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Efficacy predictors of third-generation cephalosporins in treating spontaneous bacterial peritonitis

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Abstract

Objective: Third-generation cephalosporins (3rd GCs) have recently become controversial as the first-line strategy for empirical spontaneous bacterial peritonitis (SBP) treatment. This study aimed to identify SBP treatment efficacy predictors of 3rd GCs.

Methods: In this retrospective cohort study, 279 cirrhosis patients with SBP who received 3rd GC monotherapy for initial empirical treatment from 2013 to 2019 were included. Nonresponse was defined as a decreased ascites polymorphonuclear (PMN) count < 25% from baseline after 48 hours of antibacterial treatment. Multivariate regression analysis was used to identify efficacy predictors of 3rd GCs in treating SBP. Kaplan–Meier analysis was used to evaluate survival data.

Results: The nonresponder group included 120 patients with no response, and the responder group included 159 patients with responses. The response rate to 3rd GCs was 57.0% among all patients. The common pathogens were *Escherichia coli* (40.6%), *Staphylococcus* (15.6%), *Klebsiella pneumonia* (12.5%), and *Streptococcus* (12.5%) in 32 ascites culture isolates. Nosocomial SBP (NSBP) (odds ratio [OR]: 2.371, 95% confidence interval [CI]: 1.323–4.249, P = .004), pneumonia (OR: 11.561, 95% CI: 1.876–71.257, P = .008), recurrent SBP (OR: 3.386, 95% CI: 1.804–6.357, P < .001), platelet count (≥113.5 × 10^9/L) (OR: 3.515, 95% CI: 1.973–6.263, P < .001), and ascites PMN count (≤0.760 × 10^9/L) (OR: 4.967, 95% CI: 2.553–9.663, P < .001) were independent predictors of nonresponse to 3rd GCs against SBP. Survival plot analysis at 30 days showed worse survival for the nonresponders (P = .003).

Conclusion: NSBP, pneumonia, recurrent SBP, increased platelet count, and lower ascites PMN count were independent predictors of nonresponse to 3rd GC in treating SBP. Nonresponse to initial antibiotic treatment was associated with worse survival.

Abbreviations: 3rdGC = third-generation cephalosporin, CASBP = community-acquired SBP, CI = confidence interval, GNB = gram-negative bacteria, GPB = gram-positive bacteria, MDR = multidrug-resistant, OR = odds ratio, PMN = polymorphonuclear, PPI = proton pump inhibitor, ROC = receiver operating characteristic, SBP = spontaneous bacterial peritonitis.

Keywords: efficacy, predictor, spontaneous bacterial peritonitis, third-generation cephalosporin

1. Introduction

Spontaneous bacterial peritonitis (SBP) is a common complication of cirrhosis, with an incidence of ≈14.6%[1] and a 30-day mortality as high as 24.1% to 26.1%.[2,3] Antibiotics are the main means to treat SBP, among which third-generation cephalosporins (3rd GCs) are classic first-line drugs for initial empirical treatment.[4]

In recent years, with the gradual spread of bacterial drug resistance, negative reports about SBP treatment with 3rd GCs have been increasing. Research shows that the drug resistance rates of pathogens of community-acquired SBP (CASBP) and nosocomial SBP (NSBP) to 3rd GCs are as high as 33.8% and 54.3%, respectively.[5] In NSBP cases, the proportion of pathogens that are multidrug-resistant (MDR) bacteria can be as high as 22% to 73%.[6] The composition of SBP pathogens has also changed, with the proportion of gram-positive bacteria (GPB) increasing. In Asia, Europe, North America, South America, and Africa, the highest proportions of GPB have reached 53%, 68.3%, 73.9%, 63.6%, and 73.2%, respectively.[7] The response rate of SBP to empirical treatment with 3rd GCs is only 56.3% to 59%.[8,9] Given this situation, some scholars have recommended that drugs that can cover vancomycin-resistant enterococci, methicillin-resistant staphylococci, and gram-negative bacteria (GNB) producing extended-spectrum β-lactamases should be selected as the first choice for empirical treatment of SBP instead of 3rd GCs.[10]

Different conclusions regarding the effects of 3rd GCs have been reached. Badawy et al[11] found that the response rate of SBP to cefotaxime could be as high as 81% and, therefore,

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concluded that cefotaxime was still a reliable choice for the first-line treatment of SBP. Sunjaya et al[12] found that the drug resistance rate of SBP pathogens against 3rd GCs was only 10% and concluded that 3rd GCs were effective for empirical treatment of CASBP and healthcare-related SBP patients without liver cancer. Solá et al[13] thought that 3rd GCs were a good first choice for treatment of CASBP. These results indicated that 3rd GCs can still be used as the first choice for some SBP cases.

In fact, the effectiveness of 3rd GCs in treating SBP is not only related to the species and drug resistance of the pathogenic bacteria but also associated with the general condition, underlying diseases, and severity of illness of the patient. Therefore, we aim to identify some efficacy predictors of 3rd GCs in treating SBP with the goal of helping clinicians rationally choose antibiotics.

2. Methods

2.1. Subjects

This was a retrospective, single-center cohort study. The research center was a grade III level A public hospital in China. From January 2013 to December 2019, a total of 290 cirrhosis patients with SBP who received 3rd GC monotherapy for initial empirical treatment in The Ninth Hospital of Nanchang were enrolled consecutively. Among 290 patients, 11 were excluded for the following reasons: 2 suffered from tuberculosis, 3 suffered from acquired immunodeficiency syndrome, 1 had fungal ascites, and 5 had missing data. Finally, 279 patients were included in the study. The study protocol was approved by the Ethics Committee of The Ninth Hospital of Nanchang (approval No. [2017] Lun Jian Shen Zi [03]). All the data were gathered anonymously, and the requirement for informed consent was exempted by the ethics committee.

2.2. Diagnosis and definition

Cirrhosis was diagnosed based on imaging evidence, clinical manifestations, and laboratory tests. SBP was diagnosed based on an ascites polymorphonuclear (PMN) count $\geq 0.25 \times 10^9$/L in the absence of an intra-abdominal source of infection, and with at least one sign of infection (e.g., abdominal pain and/or tenderness, fever, unexplained encephalopathy, worsening of liver and/or renal function, altered white blood cell count, and gastrointestinal bleeding).[4] Nonresponse was defined as an ascites PMN count decrease < 25% from baseline after 48 hours of treatment, whereas a decrease in the ascites PMN count ≥25% from baseline represented a response.[4] Nosocomial infection was defined as an infection occurring >48 hours after hospitalization, and earlier onset was considered community-acquired infection.[5] Broad-spectrum antibiotic exposure was defined as having received broad-spectrum antibiotic treatment within 3 months before the onset of SBP. Pneumonia was diagnosed simultaneously with SBP and initially treated with the same antibiotic as for SBP. The use of a proton pump inhibitor (PPI) was defined as the use of any PPI for at least 1 week within 1 month before the onset of SBP. The use of propranolol was defined as the administration of propranolol for at least 2 weeks before the onset of SBP.

2.3. Data collection

General data, medical history characteristics, clinical manifestations, laboratory test results, and survival data were collected. Among them, the clinical manifestations and laboratory test results were the values on the day of SBP diagnosis before antibiotic use. Candidate efficacy predictors of 3rd GCs in treating SBP were chosen based on previous research[12,13] and our clinical judgment. The Child–Pugh score[14] and Model for End-Stage Liver Disease score[15] were calculated with reference to the literature. The ascites cell count was determined by automated flow cytometry.

2.4. Statistical analysis

Student *t* test or the rank sum test was used to examine continuous variables, and the χ^2test or Fisher exact test was adopted to examine categorical variables. Binary multiple regression (forward conditional method) was used for multivariate analysis. A receiver operating characteristic (ROC) curve was drawn to evaluate the prediction accuracy of the predictors, and the best cutoff value of a predictor was defined according to the maximum Youden index. The Kaplan–Meier method and log-rank test were used to evaluate survival data. $P < .05$ was considered statistically significant. SPSS 26.0 (SPSS, Inc, Chicago, IL) was used for data analysis. As this study was exploratory in design, the sample size and power of the test were not estimated formally.

3. Results

3.1. General data

After initial treatment with 3rd GCs, 120 patients with no response were included in the nonresponder group, and 159 patients with response were included in the responder group. Among all 279 patients, only 57.0% presented a response to initial empirical treatment with 3rd GCs. The study population had an age range of 25 to 80 years, 81.4% of the patients were male, and most (70.6%) patients had hepatitis B as the cause of cirrhosis. No significant differences in general data were found between the nonresponder group and the responder group ($P > .05$). Details are shown in Table 1.

The 3rd GCs used for initial treatment of CASBP cases (n = 175) and NSBP cases (n = 104) included ceftazidime (30.9% vs 26.9%), ceftriaxone (9.7% vs 17.3%), cefotaxime (36.6% vs 35.6%), and cefoperazone (22.9% vs 20.2%), and difference in the constituent ratio of 3rd GCs was not significant ($\chi^2 = 3.572$, $P = .312$).The response rate of CASBP cases to 3rd GCs (64.6%, 113/175) was higher than that of NSBP cases (44.2%, 46/104), and the difference was significant ($\chi^2 = 11.001$, $P = .001$).

3.2. Medical history characteristics, clinical manifestations, and laboratory tests

Platelet counts and the proportions of broad-spectrum antibiotic exposure, NSBP, pneumonia, and recurrent SBP in the nonresponder group were higher than those in the responder group ($P < .05$), whereas serum alanine aminotransferase, ascites nucleated leukocyte counts, and ascites PMN counts were lower in the nonresponder group ($P < .05$). No significant differences in other features were noted between the 2 groups ($P > .05$). Details are shown in Tables 2 and 3.

The response rates of patients with broad-spectrum antibiotic exposure, pneumonia, and recurrent SBP to 3rd GCs were 40.0% (18/45), 16.7% (2/12), and 33.3% (27/81), respectively, as shown in Table 2.

At the best cutoff values of $\geq 113.5 \times 10^9$/L, ≤33.5u/L, $\leq 1.135 \times 10^9$/L, and $\leq 0.760 \times 10^9$/L, platelet count, alanine aminotransferase, ascites nucleated leukocyte count, and ascites PMN count had 0.550, 0.667, 0.528, and 0.453 sensitivity, 0.723, 0.500, 0.733, and 0.867 specificity, and Youden index values of 0.273, 0.167, 0.262, and 0.319 for predicting no response to 3rd GCs, respectively; the areas under the ROC curve were 0.656, 0.575, 0.615, and 0.670, all $P < .05$, respectively (Fig. 1).

3.3. Multivariate analysis

The candidate predictors with significant differences in univariate analysis were further examined in the multivariate analysis.

Table 1

General data.

Candidate predictors	Nonresponder (n = 120)	Responder (n = 159)	Statistics	*P*
Sex (male), n (%)	96 (80.0)	131 (82.4)	$x^2 = 0.258$	.612
Age (yr), (mean ± SD)	53.4 ± 12.4	50.8 ± 11.9	t = 1.750	.081
Cause of cirrhosis, n (%)			No statistics	.088
Hepatitis B	81 (67.5)	116 (73.0)		
Alcohol	6 (5.0)	13 (8.2)		
Hepatitis C	6 (5.0)	0 (0)		
Schistosomiasis	3 (2.5)	5 (3.1)		
Hepatolenticular degeneration	1 (0.8)	0 (0)		
Secondary biliary	1 (0.8)	0 (0)		
Hepatitis B + alcohol	9 (7.5)	11 (6.9)		
Hepatitis B + schistosomiasis	5 (4.2)	7 (4.4)		
Hepatitis C + secondary biliary	0 (0)	1 (0.6)		
Unknown cause	8 (6.7)	6 (3.8)		
3rd GC used for initial treatment, n (%)			$\chi^2 = 1.983$	.576
Ceftazidime	39 (32.5)	43 (27.1)		
Ceftriaxone	13 (10.8)	22 (13.8)		
Cefotaxime	45 (37.5)	56 (35.2)		
Cefoperazone	23 (19.2)	38 (23.9)		
Child–Pugh score, median (IQR)	10.0 (8.3–12.0)	10.0 (9.0–12.0)	Z = −0.907	.365
MELD score, median (IQR)	12.0 (7.1–19.4)	14.7 (10.1–19.8)	Z = −1.875	.061

3rd GC = third-generation cephalosporin, IQR = interquartile range, MELD = model for end-stage liver disease, SD = standard deviation.

Table 2

Medical history characteristics and clinical manifestations.

Candidate predictors	Nonresponder (n = 120)	Responder (n = 159)	Statistics	*P*
Diabetes mellitus, n (%)	15 (12.5)	19 (11.9)	$\chi^2 = 0.019$	.889
Previous history of splenectomy, n (%)	11 (9.2)	16 (10.1)	$\chi^2 = 0.063$	.802
Liver cancer, n (%)	26 (21.7)	37 (23.3)	$\chi^2 = 0.101$	.751
History of BAE, n (%)	27 (22.5)	18 (11.3)	$\chi^2 = 6.318$	.012
Nosocomial SBP, n (%)	58 (48.3)	46 (28.9)	$\chi^2 = 11.011$	.001
Recurrent SBP, n (%)	54 (45.0)	27 (17.0)	$\chi^2 = 26.058$	<.001
Prophylaxis with norfloxacin, n (%)	5 (4.2)	6 (3.8)	$\chi^2 = 0.021$	.886
Use of proton pump inhibitor, n (%)	19 (15.8)	23 (14.5)	$\chi^2 = 0.0217$	.883
Use of propranolol, n (%)	7 (5.8)	11 (6.9)	$\chi^2 = 0.014$	.905
Body temperature (°C), median (IQR)	36.8 (36.5–37.1)	36.8 (36.5–37.4)	Z = −1.105	.269
Abdominal pain, n (%)	17 (14.2)	20 (12.6)	$\chi^2 = 0.150$	.699
Abdominal tenderness, n (%)	48 (40.0)	67 (42.1)	$\chi^2 = 0.129$	.719
Abdominal rebound tenderness, n (%)	43 (35.8)	75 (47.2)	$\chi^2 = 3.601$	.058
Ascites volume, n (%)			$\chi^2 = 1.464$	.226
Mild	27 (22.5)	46 (28.9)		
Moderate-large	93 (77.5)	113 (71.1)		
Pneumonia, n (%)	10 (8.3)	2 (1.3)	$\chi^2 = 8.318$	.004
Gastrointestinal bleeding, n (%)	2 (1.7)	3 (1.9)	$\chi^2 = 0.019$	.891
Infectious shock, n (%)	1 (0.8)	1 (0.6)	$\chi^2 = 0.040$	.841
Hepatic encephalopathy, n (%)	11 (9.2)	6 (3.8)	$\chi^2 = 3.476$	.062

BAE = broad-spectrum antibiotic exposure, IQR = interquartile range, SBP = spontaneous bacterial peritonitis.

The results showed that 5 indicators, including NSBP (odds ratio [OR]: 2.371, 95% confidence interval [CI]: 1.323–4.249, $P = .004$], pneumonia (OR: 11.561, 95% CI: 1.876–71.257, $P = .008$), recurrent SBP (OR: 3.386, 95% CI: 1.804–6.357, $P < .001$), platelet count ($\geq 113.5 \times 10^9$/L) (OR: 3.515, 95% CI: 1.973–6.263, $P < .001$), and ascites PMN count ($\leq 0.760 \times 10^9$/L) (OR: 4.967, 95% CI: 2.553–9.663, $P < .001$) were independent predictors for no response to 3rd GCs against SBP. Details are shown in Table 4.

3.4. Microbiological profile

Ascites and blood cultures were conducted in all patients. Of the 279 cases of SBP, 32 (11.5%) had positive ascites cultures. GNB were isolated from 19 cultures (59.4%), and 13 cultures (40.6%) grew GPB. The main organisms found included 13 *Escherichia coli* strains (40.6%), 5 *Staphylococcus* strains (15.6%), 4 *Klebsiella pneumoniae* strains (12.5%), and 4 *Streptococcus* strains (12.5%). The microbiological patterns of ascites cultures in CASBP and NSBP are shown in Table 5. Additionally, 73.3% (11/15) of 3rd GC-resistant strains were found in the nonresponder group and 11.8% (2/17) in the responder group; the coincidence rate of the drug sensitivity test and antibiotic effectiveness was 81.3% (26/32) in positive ascites culture cases.

Only 3 cases of SBP had positive blood cultures, the organisms of which were all *E coli* strains and consistent with ascites cultures: 2 were 3rd GC-sensitive and 1 was extended-spectrum β-lactamases positive.

3.5. Survival data

A total of 55 of 279 (19.7%) patients died 30 days after SBP onset. The 30-day mortality rate was higher in the nonresponder

Table 3

Laboratory tests.

Candidate predictors	Nonresponder (n = 120)	Responder (n = 159)	Statistics	*P*
Blood test				
WBC (×10⁹/L), median (IQR)	6.1 (4.4–8.2)	6.2 (4.2–8.7)	Z = −0.263	.793
NEU%, median (IQR)	72.9 (64.6–79.6)	75.1 (65.3–81.1)	Z = −1.254	.210
HGB (g/L), (mean ± SD)	106.3 ± 24.5	104.2 ± 20.4	t = −0.746	.456
PLT (×10⁹/L), median (IQR)	119.0 (71.0–157.8)	71.0 (49.0–123.0)	Z = −4.468	<.001
ALT (u/L), median (IQR)	34.0 (20.3–81.8)	51.0 (29.0–94.0)	Z = −2.147	.032
AST (u/L), median (IQR)	65.5 (36.0–129.5)	84.0 (48.0–134.0)	Z = −1.828	.068
TBIL (μmol/L), median (IQR)	55.7 (23.1–80.1)	55.6 (35.5–97.9)	Z = −0.844	.399
ALB (g/L), (mean ± SD)	28.6 ± 5.3	27.9 ± 5.2	t = −1.072	.284
BUN (mmol/L), median (IQR)	5.2 (3.4–7.3)	5.5 (4.0–7.9)	Z = −0.857	.391
Cr (μmol/L), median (IQR)	72.0 (59.0–90.8)	73.0 (59.0–95.0)	Z = −0.458	.647
Na (mmol/L), median (IQR)	136.3 (131.9–139.1)	136.4 (132.1–138.7)	Z = −0.154	.877
Bicarbonate (mmol/L), median (IQR)	21.2 (21.0–23.8)	21.7 (20.6–25.0)	Z = −0.722	.470
PT (s), median (IQR)	17.1 (15.1–23.7)	19.1 (16.3–22.5)	Z = −1.632	.103
INR, median (IQR)	1.4 (1.2–2.1)	1.6 (1.3–2.0)	Z = −1.901	.057
Ascites examination				
NL count (×10⁹/L), median (IQR)	0.810 (0.623–1.258)	1.200 (0.640–2.590)	Z = −3.298	.001
PMN count (×10⁹/L), median (IQR)	0.353 (0.288–0.559)	0.648 (0.325–1.619)	Z = −4.616	<.001
Percentage of PMN count (%), median (IQR)	50.7 (34.2–64.8)	57.0 (43.0–75.0)	Z = −1.867	.062
SAAG (g/L), (mean ± SD)	18.9 ± 5.7	20.0 ± 4.9	t = −1.692	.092

ALB = albumin, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BUN = blood urea nitrogen, Cr = creatinine, HGB = hemoglobin, INR = international normalized ratio, IQR = interquartile range, Na = sodium, NEU% = neutrophil percentage, NL = nucleated leukocyte, PLT = platelet, PMN:polymorphonuclear, PT = prothrombin time, SAAG = serum-ascites albumin gradient, SD = standard deviation, TB = total bilirubin, WBC = white blood cell.

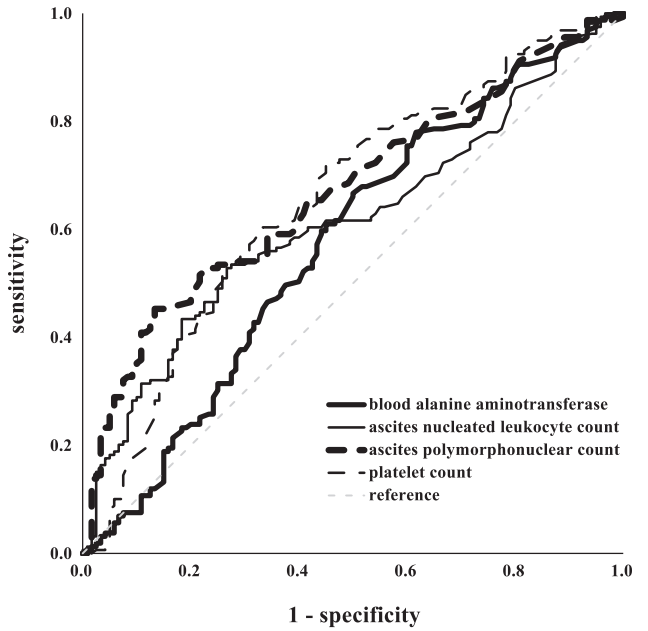

Figure 1. Receiver operating characteristic curve of the platelet count, alanine aminotransferase, ascites nucleated leukocyte count, and ascites polymorphonuclear count in predicting the efficacy of third-generation cephalosporins against spontaneous bacterial peritonitis.

group (27.5%, 33/120) than in the responder group (13.8%, 22/159), χ^2 = 8.067, *P* = .005. Survival plot analysis at 30 days (Fig. 2) also showed worse survival for the nonresponder group and better survival for the responder group (χ^2 = 8.648, *P* = .003).

The most common cause of death was septic shock in both the nonresponder group (18/33, 54.5%) and the responder group (8/22, 36.4%), and the cause of death did not differ between groups (*P* = .797). Details are shown in Table 6.

4. Discussion

This study found that NSBP was an independent predictor for treatment failure of SBP by 3rd GCs, and only 44.2% of NSBP cases responded to 3rd GCs. Related studies have confirmed that NSBP is more often caused by pathogenic bacteria that are resistant to 3rd GCs and have a high risk of death,[16,17] which is the main reason why 3rd GCs have poor efficacy against some NSBP cases. Significantly, in the subgroup analysis of Fiore et al,[5] the data after 2008 and the data in China showed that the drug resistance risk of pathogens in CASBP was not lower than that of NSBP, suggesting that 3rd GCs might not be effective to treat CASBP in certain areas. In this study, the response rate of CASBP cases to 3rd GCs was only 64.6%, which may be an early warning for the 3rd GC therapy in CASBP.

Pneumonia was an independent predictor for poor efficacy of 3rd GCs in treating SBP in this study, and patients with pneumonia had a very low response rate to 3rd GCs (16.7%). The study of Niu et al[18] showed that pulmonary infection is a risk factor for the death of hospitalized SBP patients, suggesting that pulmonary infection will increase the difficulty of SBP treatment. For patients with infection at 2 sites at the same time, first, their bacterial load is heavy, so it may be difficult to achieve an effective antibacterial concentration with a conventional dose of 3rd GC. Second, the pathogenic bacteria may be plural bacteria, which cannot be completely covered by the 3rd GC. Third, patients are prone to multiple infections, suggesting poor immune function. These factors may be the reason for the poor efficacy of 3rd GC in SBP patients with pneumonia.

In this study, recurrent SBP was an independent predictor for poor efficacy of 3rd GC against SBP, and only 33.3% of recurrent SBP cases responded to 3rd GC. Conversely, Kim et al[19] found that more than 90% of SBP patients with initial onset responded to cefotaxime for initial empirical treatment. Because secondary prophylaxis and recurrent hospitalization are associated with broad-spectrum antibiotic exposure, patients suffering from SBP recurrently are more likely to experience drug-resistant bacterial infection; meanwhile, recurrent infection attacks will also cause the body's immune function and liver function to worsen, which will ultimately lead to poor efficacy of 3rd GC.

An increased platelet count could predict poor efficacy of 3rd GC in this study. Mishra et al[20] found that thrombocytosis can be used to predict severe bacterial infection, and Johansson et al[21] proposed that some gram-positive bacteria can induce platelet activation and aggregation. In this study, SBP patients with higher platelet counts were more likely to have no response

Table 4

Multivariate analysis of predictors for no response to 3rd GCs against SBP.

Predictors	Regression coefficient	OR	95% CI of OR	P
Nosocomial SBP	0.863	2.371	1.323–4.249	.004
Pneumonia	2.448	11.561	1.876–71.257	.008
Recurrent SBP	1.220	3.386	1.804–6.357	<.001
Platelet count (≥113.5 × 10^9/L)	1.257	3.515	1.973–6.263	<.001
Ascites PMN count (≤0.760 × 10^9/L)	1.603	4.967	2.553–9.663	<.001
Constant	–2.733	0.065	NA	<.001

CI = confidence interval, OR = odds ratio, PMN = polymorphonuclear, SBP = spontaneous bacterial peritonitis.

Table 5

Microbiological patterns of ascites cultures in CASBP and NSBP.

	CASBP (n = 18)	NSBP (n = 14)	Statistics	P
Bacterial species, n (%)			No statistics	.165
Escherichia coli	5 (27.8)	8 (57.2)		
Staphylococcus	2 (11.1)	3 (21.4)		
Klebsiella pneumoniae	3 (16.7)	1 (7.1)		
Streptococcus	4 (22.2)	0 (0.0)		
Enterococcus faecalis	1 (5.6)	1 (7.1)		
Corynebacterium	2 (11.1)	0 (0.0)		
Providencia rettgeri	0 (0.0)	1 (7.1)		
Nonfermenting *Bacillus*	1 (5.6)	0 (0.0)		
Gram-negative bacteria, n (%)	9 (50.0%)	10 (64.3%)	$\chi^2 = 0.742$	.389
MDR strains, n (%)*	6 (33.3)†	9 (64.3)‡	$\chi^2 = 1.914$	.167
3rd GC-resistant strains, n (%)	4 (22.2)	7 (50.0)	$\chi^2 = 1.603$	.206

3rd GC = third-generation cephalosporin, CASBP = community-acquired spontaneous bacterial peritonitis, MDR = multidrug-resistant, NSBP = nosocomial spontaneous bacterial peritonitis.
*No imipenem- or vancomycin-resistant strains were found.
†Two of which were ESBLs-positive *E coli* strains.
‡Four of which were ESBLs positive *E coli* strains and 2 of which were methicillin-resistant *Staphylococci* strains.

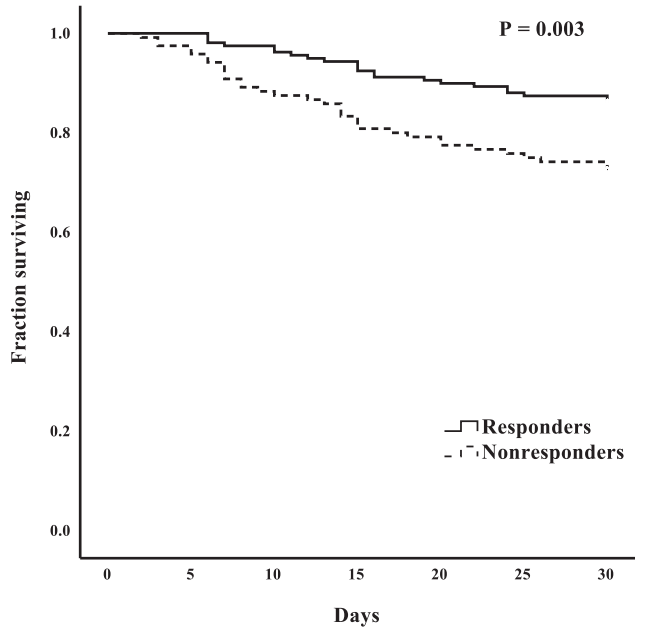

Figure 2. Survival plot for nonresponders and responders among patients with spontaneous bacterial peritonitis initially treated with third-generation cephalosporins.

Table 6

Analysis of cause of death.

Cause of death	Total (n = 55)	Nonresponder (n = 33)	Responder (n = 22)	Statistics	P
Septic shock, n (%)	26 (50.9)	18 (54.5)	8 (36.4)	No statistics	.797
Hepatorenal syndrome, n (%)	11 (20.0)	6 (18.2)	5 (22.7)		
Hepatic encephalopathy, n (%)	6 (10.9)	3 (9.1)	3 (13.6)		
Hepatic failure, n (%)	5 ((9.1)	2 (6.1)	3 (13.6)		
Gastrointestinal bleeding, n (%)	4 (7.3)	2 (6.1)	2 (9.1)		
Multiorgan failure, n (%)	3 (5.5)	2 (6.1)	1 (4.5)		

to 3rd GC, which might be because increased platelets represent serious infection and gram-positive bacterial infection.

A lower ascites PMN count in this study could predict poor efficacy of 3rd GCs. Ariza et al[22] found obvious differences in the ascites PMN count of SBP caused by different strains, whereas the ascites PMN count related to 3rd GC drug-resistant bacteria tended to be lower. Fiuza et al[23] confirmed that patients with advanced liver cirrhosis have defective neutrophil function, as these cells have a weak ability to migrate to the infection site and phagocytose. These results suggest that the pathogenic bacteria in SBP patients with relatively low ascites PMN counts may be drug-resistant bacteria, and their neutrophil function defects may be serious; therefore, treatment with 3rd GCs may achieve little response.

In this study, the response rate of SBP patients to 3rd GCs was 57.0%, which is similar to some reports (56.3%–59%)[8,9] but obviously lower than the results of Badawy et al (81%).[11] Different pathogen spectra and severities of patients may be responsible for this inconsistency.

The common pathogens of SBP in the present study were *E coli*, *Staphylococcus*, *K pneumoniae*, and *Streptococcus*, which is similar to the findings of a previous study in China.[24]The proportion of MDR bacteria in this study was at a high level (46.9%), possibly because the study population included more NSBP and previous broad-spectrum antibiotic exposure cases. There were more 3rd GC-resistant and MDR strains in NSBP cases than in CASBP cases in this study, which is consistent with the current general knowledge. However, this difference was not significant, which may be associated with the small sample size. Generally, the positive rate of ascites culture is limited, and it will take ≥3 days after the onset of SBP for the drug resistance to be available. As a result, some effective and quick-acting factors in this study are also indispensable in guiding antibiotic treatment, although our results showed that the coincidence rate of the drug sensitivity test and antibiotic effectiveness was high.

This study showed that higher 30-day mortality was associated with poorer efficacy of 3rd GCs and that nonresponders experienced worse survival, indicating that being initially treated with effective antibiotics is critical for SBP patients.

This study has several limitations. Some common indicators of infection (e.g., procalcitonin) were absent in this study due to the retrospective nature of the data. Because more powerful antibiotics rather than 3rd GCs are preferred for initial use in

treating SBP patients with severe conditions, such as hyperpyrexia, septic shock, or acute respiratory distress syndrome in our hospital, the study population lacks these patients, which can lead to selection bias. Approximately 20% of patients in this study have liver cancer. Cancerous ascites can also lead to an increased ascites cell count, and the peritoneal culture positivity rate is at a low level in this study, which may result in false-positive diagnoses of infection. This condition may affect the identification of infection and the study results.

5. Conclusion

This study showed that the response rate of SBP patients to 3rd GCs was 57.0%. NSBP, pneumonia, recurrent SBP, an increased platelet count, and a lower ascites PMN count were independent predictors of no response to 3rd GCs in treating SBP. Nonresponse to initial antibiotic treatment was associated with worse survival.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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