Development and validation of a modified albumin-bilirubin grade and α-fetoprotein score (mALF score) for hepatocellular carcinoma patients receiving atezolizumab and bevacizumab.

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Abstract

Aim

This study aims to validate the modified albumin-bilirubin grade and α-fetoprotein score (mALF score).

Methods

This retrospective study included a total 426 hepatocellular carcinoma (HCC) patients receiving atezolizumab and bevacizumab (Atez/Bev) at 22 institutions in Japan from September 2020 to January 2022. Each patient was randomized 3:2 to a training set (n = 255) and a validation set (n = 171). We investigated prognostic factors in the training set and developed an easily applicable mALF score. This score was evaluated in the validation set.

Results

We built the mALF score using mALBI grade 2b or 3 (HR 2.36, 95% CI 1.37–4.05, p = 0.002) and α-fetoprotein ≧ 100 ng/ml (HR 2.61, 95% CI 1.49–4.55, p < 0.001), which were identified as unfavorable prognostic factors in a multivariate analysis. The 1-year OS rates were 82.7% (95% CI 68.9–90.8) in patients who meet neither of the criteria (mALF 0 points, n = 101), 61.7% (95% CI 44.5–74.9) in patients who meet either of the two criteria (mALF 1 point, n = 109), and 24.6% (95% CI 9.0-44.3) in patients who meet both criteria (mALF 2 points, n = 45); the difference was statistically significant (p < 0.001). The median PFS in patients with mALF 0, 1, and 2 points was 9.5 months (95% CI 4.3-NA), 6.6 months (95% CI 6.0–8.0), and 3.8 months (95% CI 3.0-5.2), respectively, which amounted to a significant difference (p < 0.001). These results were confirmed in the validation set (1-year OS rates, 0/1/2 points = 94.2%/62.1%/46.3%, p < 0.001; median PFS, 0/1/2 points = 9.3/6.7/4.7 months, p = 0.018).

Conclusions

The mALF score can reliably predict the prognosis of HCC patients receiving Atez/Bev.

Introduction

The choices of systemic therapies for advanced hepatocellular carcinoma (HCC) have increased. Although three regimens, namely atezolizumab and bevacizumab (Atez/Bev) [1], lenvatinib [2], and sorafenib [3, 4], have already been approved as first-line treatments, Atez/Bev is recommended for first-line treatment according to recent guidelines [5, 6], and is commonly used worldwide. While the expression of PD-L1 [7], and activated Wnt/β-catenin signaling [8, 9] may be promising biomarkers to predict the clinical outcome of immune checkpoint inhibitors, reliable biomarkers are still lacking. Moreover, the predicting the survival of HCC patients receiving immune checkpoint inhibitor (ICI) treatment remains challenge. It is important to establish a simple scoring system that reflects the preserved liver function and oncologic prognostic

factors. Therefore, the aim of current study was to newly develop and validate a simple score that can be applied to predict survival in patients treated with Atez/Bev.

Methods

Participants

The present retrospective study included 426 HCC patients who received atezolizumab (1200 mg/body) and bevacizumab (15 mg/kg body weight) intravenously every 3 weeks in 22 institutions in Japan. Between September 2020 and January 2022, a total of 426 patients were included. We did not exclude any patients. These eligible patients were randomized 3:2 to a training set (n = 255) and a validation set (n = 171) (Fig. 1).

Baseline characteristics, including age, sex, body mass index, chronic liver disease, biochemical parameters, liver function, and tumor stage were collected. The liver function was assessed according to the Child-Pugh score, and modified albumin-bilirubin (mALBI) grade [10]. The tumor stage was determined based on the Barcelona Clinic Liver Cancer (BCLC) system [6].

Evaluation on therapeutic outcome of Atez/bev treatment

The Atez/Bev treatment was continued until the presence of disease progression or unacceptable adverse events were found. The tumor response was assessed according to the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST ver.1.1). The best radiological response was classified as a complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) based on local review. Progression-free survival (PFS) was computed from the date on which treatment with Atez/Bev was initiated to the date of disease progression or death from any cause, whichever came first. OS was calculated from the initiation date on which treatment with Atez/Bev was initiated to the date of death from any cause. Adverse events were graded based on The Common Terminology Criteria for Adverse Events version 5.0. Interruption or discontinuation of each drug was carried out according to the guidelines for Atez/Bev treatment provided by the manufacturer.

Statistical analyses

Categorical variables were reported as the number (percentage) and were compared using the chi-squared or Fisher's exact test, as appropriate. Continuous variables were reported as the median (interquartile range) and compared using Mann-Whitney U test. We used Cox proportional hazards regression models to investigate prognostic factors. The number of explanatory variables depended on the number of events. The following factors were included as explanatory variables: age, sex, BCLC stage (0 or A or B vs. C or D), mALBI grade (1 or 2a vs. 2b or 3), and AFP (< 100 ng/ml vs. ≥100 ng/ml). PFS and survival curves were drawn using the Kaplan-Meier method and analyzed by a log-rank test. All reported p-values were 2-sided and p values of < 0.05 were considered statistically significant. All statistical analyses were conducted using EZR Ver. 1.55 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [11].

Results

Patient profile in training and validation set

The patient profiles of the training and validation sets are shown in Table 1. The median age in the training set was 73 years, and 80.4% of the patients were male. Approximately 80% of the patients had a performance status (PS) of 0. The median body mass index was 23.9 (21.1, 26.1) kg/m^2. The etiologies of liver disease were as follows: (HBV, n = 46 [18.0%]; HCV, n = 86 [33.6%]; alcohol, n = 47 (18.4%); and other, n = 77 [30.1%]). Therefore, virus-related liver disease accounted for 51.4% of the cases. The Child-Pugh scores was 5 points in 151 patients (59.2%), 6 points in 87 patients (34.1%), and ≥ 7 points in 17 patients (6.7%). The median ALBI score was − 2.36 (-2.70, -2.07). Accordingly, 87 (34.1%), 68 (26.7%), 97 (38.0%), and 3 patients (1.2%) were classified as grade 1, 2a, 2b, and 3, respectively. The BCLC stages were as follows; very early, n = 4 (1.6%); early, n = 27 (10.6%); intermediate, n = 106 (41.6%); advanced, n = 115 (45.1%); and terminal, n = 3 (1.2%). There were 75 patients (29.4%) with extrahepatic spread and 42 patients (16.5%) with macrovascular invasion. The patient characteristics of the validation set were similar to those of the training set.

Table 1
Patient characteristics in the training and validation sets

Variables	Training set (n = 255)	Validation set (n = 171)	P-value
Age, years	73.0 [68.0, 79.0]	74.0 [67.5, 80.0]	0.96
Male, n (%)	205 (80.4)	139 (81.3)	0.90
PS, n (%)			
0	205 (80.4)	142 (83.0)	0.78
1	42 (16.5)	24 (14.0)	
≥ 2	8 (3.1)	5 (2.9)	
BMI (kg/m^2)	23.9 [21.1, 26.1]	22.4 [20.8, 24.8]	0.012
Cause of liver diseases, n (%)			
HBV	46 (18.0)*	32 (18.7)	1.00
HCV	86 (33.6)*	58 (33.9)	
Alcohol	47 (18.4)	31 (18.1)	
Others	77 (30.1)	50 (29.2)	
Viral-related liver disease, n (%)	131 (51.4)	90 (52.6)	0.84
Child Pugh score, n (%)			
5	151 (59.2)	101 (59.1)	1.00
6	87 (34.1)	58 (33.9)	
≥ 7	17 (6.7)	12 (7.0)	
ALBI score	-2.36 [-2.70, -2.07]	-2.42 [-2.69, -2.13]	0.77
mALBI grade, n (%)			
1	87 (34.1)	64 (37.4)	0.74
2a	68 (26.7)	39 (22.8)	
2b	97 (38.0)	67 (39.2)	
3	3 (1.2)	1 (0.6)	
Serum albumin (g/dL)	3.7 [3.3, 4.1]	3.8 [3.4, 4.1]	0.69
Total bilirubin (mg/dL)	0.8 [0.6, 1.0]	0.8 [0.6, 1.0]	0.96
Platelet count ($10^9/L$)	13.8 [10.6, 19.0]	13.7 [10.6, 18.8]	0.97
Prothrombin time (%)	91.0 [81.2, 100.0]	90.0 [83.0, 100.0]	0.56

Variables	Training set (n = 255)	Validation set (n = 171)	P-value
BCLC stage, n (%)			
Very early	4 (1.6)	1 (0.6)	0.12
Early	27 (10.6)	12 (7.0)	
Intermediate	106 (41.6)	62 (36.3)	
Advanced	115 (45.1)	96 (56.1)	
Terminal	3 (1.2)	0 (0.0)	
Extrahepatic spread, n (%)	75 (29.4)	63 (36.8)	0.11
Macrovascular invasion, n (%)	42 (16.5)	37 (21.8)	0.20
AFP ≥ 100 ng/ml, n (%)	99 (38.8)	77 (45.0)	0.23
DCP ≥ 100 mAU/ml**, n (%)	168 (66.4)	110 (64.7)	0.75
Data are reported as the median [IQR] or number (percentage).			
* Both HBs-Ag and anti-HCV Ab were positive in one patient.			
**Data were missing for three patients.			
AFP, α-fetoprotein; ALBI, albumin-bilirubin; anti-HCV Ab, anti-hepatitis C antibody; BCLC, Barcelona Clinic Liver Cancer; BMI, body mass index; DCP, des-gamma-carboxy prothrombin; HBV, hepatitis B virus; HCV, hepatitis C virus; HBs-Ag, hepatitis B virus surface antigen; mALBI, modified albumin-bilirubin; PS, performance status.			

Table 2
Results of the multivariate analysis in the training set

Variables		HR (95% CI)	P-value
Age	Per 1 year	1.02 (0.99–1.06)	0.22
Sex	Male	1	0.79
	Female	0.91 (0.44–1.89)	
BCLC stage	0 or A or B	1	0.75
	C or D	1.10 (0.61–1.98)	
mALBI grade	1 or 2a	1	0.002
	2b or 3	2.36 (1.37–4.05)	
AFP	< 100 ng/ml	1	< 0.001
	≥ 100 ng/ml	2.61 (1.49–4.55)	

AFP, α-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval; HR, hazard ratio; mALBI, modified albumin-bilirubin

The efficacy and safety of Atez/Bev and the development of the modified albumin-bilirubin grade and α-fetoprotein score (mALF score) in the training set

The best radiological response in the training set was classified as follows: CR, PR, SD, PD, and NE in CR, n = 5 (2.0%); PR, n = 62 (24.3%); SD, n = 118 (46.3%); PD, n = 36 (14.1%); and NE, n = 34 (13.3%) (Supplemental Table 1). The median PFS was 6.8 months (95% confidence interval 6.0–8.0: Supplemental Fig. 1a), and 129 events (50.6%) were identified at the time of the analysis. The median OS was not reached and the 1-year survival rate was 63.3% (95% CI 53.3–71.7: Supplemental Fig. 1b). Fifty-five patients (21.6%) were dead at the time of the analysis.

The multivariate analysis revealed that mALBI grade 2b or 3 and AFP ≥ 100 ng/ml were unfavorable factors for OS (mALBI grade 2b or 3, hazard ratio [HR] 2.36, 95% CI 1.37–4.05, p = 0.002: AFP ≥ 100 ng/ml, HR 2.61, 95% CI 1.49–4.55, p < 0.001). Given that both the mALBI grade and AFP were prognostic factors and the numerical value of the HR was similar in the multivariate analysis, we developed a simple score named the **m**odified **A**lbumin-bi**L**irubin grade and α-**F**etoprotein score (mALF score). We assigned 1 point for mALBI grade 2b or 3 and 1 point for baseline AFP ≥ 100 ng/ml. The scores of the patients were determined as follows: mALF score 0 points (mALBI grade 1 or 2a and AFP < 100 ng/ml), 1 point (either mALBI grade 2b or 3, and AFP ≥ 100 ng/ml), and 2 points (both mALBI grade 2b or 3, and AFP ≥ 100 ng/ml).

When patients were stratified according to their mALF scores, the objective response rate (ORR) and disease control rate (DCR) were numerically higher in patients with 0 points (30.7% and 77.2%, n = 101), followed by those with 1 point (27.5% and 72.5%, n = 109) and those with 2 points (13.3% and 62.2%, n = 45); the differences showed statistical significance (p = 0.08, and 0.17: Supplemental Table 1). The median PFS in patients with mALF scores of 0, 1, and 2 points was 9.5 months (95% CI 7.3-not applicable [NA]), 6.6 months (95% CI 6.0–8.0), and 3.8 months (95% CI 3.0-5.2), respectively; the difference was statistically significant (p < 0.001, concordance index 0.630: Fig. 2a). The 1-year OS rates in patients with mALF scores of 0, 1, and 2 points were 82.7% (95% CI 68.9–90.8), 61.7% (95% CI 44.5–74.9), and 24.6% (95% CI 9.0-44.3), respectively, which amounted to a statistically significant difference (p < 0.001, concordance index 0.675: Fig. 2b). There were no other significant differences among patients with mALF scores of 0, 1, and 2 points with the exception of any-grade decreased appetite (p = 0.04) and any-grade fever (p = 0.01: Table 3).

Table 3
Adverse events according to the mALF score in the training and validation sets

		Training set				Validation set			
Variables		0 points (n = 101)	1 point (n = 109)	2 points (n = 45)	P-value	0 points (n = 60)	1 point (n = 77)	2 points (n = 34)	P-value
Diarrhea	Any	5 (5.0)	12 (11.0)	4 (8.9)	0.28	4 (6.7)	1 (1.3)	1 (2.9)	0.23
	Grade ≥ 3	0 (0.0)	1 (0.9)	1 (2.2)	0.36	1 (1.7)	0 (0.0)	0 (0.0)	0.39
Liver injury	Any	10 (9.9)	11 (10.1)	5 (11.1)	0.97	5 (8.3)	11 (14.3)	8 (23.5)	0.13
	Grade ≥ 3	2 (2.0)	2 (1.8)	4 (8.9)	0.05	0 (0.0)	4 (5.2)	1 (2.9)	0.20
Elevated blood pressure	Any	17 (16.8)	18 (16.5)	7 (15.6)	0.98	12 (20.0)	8 (10.4)	2 (5.9)	0.10
	Grade ≥ 3	5 (5.0)	7 (6.4)	2 (4.4)	0.85	1 (1.7)	2 (2.6)	0 (0.0)	0.63
Gastrointestinal tract bleeding	Any	1 (1.0)	2 (1.8)	1 (2.2)	0.82	1 (1.7)	1 (1.3)	0 (0.0)	0.76
	Grade ≥ 3	1 (1.0)	1 (0.9)	0 (0.0)	0.80	1 (1.7)	1 (1.3)	0 (0.0)	0.76
Decreased appetite	Any	19 (18.8)	24 (22.0)	17 (37.8)	0.04	8 (13.3)	8 (10.4)	8 (23.5)	0.18
	Grade ≥ 3	4 (4.0)	3 (2.8)	2 (4.4)	0.84	1 (1.7)	0 (0.0)	2 (5.9)	0.10
Protein urea	Any	17 (16.8)	23 (21.1)	9 (20.0)	0.73	11 (18.3)	16 (20.8)	8 (23.5)	0.83
	Grade ≥ 3	6 (5.9)	11 (10.1)	2 (4.4)	0.36	2 (3.3)	8 (10.4)	6 (17.6)	0.07
Fever	Any	2 (2.0)	13 (11.9)	2 (4.4)	0.01	0 (0.0)	7 (9.1)	5 (14.7)	0.02
	Grade ≥ 3	0 (0.0)	4 (3.7)	0 (0.0)	0.07	0 (0.0)	0 (0.0)	1 (2.9)	0.13
General fatigue	Any	18 (17.8)	23 (21.1)	14 (31.1)	0.20	16 (26.7)	10 (13.0)	9 (26.5)	0.09
	Grade ≥ 3	2 (2.0)	1 (0.9)	0 (0.0)	0.56	2 (3.3)	1 (1.3)	0 (0.0)	0.46

		Training set				Validation set			
Hepatic edema	Any	11 (10.9)	12 (11.0)	3 (6.7)	0.69	2 (3.3)	13 (16.9)	5 (14.7)	0.04
	Grade ≥ 3	2 (2.0)	5 (4.6)	1 (2.2)	0.52	1 (1.7)	5 (6.5)	1 (2.9)	0.34

mALF score, mALBI grade and AFP score.

The performance of mALF score in the validation set

The mALF scores of the validation cohort were as follows: 0 points, n = 60 (35.1%), 1 point, n = 77 (45.0%); and 2 points, n = 34 patients (19.9%). The ORR in patients with a mALF score of 0 points was numerically higher in comparison to those with those with scores of 1 point or 2 points, but the difference was not statistically significant (p = 0.89: supplemental Table 2). The median PFS in patients with mALF scores of 0, 1, and 2 points was 9.3 months (95% CI 5.8-NA), 6.7 months (95% CI 3.8-9.0), and 4.7 months (95% CI 2.9–6.4), respectively. The 1-year OS rates in patients with a mALF score of 0 points was the highest (94.2%, 95% CI 78.5–98.5%), followed by patients with 1 point (61.7%, 95% CI 44.5–74.9) and patients with 2 points (46.3%, 95% CI 19.6–69.4). The PFS and the survival curve were well stratified by the mALF score (PFS, p < 0.018 concordance index 0.579; OS, p < 0.001 concordance index 0.602: Fig. 3a and 3b). The incidence of any-grade fever and any-grade of hepatic edema showed significant differences according to the mALF score (p = 0.02, and p = 0.04, respectively; Table 3).

Discussion

The major findings of the present study were the identification of mALBI grade 2b or 3, and AFP ≥ 100n g/ml as independent unfavorable prognostic factors in a multivariate analysis. Based on this, we built an easy, and widely applicable scoring system named the mALF score. The PFS and survival curve were well stratified by the mALF score in the training set and these results were confirmed in the validation set.

Staging systems, including the Liver Cancer Study Group of Japan staging system [12] have been used to evaluate pure tumor factors. Other staging systems, such as the BCLC staging system [6], CLIP score [13], and JIS score [14], have been used to evaluate both the liver function and tumor factors. However, the inclusion of both tumor factors and the liver function is generally complicated. New evaluation methods for patients receiving systemic therapy are needed because many therapeutic agents have been developed. The liver function plays an important role in maintaining sequential systemic therapies, resulting in prolonged survival. The precise oncologic evaluation is necessary to predict the prognosis. Moreover, although Atez/Bev is recommended as first-line treatment according to recent guidelines, there has been no simple survival estimation model for patients receiving this regimen [5, 6]. Accordingly, we built a simple applicable score that includes both the liver function and tumor factors.

The ALBI score can be calculated based on only two variables: serum albumin and bilirubin [15]. According to data from a Japanese nationwide survey, the mALBI grade can evaluate the preserved liver function more precisely and accurately in comparison to the Child-Pugh classification [10]. In addition, the mALBI grade can predict and stratify the prognosis of HCC patients [10]. Indeed, the ALBI score plays an important role in predicting survival in advanced HCC patients treated with systemic agents, including atezolizumab plus bevacizumab [16], lenvatinib [17], sorafenib [18], and ramucirumab [19, 20]. These findings were in line with the present results. Recently, we reported that the early interruption of Bev due to the AEs was relevant to PFS and OS in patients receiving Atez/Bev, and that Bev treatment was likely to be interrupted in patients with mALBI grade 2b [21]. Accordingly, a relatively poor liver function leads to the interruption of Bev treatment, resulting in poor PFS and OS, which supports the present results.

AFP is a well-known tumor marker and is widely applied in the management of HCC for uses such as surveillance, diagnosis, treatment response monitoring, and prognostic factors [22]. AFP elevation is associated with a poor prognosis across all stages of HCC [23]. AFP elevation was also related to a high risk of tumor recurrence after surgical resection [24] and liver transplantation [25]. The analysis of transcriptome data, whole-exome sequencing data, and DNA methylome profiling demonstrated that AFP-high tumors showed a different phenotype, which was characterized by poor differentiation, enrichment of progenitor features and enhanced proliferation in comparison to AFP-low tumors [26]. This analysis also showed VEGF pathway enrichment in AFP-high tumors [26]. VEGF hampered the benefit and durability of the response of ICI via certain mechanisms [27]. Given these previous reports, HCC patients with AFP elevation are less responsive to Atez/Bev treatment and show a poor prognosis, which was consistent with the present results.

The ORR was numerically the highest in patients with an mALF score of 0 points in both the training and validation set, followed by those with 1 point and 2 points; however, the differences were not significant. The reason for the lack of significance is probably due to the low statistical power. In comparison to tyrosine kinase inhibitor treatment, a longer treatment period is required to achieve a tumor response in patients receiving ICI treatment. Accordingly, with a longer observation period and a larger number of cases, significant differences may be observed among the mALF scores.

There are significant differences in any-grade decreased appetite and any-grade fever in the training set, and in any-grade fever, and any-grade hepatic edema in the validation set. Any-grade fever was the only of these factors that was seems to be confirmed in the validation set. However, the incidence of any-grade fever was highest in patients with an mALF score of 1 point in the training set, followed by patients with 2 points and patients with 0 points. On the other hand, it was most frequently found in patients with an mALF score of 2 points in the validation set, followed by patients with 1 point and 0 points. That is, data concerning to any-grade fever in the training set were not confirmed in the validation set. A further study may be required to confirm whether or not the mALF score can predict the development of AEs during Atez/Bev treatment.

The present study was associated with some limitations. First, the study population was relatively small. Second, the median OS was not reached at the time of the analysis due to the relatively short observation period. A longer observation period may affect the present results. Third, this study conducted in a

retrospective manner and no patients were excluded. Therefore, patients with poor PS (≥ 2), a poor liver function (Child-Pugh score ≥ 7 or mALBI grade 3), and all BCLC stages were included.

In conclusion, the mALF score can reliably predict the prognosis of HCC patients receiving Atez/Bev.

Declarations

Statement of Ethics

All research procedures were approved by the Institutional Ethics Committee of Ehime Prefectural Central Hospital (IRB No. 30-66) (UMIN000043219) and were performed in accordance with the Declaration of Helsinki. All patients included in the present study agreed and gave their written consent for the anonymous use of their clinical data for scientific research.

Conflict of Interest Statement

Takeshi Hatanaka received lecture fees from Eisai. Satoru Kakizaki received research grants from Abbvie. Atsushi Hiraoka received lecture fees from Eli Lilly, Bayer, and Chugai. Toshifumi Tada received lecture fees from AbbVie, and Eisai. Hiroko Iijima received research grants from Abbvie, Otsuka, and Sumitomo Dainippon Pharma. Takashi Kumada received lecture fees from Eisai. The other authors declare no conflicts of interest in association with the present study.

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Author contributions

TH, SK, AH, TTad, AN, and TK contributed to the concept, design and execution of the study. TH, SK, AH, TTad, MH, KKar, JT, MA, KTak, EI, SF, KTs, TI, KTaj, HOc, SY, HT, CO, TNi, NS, KKaw, HK, TTan, HOh, KN, AM, AT, TNa, NI, TO, TA, MI, AN, YK, SN, MK, HI, and YH contributed to data curation. TH performed statistical analyses and interpreted the data. TH, SK, AH, TTad, AN, and TK reviewed and edited the manuscript. All authors have read and approved the final version of the manuscript.

Data Availability Statement

The data associated with present study are available from the corresponding author upon reasonable request.

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Figures

Figure 1

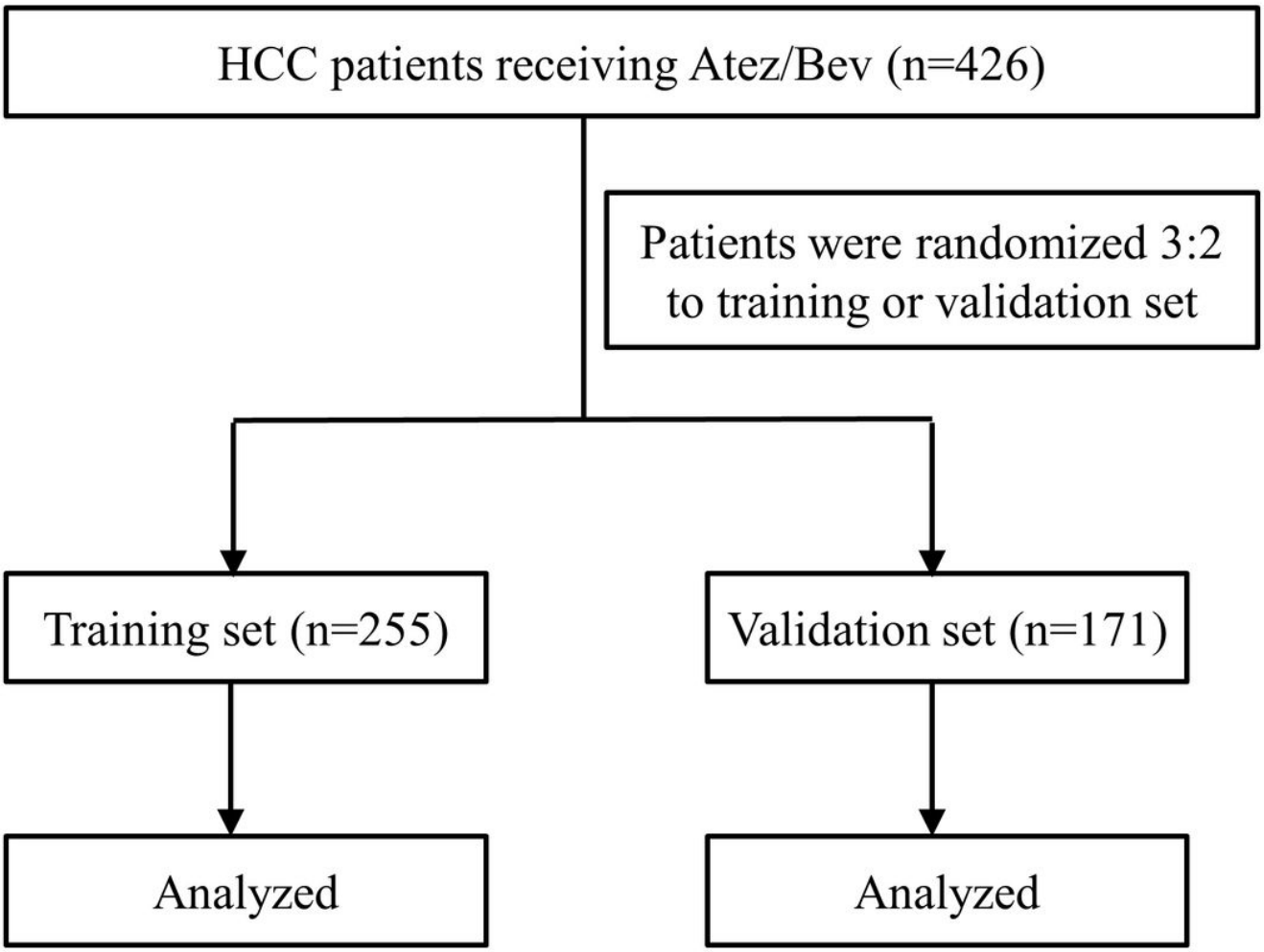

Figure 1

Flow diagram of the patients with hepatocellular carcinoma. Atez/Bev, atezolizumab and bevacizumab; HCC, hepatocellular carcinoma.

Figure 2

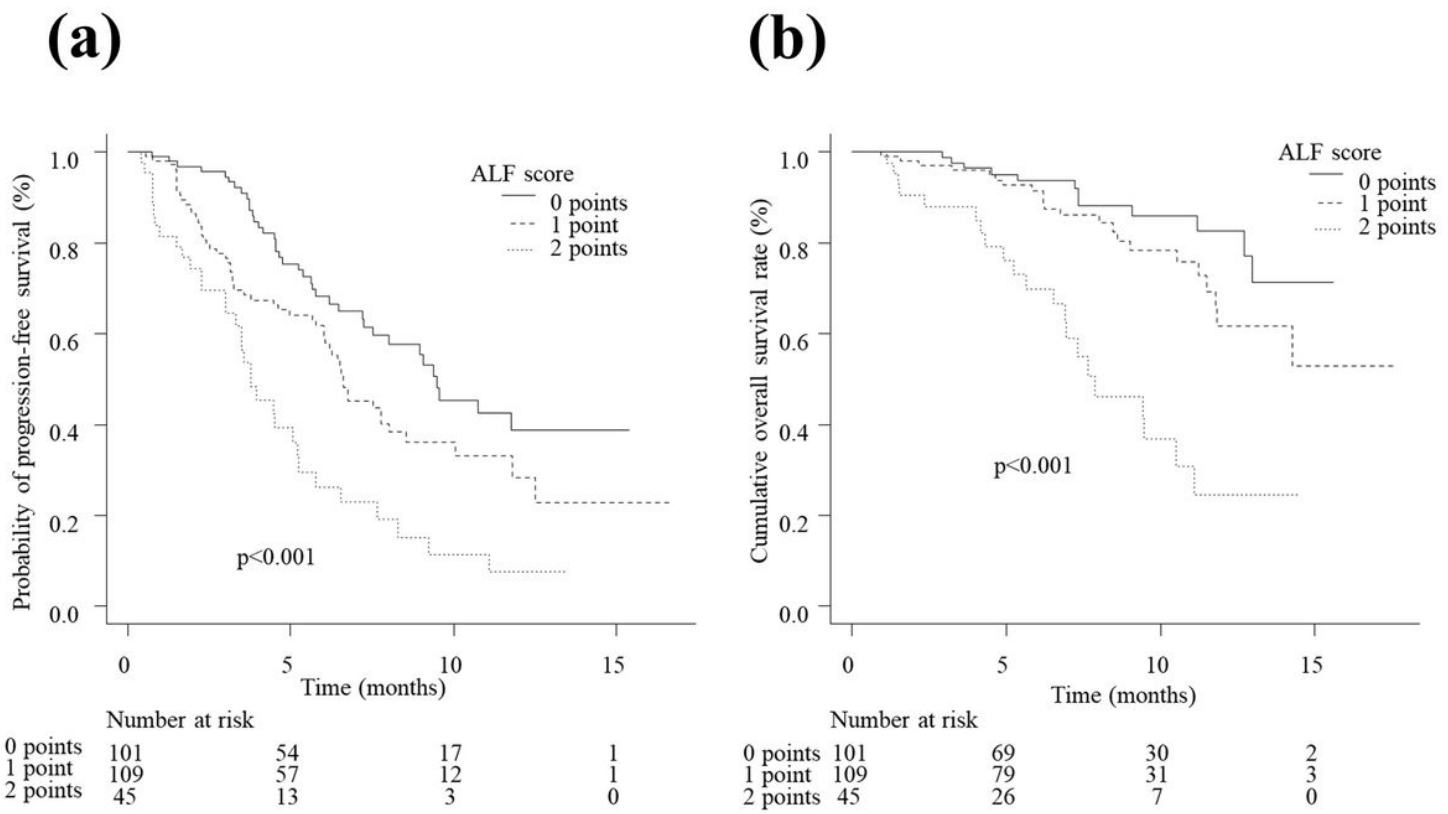

Figure 2

The PFS and OS according to the mALF score in the training set. (a) The median PFS according to the mALF scores was as follows: 0 points (n=101), 9.5 months (95% CI 7.3-not applicable); 1 point (n=109), 6.6 months (95% CI 6.0-8.0); and 2 points (n=45), 3.8 months (95% CI 3.0-5.2); this amounted to a statistically significant difference (p<0.001, concordance index 0.630). (b) The 1-year OS rates in patients with mALF scores of 0, 1, and 2 points were 82.7% (95% CI 68.9-90.8), 61.7% (95% CI 44.5-74.9), and 24.6% (95% CI 9.0-44.3), respectively, which amounted to a statistically significant difference (p<0.001, concordance index 0.675).

CI, confidence interval; mALF score, modified albumin-bilirubin grade and α-fetoprotein score; OS, overall survival; PFS, progression-free survival.

Figure 3

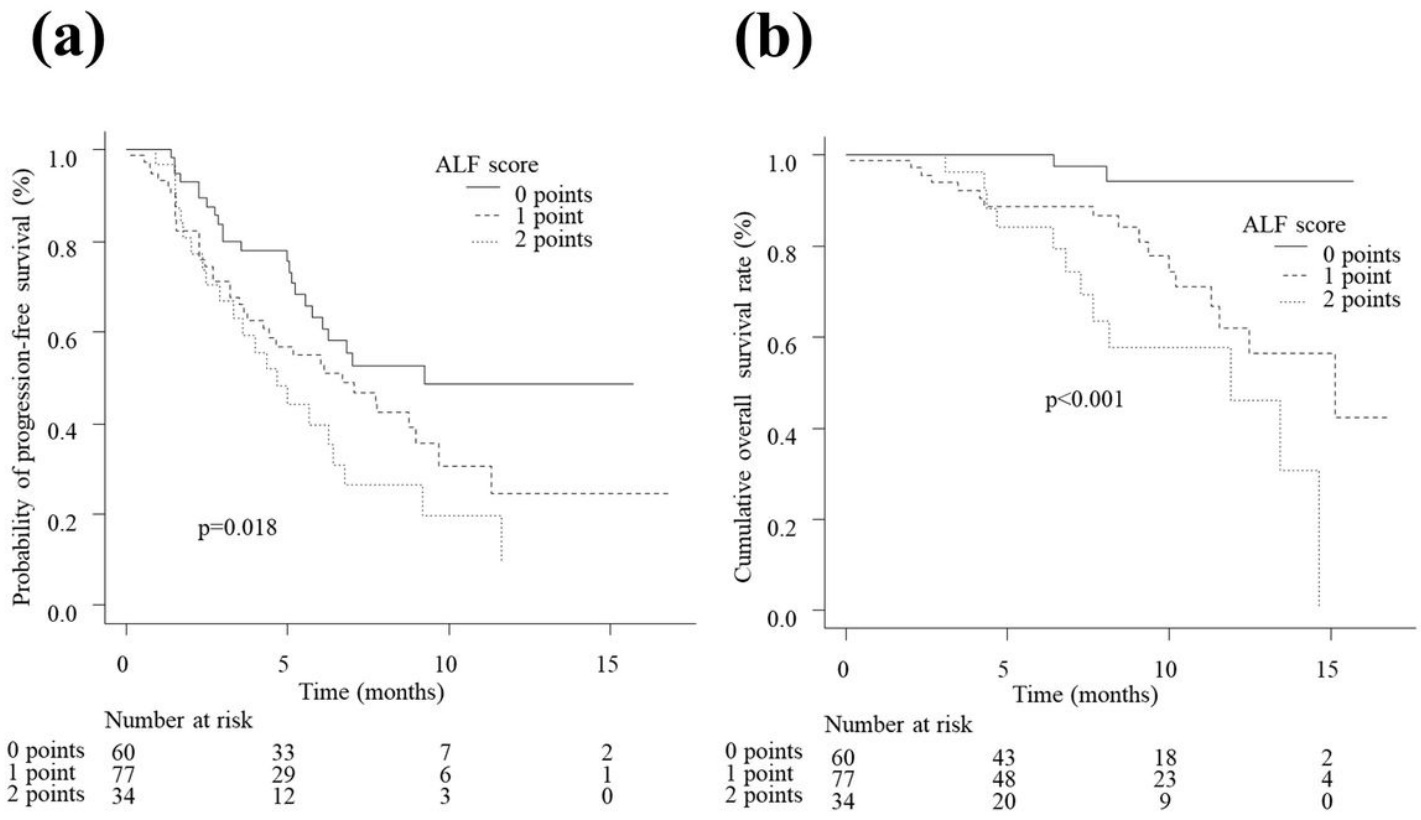

Figure 3

The PFS and OS according to the mALF scores in the validation set. (a) The median PFS according to the mALF scores was as follows: 0 points (n=60), 9.3 months (95% CI 5.8-not applicable); 1 point (n=77), 6.7 months (95% CI 3.8-9.0); and 2 points (n=34), 4.7 months (95% CI 2.9-6.4). (b) The 1-year OS rate was highest in patients with a mALF score of 0 points (94.2%, 95% CI 78.5-98.5%), followed by patients with 1 point (61.7%, 95% CI 44.5-74.9) and 2 points (46.3%, 95% CI 19.6-69.4). The PFS and survival curve were well stratified by the mALF score (PFS, p<0.018 concordance index 0.579: OS, p<0.001 concordance index 0.602).

CI, confidence interval; mALF score, modified albumin-bilirubin grade and α-fetoprotein score; OS, overall survival; PFS, progression-free survival.

Supplementary Files

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- AtezBevmALFscoreSupplementalTable2022June08.xlsx
- Sup.Figure1.tif