

Role of Baseline Albumin-Bilirubin Grade on Predict Overall Survival Among Sorafenib-Treated Patients With Hepatocellular Carcinoma in Vietnam

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Abstract

Introduction: Albumin-bilirubin (ALBI) grade has been recently used in evaluation of liver function and prognosis of patients with hepatocellular carcinoma (HCC). However, in Vietnam, the utility of ALBI grade in clinical setting has not been adequately investigated.

Methods: This is a retrospective study of 110 patients with HCC treated with sorafenib from January 2010 to November 2018 at 2 tertiary hospitals in Vietnam. Prognostic value of ALBI grade was evaluated by Kaplan-Meier survival analysis and Cox proportional regression model.

Results: Results showed that the majority of ALBI grade 1 were Child-Pugh level A (97.5%); ALBI grade 2 was seen in all Child-Pugh score groups of 5, 6, 7, ≥ 8 , whereas ALBI grade 3 was mostly reported in Child-Pugh score ≥ 8 group (83.3%). Compared with ALBI grade 3, ALBI grade 1 reduced 66.4% risk of death (hazards ratio [HR] = 0.336, 95% confidence interval [CI]: 0.115-0.981; $P = .046$). Compared with ALBI grade 3, ALBI grade 2 reduced 67.3% risk of death (HR = 0.327, 95% CI: 0.122-0.875; $P = .026$). Albumin-bilirubin grade was an independent predictor of survival outcome.

Conclusion: Baseline ALBI grade is a simple and objective approach in assessing liver functions of patients with HCC. Baseline ALBI grade is an independent predictor of survival in patients treated with sorafenib.

Keywords

hepatocellular carcinoma, albumin-bilirubin grade, sorafenib, predict overall survival, Vietnam

Received March 04, 2019. Received revised June 20, 2019. Accepted for publication June 28, 2019.

Introduction

Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide and is the second leading cause of cancer death. Latest data have demonstrated that in terms of HCC incidence, Vietnam takes the fourth place in the world after Mongolia, Egypt, and Gambia, with a standardized age incidence rate of 39.0/100 000 people in males and 9.5/100 000 people in females.¹ In Vietnam, a majority of patients are diagnosed at an advanced stage, which is associated with poorer treatment outcome.² Treatment of patients with advanced stage

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HCC is expensive and poses an economic challenge for the developing economy of Vietnam.^{3,4} Hepatitis B virus (HBV) is a major risk factor for HCC in Vietnam.³ Although a national immunization program with HBV vaccination for infants has been implemented in Vietnam for more than 15 years, there is a heavy burden of HCC in the country.

The prognosis of HCC is extremely poor, with the mortality rate being roughly equivalent to the incidence.⁴ For advanced stage, without treatment, the median survival is only 4 months.⁵ Although in recent years, there has been a significant progress in the understanding of the molecular biology of HCC, the treatment efficacy has been limited, especially in patients with advanced stage. So far, sorafenib, a multikinase inhibitor, has demonstrated significant survival benefits in phase III trials in the United States and Europe (the Sorafenib Hepatocellular Carcinoma Assessment Randomized Protocol trial) and in the Asia-Pacific region (the Asia-Pacific trial).^{5,6} The results showed that sorafenib reduced the risk of death by 31%, improved the progression-free survival by 5.5 months compared to control group (2.8 months), as well as increased the overall survival (OS) by an average of 10.7 months.^{5,6}

Liver function is an important factor affecting the choice of treatment protocols. Child-Pugh and Model for End-stage Liver Disease (MELD) scale were first introduced in 1964 and 2000, respectively, as a tool to measure liver function and are widely used in staging and prognosis of chronic liver diseases.^{7,8} However, MELD score with International Normalized Ratio (INR) is believed not to sufficiently reflect coagulopathy, and the role of MELD has not been evaluated in patients with HCC.⁷ On the other hand, the 2 parameters in Child-Pugh score, ascites and encephalopathy, are difficult to assess clinically and associated with interobserver variability.⁹ In addition, there is an interaction between albumin level and ascites. Therefore, it is necessary to develop a simpler and more objective tool to evaluate liver function in patients with HCC. Recently, Johnson et al have proposed a new liver function assessment tool for HCC, the albumin-bilirubin (ALBI) grade. The ALBI score is calculated by the formula ($\log_{10}$ bilirubin $\times$ 0.66) – (albumin $\times$ 0.085) and divided into 3 grade: grade 1 (≤ -2.6), grade 2 (> -2.6 and ≤ -1.39), grade 3 (> -1.39).¹⁰ The prognostic value of the ALBI grade has been evaluated in patients with liver cirrhosis, being comparable with that of the Child-Pugh and MELD score in predicting in-hospital mortality.^{11,12} Besides, the predictive performance of ALBI has been investigated in postoperative patients with HCC and patients treated with TACE, in which ALBI is an independent predictor of treatment outcome.^{13,14} However, data on the role of ALBI grade in patients with HCC treated with sorafenib are still limited.¹⁵ In Vietnam, ALBI grade are almost neglected in clinical practice, generally, and in HCC treatment, particularly.¹⁶

The aim of the present study is to assess the baseline ALBI grade as a prognostic factor in patients with HCC treated with sorafenib in Vietnam.

Methods

Study Design

This was a retrospective analysis in patients with advanced HCC treated with sorafenib. The protocol of this study was approved by the human research ethics committee at Hanoi Medical University in Vietnam (approval no. 129/HĐĐDDHYN October 04, 2017).

Study Participant

Inclusion and exclusion criteria. We retrospectively analyzed data from all patients who received sorafenib as treatment for advanced HCC in Vietnam National Cancer Institute and Hanoi Medical University hospital from January 2010 to November 2018. The eligibility criteria included an Eastern Cooperative Oncology Group performance status score of 2 or less and liver function of Child-Pugh score level A or level B. Patients were required to have at least 1 untreated target lesion that could be measured in one dimension, according to the Response Evaluation Criteria in Solid Tumors (RECIST). Patients were excluded if they had previously received molecularly targeted therapies or any other systemic treatment, the patients with simultaneously second cancer.

Criteria for HCC diagnosis and staging. The diagnostic criteria of HCC are based on diagnosis and treatment guideline of Vietnamese Ministry of Health.¹⁶ Patients were diagnosed with HCC if 1 of 3 following criteria was satisfied: (1) evidence of pathological diagnosis with HCC, (2) typical image of HCC on contrast-enhanced abdominal computer tomography or magnetic resonance imaging (MRI) together with Alpha-feto-protein (AFP) level higher than 400 ng/mL, or (3) typical image of HCC on contrast-enhanced abdominal computer tomography or MRI, with an increase in AFP (but less than 400 ng/mL) and evidence of chronic HBV or HCV infection. Patients were classified as having advanced disease if they were not eligible for or had disease progression after surgical or locoregional therapies.^{17,18}

Treatment Protocol, Response Evaluation, and Follow-Up

The starting dose was 400 to 800 mg per day of sorafenib (Nexavar, Bayer), which was chosen based on patients' performance status and liver function. The toxicities were evaluated after the first 2 weeks and every 4 weeks afterward. The dose would be increased, reduced, or temporarily interrupted by the development of adverse events (AEs). Treatment response defined by the RECIST 1.1 was assessed after 8 weeks. Treatment was continued until disease progression, hepatic deterioration to Child-Pugh class C, unacceptable AEs, or death. Concomitant antiviral systemic therapy was allowed. Patients with disease progression were followed up until death.

Study Setting

The study was conducted in 2 hospitals in Hanoi, the capital of Vietnam, including Vietnam National Cancer Hospital (99 patients) and Hanoi Medical University Hospital (11 patients) from January 2010 to November 2018. These are 2 major oncology hospitals in the Northern region of Vietnam.

Data Collection

Information was collected based on medical record of each case. Patients' data included age, gender, hepatitis status, tumor characteristics (tumor size, macroscopic vascular invasion, and extrahepatic metastasis), Child-Pugh score, Aspartate aminotransferase (AST) level before treatment, AFP before treatment, and ALBI score.

The ALBI score was calculated according to the baseline serum albumin and bilirubin levels ($ALBI = [\log_{10} \text{bilirubin} \times 0.66] + [\text{albumin} \times 0.085]$, where bilirubin was in $\mu\text{mol/L}$ and albumin was in g/L).⁷ Three different grades for prognostic stratification purposes were described: grade 1 (less than -2.60), grade 2 (between -2.60 and -1.39), and grade 3 (above -1.39). Overall survival was measured from the day of starting treatment to the day of death from any cause. Patients who died without tumor progression were censored.

Data Analysis and Statistical Method

Data were collected, processed, and analyzed on SPSS 20.0 software. Survival was estimated by the Kaplan–Meier method and compared by the log-rank test. Adverse events were compared among ALBI grades using the χ^2 test and Fisher exact test. The univariate and multivariate Cox proportional hazard regression models were used to calculate hazard ratios for prognostic factors of OS. The covariates included in the multivariate hazard regression model were chosen by literature review.^{19–21} The proportional hazards assumption for all covariates were tested by Schoenfeld residual-based test. No violation of the proportional hazards assumption was found. A significance level of $P < .05$ was used.

Results

Characteristics of Study Population

Table 1 showed the characteristics of the study population. There was a total of 110 eligible patients in this study. The median age was 59 years (range: 21–80) and 92.7% patients were male. The median tumor size was 60 mm. Most patients were infected with hepatitis B virus (84 patients, 76.4%). The median dose of sorafenib was 600 mg/d. The median follow-up time was approximately 6 months, and the median treatment duration was 4 months. In this study, 39 (35.4%) patients were ALBI grade 1, 66 (59.1%) patients were ALBI grade 2, and 6 (5.5%) patients were ALBI grade 3 (Table 1). The median Child-Pugh score of patients was 5.

Correlation Between the ALBI Grade and Child-Pugh Score

The proportions of patients with Child-Pugh scores of 5, 6, 7, and ≥ 8 were 76.4%, 13.6%, 4.5%, and 5.5%, respectively. Most patients with ALBI grade 1 had a Child-Pugh score of 5 (97.4%). In the group with ALBI grade 2, a wide range of Child-Pugh score from 5 to ≥ 8 was observed. A majority of patients with ALBI grade 3 had a Child-Pugh score of ≥ 8 (5 of 6 patients, 83.3%; Table 2).

Response to Sorafenib

According to RECIST 1.1 criteria, no patient had complete response and only 5 (4.5%) patients had partial response after 8 weeks of treatment. Stable disease or progression was observed in the majority of patients (54.5% and 41%, respectively). Clinical symptoms were improved in about one-third (32.7%) of patients but became more severe in another one-third (33.6%) of patients.

Overall Survival According to ALBI Grade and Other Factors

The median OS of study population was 7.1 months (95% confidence interval [CI]: 4.5–9.1 months; Figure 1). The median OS of patients with ALBI grade 1, grade 2, and grade 3 were 10.4, 6.7, and 1.8 months, respectively, with significant difference among 3 groups ($P = .008$; Figure 2).

In univariate analysis, beside ALBI and Child-Pugh classification, factors that had a positive effect on sorafenib treatment outcome included: hand-foot skin reaction (HFSR; hazards ratio [HR] = 0.477, 95% CI: 0.298–0.765; $P = .002$), macroscopic vascular invasion (HR = 0.634, 95% CI: 0.404–0.994; $P = .047$), AFP pretreatment higher than 20 ng/mL (HR = 0.518, 95% CI: 0.291–0.922; $P = .025$), and AST pretreatment higher than 80 UI/L (HR = 0.618, 95% CI: 0.392–0.973; $P = .038$; Tables 3 and 4).

In multivariate analysis, compared with ALBI grade 3, ALBI grade 1 reduced 66.4% risk of death (HR = 0.336, 95% CI: 0.115–0.981; $P = .046$). Compared with ALBI grade 3, ALBI grade 2 reduced 67.3% risk of death (HR = 0.327, 95% CI: 0.122–0.875; $P = .026$). Similarly, Child-Pugh A reduced 69.7% mortality risk (HR = 0.303, 95% CI: 0.140–0.652; $P = .002$) compared to Child-Pugh B. Albumin-bilirubin grades and Child-Pugh classification were independent predictors of survival outcome (Tables 3 and 4). In 2 different multivariate regression models using either ALBI or Child-Pugh classification, the only factor that was shown to be significantly favorable of OS in patients treated with sorafenib was the presence of HFSR (HR = 0.516, 95% CI: 0.300–0.887 and HR = 0.542, 95% CI: 0.315–0.932; Tables 3 and 4).

Table 1. Characteristics of Patients.

Characteristics	Total, N = 110	ALBI Grade		
		Grade 1, N = 39	Grade 2, N = 65	Grade 3, N = 6
Age (year) ^a	59 (21 to 80)	54 (49 to 61)	60 (55 to 67)	65.5 (63 to 69)
Sex (male) ^b	102 (92.7%)	33 (84.6%)	64 (98.5%)	5 (83.3%)
Tumor size (mm) ^c	60 (39.5 to 93.5)	50.5 (34.5 to 76)	65 (40 to 95)	91.5 (78 to 130)
Viral infection status ^b				
HBV (+)	84 (76.4%)	28 (71.8%)	50 (76.9%)	6 (100%)
HCV (+)	4 (3.6%)	1 (2.6%)	3 (4.6%)	0
HBV (+) and HCV (+)	1 (0.9%)	0	1 (1.5%)	0
HBV (–) and HCV (–)	21 (19.1%)	10 (25.6%)	11 (16.9%)	0
Macroscopic vascular invasion ^b	42 (38.2%)			
Extrahepatic metastasis ^b	61 (55.5%)	25 (64.1%)	36 (55.4%)	0
ECOG status ^b				
0	93 (84.5%)	38 (97.4%)	54 (83.1%)	1 (16.7%)
1	17 (15.5%)	1 (2.6%)	11 (16.9%)	5 (83.3%)
Sorafenib treatment ^c				
Median dose	600 (400 to 800)	600 (467 to 800)	550 (400 to 800)	480 (400 to 600)
Starting dose				
800 mg/d group ^b	48 (43.6%)	19 (48.7%)	37 (56.9%)	6 (100%)
<800 mg/d group ^b	62 (56.4%)	20 (51.3%)	28 (43.1%)	0
Time following (month)—range ^c	5.86 (3.32 to 14.55)	8.11 (4.50 to 22.82)	5.32 (2.59 to 13.17)	2.17 (1.77 to 9.33)
Number of treatment cycles ^c	4 (2 to 6)	4 (3 to 10)	4 (2 to 5)	2 (1 to 5)
Hand-foot skin reaction ^b	40 (36.4%)	23 (59.0%)	17 (26.2%)	0
AFP pretreatment ^c	423 (24 to 2284)	1003 (14 to 3000)	392 (27 to 2000)	609 (387 to 20 000)
≥20 ng/mL	86 (78.2%)	28 (71.8%)	52 (80.0%)	6 (100%)
<20 ng/mL	24 (21.8%)	11 (21.2%)	13 (20.0%)	0
Albumin pretreatment ^c	39.5 (36 to 42.4)	43.2 (42 to 46)	37 (35 to 40)	29 (25 to 32)
Bilirubin pretreatment ^c	13 (9.7 to 19.7)	10.5 (6.9 to 12.2)	15.4 (11.8 to 20.6)	31.4 (28.1 to 70.3)
INR pretreatment ^c	1.05 (0.99 to 1.17)	1.03 (0.95 to 1.08)	1.08 (1.00 to 1.18)	1.22 (1.08 to 1.29)
Child-Pugh score ^c	5 (5 to 5)	5 (5 to 5)	5 (5 to 6)	8 (8 to 8)
ALBI score ^c	–2.44 (–2.79 to –1.97)	–2.91 (–3.02 to –2.78)	–2.23 (–2.44 to –1.87)	–1.11 (–1.22 to –0.94)

Abbreviations: ALBI, albumin-bilirubin; ECOG, Eastern Cooperative Oncology Group; HBV, hepatitis B virus; HCV, hepatitis C virus; IQR, interquartile range.

^aValues are presented as median (range).

^bValues are presented as number (percentage).

^cValues are presented as median (IQR).

Table 2. Correlation Between the ALBI Grade and Child-Pugh Score.^a

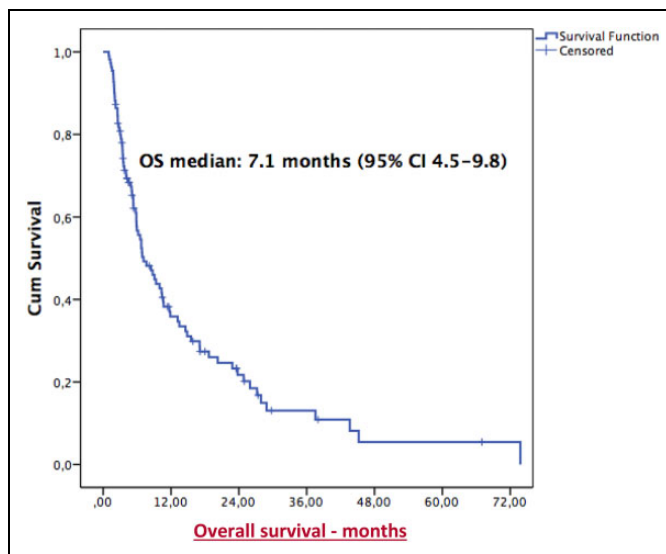
ALBI/ Child-Pugh	Child-Pugh Score—n (%)				Total	P
	5	6	7	≥8		
ALBI grade						
1	38 (97.4)	1 (2.6)	0	0	39	<.001
2	46 (70.8)	14 (21.5)	4 (6.2)	1 (1.5)	65	
3	0	0	1 (16.7)	5 (83.3)	6	
Total	84	15	5	6	110	

Abbreviation: ALBI, albumin-bilirubin.

^aP value is estimated by Fisher exact test.

Adverse Events of Sorafenib Treatment

There were 4 major AEs of treatment in our study, in which HFSR was the most common one (occurred in 40 patients, 36.4%), followed by high elevated liver enzymes (36 patients, 32.7%). Statistically significant difference among 3 ALBI

**Figure 1.** Overall survival of patients with hepatocellular carcinoma (HCC) treated with sorafenib.

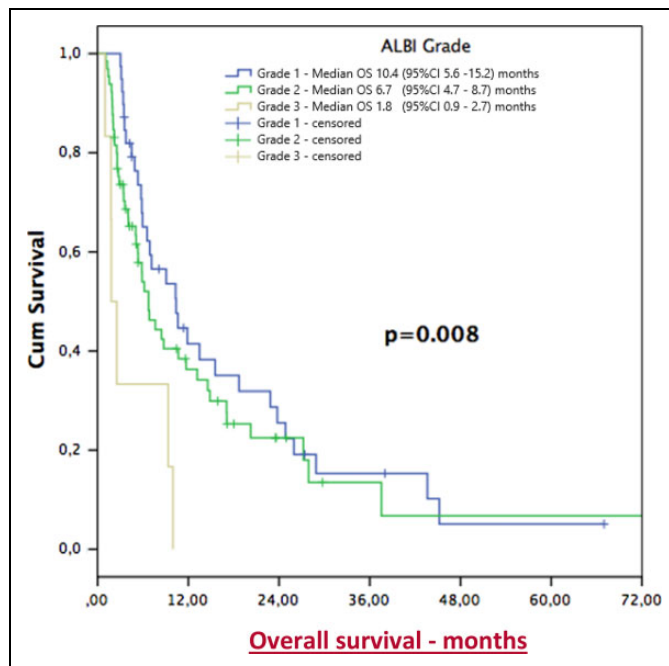


Figure 2. Overall survival of patients in each albumin-bilirubin (ALBI) grade by Kaplan-Meier survival analysis. Median overall survival (OS) of ALBI grade 1, ALBI grade 2, and ALBI grade 3 were 10.4 months, 6.7 months, and 1.8 months, respectively ($P = .008$).

grades was only seen in the rate of HFSR ($P < .001$, see more details in Table 5).

Discussion

Our study concentrated on evaluating the role of ALBI grade as a predictor of sorafenib treatment outcome in Vietnamese patients with HCC. In general, HCC prognosis depends on 2 important factors: the extent of disease spread and liver function.²²⁻²⁴ Median OS of the study population was 7.1 months, lower than the result of sorafenib treatment in the Sorafenib HeProtocolpatocellular Carcinoma Assessment Randomized (SHARP) trial (10.7 months), but similar to that of the Asia-Pacific (AP) trial (7.8 months).^{5,6} The difference in OS among different studies might be explained by the different characteristics in study population, especially the proportion of hepatitis B infection and the disease burden.^{5,17,25}

When we assessed the relationship between ALBI grades and Child-Pugh classification, we found that in patients with Child-Pugh A, 39.4% (39/99 patients) had ALBI grade 1 and 60.1% (60/99) had ALBI grade 2. Similarly, Child-Pugh B group was also divided into 5 patients with ALBI grade 2 and 6 patients with ALBI grade 3. Thus, ALBI grade provided certain additional stratification value, especially in patients with Child-Pugh level A, who accounted for the majority of patients receiving sorafenib. In terms of survival among different groups, ALBI grade separated the study population into 3 groups with different time of survival ($P < .05$), while Child-Pugh classification only classified our patients into 2 groups.

Hiraoka et al reported that Child-Pugh score was unable to distinguish the difference in liver function between patients with Child-Pugh score 6 (level A) and score 7 (level B).⁹ Kuo et al also suggested that ALBI grade might further discriminate the liver function among patients with Child-Pugh A classification.²¹ Besides, a large-scale study on patients with HCC, the group of patients with Child-Pugh A consisted of a better risk group (ALBI grade 1) and a relatively poorer risk group (ALBI grade 2), with a median survival difference of nearly 6 months.¹⁰

In the multivariate analysis of factors affecting sorafenib treatment results, we found that ALBI grade was a significant predictor. Compared with ALBI grade 3, ALBI grade 1 and ALBI grade 2 decreased 66.4% and 67.3% risk of death, respectively, with significant differences in OS. Some authors had also evaluated the role of ALBI grade in the prognosis of HCC treatment, in which the results showed that ALBI grade was an independent prognostic factor in patients with HCC undergoing liver resection.²⁰ Albumin-bilirubin grade was also a factor that accurately predicted the outcome in patients with high risk of TACE.^{13,26} However, there has not been many reports about the predictive value of ALBI grades in patients with HCC treated with sorafenib. In a study of 89 patients using sorafenib for treatment of HCC, there were no patients with ALBI grade 3 and no significant difference in OS were observed between ALBI grade 1 and grade 2.¹⁹ Therefore, the authors used ALBI score of -2.118 as a cutoff value to subdivide patients with ALBI grade 2 into 2 groups, ALBI 2A and ALBI 2B. A significant difference in OS was observed between ALBI grade 2A and 2B as well as ALBI 1 and ALBI 2B, leading to the suggestion that sorafenib may be indicated for patients with ALBI grade 1 and a subset of patients with ALBI grade 2.¹⁹ In another study on 260 patients with HCC who failed with sorafenib treatment, a multivariate analysis also reported a HR of 2.35 (95% CI: 1.43-3.87) of baseline ALBI grade in predicting OS.²¹ In our study, Child-Pugh was also an independent prognostic factor of survival with a similar HR compared to ALBI grade. Consistent with our study, data from other studies on patients in different geographic regions showed that performance of ALBI score in predicting HCC survival was at least as well as Child-Pugh score.^{9,10} In addition, ALBI grade offers a simpler and more objective way to assess liver function and therefore can be a useful tool in evaluation of patients with HCC treated with sorafenib.

Although to our best knowledge, this is the first study in Vietnam to evaluate the prognostic role of ALBI grade in patients with HCC treated with sorafenib, our study had some limitations. Firstly, it was a retrospective study in patients with HCC treated with sorafenib. Secondly, we did not further investigate the prognostic value of subgroups of grade 2 (grade 2A and 2B), as suggested in a previous study. Thirdly, the site for data collection was limited to cancer centers in Northern region of Vietnam and did not fully capture the characteristics of patients with HCC of the whole country. Fourth, in our study, the proportion of HCV infection in our

Table 3. Univariate Analysis and Multivariate Analysis of some Factors in Overall Survival.

ALBI/Child-Pugh	Univariate Analysis				Multivariate Analysis		
	n	HR	95% CI	P	HR	95% CI	P
ALBI grade							
1	39	0.259	0.106-0.635	.003	0.336	0.115-0.981	.046
2	65	0.334	0.141-0.793	.013	0.327	0.122-0.875	.026
3	6	Reference	—	—	Reference	—	—
HFSR ^a	40	0.477	0.298-0.765	.002	0.516	0.300-0.887	.017
No extrahepatic metastasis ^b	49	0.796	0.513-1.234	.307	0.616	0.380-0.997	.049
No MVI ^c	42	0.634	0.405-0.994	.047	0.693	0.423-1.134	.144
AFP < 20 ng/mL ^d	86	0.518	0.291-0.922	.025	0.667	0.353-1.259	.212
No HBV infection ^e	84	0.604	0.363-1.004	.052	0.608	0.344-1.072	.085
Sorafenib dosage, 800 mg/d ^f	49	0.707	0.453-1.104	.127	0.933	0.576-1.512	.779
AST ≤ 80 UI/L ^g	36	0.618	0.392-0.973	.038	0.947	0.531-1.69	.854

Abbreviations: ALBI, albumin-bilirubin; CI, confidence interval; HBV, hepatitis B virus; HFSR, hand-foot skin reaction; HR, hazards ratio; MVI, macroscopic vascular invasion.

^aNo HFSR as reference.

^bPresence of extrahepatic metastasis as reference.

^cPresence of MVI as reference.

^dAFP ≥ 20 ng/mL as reference.

^eHBsAg(+) as reference.

^fSorafenib dose < 800 mg/d as reference.

^gAST > 80 UI/L as reference.

Table 4. Univariate Analysis and Multivariate Analysis of Some Factors in Overall Survival.

ALBI/Child-Pugh	Univariate Analysis				Multivariate Analysis		
	n	HR	95% CI	P	HR	95% CI	P
Child-Pugh classification ^a							
A	99	0.297	0.154-0.575	<.001	0.303	0.140-0.652	.002
B	11	Reference					
HFSR ^b	40	0.477	0.298-0.765	.002	0.542	0.315-0.932	.027
No extrahepatic metastasis ^c	49	0.796	0.513-1.234	.307	0.602	0.363-1.000	.05
No MVI ^d	42	0.634	0.405-0.994	.047	0.601	0.361-1.002	.051
AFP < 20 ng/mL ^e	86	0.518	0.291-0.922	.025	0.730	0.383-1.392	.340
No HBV infection ^f	84	0.604	0.363-1.004	.052	0.530	0.286-0.983	.044
Sorafenib dosage, 800 mg/d ^g	49	0.707	0.453-1.104	.127	0.944	0.570-1.561	.822
AST ≤ 80 UI/L ^h	36	0.618	0.392-0.973	.038	0.874	0.481-1.588	.659

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HFSR, hand-foot skin reaction; HR, hazards ratio; MVI, macroscopic vascular invasion.

^aNo patients had Child-Pugh C.

^bNo HFSR as reference.

^cPresence of extrahepatic metastasis as reference.

^dPresence of MVI as reference.

^eAFP ≥ 20 ng/mL as reference.

^fHBsAg(+) as reference.

^gSorafenib dose < 800 mg/d as reference.

^hAST > 80 UI/L as reference.

p < 0.05 for statistically significant difference are in bold.

Table 5. Adverse Events Among Different ALBI Grades.

Adverse Events	Total, N = 110	ALBI Grade			P Values ^a
		Grade 1, N = 39	Grade 2, N = 65	Grade 3, N = 6	
HFSR	40 (36.4%)	23 (59.0%)	17 (26.2%)	0	<.001
Increased liver enzymes	36 (32.7%)	9 (23.1%)	26 (40.0%)	1 (16.7%)	.146
Fatigue	28 (25.5%)	10 (25.6%)	16 (24.6%)	2 (33.3%)	.818
Mucositis	7 (6.4%)	5 (12.8%)	2 (3.1%)	0	.168

Abbreviations: ALBI, albumin-bilirubin; HFSR, hand-foot skin reaction.

^aAll comparisons were performed using Fisher exact test.

study was less than 5%, which made it difficult to assess the impact of HCV infection on the relationship between ALBI grade and survival. Therefore, there should be further prospective, randomized studies to fully assess the prognostic value of ALBI score in patients with advanced HCC treated with sorafenib.

In conclusion, ALBI grade showed more detail in evaluating liver function especially in patients with Child-Pugh level A. Baseline ALBI grade was an independent predictor of survival in patients treated with sorafenib. Therefore, the use of baseline ALBI grade should be encouraged in prognosis of patients with HCC in Vietnam.

Authors' Note

Nguyen Thi Thu Huong and Nguyen Van Hieu are equal contributors and co-primary authors. The protocol of this study was approved by the Human Research Ethics Committee at Hanoi Medical University in Vietnam (approval no. 129/HĐĐDHYHN October 04, 2017). All patients provided written informed consent prior to enrollment in the study.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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