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Research Letter

Delay in Paracentesis and Clinical Outcomes in Hospitalized Patients with Cirrhosis and Ascites

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Cirrhosis of the liver is a common cause of death worldwide, including in the U.S., and contributes significantly to the healthcare burden.[1–3] Ascites is the most frequent complication in hospitalized patients with cirrhosis.[4,5] The American Association for the Study of Liver Diseases and the European Association for the Study of the Liver recommend large volume paracentesis (LVP) for hospitalized patients with cirrhosis and ascites.[5,6] However, paracentesis is often delayed (performed after 12–24 h of admission) in hospitalized patients.[7,8] Common reasons for this delay include weekend admissions, older age, comorbid conditions, coagulopathy, and the involvement of interventional radiology in performing the paracentesis.[9,10] Studies have shown that a delay in paracentesis is associated with higher mortality[11,12] and increased healthcare resource utilization.[13] However, population-level data on trends in delayed paracentesis and its association with patient outcomes are limited.

The National Inpatient Sample (NIS) database, representing over seven million hospital discharges from 46 states, includes up to 25 discharge diagnoses using ICD codes. The NIS database represents approximately 97% of the U.S. population. Hospitalizations involving LVP were identified (2016–2019) using discharge ICD-10 procedure codes (0W9G30Z, 0W9G3ZX, or 0W9G3ZZ). Hospitalizations with missing outcome data were excluded. Other covariates, confounders, and outcomes for analysis were identified using ICD-10 discharge diagnosis or procedure codes (Supplementary Table 1).[14]

The primary outcome was in-hospital mortality, while secondary outcomes included length of stay in days and total hospital charges in USD. Using the variable of procedure day, delayed LVP was defined as the first LVP being performed more than 24 h after admission. Trends in delayed LVP were analyzed using the Armitage trend test. A logistic regression model was built to examine variables associated with delayed LVP. Hospitalizations with delayed LVP were compared to those without delay for in-hospital mortality, liver disease complications, and hospital resource use. Logistic regression models were built to determine the association between delayed LVP and outcomes. Clinically relevant variables and those differing at baseline were entered into the models to examine the independent association of delayed LVP with respective outcomes.

Of 496,138 hospitalizations with a discharge diagnosis of cirrhosis between 2016 and 2019, 100,482 (24.3%) had ascites and underwent LVP during hospitalization. Of these, 94,787 hospitalizations (mean age 57.7 years, 35.9% females, 68.1% Caucasians, 10.8% obese, 30.3% with diabetes mellitus, 68.2% with alcohol-related liver disease, 22.4% weekend hospitalizations) were analyzed. A total of 39,350 (41.5%) hospitalizations experienced a delay in LVP (Supplementary Fig. 1).

Trends in LVP and delays during hospitalization

Although the proportion of hospitalizations receiving LVP was significantly lower in 2019 ($P < 0.001$), the numerical decrease was small (from 20.9% to 20.3%). Delayed LVP increased over time, from 41.2% in 2016 to 42.8% in 2019 (Fig. 1A).

Baseline characteristics comparing hospitalizations based on delay in performing LVP

Hospitalizations with delayed LVP, compared to those without delay, involved older patients and were more likely to involve females, Black patients, obese individuals, and those with diabetes (Table 1). In a logistic regression model controlling for baseline characteristics and the calendar year of admission, weekend admission was most strongly associated with delayed LVP, with an odds ratio (95% confidence interval) of 1.66 (1.59–1.72). Other variables associated with delayed LVP included patient age, obesity, and admission to urban hospitals. In contrast, Medicaid and uninsured patients versus those with Medicare insurance had lower odds of delayed LVP (Supplementary Table 2).

Delayed LVP and liver disease complications

Acute kidney injury (AKI) was the most common complica-

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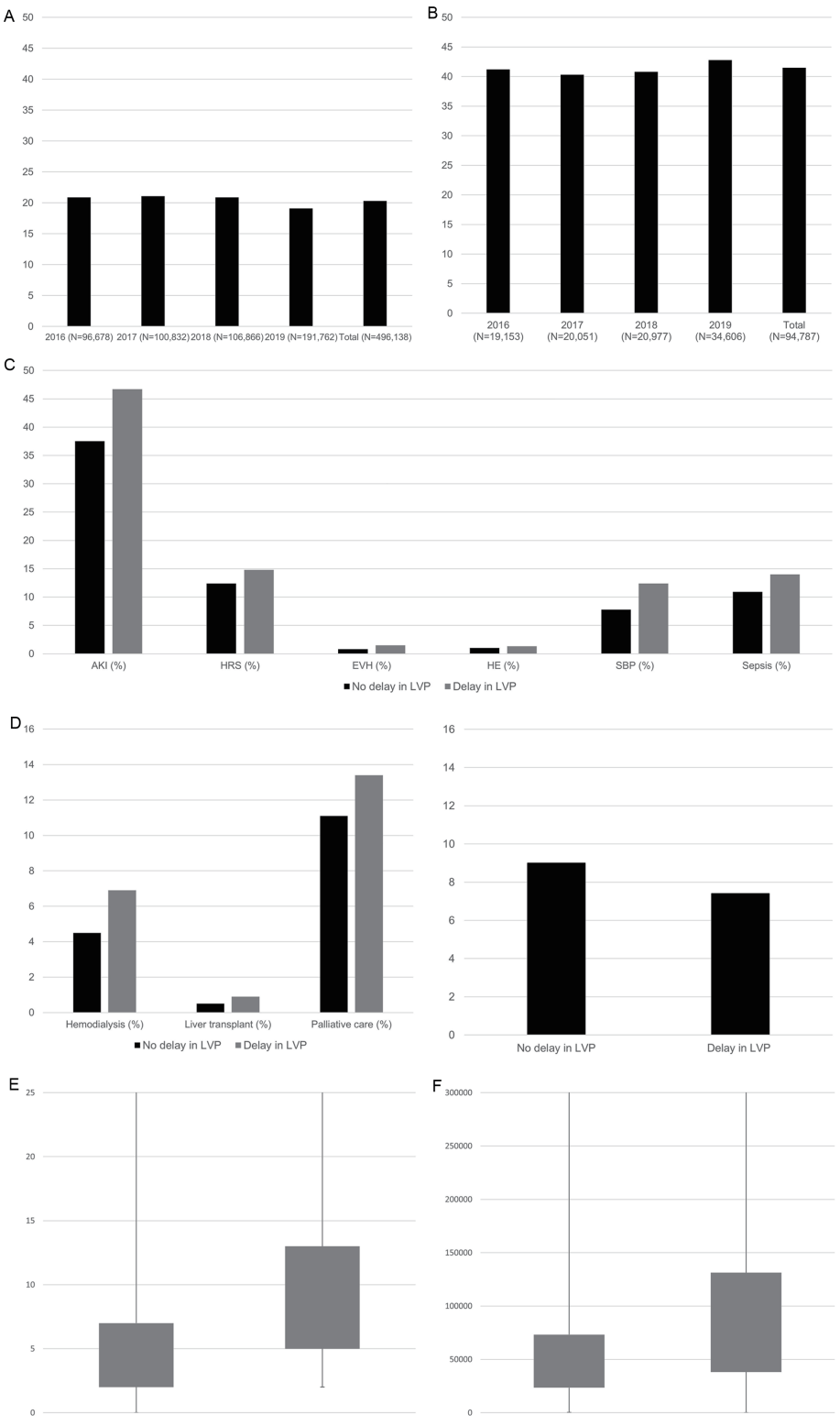

Fig. 1. (A–B) Trends between 2016 and 2019 for (A) large volume paracentesis (LVP) and (B) delay in LVP during hospitalization. (C) Proportion of hospitalizations associated with cirrhosis complications, comparing hospitalizations without vs. with delayed large volume paracentesis (LVP). (D) Proportion of hospitalizations associated with the use of hospital resources, comparing hospitalizations without vs. with delayed large volume paracentesis (LVP). (E–F) Box plots showing the mean length of stay in days (E) and total hospital charges in USD per hospitalization (F), comparing hospitalizations without vs. with delayed large volume paracentesis (LVP). AKI, acute kidney injury; HRS, hepatorenal syndrome; EVH, esophageal variceal hemorrhage; HE, hepatic encephalopathy; SBP, spontaneous bacterial peritonitis.

Table 1. Baseline characteristics comparing hospitalizations without vs. with delayed large volume paracentesis (LVP)

	Total hospitalizations (N = 94,787)	No delay in LVP (N = 55,437)	Delay in LVP (N = 39,350)	*P*
Mean age, SD	57.7, 11.8	57.3, 11.7	58.3, 12	<0.001
% Female	34,003 (35.9)	19,762 (35.7)	14,241 (36.2)	0.088
% Caucasians	62,799 (68.1)	36,696 (68.1)	26,103 (68.2)	
% AA	8,837 (9.4)	4,910 (9.1)	3,727 (9.7)	<0.001
% Hispanics	14,875 (16.1)	8,880 (16.5)	5,995 (15.7)	
% Weekend admissions	21,258 (22.4)	10,420 (18.8)	10,838 (27.5)	<0.001
% Medicare	36,001 (38)	20,299 (36.7)	15,702 (40)	
% Medicaid	28,443 (30.1)	17,037 (30.8)	11,406 (29)	<0.001
% Private	20,555 (21.7)	12,023 (21.7)	8,532 (21.7)	
Obese (%)	6,475 (10.8)	3,750 (10.5)	2,725 (11.1)	0.024
Diabetes mellitus (%)	28,697 (30.3)	16,532 (29.8)	12,165 (30.9)	<0.001
% Rural	4,380 (4.6)	2,681 (4.8)	1,699 (4.3)	
% Non-teaching urban	18,202 (19.2)	10,632 (19.2)	7,570 (19.2)	<0.007
% Teaching urban	72,205 (76.2)	42,124 (76)	30,081 (76.4)	
% Small size hospital	15,671 (16.5)	9,245 (16.7)	6,426 (16.3)	
% Moderate size hospital	24,337 (27.8)	15,376 (27.7)	10,961 (27.9)	0.368
% Large size hospitals	52,779 (55.7)	30,816 (55.6)	21,963 (55.8)	
% ALD	64,165 (68.2)	38,448 (69.4)	26,209 (66.6)	
% Chronic viral hepatitis	13,475 (16.4)	7,878 (14.2)	5,597 (14.2)	<0.001
% NASH	5,180 (5.5)	2,960 (5.3)	2,220 (5.6)	

SD, standard deviation; AA, African Americans; ALD, alcohol-associated liver disease; NASH, non-alcoholic steatohepatitis.

tion and occurred more frequently among hospitalizations with delayed LVP (46.7% vs. 35.7%, $P < 0.001$). Hepatorenal syndrome (HRS) was also more common with delayed LVP (14.8% vs. 12.4%, $P < 0.001$). Other complications of cirrhosis, including esophageal variceal hemorrhage, hepatic encephalopathy, spontaneous bacterial peritonitis (SBP), and sepsis, were also more frequent in cases of delayed LVP (Fig. 1C). In a logistic regression model controlling for baseline characteristics and the calendar year of hospitalization, delayed LVP was associated with AKI or HRS [1.41 (1.37–1.48)], SBP or sepsis [1.20 (1.16–1.25)], and variceal bleeding or hepatic encephalopathy [1.57 (1.42–1.75)] (Table 2). Interestingly, the calendar year was associated with 34% lower odds of variceal bleeding or hepatic encephalopathy. Regarding liver disease etiology, non-alcoholic steatohepatitis and alcohol-related liver disease versus chronic viral hepatitis were associated with higher odds of AKI or HRS, but lower odds for sepsis, SBP, variceal bleeding, or hepatic encephalopathy (Table 2).

Delayed LVP and in-hospital mortality

A total of 7,655 (8.1%) hospitalizations resulted in in-hospital mortality, which was higher among those with delayed LVP (9% vs. 7.4%, $P < 0.001$). In a logistic regression model controlling for baseline characteristics and the calendar year of hospitalization, delayed LVP was associated with 21% higher odds of in-hospital mortality [1.21 (1.14–1.28)]. Other variables associated with in-hospital mortality included older age, Asian or other versus Caucasian race, and admission to urban teaching hospitals versus rural locations. Interestingly, in-hospital mortality decreased by 6% annually (Table 2).

Delayed LVP and use of hospital resources

Procedures such as hemodialysis, liver transplant, and palliative care consultations were more frequently utilized in hospitalizations associated with delayed LVP (Fig. 1D). This translated into longer hospitalization durations (10.8 vs. 6.0 days) and higher total hospital charges (USD 120K vs. USD 67K) per hospitalization (Fig. 1E, F).

Our study of hospitalizations for cirrhosis shows that LVP is delayed in over 40% of cases, and this delay is increasing over time. Furthermore, delayed LVP is associated with liver and renal complications, in-hospital mortality, and increased use of hospital resources.

In this national database of hospitalizations with a discharge diagnosis of cirrhosis, only 20.3% received LVP, which is similar to another recently reported experience, where 21.6% of Veterans received paracentesis during hospitalization.[7] In that study, 35.2% of paracenteses were delayed.[7] The rate of delayed paracentesis in our study is slightly higher at 40.3%, likely because the denominator in our study is hospitalizations, and a given patient may have been admitted multiple times throughout the year. Other studies have reported delays in paracentesis in 65–82% of cases.[10,12] Data from single centers and the use of a 12-h cut-off from admission to define delayed paracentesis may explain the higher prevalence of delay in those studies.[10,12]

We also observed an increasing prevalence of delayed LVP over time, although this trend was not observed after con-

Table 2. Logistic regression models examining variables associated with liver disease complications and in-hospital mortality among hospitalizations with cirrhosis in the US (2016–2019). Data are presented as odds ratio (95% confidence intervals)

Variable	AKI or HRS	SBP or sepsis	EVH or HE	In-hospital mortality
Delayed LVP	1.41 (1.37–1.46)	1.20 (1.16–1.25)	1.57 (1.42–1.75)	1.21 (1.14–1.28)
Calendar Year	1.00 (0.98–1.02)	1.00 (0.98–1.03)	0.66 (0.62–0.71)	0.94 (0.90–0.97)
Weekend admission	0.97 (0.94–1.01)	1.15 (1.09–1.20)	1.12 (0.99–1.27)	1.05 (0.98–1.13)
ALD vs. chronic viral hepatitis	1.14 (1.09–1.20)	0.93 (0.88–0.98)	0.80 (0.70–0.92)	1.02 (0.94–1.11)
NASH vs. chronic viral hepatitis	1.49 (1.33–1.67)	0.82 (0.71–0.95)	0.71 (0.47–1.05)	0.87 (0.68–1.10)
Age of the patient in years.	1.013 (1.011–1.05)	0.993 (0.991–0.998)	1.00 (0.99–1.02)	1.013 (1.01–1.016)
Female vs. Male sex	0.94 (0.91–0.98)	1.04 (0.99–1.08)	0.99 (0.89–1.11)	0.96 (0.90–1.03)
AA vs. Caucasian race	1.19 (1.17–1.26)	0.88 (0.82–0.95)	0.88 (0.72–1.07)	1.08 (0.98–1.20)
Hispanic vs. Caucasian race	1.03 (0.98–1.08)	1.13 (1.07–1.19)	0.94 (0.81–1.09)	0.95 (0.87–1.04)
Asian or other vs. Caucasian race	1.12 (1.05–1.20)	1.23 (1.13–1.33)	1.25 (1.03–1.52)	1.19 (1.06–1.35)
Medicaid vs. Medicare pay	0.95 (0.91–0.99)	0.94 (0.89–0.99)	1.20 (1.03–1.39)	1.09 (0.99–1.19)
Private vs. Medicare pay	1.18 (1.13–1.24)	1.01 (0.95–1.07)	1.15 (0.99–1.35)	1.05 (0.96–1.15)
Other vs. Medicare pay	0.79 (0.74–0.84)	0.85 (0.79–0.92)	1.11 (0.91–1.35)	1.07 (0.96–1.20)
Obesity	1.13 (1.07–1.19)	0.96 (0.90–1.03)	0.94 (0.78–1.12)	0.88 (0.79–0.98)
Diabetes mellitus	1.12 (1.08–1.16)	0.83 (0.79–0.88)	0.99 (0.87–1.12)	0.65 (0.60–0.70)
Urban non-teach vs. rural	1.18 (1.08–1.29)	0.98 (0.88–1.09)	1.19 (0.88–1.61)	0.99 (0.84–1.18)
Urban teach vs. rural	1.60 (1.47–1.75)	1.03 (0.93–1.14)	1.22 (0.92–1.62)	1.26 (1.08–1.48)

AKI, acute kidney injury; HRS, hepatorenal syndrome; SBP, spontaneous bacterial peritonitis; EVH, esophageal variceal hemorrhage; HE, hepatic encephalopathy; AA, African Americans; ALD, alcohol-associated liver disease; NASH, non-alcoholic steatohepatitis.

trolling for baseline characteristics. Weekend admissions and older age were associated with delayed paracentesis in our study, which has been shown in previous research as well.[10] In addition to lack of insurance, we found that delayed LVP was associated with hospitals located in urban areas. The increasing number of hospitalizations in urban teaching hospitals over time likely explains this finding. It is speculated that paracentesis being performed by interventional radiology experts in most teaching and academic hospitals contributes to the delay in these centers, as paracentesis performed by emergency room physicians has been shown to reduce the delay. In another study, paracentesis performed by emergency room physicians was associated with reduced odds of delay.[10]

The association of delayed LVP with higher mortality, increased hospital resource use, and liver disease complications has been reported in previous studies.[7,11,12] For example, Veterans with delayed LVP were at higher risk for AKI, intensive care unit admission, and mortality during hospitalization.[7] In another study, delayed paracentesis was associated with hepatic encephalopathy, HRS, and infections.[12] Delayed paracentesis may lead to a delay in SBP diagnosis, which may explain the negative association with patient outcomes and the increased length of stay, as observed in our study.[12,13] It may also contribute to the risk of emergency room visits within 30 days of hospital discharge.[13] We also observed novel findings that negative patient outcomes were associated with increased hospitalization costs, increased use of procedures such as hemodialysis and liver transplantation, and greater use of ancillary services, particularly palliative care consults. Clearly, delaying LVP should be avoided, especially in patients with a high suspicion of SBP.

The large, geographically diverse sample from the NIS database is a strength of our study. However, our study has several limitations inherent to a retrospective cohort design, such as missing baseline data (e.g., laboratory values, treatments received, and post-discharge follow-up) and the potential misclassification of outcomes and diagnoses, which were extracted using ICD-10 codes. As a result, we were unable to examine the true association of delayed LVP with outcomes or other factors like disease severity, short-term mortality, and readmissions.

In conclusion, delayed LVP is associated with worse clinical outcomes and a higher healthcare burden among patients hospitalized with cirrhosis and ascites. Further prospective studies are needed to validate these findings, assess their generalizability, and explore the underlying mechanisms.

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Conflict of interest

AKS has been an Associate Editors of *Journal of Clinical and Translational Hepatology* since 2021. The other author has no conflict of interests related to this publication.

Author contributions

AKS and YFK conceptualized and designed the study, performed statistical analyses, interpreted the data, and supervised the manuscript preparation. AKS wrote and finalized the initial draft of the manuscript. All authors approved the final version and the publication of the manuscript.

Ethical statement

Participants were de-identified and sourced from a public database. All NIS participants provided informed consent.

Data sharing statement

Data will be available upon request and approval from the corresponding author.

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