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Hemorrhagic ascites. Clinical presentation and outcomes in patients with cirrhosis

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Abstract

Background & Aims—Hemorrhagic ascites can pose diagnostic and therapeutic dilemmas in patients with cirrhosis. We aimed at exploring the characteristics and outcomes of patients with cirrhosis and hemorrhagic ascites.

Methods—The records of all patients with cirrhosis and ascites, who underwent paracentesis between 2003 and 2010 at Parkland Memorial Hospital, were retrospectively reviewed. Hemorrhagic ascites was defined as an ascitic fluid red blood cell (RBC) count $\geq 10,000/\mu\text{l}$. We compared each patient with 3 age- and gender-matched controls (cirrhotic patients with ascites and an ascitic RBC count $<10,000/\mu\text{l}$). Survival curves were generated using Kaplan–Meier plots and compared using the log rank test.

Results—1113 cirrhotic patients underwent paracentesis; 214 (19%) had hemorrhagic ascites. Patients with hemorrhagic ascites had higher rates of spontaneous bacterial peritonitis ($p < 0.001$), acute kidney injury (AKI, $p < 0.001$), and were more likely to require intensive care unit (ICU)-level care ($p = 0.01$) compared to patients without hemorrhagic ascites. Patients with hemorrhagic ascites had a higher mortality than controls at one month (87% vs. 72%), 1 year (72% vs. 50%) and 3 years (61% vs. 41%). Using multivariate regression analysis, hemorrhagic ascites was also an independent predictor of mortality (HR 1.34, 95% CI 1.07–1.68) after adjusting for the model for end-stage liver disease score (HR 1.04, 1.03–1.05), ICU-level care (HR 2.02, 1.63–2.51) and presence of hepatocellular carcinoma (HR 2.27, 1.61–3.19).

Conclusions—Patients with hemorrhagic ascites had a significantly higher rate of ICU care, AKI, and mortality than patients with portal hypertension and ascites but without hemorrhagic ascites. We conclude that hemorrhagic ascites is a marker of advanced liver disease and poor outcome.

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Conflict of interest

The authors have declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

Keywords

Liver; Portal hypertension; Mortality; MELD; Survival

Introduction

Ascites is the most common complication of cirrhosis and a frequent reason for hospital admission in cirrhotic patients [1]. Further, ascites portends a poor outcome; approximately 15% of cirrhotic patients hospitalized for ascites management will die in 1 year and 44% will die within 5 years [1,2]. Hemorrhagic ascites is an uncommon but problematic complication in patients with cirrhosis and ascites. Although it is encountered in less than 5% of patients with cirrhosis [3], and is atypical of most ascites, it frequently poses a diagnostic and therapeutic dilemma when present, as there is often controversy in determining the etiology and appropriate management [4].

We have observed that patients with cirrhosis and hemorrhagic ascites have a poor outcome. Few studies have evaluated hemorrhagic ascites or hemoperitoneum in non-critical care settings, with most of the available literature being case reports or small case series [3,5–12]. Thus, here, we have hypothesized that patients with hemorrhagic ascites have unique clinical features and perhaps poorer outcomes than commonly believed. Therefore, the goals of this study were to characterize the features of patients with hemorrhagic ascites and cirrhosis, to understand the etiologies of hemorrhagic ascites in this population, and to explore clinical outcomes.

Patients and methods

Study population and design

This retrospective case-control analysis included consecutive patients with cirrhosis, admitted to Parkland Memorial Hospital from January 2003 to June 2010, with ascites and hemorrhagic ascites (defined as RBC in ascitic fluid $\geq 10,000/\mu\text{l}$). Patients were initially identified by International Classification of Diseases, 9th revision (ICD-9) codes for cirrhosis (571; 571.2; 571.5; 571.6) and the Current Procedural Terminology (CPT) code for paracentesis (49080). The electronic and paper charts were then manually reviewed by one investigator (N.U.) to verify the diagnosis of cirrhosis and ascites. We compared this group to an age- and gender-matched control group of cirrhotic patients with ascites and ascitic RBC count $<10,000/\mu\text{l}$ (3 controls: 1 case). The control patients were admitted during the same time period and matched using age (within 2 years) and gender. The study was approved by the Institutional Review Board at the University of Texas Southwestern Medical Center.

Data collection

We collected 296 unique clinical and laboratory variables for each patient at the time of presentation and hospital admission. Among the variables collected were demographics, detailed clinical history, laboratory data, and imaging results. Clinical and historical data included the etiology of liver disease, co-morbidities, gastrointestinal bleeding, hepatic

encephalopathy, bacteremia (diagnosed with a positive blood culture upon hospital admission), as well as laboratory data including bilirubin, albumin, prothrombin time/international normalized ratio (INR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine and serum electrolytes. Outcomes were reported through the course of the index hospitalization and follow-up.

Definitions

Cirrhosis was defined based on clinical features, including a history consistent with chronic liver disease as well as a documented complication of chronic liver disease (i.e., ascites, varices, hepatic encephalopathy), and/or imaging consistent with cirrhosis, and/or liver histology consistent with cirrhosis. The etiology of liver disease was determined according to the following criteria: (1) hepatitis C virus (HCV) cirrhosis was defined by the presence of cirrhosis in a person seropositive for hepatitis C virus (antibody or RNA); (2) hepatitis B virus (HBV) cirrhosis was defined by the presence of cirrhosis in a patient seropositive for hepatitis B virus (hepatitis B surface antigen or HBV DNA); (3) alcoholic cirrhosis was determined from the provider's note in the presence of a history of alcohol abuse or dependence and the absence of other known liver disease; and (4) other causes of cirrhosis as diagnosed by the provider but not falling into the aforementioned categories (i.e., primary biliary cirrhosis, cryptogenic, non-alcoholic fatty liver disease).

Ascites was classified as small, moderate, or large, based on review of the admission note and available imaging. In brief, grade 1 ascites or small ascites was defined as ascites detectable only by ultrasound examination, grade 2 or moderate ascites was defined as moderate symmetrical distention of abdomen described on the admission note, and grade 3 or large ascites was defined as obvious abdominal distention seen during physical exam or ultrasound [13]. We classified bloody ascites into 2 main categories: (1) ascitic fluid RBC count >50,000/ μ l (hematocrit value more than 0.5%) and (2) ascitic fluid RBC count 10,000/ μ l [5,14]. This classification was made with the explicit intent of exploring possible differences between groups.

Definitions for the different etiologies of hemorrhagic ascites, agreed upon *a priori*, were as follows: hemorrhagic ascites related to hepatocellular carcinoma (HCC) was defined by ascitic fluid RBC count 10,000/ μ l and imaging, suggestive that hemoperitoneum was likely secondary to HCC, including bleeding from a liver mass, localized hematoma or "sentinel clot" close to the tumor, a liver mass 5 cm or a mass of any size close to the surface (1 cm) [4,15,16]. Hemorrhagic ascites secondary to blunt trauma was defined by ascitic fluid RBC count 10,000/ μ l and documented history of fall, motor vehicle accident, with blunt trauma to abdomen prior to presentation. Iatrogenic hemorrhagic ascites was defined by ascitic fluid RBC count 10,000/ μ l and documented history of paracentesis (diagnostic or therapeutic), transjugular intrahepatic portosystemic shunt, or other abdominal procedure (liver biopsy) before diagnosis, and either of the following scenarios: (a) no evidence of hemorrhagic ascites before the procedure then development of hemorrhagic ascites within 7 days after procedure or (b) hemorrhagic ascites on initial paracentesis with evidence of intra-peritoneal bleeding at the procedure site on imaging study [6,17,18]. Spontaneous hemorrhagic ascites was defined by ascitic fluid RBC count 10,000/ μ l and without

apparent cause found. This category was a diagnosis of exclusion, as other potential causes for hemorrhagic ascites were excluded based on the above detailed criteria [4].

HCC was defined according to 2005 AASLD criteria (<http://www.aasld.org/practiceguidelines/pages/default.aspx>). Patients with HCC were classified based on the Milan criteria; thus, patients meeting the Milan criteria had a solitary tumor ≤ 5 cm, or three or fewer lesions none >3 cm and no evidence of tumor invasion of blood vessels or lymph nodes [19]. Finally, continued follow-up of patients was used to verify absence of HCC in those without HCC at the time of presentation.

Hepatic encephalopathy was classified according to the West Haven Criteria as described [20]. In brief, we considered four categories. Grade 1, defined as trivial lack of awareness, euphoria, anxiety, or shortened attention span. Grade 2, defined as lethargy, minimal disorientation for time or place, subtle personality change. Grade 3, characterized by somnolence to semi stupor, but responsiveness to verbal or noxious stimuli, confusion, and gross disorientation. Grade 4 defined as coma, unresponsiveness to verbal or noxious stimuli.

Sepsis was defined according to the American College of Chest Physicians and the Society of Critical Care Medicine recommendations [21]. In brief, sepsis was defined as the systemic inflammatory response syndrome (SIRS) due to a confirmed infection. The classification of AKI was defined as an abrupt (within 48 h) increase in serum creatinine (either 0.3 mg/dl absolute increase or 50% increase over baseline) [22] to a serum creatinine value of 1.5 mg/dl or greater. A cut-off value of 1.5 mg/dl was used because prior studies have shown that patients with creatinine values of 1.5 mg/dl or greater have significantly decreased renal function [23,24].

Spontaneous bacterial peritonitis was defined by a positive ascitic fluid culture.

Each patient's clinical course, including survival through June 2011, was recorded through review of the electronic medical record. Survival status of patients not currently followed up or those patients known to have died was verified through the Social Security Death Index.

Statistical analysis

All data values were expressed as median (range) unless otherwise stated. Demographics, clinical and laboratory characteristics of patients with and without hemorrhagic ascites were compared. Chi-squared test was used for categorical variables and *t* tests were used for continuous variables, with *p*-values less than 0.05 being considered significant. The primary outcome for this study was all-cause mortality. Survival curves were generated using Kaplan–Meier plots and compared using log rank test. Cox multivariate regression analysis was performed to determine factors associated with mortality. Tested predictors included age, ethnicity, gender, etiology of liver disease, model of end-stage liver disease (MELD), presence of hemorrhagic ascites, severity of ascites, severity of hepatic encephalopathy, requirement for ICU-level care, history of HCC, and laboratory data at presentation (leukocyte count, hemoglobin level, and sodium level). We did not include laboratory results such as bilirubin, creatinine, and INR in the regression model as these are components of the

MELD score. Likewise, vasopressor requirement was considered to be collinear with ICU-level care and transfusion requirement collinear with hemoglobin levels, so neither of these variables was tested. Statistical analysis was defined as p value less than 0.05 for both univariate and multivariate analysis. All data analysis was performed using Stata 11.0 (College Station, TX, USA).

Results

Patient characteristics

A total of 1113 unique patients with cirrhosis who underwent paracentesis were admitted to the hospital from January 2003 to June 2010. Hemorrhagic ascites was identified in 214 (19%) patients, who were compared to 642 age- and sex-matched controls (Table 1). The median age of the entire cohort was 51 years (range 22–79) and over three-fourths of patients were male. The most common etiologies of liver disease were HCV and alcohol-induced, similar to previous studies for this patient population [23,25].

Clinical presentation

Several clinical features were significantly different in patients with hemorrhagic ascites compared to controls. A complaint of abdominal swelling was more common in the hemorrhagic ascites group compared to the control group (80% vs. 29%, $p < 0.001$). Patients with hemorrhagic ascites were more likely to present with fever ($p < 0.001$), abdominal pain ($p < 0.001$), and dyspnea ($p < 0.001$) than controls. This may be related to a higher proportion of patients with large ascites among those with hemorrhagic ascites than controls ($p < 0.001$). There were no significant differences in the presence on admission of grade 3 or grade 4 encephalopathy between the two groups.

There were no major differences in the clinical presentation in patients with ascitic fluid RBC counts of 10,000–50,000/ μ l and $>50,000/\mu$ l; a similar proportion of patients presented with abdominal swelling (77% vs. 84%, $p = 0.33$), fever (23% vs. 28%, $p = 0.54$), abdominal pain (72% vs. 71%, $p = 0.22$), dyspnea (47% vs. 55%, $p = 0.31$), nausea (31% vs. 34%, $p = 0.68$), vomiting (26% vs. 31%, $p = 0.49$), light-headedness (14% vs. 19%, $p = 0.43$), respectively. There was a trend toward an increased frequency of grade 3 or 4 encephalopathy in the group with an ascitic fluid RBC count $>50,000/\mu$ l (16% vs. 27%), but this difference was not statistically significantly different ($p = 0.07$).

Both control and hemorrhagic ascites patients had substantial liver dysfunction, as evidenced by median MELD scores of 16 (6–46) and 18 (6–46), respectively, although this was significantly higher among those with hemorrhagic ascites ($p < 0.001$). The median albumin was 2.5 g/dl in patients with hemorrhagic ascites, lower than the median albumin of 2.8 g/dl among controls ($p < 0.01$). Additionally, patients with hemorrhagic ascites had higher levels of bilirubin (3.0 vs. 2.5 mg/dl, $p = 0.04$), creatinine (1.1 vs. 1.0 mg/dl, $p = 0.004$), and INR (1.5 vs. 1.4, $p = 0.009$), while having lower hemoglobin levels (10 vs. 11 g/dl, $p = 0.001$) upon presentation than controls. There were no significant differences in the level of leukocyte count, platelet count, plasma sodium, or alpha-fetoprotein.

Etiology

Patients with hemorrhagic ascites were divided into two groups: ascitic fluid RBC count of 10,000–50,000/ μ l ($n = 133$) and RBC count $>50,000/\mu$ l ($n = 81$). Spontaneous hemorrhagic ascites was the most common cause in both groups (72% and 52% respectively), followed by HCC related (13% and 24%) and iatrogenic (11% and 17%) (Table 2). Among the 28 cases of iatrogenic hemorrhagic ascites, 27 were related to prior paracentesis, and 1 to prior TIPS placement.

Three patients with spontaneous hemorrhagic ascites had a paracentesis that was performed 8 days (9 days, 12 days, and 30 days) or more before the event. In all these cases, the initial ascitic fluid met the criteria of hemorrhagic ascites. Imaging was performed in all the 3 cases and there was no evidence of bleeding from paracentesis site, or any vascular bleeding. Neither of these cases met criteria for HCC or had a history of prior blunt trauma.

In the spontaneous hemorrhagic ascites group, 7 patients had a concomitant diagnosis of HCC. All of them had masses <5 cm, without evidence of tumor bleeding, sentinel clot by imaging, or tumor close to the surface (<1 cm). They had no paracentesis or history of trauma prior to the index paracentesis.

In the hemorrhagic ascites group with HCC, 5 patients had tumors less than 5 cm, but all of them had evidence of bleeding by imaging (HCC close to the surface, ($n = 2$) or sentinel clot ($n = 3$)). In this group, 1 patient had an ascitic fluid RBC count of $<10,000/\mu$ l, 5 days prior to the index paracentesis that showed hemorrhagic ascites; imaging after the finding of hemorrhagic ascites revealed a localized hematoma close to the tumor. There were 44 patients with HCC, including 26 “beyond” Milan criteria.

Clinical course and outcomes

Patients with hemorrhagic ascites had a significantly higher need for transfusion ($p < 0.001$), ICU-level care ($p = 0.01$), and vasopressor use ($p < 0.001$) than patients with non-hemorrhagic ascites; they experienced more SBP ($p < 0.001$), AKI ($p < 0.001$) and sepsis ($p < 0.01$) (Table 3). The overall 1-month, 1-year and 3-year survival rates among patients with hemorrhagic ascites were 72%, 50% and 41% respectively, with a median survival of 1.0 year. These rates were lower than survival rates in patients without hemorrhagic ascites, who had 1-month, 1-year and 3-year patient survival rates of 87%, 72%, and 61%, respectively, and a median survival of 5.6 years (Fig. 1).

Patients with hemorrhagic ascites were divided into sub-groups (Fig. 2) to evaluate differences in survival. Patients with ascitic fluid RBC counts of 10,000–50,000/ μ l had 1-month, 1-year and 3-year survival rates of 75%, 51%, and 44%, respectively, with a median survival of 1.4 years, higher than that in patients with ascitic fluid RBC count $>50,000/\mu$ l (1-month, 1-year and 3-year survival rates of 68%, 44%, and 36%, respectively, with a median survival of 0.5 years).

Differences in mortality by etiology of hemorrhagic ascites were assessed. Patients with spontaneous hemorrhagic ascites had a median survival of 1.3 years (1-month and 1-year survival rates of 75% and 52%, respectively), which was not significantly different than that

in patients with other etiologies of hemorrhagic ascites ($p = 0.76$). Cases with iatrogenic hemorrhagic ascites had a trend toward better survival (1-month and 1-year survival rates of 86% and 68%, respectively); however, this difference was not statistically significant when compared to other etiologies of hemorrhagic ascites ($p = 0.07$). HCC related hemorrhagic ascites cases had significantly worse survival when compared to other etiologies ($p = 0.001$), with 1-month and 1-year survival rates of 50% and 25%, respectively.

We performed uni- and multivariate logistic regression analysis to identify clinical and laboratory variables that could have prognostic value for predicting mortality in the entire cohort of patients with ascites (Table 4). Univariate predictors of increased mortality included the following: the presence of hemorrhagic ascites, MELD score, ICU need; concomitant diagnosis of HCC; large ascites; grade 3 or grade 4 encephalopathy; the presence of HCV; WBC count, hemoglobin level and sodium level. On multivariate analysis, hemorrhagic ascites remained a significant independent predictor of mortality (HR 1.34, 95% CI 1.07–1.68) after adjusting for markers of illness, including MELD score (HR 1.04, 95% CI 1.03–1.05) and need for ICU-level care (HR 2.02, 95% CI 1.63–2.51), as well as co-morbid conditions, including HCC (HR 2.27, 95% CI 1.61–3.19) and HCV (HR 1.34, 95% CI 1.10–1.63).

With regard to patients with spontaneous hemorrhagic ascites, follow-up paracentesis was frequently performed. Among the 138 cases of spontaneous hemorrhagic ascites, 64 had at least one repeat paracentesis. The number of subjects with hemorrhagic ascites on repeat paracentesis decreased over time, from 19/22 in less than 7 days, to 12/30 between 7 days and 3 months, to 2/12 after an interval of more than 3 months.

Discussion

Here, we present data from a cohort of 214 patients with cirrhosis and hemorrhagic ascites. We demonstrate that hemorrhagic ascites occurs most often in patients with advanced liver disease. We also found that these patients have a poor prognosis, with a significantly higher rate of ICU care, AKI, and overall mortality than age- and gender-matched control patients with portal hypertension and ascites, but without hemorrhage.

In the majority of patients with hemorrhagic ascites, a specific cause could not be identified; 72% of patients with ascitic RBC count of 10,000–50,000/ μ l and 52% of patients with RBC count $>50,000/\mu$ l in their ascitic fluid had spontaneous or idiopathic hemorrhagic ascites. Iatrogenic and HCC related hemorrhagic ascites were notable in the cohort; hemorrhagic ascites secondary to trauma was uncommon. The findings are consistent with data from a small series of 39 cases in which 33% to 51% of patients (this range represents the lowest and highest estimates based on extrapolation of missing data) with cirrhosis and grossly bloody ascites had spontaneous bloody ascites, followed by hemorrhagic ascites secondary to HCC in 11 cases (28%), secondary to procedures in 6 cases (15%), and due to blunt abdominal trauma in 1 case (2%) [3].

The mechanism whereby RBCs spontaneously appear in ascites is unclear, but has been postulated to be related to portal hypertension. It is likely to be due to one of two processes:

(1) leakage from the interstitial spaces of the liver or splanchnic bed in a manner similar to red cell diapedesis in systemic venous hypertension or (2) intra-abdominal bleeding from a small vessel (likely a thin-walled, portosystemic collateral) or an abdominal cavity varix [4]. The only prior study that described specific cases with spontaneous hemorrhagic ascites found no association with clinical evidence of hemodynamic instability [3], suggesting an insidious process. While the blood was noted incidentally at routine paracentesis, it was not a benign condition in the small series of 15 patients with spontaneous hemorrhagic ascites. As in our study, patients in this case series had a poorer prognosis than control patients with ascites and no hemorrhage [3]. Our data expand this small series and emphasize that mortality in patients with spontaneous hemorrhagic ascites is high.

Patients with cirrhosis and hemorrhagic ascites may also present acutely, with sudden abdominal pain and distention followed by hypotension, particularly if secondary to ruptured varices [3,4] or rupture of an HCC. The true frequency of variceal rupture is difficult to estimate because laparotomy is generally necessary to confirm this diagnosis [26]. Angiography locates the site in only one-third of the cases [4,26]. Mortality is extremely high (up to 75%) and survival is dismal. Similarly, rupture of HCC is associated with very poor outcomes.

Our analysis revealed that patients with cirrhosis and hemorrhagic ascites of any severity had decreased survival (median 1 year) when compared with age- and gender-matched cirrhotic patients with non-hemorrhagic ascites (median 5.6 years). Similarly, prior reports emphasized that patients with cirrhosis and hemoperitoneum, especially due to rupture of HCC or of an abdominal cavity varix, had high mortality [3,4,26]. We also found that patients with hemorrhagic ascites related to HCC have worse survival than patients with hemorrhagic ascites due to other etiologies. Additionally, we found that an ascitic RBC count of 10,000–50,000/ μ l had a median survival of 1.4 years, higher than patients with an ascitic fluid RBC count >50,000/ μ l, who had a median survival of only 0.5 years. This raises the possibility that decreased survival may correlate with the severity of hemorrhagic ascites.

Although our study has several important strengths, including its large size, robust data collection, mortality assessment, case-control design, and substantial long-term follow-up, we recognize several limitations. First, the study was retrospective in design, and this could have limited the analysis of variables. However, we examined a very large number of variables, and it is unlikely that any significant clinical variables were omitted. Additionally, the retrospective nature of this study may have confounded the precise determination of the etiologies of hemorrhagic ascites and theoretically, could be a source of selection bias. To mitigate this potential limitation, we used precise definitions for the different types of hemorrhagic ascites and implemented these *a priori*. Other concerns include the accuracy of reporting clinical characteristics, such as altered mental status or asterixis. Nonetheless, we feel that the notable strengths of this study outweigh its limitations.

In summary, our data indicate that hemorrhagic ascites in cirrhotic patients is associated with advanced liver disease, higher MELD, higher rate of ICU care, AKI, and greater overall mortality. In addition, we show that hemorrhagic ascites itself is associated with

decreased survival in cirrhotic patients with portal hypertension and ascites. These data raise the possibility that an improved prognostic score for patients with cirrhosis and ascites should include well-defined clinical features, such as hemorrhagic ascites.

Abbreviations

RBC	red blood cell
AKI	acute kidney injury
MELD	Model for End-Stage Liver Disease
INR	international normalized ratio
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HBV	hepatitis B virus
SBP	spontaneous bacterial peritonitis
SIRS	systemic inflammatory response syndrome

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Fig. 1. Survival of patients with hemorrhagic ascites

Cases represent patients with hemorrhagic ascites and controls represent patients with ascites alone as defined in the Patients and methods section. The overall 1-month, 1-year, and 3-year patient survival rates in cases with hemorrhagic ascites were 72%, 50%, and 41%, respectively, with a median survival of 1 year. These rates were lower than survival rates in the control group. Patients without hemorrhagic ascites had a 1-month, 1-year and 3-year patient survival of 87%, 72%, 61% respectively, with a median survival of 5.6 years.

Fig. 2. Survival of patients with hemorrhagic ascites based on ascitic RBC count

Patients with hemorrhagic ascites were divided into two groups. Patients with ascitic fluid RBC counts of 10,000–50,000/ μ l had 1-month, 1-year, and 3-year survival rates of 75%, 51%, and 44%, respectively, with a median survival of 1.4 years, higher than patients with ascitic fluid RBC count >50,000/ μ l (1-month, 1-year and 3-year survival rates of 68%, 44%, and 36% respectively with a median survival of 0.5 years).

Table 1

Demographic and clinical characteristics (n = 856).

Variables	Controls (n = 642) Median (range)	Cases (n = 214) Median (range)	p value
Age (yr)	51 (22–79)	51 (24–77)	0.9500
Ethnicity			<0.001
African American (%)	178 (28)	54 (25)	
Asian (%)	14 (2)	3 (2)	
Caucasian (%)	252 (40)	56 (26)	
Hispanic (%)	188 (29)	99 (46)	
Other (%)	10 (1)	2 (1)	
Gender			1.0
Female (%)	138 (22)	46 (22)	
Ascites characteristics			<0.001
Small ascites (%)	377 (59)	17 (8)	
Moderate ascites (%)	60 (9)	86 (40)	
Large ascites (%)	202 (32)	111 (52)	
Symptoms and signs			
Abdominal swelling (%)	188 (29)	171 (80)	<0.001
Fever (%)	83 (13)	54 (25)	<0.001
Abdominal pain (%)	168 (26)	141 (66)	<0.001
Dyspnea (%)	142 (22)	108 (50)	<0.001
Nausea (%)	87 (14)	69 (32)	<0.001
Vomiting (%)	78 (12)	59 (28)	<0.001
Lightheadedness (%)	27 (4)	33 (15)	<0.001
Etiology of cirrhosis			0.48
Alcohol (%)	246 (38)	71 (33)	
Hepatitis C virus (%)	318 (50)	111 (52)	
Hepatitis B (%)	27 (4)	9 (4)	
Other (%)	51 (8)	23 (11)	
Laboratory results			
MELD score *	16 (6–46)	18 (6–46)	<0.001
Bilirubin (mg/dl)	2.5 (0.2–53.9)	3 (0.3–41)	0.04
Albumin (g/dl)	2.8 (1.3–5.2)	2.5 (1.3–4.5)	<0.001
INR	1.4 (0.9–6.1)	1.5 (0.9–5.8)	0.009
AST (U/L)	73 (12–4009)	55 (5–5988)	0.90
ALT (U/L)	36 (5–1758)	27 (3–1264)	0.05
Platelets ($\times 10^9/L$)	112.5 (9–2631)	101 (11–660)	0.12
Hemoglobin (g/dl)	11.2 (3.0–17.8)	10.2 (4–16.9)	0.001
WBC ($\times 10^9/L$)	7.5 (1.5–40.4)	7.5 (1.9–30.8)	0.87

Variables	Controls (n = 642) Median (range)	Cases (n = 214) Median (range)	p value
Creatinine (mg/dl)	1 (0.5–26)	1.1 (0.4–17.6)	0.004
BUN (mg/dl)	15 (2–168)	21 (1–190)	<0.001
Sodium (mEq/L)	134 (105–148)	133 (96–152)	0.25

Controls = ascitic RBC <10,000 RBC/ μ l.

Cases = ascitic RBC $\geq$ 10,000 RBC/ μ l.

* Calculated at time of admission.

MELD, Model for End-Stage Liver Disease; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

Table 2

Etiology of hemorrhagic ascites (n = 214).

Etiology	Ascites RBC		<i>p</i> value
	10,000–50,000/ μ l n = 133 (%)	>50,000/ μ l n = 81 (%)	
Spontaneous	96 (72)	42 (52)	0.003
HCC	17 (13)	19 (24)	0.06
Iatrogenic	14 (11)	14 (17)	0.21
Trauma	1 (1)	1 (1)	1.0
Other	5 (3)	5 (6)	0.51

HCC, hepatocellular carcinoma.

Table 3

Complications and outcomes.

Complications	Controls n = 642 (%)	Cases n = 214 (%)	p value
Need for transfusion	146 (23)	99 (46)	<0.001
ICU admission	150 (23)	68 (32)	0.01
Acute kidney injury	92 (14)	84 (40)	<0.001
Need for vasopressors	40 (6)	32 (15)	<0.001
Sepsis	27 (4)	30 (14)	<0.001
SBP	16 (3)	57 (27)	<0.001

Controls = ascitic RBC 0 to <10,000 RBC/ μ l, n = 642.Cases = ascitic RBC $\geq$ 10,000 RBC/ μ l, n = 214.

SBP, spontaneous bacterial peritonitis; ICU, intensive care unit.

Table 4

Predictors of survival.

Variable	Univariate analysis HR (CI)	Multivariate analysis HR (CI)
Hemorrhagic ascites	1.70 (1.38–2.09)	1.34 (1.07–1.68)
MELD	1.05 (1.04–1.06)	1.04 (1.03–1.05)
Need for ICU level care	2.30 (1.88–2.81)	2.02 (1.63–2.51)
History of HCC	2.87 (2.07–3.97)	2.27 (1.61–3.19)
HCV infection	1.32 (1.10–1.61)	1.34 (1.10–1.63)
Large ascites	1.64 (1.31–2.05)	1.19 (0.94–1.50)
Hepatic encephalopathy grade 3	1.64 (1.31–2.05)	1.19 (0.94–1.50)
Hb >10 g/dl	0.77 (0.63–0.93)	0.94 (0.76–1.15)
WBC >10 × 10 ⁹ /L	1.46 (1.19–1.79)	1.20 (0.98–1.48)
Na <125 mEq/L	0.63 (0.47–0.87)	0.81 (0.59–1.12)

Large ascites and encephalopathy grades are as defined in Patients and methods.