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The long-term mortality of spontaneous bacterial peritonitis in cirrhotic patients: A 3-year nationwide cohort study

LIVER

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Original Article

ABSTRACT

Background/Aims: There is no nationwide population-based study for the long-term mortality after single episode of spontaneous bacterial peritonitis (SBP) in cirrhotic patients. Our study showed the short-term and long-term mortalities, and identified the mortality risk of SBP.

Materials and Methods: The National Health Insurance Database, derived from the Taiwan National Health Insurance program, was used to collect data from 16,992 cirrhotic patients. These cirrhotic patients were classified into three groups: SBP group (n=451, 2.7%), ascites without SBP group (n=2,564, 15.1%), and non-ascites (n=13,977, 82.3%) group. Each patient was followed up to 3 years after the initial hospitalization.

Results: The 30-day mortalities in SBP, ascites without SBP, and non-ascites groups were 24.2%, 14.1%, and 8.1%, respectively. The 3-year mortalities in SBP, ascites without SBP, and non-ascites groups were 66.5%, 61.1%, and 41.5%. After Cox's regression analysis adjusted by the patients' age, gender, and underlying medical disorders, the SBP patients (hazard ratio=2.52) and ascites without SBP patients (hazard ratio=1.91) have higher risk for 3-year mortality than those without ascites.

Conclusion: Cirrhotic patients with SBP have a 2.5-fold increase of 3-year mortality, compared to those without ascites.

Keywords: Cirrhosis, spontaneous bacterial peritonitis, ascites

INTRODUCTION

The previous studies showed the mortality of cirrhotic patients after an episode of spontaneous bacterial peritonitis (SBP) is around 20% to 30% (1,2). Although the 30-day or in-hospital mortality of -SBP in cirrhotic patients is well understood, there is no nationwide population-based cohort study for the long-term mortality after a single episode of SBP. In this study, we used the national population-based dataset to determine the overall long-term mortality of SBP in cirrhotic patients, and identify the mortality risk of SBP.

MATERIALS AND METHODS

Database

This study was approved by the Taiwan National Health Research Institute with application and agreement number of 100101. The database used in this retrospective study was from the National Health Insurance research database in Taiwan. The database was established and maintained by the Taiwan National Health Insurance Bureau and the National Health Research Institute. The Taiwan national Health Insurance program was developed in 1995 and included nearly all citizens residing in Taiwan. The National Health Insurance Bureau covers >95% of Taiwan's population in 2004. All the study protocols needed to be evaluated by the National Health Research Institute for protection the privacy of the patients and health care providers.

Study sample

This retrospective study included patients who were first discharged with the diagnosis of SBP between July 1, 2004 and December 31, 2004. Because of the diffe-

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rent etiology of cirrhosis in the younger patients, the patients >30 years of age were included. As previous studies, we defined SBP as a patient with the ICD-9-CM diagnosis code for both cirrhosis (571.2 and 571.5) and peritonitis (567.2, 567.8, or 567.9) (3,4). We also checked the other diagnostic codes of the included patients. When the patients had other diagnostic coding for secondary peritonitis, like appendicitis, hollow organ or biliary tract perforation, ischemic bowel disease, peritoneal dialysis catheter-related peritonitis, as well as those having an additional procedure code for abdominal surgery, they were not included. Because primary biliary cirrhosis is a chronic autoimmune cholestatic liver disorder and is a liver disease of a different mechanism, cases with biliary liver cirrhosis were not included in our study (5,6). In this study, we defined ascites as a patient with the ICD-9-CM diagnosis code 789.5 or received the procedure of paracentesis in hospitalization.

A total of 16,992 cirrhotic patients who was first hospitalized during the study period were enrolled. The cirrhotic patients were classified into three groups according to baseline clinical conditions: SBP (n=451, 2.7%), ascites without SBP (n=2,564, 15.1%), and non-ascites group (n=13,977, 82.3%). Each patient was followed up to death, or up to 3 years from their first hospitalization during the study period.

Statistical analyses

The SPSS statistical package (SPSS System for Windows, version 13.0) was used to perform the analyses in this study. Pearson's Chi-squared or Fisher's exact 2-tailed test was used to examine nominal data, and One-Way ANOVA test used for continuous data. The mortality in these three groups was calculated respectively from 30 days to 3-year. In this follow-up study, Cox proportional hazard regressions was used to analyze the mortality risk in these three groups. Hazard ratios with 95% confidence intervals (CI) using a significance level of 0.05 for this study were also calculated.

The comorbid medical disorders included alcoholism (ICD-9-CM codes 291, 303, 305.00-305.03, 571.0-571.3), diabetes mellitus (ICD-9-CM code 250), hepatocellular carcinoma (HCC) (ICD-9-CM code 155.0), renal failure (ICD-9-CM code 548, 585, 586, or other procedure code may relate to renal failure), hepatic encephalopathy (ICD-9-CM code 572.2), esophageal variceal (EV) bleeding (ICD-9-CM code 456.0, 456.20), and peptic ulcer bleeding (ICD-9-CM code: 531.0, 531.2, 531.4, 531.6, 532.0, 532.2, 532.4, 532.6, 533.0, 533.2, 533.4 and 533.6) (7). The comorbid diseases were considered if the condition was noted at the first time of admission.

RESULTS

Of the total 16,992 cirrhotic patients, mean age was 59.6±14.1 years. The male was 70.8 %. Table 1 showed the distribution of demographic characteristics for cirrhotic patients in the three groups individually. Table 2 showed the 30-day, 60-day, 90-day, 180-day, 1-year, 2-year, and 3-year mortalities of cirrhotic patients among three groups. In SBP group, the overall mortality was from 24.2% in 30 days to 66.5 % in 3 years. In ascites without SBP group, the mortality was from 14.1 % in 30 day to 61.1 % in 3 years. In non-ascites group, the mortality was from 8.1 % in 30 days to 41.5 % in 3 years.

Table 1. Demographic characteristics among SBP group, ascites without SBP group, and non-ascites group

	SBP group (n=451)	Ascites without SBP group (n=2,564)	Non-ascites group (n=13,977)	p value
Male, no. (%)	320 (71.0)	1793 (69.9)	9923 (71.0)	0.551
Age, yr	57.4±14.1	59.4±14.2	59.7±14.1	0.002
HCC, no. (%)	85 (18.8)	625 (24.4)	3874 (27.7)	<0.001
HE, no. (%)	59 (13.1)	314 (12.2)	1055 (7.5)	<0.001
EV bleeding	50 (11.1)	317 (12.4)	1294 (9.3)	<0.001
PUB, no. (%)	22 (4.9)	150 (5.9)	979 (7.0)	0.027
Alcoholism, no. (%)	95 (21.1)	481 (18.8)	2673 (19.1)	0.517
Diabetes, no. (%)	53 (11.8)	421 (16.4)	2747 (19.7)	<0.001
Renal failure, no. (%)	42 (9.3)	131 (5.1)	732 (5.2)	0.001

SBP: spontaneous bacterial peritonitis; HCC: hepatocellular carcinoma; HE: hepatic encephalopathy; EV: Esophageal varies; PUB: peptic ulcer bleeding

Table 2. The long-term and short-term mortalities of SBP group, ascites without SBP group, and non-ascites group

Time	SBP group (n, %)	Ascites without SBP group (n, %)	Non-ascites group (n, %)
30 days	109 (24.2)	362 (14.1)	1128 (8.1)
60 days	139 (30.8)	583 (22.7)	1633 (11.7)
90 days	164 (36.4)	736 (28.7)	1998 (14.3)
180 days	208 (46.1)	940 (36.7)	2730 (19.5)
1 year	243 (53.9)	1166 (45.4)	3632 (26.0)
2 years	277 (61.4)	1412 (55.1)	4866 (34.5)
3 years	300 (66.5)	1566 (61.1)	5806 (41.5)

SBP: spontaneous bacterial peritonitis

The Cox regression was performed to identify the mortality risks of SBP and ascites. Table 3 showed the result of the Cox regression. The hazard ratio of SBP and ascites for 3-year mortality of cirrhotic patients were 2.52 (95% confidence interval =2.24-2.83, p<0.001), and 1.91 (95% confidence interval =1.81-2.02, p<0.001), respectively, compared to those without ascites. The Figure 1 demonstrated the Kaplan-Meier survival curve in the three groups and the log-rank test revealed statistically difference in each groups (p<0.001).

DISCUSSION

This is the first nationwide population-based study for demonstrating the long-term mortality of SBP. The large case numbers

Table 3. Adjusted hazard ratios of risk factors for 3-year mortality in cirrhotic patients

Variable	Hazard ratio	95% confidence interval	p value
Ascites conditions			
SBP	2.52	2.24-2.83	<0.001
Ascites without SBP	1.91	1.81-2.02	<0.001
No ascites	1		
HCC	1.93	1.84-2.07	<0.001
HE	1.91	1.78-2.05	<0.001
Renal failure	2.02	1.85-2.20	<0.001
Age	1.02	1.01-1.02	<0.001
EV bleeding	1.16	1.08-1.25	<0.001
Male	1.32	1.26-1.40	<0.001

SBP: spontaneous bacterial peritonitis; HCC: hepatocellular carcinoma; HE: hepatic encephalopathy; EV: esophageal varies

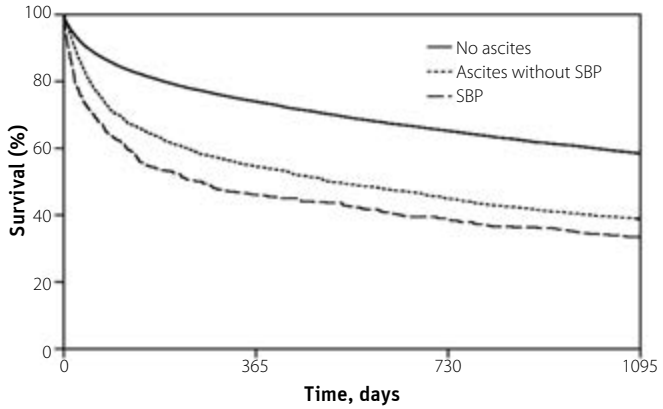

Figure 1. Kaplan-Meier survival curve for cirrhotic patients in the 3 year follow-up period.

and 3-year follow-up period provided an overview and a reliable result for the mortality risk after a single episode of SBP. Our study also showed clear long-term and short-term mortalities of SBP in cirrhotic patients. Using a nationwide population-based dataset, this study assessed the stepwise 1-, 2-, 3-, 6-, 12-, 24-, and 36-month mortalities of SBP in cirrhotic patients. The hazard ratios of SBP and ascites for 3-year mortality of cirrhotic patients were also calculated for identifying their actual mortality risks, compared to those without ascites.

Bacterial infectious disease is usually an acute process, and the final result is almost either complete recovery or leading to death. Therefore, the result of long-term mortality after a single episode of bacterial infection is less significant. However, SBP in cirrhotic patients is a special infectious disease. By definition, cirrhotic patients have SBP only when they have ascites. Cirrhotic patients with SBP are in a more decompensated status of liver. The development of SBP is not only a simple infectious disease but also can reflect the underlying decompensated status of liver cirrhosis. Therefore, it is necessary to understand the mortality effect of SBP for long-term mortality of cirrhotic patients. This is the reason why the study period of our study was extended to 3 years for evaluating the mortality risk of SBP. In our study, the cirrhotic patients were classified into SBP group, ascites without SBP group, and non-ascites group. This design is more reliable to demonstrate the mortality risk of SBP. In this study, cirrhotic patients with SBP had higher long-term mortality risk than the other two groups. The other prognostic factors for 3-year mortality of cirrhotic patients were HCC, hepatic encephalopathy, renal failure, age, EV bleeding, and male. These findings were similar to previous studies (8-14).

Although the in-hospital mortality of SBP was variable in previous studies, it was most in 20-30% (1,2). In the study published during 2000-2009, the 30-day and 1-year mortality of SBP was high as 31.9% and 59.8% (15). Using this nationwide population-based database, our study revealed a somewhat lower 30-day and 1-year mortality rate as 24.2% and 53.9%. There was limited data for the long term mortality of SBP. Our study demonstrated that the overall 3-year mortality after a SBP episode was 66.5%. The somewhat lower mortality rate in our study may actually show the real world condition in clinical practice. The cases in previous studies were mostly from tertiary hospital and patients in these hospitals may have more complicated conditions than that in the usual community hospitals. Our study, using the nationwide population-based data could avoid this bias and actually provided the reliable national data –for short-term and long-term mortalities of SBP in cirrhotic patients.

Nonetheless, there are some limitations worth of mention. First, the major limitation of this study is that some basic lab data (such as creatinine, bilirubin, prothrombin time, and albumin., etc) is not available in this database. It is not possible to calculate the model for end stage liver disease (MELD) score or Child-Paul score in our study. However, we used other founding factor to correct this problem, including esophageal variceal bleeding, hepatic encephalopathy, HCC and renal failure. Although not always correct, cirrhotic patients with such major complications may actually be in more decompensated states. Secondly, the etiology of cirrhosis in our study was divided into alcoholic-related and non-alcoholic related. However, exact etiology of non-alcoholic liver cirrhosis was not identified in this national population-based study. However, the etiology of liver cirrhosis in Taiwan has been well-established in previous reports and is known to be mostly related to the hepatitis B or C virus, especially hepatitis B virus (16,17). In the present study, alcoholic liver cirrhosis was accounted for about 20% of the cases whereas the remaining 80% of cirrhotic patients were non-alcohol related, which was also compatible with previous studies. Finally, the mild or transient deterioration of renal function would not be detected by ICD-9 coding numbers because of the lacking of suitable ICD-9 coding numbers. This can exp-

lain why the renal dysfunction is lower in our study comparing to previous studies (11,18-20). Despite these limitations, this study is the complete nationwide population-based study for identifying the mortality risk of SBPin cirrhotic patients.

In summary, this study showed the mortality risk of SBP in cirrhotic patients. Cirrhotic patients with SBP have a 2.5-fold increase of 3-year mortality, compared to those without ascites.

Ethics Committee Approval: the Institutional Review Board of the Buddhist Dalin Tzu Chi General Hospital Taiwan (IRB: B1010410)

Informed Consent: The review board waived the requirement for written informed consent from the patients involved.

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Conflict of Interest: No conflict of interest was declared by the authors.

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