



## Are Patients Hospitalized with Cirrhosis and Ascites Receiving Appropriate Diagnostic Paracentesis?

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### Abstract

**Background and Aim:** Ascites is the most common complication of cirrhosis, and is associated with increased mortality. Diagnostic paracentesis is recommended for patients who are admitted to the hospital with ascites. However, it is unknown if diagnostic paracentesis in Canadian teaching hospitals are done according to recommended guidelines. We analyzed the rate of paracentesis, determined barriers for not performing paracentesis and the association of not performing paracentesis with mortality.

**Method:** We conducted a retrospective chart review of inpatient records from January 2010 to May 2014 at Hamilton Health Sciences (Hamilton, Ontario). We used electronic medical records to identify patients with cirrhosis and ascites who were admitted with a primary or secondary diagnosis of ascites, spontaneous bacterial peritonitis or hepatic encephalopathy. All patients have to have a secondary diagnosis of cirrhosis. Primary point of interest was the performance of diagnostic paracentesis. We determined barriers for not performing and delaying paracentesis > 1 day after admission. We used multiple logistic regression to study the association between age, Charlson score (comorbidity score), model of end stage liver disease (MELD) score and weekend admission for patients who received and did not receive paracentesis. Mortality and hospital stay were compared for those who received and did not receive paracentesis.

**Results:** Of 228 eligible admissions, 131 (57.5%, 95% CI 20.8%-64.0%) admissions received diagnostic paracentesis. 97 (74%) patients received paracentesis < 24 hours after admission. After adjusting for other covariates, none of the predictors were significantly associated with the performance of paracentesis. In patients who did not receive paracentesis, 57 (79.4 %) had no documented reason for not receiving paracentesis. In patients who received delayed paracentesis, 19 (55.9 %) were related to seeking ultrasound guidance/marking. There was a statistical significant increase in the mean length of hospital stay in patients with a delayed paracentesis (12.6) compared to those with early paracentesis (8.2) ( $P = 0.02$ ). There was no statistically significant difference in in-hospital mortality in patients who underwent paracentesis 15 (11.5 %) compared to those who did not undergo paracentesis 10 (10.3 %).

**Conclusion:** In these two Canadian teaching centers, paracentesis was underutilized for patients admitted with ascites and cirrhosis. There was no clear documented reason for not receiving paracentesis in many patients. We found an increased reliance on ultrasound guidance resulted in delayed paracentesis. Delaying paracentesis was associated with longer hospital stay. Larger studies are needed to determine the effect of not performing paracentesis on mortality.

### Keywords

Paracentesis, Ascites, Liver Cirrhosis, Gastrointestinal bleeding, Spontaneous Bacterial Peritonitis

### Background

Liver cirrhosis is a major public health problem worldwide [1]. In 2008, a total of 2748 deaths were related to chronic liver disease and liver cirrhosis in Canada (eleventh leading cause of death) [1]. In cirrhotic patients, ascites is the most common complication to develop and its development increases the risk of mortality and morbidity [2-4]. In patients with compensated cirrhosis, approximately 50% will develop ascites over a 10-year observation period [2]. Ascites is the most common cause of hospital admissions in patients with cirrhosis [5]. In hospitalized patients with cirrhotic ascites, spontaneous bacterial peritonitis (SBP) is a common and severe complication, occurring in 32-34% of patients [6]. The in-hospital prevalence of SBP in unselected cirrhotic patients with ascites ranges between 10-30% [7] and the in-hospital mortality rate is as high as 30% [8].

Many studies confirm that diagnostic paracentesis is a safe procedure with very low risk of complications [9,10]. Abdominal paracentesis with appropriate ascitic fluid analysis is probably the most rapid and cost-effective method of diagnosing the cause of ascites. Also, in view of the high prevalence of ascitic fluid infection at the time of admission to hospital, an admission paracentesis may detect unexpected infection [11]. Practice guidelines have long recommended the performance of diagnostic paracentesis for patients hospitalized with ascites [11,12].

A recent set of quality indicators suggests that performing a diagnostic paracentesis is one of the most important quality indicators in the care of patients hospitalized with cirrhotic ascites [13]. Medical care for cirrhosis and ascites can delay complications and improve quality and quantity of life [14,15].

Two studies estimated the frequency of diagnostic paracentesis in the United States where it was determined that the procedure was performed in less than 60% and 61% of patients, respectively [16,17]. Orman et al. studied the association between performance of paracentesis and mortality and length of hospital stay. They found that performance of paracentesis is associated with lower mortality [17]. However, they were unable to determine barriers/reasons for

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**Table 1:** Baseline characteristics of patients hospitalized with cirrhosis and ascites.

Variables	Sample Size	Mean (SD)	Median	Range
Age	228	62.4 (10.9)	61.0	30 - 83
Charlson Score (Excluding liver Disease)	228	1.9 (1.8)	1.0	0 - 8
MELD	228	17.4 (6.9)	16.0	6 - 42
Length of stay (Excluding expired patients)	203	8.3 (9.1)	5.0	1 - 55

**Table 2A:** Characteristics of cirrhotic patients admitted with ascites according to the receipt of paracentesis.

Variables	Paracentesis (n = 131)	No Paracentesis (n = 97)	P value
Age (mean; SD)	62.0 (11.0)	62.9 (10.7)	0.56
Charlson scores (excluding liver disease) (mean; SD)	1.7 (1.7)	2.1 (1.9)	0.09
MELD (mean; SD)	18.0 (6.6)	16.6 (7.3)	0.13
Length of stay (116 vs 87)	9.3 (8.6)	6.9 (9.5)	0.05
Men (n; %)	76 (58.0%)	59 (60.8%)	0.69
Weekday admission (n; %)	99 (75.6%)	67 (69.1%)	0.30
Death (n; %)	15 (11.5%)	10 (10.3%)	0.83

underutilizing paracentesis. Kanwal et al. also reported a reduction in mortality in those who received paracentesis [16]. To our knowledge, there are no existing Canadian data regarding the utilization of diagnostic paracentesis and its effect on mortality.

## Aim

The aim of our study is to determine the rate of diagnostic paracentesis in our tertiary-care center (Hamilton Health Sciences) in a single Canadian city in patients hospitalized with cirrhosis and ascites. We sought to identify barriers for delaying or not performing paracentesis. We also determined if cirrhotic patients with spontaneous bacterial peritonitis (SBP) or gastrointestinal bleeding received appropriate antibiotics. We assessed patient factors, which may predict the receipt of paracentesis. We studied the association of paracentesis performance on mortality and length of hospital stay.

## Methods

A retrospective chart review was conducted from January 2010 to May 2014 at Hamilton Health Sciences (Hamilton, Ontario, Canada). We used data derived from the Hamilton Health Sciences electronic medical records (Meditech and Sovera) to search for patient's  $\geq 18$  years old with a primary admission diagnosis of ascites or SBP. We also included patients with a primary admission diagnosis of hepatic encephalopathy or variceal gastrointestinal bleeding provided that they also had a secondary admission diagnosis of ascites. All patients were required to have a diagnosis of cirrhosis.

Ascites had to be confirmed on admission by physical exam such as a positive fluid wave, presence of shifting dullness or abdominal distension and/or detectable ascites on diagnostic imaging studies such as ultrasound (US), magnetic resonance imaging (MRI) or computerized tomography (CT) scan which had been completed during the admission period. Patients transferred from different centers were excluded to avoid misclassifying patients who had already received a paracentesis prior to transfer. We excluded patients with a cardiac or renal cause of ascites. We identified patients who underwent paracentesis by searching the medical record for ascitic fluid cell count, differential and culture for each admitted patient. We determined the timing of paracentesis performance (early ( $\leq 24$  hours) versus late ( $> 24$  hours)). The following variables were collected: age, sex, Charlson score (comorbidity score, excluding liver disease) [18], model of end stage liver disease (MELD) score, weekend versus week admission, receipt of antibiotics (treatment of SBP or prophylaxis for gastrointestinal bleeding), length of hospital stay (excluding expired patients), mortality and reasons for not performing and delaying paracentesis.

The primary outcome was the performance and timing of diagnostic paracentesis in patients admitted with cirrhosis and ascites. The secondary outcome was to determine the association between the following variables (age, Charlson score, MELD score and weekend versus week admission) and performance of

paracentesis. Categorical variables were compared by Fisher's exact test and continuous variables were compared by Student T-test. Multiple logistic regressions was used to determine the association of paracentesis performance with age, Charlson score, MELD score and weekend versus week admission.

A p-value of  $< 0.05$  was considered statistically significant. Analyses were performed by using IBM SPSS version 22 (Armonk, NY: IBM Corp.).

Each patient record was reviewed by a clinician who was not involved in the patients care (HB). Data was abstracted using a standardized data collection instrument. Data analysis was performed by an independent investigator who was not involved in data abstraction (CY). This study was approved by the Hamilton Integrated Research Ethics Board.

## Results

### Study sample characteristics

A total of 228 admissions were included in the study during the period of the analysis. The mean age of patients studied was 62.4 years (range 30-83). Of the 228, 135 (59.2%) were males. The mean of MELD score was 17.4 (range 6-42) and Charlson score 1.9 (range 0-8). The mean length of stay (excluding expired patients) was 8.3 (range 1-55) (Table 1).

### Patients who underwent diagnostic paracentesis

131/228 (57.5%, 95% CI 20.8-64.0%) admissions received diagnostic paracentesis. The receipt of paracentesis was higher in men (58.0%) than in women (42.0%). The mean MELD score was higher in patients with paracentesis performance (18.0) than patients that did not receive paracentesis (16.6). The mean Charlson score was lower in patients who received paracentesis (1.7) than in patients who did not receive paracentesis (2.1). Patients admitted on a weekend were less likely to undergo paracentesis (24.4%) compared to weekday admission (30.9%). The mean length of hospital stay was higher in patients who received paracentesis (9.3) compared to patients who did not receive paracentesis (6.9) (Table 2A). After adjusting for other covariates none of the predictors was associated significantly with the performance of paracentesis (Table 2B).

### Patients receiving antibiotics

Seventy-six patients of the 228 received antibiotics. We evaluated the receipt of antibiotics for indicated reasons, which includes SBP and gastrointestinal bleeding. Fifty-six (24.6%) patients had an indicated reason, 21 for SBP and 35 for gastrointestinal bleeding. Four (7.1%) with gastrointestinal bleeding did not receive antibiotics. Twenty (8.8%) patients received antibiotics with no indicated reasons.

### Barriers for not receiving paracentesis

Upon review of the 97 admissions that did not receive paracentesis,

**Table 2B:** Adjusting for other covariates by using multiple logistic regression.

Variables	B	Sig.	Exp (B)	95 % CI
Age	- 0.005	0.713	0.995	0.971 - 1.020
Charlson score	- 0.131	0.082	0.877	0.756 - 1.017
MELD	0.031	0.132	1.031	0.991 - 1.073
Time of admission	0.337	0.267	1.401	0.773 - 2.541

**Table 3:** Barriers for non-adherence to paracentesis performance.

Reason for non-adherence	Frequency	Percent
Small amount of ascites	20	20.6
Not documented	57	58.8
Recent paracentesis	6	6.2
Coagulopathy	3	3.1
Unsuccessful paracentesis	10	10.3
Refusal	1	1.0
Total	97	100.0

57 (79.4%) had no clear documented reason. Three (3.1%) were related to coagulopathy and 6 (6.2%) were related to having a recent paracentesis. Twenty had only a small amount of ascites on ultrasound and 10 had an unsuccessful attempt of paracentesis. One patient refused paracentesis. **Table 3** summarizes barriers for not performing paracentesis.

### Delayed paracentesis

One hundred and thirty-one patients received paracentesis. Ninety-seven (74 %) patients received paracentesis < 24 hours after admission. Twenty-six percent had delayed paracentesis. The mean age of patients with delayed paracentesis was younger (60.3) than patients with early paracentesis (62.6). Delayed paracentesis was more likely in women (55.9%) than in men (44.1%). We found that patients with delayed paracentesis had lower MELD score (17.5) than patients with early paracentesis (18.1). Early paracentesis was higher in patients admitted during a weekday compared to a weekend admission. There was a statistical significant increase in the mean length of hospital stay in patients with a delayed paracentesis (12.6 days) compared to those with early paracentesis (8.2 days) ( $P = 0.02$ ). **Table 4** compares the characteristic of patients with early versus late paracentesis.

### Reasons for delaying paracentesis

Paracentesis was delayed in 34 of the 131 patients who underwent paracentesis. Nineteen (55.9%) of delayed paracentesis were related to seeking ultrasound marking. Two (5.9 %) patients were referred to interventional radiology for US guided paracentesis. Twelve (35.3%) had no documented reason for delayed paracentesis. One (2.9%) patient was described as being too sick to receive paracentesis. **Table 5** summarizes the reasons for delaying paracentesis.

### Effect of receiving paracentesis on mortality

Twenty-five of the 228 admissions expired during hospitalization. The mean age of those who expired was 64.3. The Charlson score and MELD score were 2.6 and 24.9, respectively (**Table 6**). A total of 15 (11.5 %) who underwent paracentesis expired compared to 10 (10.3%) who did not undergo paracentesis. The mortality rate in patients with late paracentesis was (11.8 %) compared to early paracentesis (11.3%).

### Discussion

Our retrospective chart review reports on the utilization and timing of paracentesis in patients admitted to hospital with cirrhosis and ascites. We demonstrated that only 57.5% of patients admitted to hospital with cirrhosis and ascites underwent paracentesis. Moreover, of those who underwent a paracentesis, only 74% received it within 24 hours of hospital admission. Therefore, only 42.5% of all eligible patients received timely paracentesis which clearly falls below the accepted standard of care. Similar to findings of Kanwal et al. [16], our study showed that patients with higher MELD scores were more likely to receive a paracentesis. We believe this reflects the fact that

**Table 4:** Comparing the characteristics of patients with early versus late paracentesis.

Variables	Early Paracentesis (n = 97)	Late paracentesis (n=34)	P values
Age (mean; SD)	62.6 (10.2)	60.3 (13.0)	0.29
Charlson scores excluding liver disease (mean; SD)	1.7 (1.7)	1.7 (1.9)	0.99
MELD (mean; SD)	18.1 (6.9)	17.5 (5.5)	0.64
Length of stay (86 vs 30)	8.2 (8.3)	12.6 (9.0)	0.02
Men (n; %)	61 (62.9%)	15 (44.1%)	0.07
Weekday admission (n; %)	72 (74.2%)	27 (79.4%)	0.65
Death (n;%)	11 (11.3%)	4 (11.8%)	1.00

**Table 5:** Reasons for delaying paracentesis.

Reasons	Frequency	Percent
US Guidance/Marking	19	55.9
Not documented	12	35.3
Too sick	1	2.9
IR Guided	2	5.9
Total	34	100.0

**Table 6:** Characteristics of expired patients.

Variables	No	Minimum	Maximum	Mean	SD
Charlson Score Excluding liver disease	25	0	8	2.60	2.217
MELD	25	9	40	24.88	8.418
Age	25	37	80	64.32	11.010

those with higher MELD scores are more likely to have large/tense ascites. Additionally, there may be a perception amongst physicians that those with higher MELD scores are more likely to have SBP, which potentially explains the higher likelihood of undergoing a paracentesis in these patients. Patients with lower Charlson score (comorbidity score) were more likely to receive paracentesis. Thus, the presence of multiple comorbidities reduced the likelihood of receiving a paracentesis in our study. A similar finding was also reported by Kanwal et al. [16]. This may be explained by the fact that the ascites in patients with multiple comorbidities, may not be the major issue requiring hospitalization. Therefore, the physician may be more focused on the other comorbid conditions/problems. Patients were more likely to receive a paracentesis if admitted on a weekday compared to being admitted on a weekend. This is likely in part related to the reduction in available house staff during a weekend, which thereby increases the physician workload and reduces the time available to perform the procedure. Orman et al. also found that admission during a weekend reduced the likelihood of receiving a paracentesis [17].

We sought to understand the reasons for not performing a paracentesis. Unfortunately, there was no documented reason for the failure to perform a paracentesis in almost 60% of patients. We hypothesize that a major reason for not performing a paracentesis may be related to the physician's low index of suspicion for a diagnosis of SBP, likely based on the absence of classic features of infection. However, it is important to note that the in-hospital prevalence of SBP in unselected cirrhotic patients with ascites ranges between 10-30% [7]. Moreover, a substantial portion of patients with SBP lack typical features such as abdominal pain, fever and/or leukocytosis [19]. We were encouraged by our finding that coagulopathy was an uncommon documented reason for failing to perform a paracentesis. There is substantial evidence supporting that paracentesis is a safe procedure in those with cirrhosis-related coagulopathy [20,21].

Our study was unable to demonstrate a difference in mortality between patients that received paracentesis and those who did not. This may be related to our limited sample size. In a recent study with more than 17000 patients mortality was significantly higher in patients that did not receive paracentesis [17]. In this study, we found a higher mean age, MELD score and Charlson score in those patients who expired. The exact cause of death in these patients, however, was not clear.

Our study demonstrated that approximately 25% of patients underwent paracentesis greater than 24 hours after admission (delayed paracentesis). We identified a reliance on ultrasound guidance or marking as a major barrier to timely paracentesis. At our centre, the availability of portable bedside ultrasound is limited and we cannot routinely obtain an ultrasound through the radiology department after regular business hours or on a weekend. This translates, therefore, into delaying of paracentesis in many patients. We believe this is substandard care since most diagnostic paracentesis can be performed safely and effectively without ultrasound marking or guidance.

In a study by Kim et al, in-hospital mortality increased 2.7-fold in patients who had a delayed paracentesis [22]. We were unable to demonstrate a difference in mortality in our study in those who had a delayed paracentesis. Our study was limited, however, by small numbers and was not powered to answer this question.

The length of stay in hospital was longer in those who had a paracentesis (versus those who did not) and in patients whose paracentesis was delayed (versus early paracentesis). In our study, the longer hospital stay in patients who underwent paracentesis was likely related to their diagnosis of SBP, which generally required intravenous antibiotics and albumin infusions thereby preventing early discharge. Orman et al. also demonstrated an increased length of stay in those undergoing paracentesis which was mainly related to paracentesis complications such as ascites leak and bleeding [17]. This was not observed in our study.

We assessed the appropriateness of antibiotic usage in patients with a clear indication (either to treat SBP or as prophylaxis against SBP in setting of a gastrointestinal hemorrhage). Overall, 92.9 % received antibiotics appropriately in our study. Twenty (11.6%) patients received antibiotics with no clear indicated reason, which suggests that empirical use of antibiotics is fairly common. This has implications in terms of antimicrobial resistance and risk for acquiring nosocomial infections such as *Clostridium difficile*. It is important to remember however, that some of these patients may have had an alternative reason to receive antibiotics such as urinary tract infection, pneumonia etc. Therefore, the number of patients receiving inappropriate antibiotics may be an overestimate. Kanwal et al. showed that nearly all patients with an indication received antibiotics appropriately [16].

Our study has several limitations. The retrospective nature of the study lead to inclusion of patients with only small amounts of ascites (some only detectable by imaging). These patients often do not require paracentesis yet they were included in our analysis. This may have lead to an underestimate of the rate of necessary paracentesis at our centre. As a chart review, we relied on documentation in the patient's chart which was quite variable in terms of the level of information and detail. In many cases, a reason for failing to perform or delaying a paracentesis could not be identified thereby limiting our ability to truly determine reasons for the underutilization/suboptimal timing of paracentesis. Our study was small and therefore had limited power to determine the association of paracentesis performance and timing with mortality. This was a single centre study, which may not be generalizable to other centres.

## Conclusion

Diagnostic paracentesis is underutilized or often delayed at our tertiary care hospital. Reliance on ultrasound guidance/markings leads to delayed paracentesis, which in turn, appears to increase hospital length of stay. We were unable to demonstrate that paracentesis performance impacts on mortality but this may have been related to our small study size and the retrospective nature of our study. Education of our trainees and colleagues regarding the importance and ease of performing a diagnostic paracentesis may improve this important quality indicator in the management of patients with cirrhosis and ascites.

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