)	50 (3.4%)	19 (2.5%)	0.321
Fluroquinolones	818 (10.2%)	171 (11.7%)	60 (8.0%)	**0.022**
Rifaximin	661 (8.2%)	117 (8.0%)	39 (5.2%)	**0.012**
Lactulose	1433 (17.9%)	329 (22.5%)	94 (12.5%)	**<0.001**
Carvedilol	315 (3.9%)	43 (2.9%)	23 (3.1%)	0.112
Nadolol	74 (1.0%)	14 (1.0%)	7 (1.0%)	0.992
Propranolol	655 (8.2%)	111 (7.6%)	46 (6.1%)	0.117
Selective β-Blockers	605 (7.5%)	118 (8.1%)	49 (6.5%)	0.414
Diuretics	3114 (38.8%)	681 (46.6%)	224 (29.7%)	**<0.001**
PPI	1926 (24.0%)	335 (22.9%)	143 (19.0%)	**0.006**
Statins	667 (8.3%)	104 (7.1%)	71 (9.4%)	0.142
Outcomes				
Median LOS (Days)	3.00 (1.00–7.00)	2.00 (1.00–5.00)	8.00 (5.00–16.00)	**<0.001**

	No Paracentesis (n = 8021)	**paracentesis ± 1 Day (n = 1462)**	**Paracentesis >1 Day (n = 754)**	***p*-value**
Inpatient AKI	1720 (21.4%)	318 (21.7%)	255 (33.8%)	**<0.001**
30-Day Readmission	2029 (25.3%)	416 (28.5%)	150 (19.9%)	**0.002**
Inpatient ICU transfer	769 (9.6%)	78 (5.3%)	131 (17.4%)	**<0.001**
Inpatient Death	824 (10.3%)	89 (6.1%)	96 (12.7%)	**<0.001**
30-day Death	968 (12.1%)	203 (13.9%)	140 (18.6%)	**<0.001**
Inpatient LT	15 (<1.0%)	5 (<1.0%)	2 (<1.0%)	0.316
30-day LT	11 (<1.0%)	3 (<1.0%)	3 (<1.0%)	0.165

AKI: acute kidney injury, CKD: chronic kidney disease, ICU: intensive care unit, LOS: length of stay, LT: liver transplantation, MELD-Na: Model for End-stage Liver Disease-Sodium, PPI: proton pump inhibitors, SBP: spontaneous bacterial peritonitis, TMP-SMX: trimethoprim-sulfamethoxazole, WBC: white blood cell count, CCI: Charlson Comorbidity index. Bold text shows headings and statistically significantly differences

Table 2:

Results from Unadjusted Models

Outcome	**Odds Ratio (95% CI),** ***Late Paracentesis vs. Early Paracentesis***	**Odds Ratio (95% CI),** ***No Paracentesis vs. Early Paracentesis***
Death (inpatient)	2.25 (1.66, 3.05), $p<0.0001$	1.77 (1.42, 2.23), $p<0.0001$
Death (30-days)	1.41 (1.12, 1.79), $p=0.004$	0.85 (0.72, 1.00), $p=0.06$
ICU transfer	3.73 (2.78, 5.03), $p<0.0001$	1.88 (1.49, 2.41), $p<0.0001$
AKI during admission	2.34 (1.89, 2.91), $p<0.001$	1.09 (0.95, 1.26), $p=0.214$

AKI, acute kidney injury; ICU, intensive care unit

Table 3:

Results from Adjusted Multivariable Models

Outcome	Odds Ratio (95% CI)	*p*-value
Inpatient death		
Group	Late vs. early paracentesis: 1.54 (1.03, 2.29) No vs. early paracentesis : 1.42 (1.05, 1.93)	Overall: 0.046 Late vs. early paracentesis: 0.034 No vs. early paracentesis: 0.024
MELD-Na	1.08 (1.07, 1.09)	<0.001
Serum Albumin	0.82 (0.71, 0.96)	0.013
log-WBC	1.92 (1.62, 2.28)	<0.001
Etiology of Cirrhosis	Alcohol vs. Other: 0.76 (0.60, 0.97)	Alcohol vs. Other: 0.027
PPI	0.70 (0.53, 0.91)	0.009
Diuretics	0.73 (0.58, 0.91)	0.007
Variceal Bleed	1.85 (1.33, 2.54)	<0.001
SBP infection	2.40 (1.82, 3.14)	<0.001
Death (30-days)		
Group	Late. vs. early paracentesis: 1.38 (1.01, 1.87) No vs. early paracentesis: 1.02 (0.82, 1.28)	Overall: 0.05 Late vs. early paracentesis: 0.041 No vs. early paracentesis: 0.842
MELD-Na	1.06 (1.05, 1.07)	<0.001
log-WBC	1.48 (1.29, 1.69)	<0.001
Etiology of Cirrhosis	Alcohol vs. Other: 0.61 (0.51, 0.73)	Alcohol vs. Other: <0.001
ICU transfer		
Group	Late vs. early paracentesis: 2.43 (1.71, 3.47) No vs. early paracentesis: 2.01 (1.53, 2.69)	Overall: <0.001 Late vs. early paracentesis: <0.001 No vs. early paracentesis:<0.001
MELD-Na	1.04 (1.03, 1.05)	<0.001
log-WBC	1.37 (1.18, 1.57)	<0.001
Etiology of Cirrhosis	Alcohol vs. Other: 0.66 (0.54, 0.80)	Alcohol vs. Other: <0.001
Complexity	1a/1b/1c vs 2/3: 1.94 (1.27, 3.12)	0.003
PPI	0.76 (0.60, 0.94)	0.013
Rifaximin	0.56 (0.36, 0.83)	0.006
Diuretics	0.71 (0.59, 0.86)	<0.001
Variceal Bleed	1.87 (1.42, 2.44)	<0.001
Non-SBP infection	1.65 (1.25, 2.17)	<0.001
SBP infection	1.79 (1.38, 2.30)	<0.001
AKI development		
Group	Late vs. early paracentesis: 2.16 (1.59, 2.94) No vs. early paracentesis: 1.34 (1.09, 1.66)	Overall: <0.001 Late vs. early paracentesis: <0.001 No vs. early paracentesis: 0.006
MELD-Na	1.12 (1.11, 1.13)	<0.001
Serum Albumin	1.11 (1.01, 1.23)	0.033
log-WBC	1.80 (1.57, 2.06)	<0.001

Outcome	Odds Ratio (95% CI)	*p*-value
Etiology of Cirrhosis	Alcohol vs. Other: 0.67 (0.56, 0.81)	Alcohol vs. Other: <0.001
Complexity	1a/1b/1c vs 2/3: 1.65 (1.19, 2.33)	0.004
Lactulose	0.73 (0.60, 0.90)	0.003
Rifaximin	0.74 (0.56, 0.98)	0.034
Prior CKD	2.48 (2.08, 2.95)	<0.001
Non-SBP infection	1.77 (1.33, 2.37)	<0.001
SBP infection	1.34 (1.03, 1.76)	0.030

AKI: acute kidney injury, CKD: chronic kidney disease, ICU: intensive care unit, MELD-Na: Model for End-stage Liver Disease-Sodium, PPI: proton pump inhibitors, WBC: white blood cell count.