Imaging and clinical predictors of spontaneous bacterial peritonitis diagnosed by ultrasound-guided paracentesis

Andrew Sideris, Pooja Patel, Hearns W. Charles, MD, James Park, MD, David Feldman, MD, and Amy R. Deipolyi, MD, PhD

Spontaneous bacterial peritonitis (SBP) is a potentially life-threatening complication of ascites diagnosed by paracentesis. We determined predictors of SBP to facilitate patient selection. The 301 paracenteses performed in 119 patients (51 women, 68 men) from July to November 2015 were retrospectively reviewed. Presentation, lab data, depth of the deepest ascites pocket on ultrasound, total volume of ascites removed, absolute neutrophil count, and complications were studied. Of 301 paracenteses, 16 (5%) diagnosed SBP. On univariate analysis, SBP was associated negatively with history of cirrhosis and positively with history of cancer, abdominal pain, greater depth of the fluid pocket, prior SBP, and leukocytosis. Multivariate analysis using these variables to predict SBP was significant ($P < 0.0001$); only depth of the largest fluid pocket ($P = 0.008$) and complaint of abdominal pain ($P = 0.006$) were independent predictors. Receiver-operator curve analysis showed that a 5-cm cutoff of pocket depth yielded 100% sensitivity and 32% specificity. Two (0.1%) hemorrhagic complications occurred, one causing death and one necessitating laparotomy. In conclusion, deeper ascites pockets and abdominal pain are independent predictors of SBP. When the largest ascites pocket is <5 cm, the probability of SBP is nearly negligible. Given the potential for hemorrhagic complications, findings may help triage patients for paracentesis.

Paracentesis is recommended for symptomatic relief, diagnosis of ascites etiology, and exclusion of spontaneous bacterial peritonitis (SBP), which can be fatal in 20% of patients (1, 2). Paracentesis has been shown to shorten hospital stay and prevent complications such as hyponatremia, hepatic encephalopathy, and hepatorenal syndrome (3). One major complication of paracentesis is hemorrhage, with an incidence of <1% (4). Studies have not defined risk factors for bleeding complications (5). Given its low complication rate and diagnostic and therapeutic value, paracentesis is performed on a large scale. Among nearly 18,000 admissions for ascites or encephalopathy, diagnostic workup for over 60% of patients included paracentesis (6). Given that the exposure to paracentesis procedures is so large, hemorrhage, while rare, is encountered. Certain paracenteses are performed only for diagnostic purposes, to evaluate for SBP, an uncommon diagnosis (7). Given the rarity of SBP and the potential for hemorrhagic complications, it would be helpful to define factors associated with SBP to aid in patient selection and avoid unnecessary adverse events. The aim of this study was to identify patient and imaging characteristics that increased the risk for SBP to optimize the diagnostic role of paracentesis and minimize patient exposure to procedural risks.

METHODS

This retrospective study was approved by the institutional review board and was compliant with the Health Insurance Portability and Accountability Act. Consecutive ultrasound-guided paracentesis procedures from July 2015 to November 2015 at a single institution were analyzed. Indications were for therapeutic and/or diagnostic purposes. Paracentesis was performed by physician members of the vascular and interventional radiology section. After preparing and draping in usual sterile technique and administering lidocaine for local anesthesia, using ultrasound guidance an 8Fr pigtail drainage catheter (Total Abscession, Angiodynamics, Latham, NY) or an 18-gauge needle was advanced into the largest pocket and secured to the skin for drainage, with an image of the largest pocket saved, as described previously (4). All specimens were sent for evaluation of cell count and culture. For therapeutic paracentesis, all fluid was removed; for paracentesis performed only for diagnostic purposes, 20 to 60 cc were removed. SBP was defined by absolute neutrophil count (ANC) ≥250 cells/mm^3 and/or positive fluid culture (8). Ascitic fluid characteristics and the patient's underlying condition, presenting symptoms, and laboratory data were also analyzed. In total, 309 paracentesis procedures were performed over the study period. Eight were excluded due to the absence of laboratory or imaging data. The 301 remaining procedures were performed in 119 patients (51 women, 68 men) with a mean age of 62.5 ± 1.2 years.

From New York University School of Medicine, New York, New York (Sideris, Patel); South Florida Vascular Associates, Coconut Creek, Florida (Charles); New York University Hepatology Associates, New York University Langone Medical Center, New York, New York (Park, Feldman); and Interventional Radiology Service, Memorial Sloan Kettering Cancer Center, New York, New York (Deipolyi).

Corresponding author: Amy Deipolyi, MD, PhD, Interventional Radiology Service, Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY 10065 (e-mail: deipolya@mskcc.org).

Statistical analysis was performed with GraphPad Prism 7 (GraphPad Software, San Diego, CA), with $P < 0.05$ used for statistical significance. Data are presented as mean ± standard error. Student's *t* test and Fischer's exact tests were used to compare means and frequencies. Logistic regression was used to assess the impact of laboratory and clinical variables on the outcome of SBP or complications.

RESULTS

Of the 301 procedures, 185 were performed in men and 116 in women. Of the 301 ultrasound-guided paracenteses, 219 cases were associated with liver cirrhosis, 105 with cancer, and 45 cases with both liver cirrhosis and cancer. Of the 301 paracenteses studied, 16 resulted in diagnoses of SBP (5%), whereas 275 did not. Fifteen of the 16 cases were diagnosed based on ANC ≥ 250 cells/mm^3; the other case was diagnosed based on a positive culture with *Citrobacter freundii* and had an ANC of 123 cells/mm^3. Of the remaining 15 cases, 13 had negative cultures and 2 had positive cultures *(Enterococcus faecium* and *Citrobacter freundii).* Among the 275 negative cases, three had positive cultures considered contaminants (one with *Staphylococcus simulans* and two with *Propionibacterium acnes).*

Univariate analysis comparing positive and negative cases demonstrated that positive cases significantly differed from negative cases in having decreased diagnosis of cirrhosis, increased diagnosis of any type of cancer, more abdominal pain, a larger depth of the largest fluid pocket, increased rate of prior SBP, and increased serum white blood cell count *(Table).* In contrast, serum sodium, total ascites drained, the presence of fever or confusion, gender, age, and indication for diagnostic evaluation only did not significantly differ between groups. There was a positive correlation between the depth of the largest pocket and total volume of ascites drained ($r = 0.37$, $P < 0.0001$).

Table. Univariate analysis comparing cases with and without a diagnosis of spontaneous bacterial peritonitis

Variable	No SBP (n = 275)	SBP (n = 16)	*P* value
Abdominal pain	20%	75%	<0.001
Fever	2.5%	6.3%	0.36
Confusion	3.5%	6.3%	0.46
Cirrhosis	73%	31%	<0.001
Cancer	31%	69%	0.004
Diagnostic only	6.3%	0%	0.61
Male gender	63%	38%	0.06
Age (years)	63.0 ± 0.7	61.9 ± 3.7	0.71
Prior SBP	19%	50%	0.008
Sodium	133.6 ± 0.7	135.8 ± 1.4	0.47
White blood cell count (cells/cc^3)	6.5 ± 0.3	11.0 ± 1.5	<0.001
Depth of largest pocket (cm)	6.2 ± 0.2	7.7 ± 0.4	0.008
Total volume drained (L)	4.7 ± 0.2	4.6 ± 0.8	0.83

SBP indicates spontaneous bacterial peritonitis.

Next, multiple logistic regression was performed to assess the impact of the variables with significant differences on univariate analysis (prior SBP, diagnosis of cirrhosis, diagnosis of cancer, abdominal pain, depth of largest fluid pocket, and serum white blood cell count) on the diagnosis of SBP. Only two variables were independent predictors, specifically the depth of the largest fluid pocket ($P = 0.008$) and complaint of abdominal pain ($P = 0.006$). A receiver-operator curve analysis of pocket depth and SBP diagnosis had an area under the curve of 0.73 ($P = 0.002$); at a cutoff of 5 cm, sensitivity was 100% and specificity was 32%.

Of the 301 cases, there were two major adverse events (0.67%), specifically hemorrhage requiring emergent laparotomy and hemorrhage resulting in death. A multiple logistic regression was performed with all the variables assessed for SBP plus platelet count and international normalized ratio (INR) as input variables, and hemorrhagic complication as the outcome variable. The resultant model was not significant ($P = 0.06$) and there were no independent predictors. The average platelet count for cases with and without complications was 77.5 and 148.9 K/μL ($P = 0.39$). The average INR for cases with and without complications was 1.2 and 1.3 ($P = 0.39$).

DISCUSSION

Multiple variables, including abdominal pain, cirrhosis, cancer, prior SBP, white blood cell count, and amount of ascites, may be associated with SBP (9). The primary finding of this study is that only abdominal pain and depth of the largest fluid pocket were independent predictors of SBP. Though abdominal pain is considered the hallmark of SBP (10), its utility as a tool to predict a positive diagnosis of SBP is limited by its low specificity, as accumulation of ascites alone can lead to abdominal pain. Increased depth of fluid pocket was associated with SBP. Despite the positive correlation between largest pocket depth and total ascites volume drained, total volume drained did not differ between patients with and without SBP. This may be because not all of the fluid was removed in every patient, or a certain threshold amount of fluid is needed to create conditions permissive of SBP. Depth of largest pocket is an indirect estimate of the total volume of ascites and is readily measurable with ultrasound and therefore is useful as a clinical tool. Receiver-operator curve analysis and the finding that no patient with a fluid pocket <5 cm in depth had SBP suggest that a 5-cm cutoff may help to exclude certain patients with low-volume ascites from the need for paracentesis, potentially avoiding unnecessary exposure to procedure-related risks. This patient population is of particular importance to interventional radiologists, who are likely to be consulted in cases of small-volume ascites necessitating ultrasound guidance.

In this study, clinical findings such as fever and confusion were not helpful in selecting patients for paracentesis. Indeed, overall physician clinical impression carries a low sensitivity of 76% and specificity of 34% (11). In our study, none of the paracenteses performed for diagnostic purposes

only yielded a diagnosis of SBP, suggesting that clinicians were not successful in selecting patients at high risk of SBP. Given the difficulty of predicting which patients have SBP based on clinical features, and the low frequency of SBP (6% in the current study) in all patients undergoing paracentesis, knowledge that SBP is exceedingly rare in patients with minimal ascites is helpful.

The overall major adverse event rate in this study was 0.9%, including two hemorrhagic complications. No risk factors were identified, possibly due to the low number of cases. In both cases, INR was <1.5 and platelet count >50. Similarly, bleeding after paracentesis has not been reported to be related to operator experience, elevated INR, or low platelet count (5). Ascitic fluid leakage and bowel perforation and infection are other major adverse events associated with SBP (12), but did not occur in any of the procedures in our series. As there are no known variables predictive of major adverse events including bleeding, it is important to define selection criteria and exclude patients for diagnostic paracentesis. Though the reported mortality rate associated with paracentesis is small, 0.16% to 0.39% (5, 12), our findings suggest that certain patients could be excluded based on the ascites pocket depth to minimize the exposure to potential adverse events.

The primary limitations of this study are based on its single-center retrospective nature. Our sample size of 301 procedures performed over the course of 6 months at our institution may not be sufficient to identify risk factors of rare outcomes, e.g., adverse events. Given that only 2 adverse events were observed in our study, the statistical power to identify risk factors was limited. A prospective study can validate our findings regarding the suggested 5-cm threshold for selecting patients for diagnostic paracentesis. It was interesting that total ascites drained correlated to depth of the largest pocket, but did not differ between patients with and without SBP. One study limitation is that the presence of loculations was not documented in the chart, and therefore it is possible that not all the fluid was removed. Also, we report a higher than expected rate of SBP among patients with a cancer diagnosis. Future studies could assess whether malignancy-related SBP is associated with undocumented liver failure and portal hypertension (13, 14).

1. Pericleous M, Sarnowski A, Moore A, Fijten R, Zaman M. The clinical management of abdominal ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: a review of current guidelines and recommendations. *Eur J Gastroenterol Hepatol* 2016;28(3):e10–e18.
2. Rimola A, García-Tsao G, Navasa M, Piddock LJV, Planas R, Bernard B, Inadomi JM. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. *J Hepatol* 2000;32(1):142–153.
3. Moore CM, Van Thiel DH. Cirrhotic ascites review: pathophysiology, diagnosis and management. *World J Hepatol* 2013;5(5):251–263.
4. McGibbon A, Chen GI, Peltekian KM, van Zanten SV. An evidence-based manual for abdominal paracentesis. *Dig Dis Sci* 2007;52(12):3307–3315.
5. Pache I, Bilodeau M. Severe haemorrhage following abdominal paracentesis for ascites in patients with liver disease. *Aliment Pharmacol Ther* 2005;21(5):525–529.
6. Orman ES, Hayashi PH, Bataller R, Barritt AS. Paracentesis is associated with reduced mortality in patients hospitalized with cirrhosis and ascites. *Clin Gastroenterol Hepatol* 2014;12(3):496–503.
7. Castellote J, Girbau A, Maisterra S, Charhi N, Ballester R, Xiol X. Spontaneous bacterial peritonitis and bacterascites prevalence in asymptomatic cirrhotic outpatients undergoing large-volume paracentesis. *J Gastroenterol Hepatol* 2008;23(2):256–259.
8. Solà E, Solé C, Ginès P. Management of uninfected and infected ascites in cirrhosis. *Liver Int* 2016;36(Suppl 1):109–115.
9. Such J, Runyon BA. Spontaneous bacterial peritonitis. *Clin Infect Dis* 1998;27(4):669–674.
10. McHutchison J, Runyon B. Spontaneous bacterial peritonitis. In Surawicz CM, Owen RL, eds. *Gastrointestinal and Hepatic Infections.* Philadelphia: WB Saunders, 1994:455.
11. 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):268–273.
12. De Gottardi A, Thevenot T, Spahr L, Morard I, Bresson-Hadni S, Torres F, Giostra E, Hadengue A. Risk of complications after abdominal paracentesis in cirrhotic patients: a prospective study. *Clin Gastroenterol Hepatol* 2009;7(8):906–909.
13. Bac DV, de Marie S, van Blankenstein M. Spontaneous bacterial peritonitis complicating malignancy-related ascites. *Dig Dis Sci* 1996;41(1):131–132.
14. Khan MO, Horowitz HW. Spontaneous bacterial peritonitis in patients with malignancy-related ascites: case report and review. *Infect Dis Clin Pract* 1999;8(3):122–126.