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Original Article

Prognostic Efficacy of the Albumin Grade in Patients with Hepatocellular Carcinoma

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We previously found that "albumin grade", formerly called the "ALBS grade," demonstrated significant capability for prognostic stratification in hepatocellular carcinoma (HCC) patients treated with lenvatinib. The purpose of the present study was to compare the performance of the albumin grade with that of the modified albumin-bilirubin (mALBI) grade in predicting overall survival of HCC patients with different BCLC stages and treatment types. We enrolled 7,645 Japanese patients newly diagnosed with HCC using the Akaike information criteria (AIC), likelihood ratio, and C-index in different Barcelona Clinic Liver Cancer (BCLC) stages and treatments. The albumin grade showed similar and slightly better performance than the mALBI grade for BCLC stage 0 and A and especially for patients who underwent curative surgery and ablation. In patients treated with transcatheter arterial chemoembolization, molecular targeted agents, and the best supportive care, the mALBI grade had better performance than the albumin grade. However, the differences of the indices were very small in all scenarios. Overall, the albumin grade was comparable in efficacy to the mALBI grade, showing particular benefit for patients with early-stage HCC.

Key words: albumin grade, hepatocellular carcinoma, modified albumin-bilirubin grade

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The Child-Pugh classification system is a widely accepted prognostic model for evaluating hepatic reserve [1-4]. Originally, the Child-Pugh scoring system was developed by Pugh *et al.* to grade the severity of liver dysfunction in predicting the outcome of surgery for esophageal varices [5]. The Child-Pugh score categorizes patients into three classes (A, B, and C) based on five parameters, including albumin, bilirubin, prothrombin time, presence of ascites, and encephalopathy. However, this classification system includes subjective factors such as the presence of ascites and encephalopathy; hence the classification of any individual can vary depending on the physician's judgment.

Recently, the albumin-bilirubin (ALBI) grade, which consists of only albumin and total bilirubin (T.Bil), has been proposed. The original ALBI grade showed some value for assessing liver function in patients with hepatocellular carcinoma (HCC) [6] but included patients with a wide range of liver function in its grade 2 classification. The modified ALBI (mALBI) grade, which is widely used in clinical practice today, divided ALBI grade 2 into two subgroups (2a and 2b) [7, 8]. These scores eliminate the use of subjective variables but are complicated to calculate as they involve logarithmic calculations.

To address this complexity, we developed a grading system based solely on albumin, the so-called "albumin grade," which was formerly called the "ALBS grade," derived from the modified albumin-bilirubin grade [9]. We examined the prognostic ability of the albumin grade for patients with HCC treated with lenvatinib (LEN-HCC) and reported its strong performance stratifying LEN-HCC survival. The albumin grade demonstrated comparable Akaike information criteria (AIC) and C-index values to those of the mALBI grade [9]. Notably, in cases where the T.Bil level was low, which is common in LEN-HCC, overall survival was primarily correlated with albumin rather than T.Bil, validating the use of albumin alone for prediction. However, the prognostic ability of the albumin grade for HCC in different treatment scenarios (*e.g.*, surgery, ablation, supportive care, *etc.*) remains unclear.

In this study, we compared the prognostic capabilities of the albumin and mALBI grades for HCC in various treatment scenarios using a large HCC cohort in Japan.

Materials and Methods

Patients. We analyzed the Real-life Practice Experts for HCC (RELPEC) Study Group database in Japan, which includes 7,645 patients with HCC who were newly diagnosed and treated between 1998 and 2022. HCC was diagnosed histologically or clinically in accordance with the criteria of the American Association for the Study of Liver Diseases using dynamic computed tomography, magnetic resonance imaging, and angiography [10]. Patients were categorized into six treatment groups according to their primary treatment: surgery, ablation, transcatheter arterial chemoembolization (TACE), molecular targeted agents (MTA), "others", and best supportive care (BSC).

This study complied with the ethical guidelines of the World Medical Association Declaration of Helsinki and was approved by the Ethics Committee of the Institutional Review Board of Ehime Prefectural Central Hospital (approval number: 27-34).

Calculation of the scores. The ALBI score was calculated by the following formula: $\{\log_{10}(\text{bilirubin [mg/dL]} \times 17.1) \times 0.66\} + (\text{albumin [g/dL]} \times -0.85)$; and the ALBI grade was defined based on ALBI scores as follows: grades 1 (≤ -2.60), 2 (> -2.60 to -1.39), and 3 (> -1.39) [6]. The ALBI grade 2 was further divided using a new cutoff value (ALBI score, -2.270) into two subgroups, 2a and 2b; consequently, mALBI was divided into four grades [7, 8]. The albumin grade cutoffs that corresponded to the mALBI grades 1, 2a, 2b, and 3 were albumin ≥ 4.0 g/dL, 4.0 g/dL $>$ albumin ≥ 3.5 g/dL, 3.5 g/dL $>$ albumin ≥ 2.8 g/dL, and albumin < 2.8 g/dL, respectively [9].

Prognostic ability of the albumin grade in different BCLC stages and treatment groups. To determine the prognostic ability of the albumin grade, we calculated the AIC, likelihood ratio, and C-index in different Barcelona Clinic Liver Cancer (BCLC) stages and compared them with those of the mALBI grade [11]. Similarly, we examined the AIC, the likelihood ratio, and the C-index of the albumin and mALBI grades in different treatment groups: surgery, ablation, TACE, MTA, and BSC.

Statistics. Baseline characteristics are presented as medians and interquartile ranges. Survival curves were estimated using the Kaplan-Meier method and analyzed using a log-rank test. The AIC, likelihood ratio, and C-index were calculated to evaluate the strat-

ification and predictive abilities. All statistical analyses were performed using Easy R (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [12], a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics. The baseline patient characteristics are summarized in Table 1. The median age of the patients was 70 years, and 74.2% were male. The underlying etiology of HCC was hepatitis C virus (HCV) in 57.4%, hepatitis B virus (HBV) in 12.5%, both HBV and HCV in 0.8%, and neither HBV nor HCV in 29.2%. Over half of the patients (n = 4,758; 63.2%) were categorized as having very early or early-stage HCC (BCLC stage 0 or A), and 59.0% (n = 4,513) received curative treatments such as surgery or ablation. The characteristics of the patients in each BCLC stage and treatment group are shown in Tables 2 and 3.

Prognostic ability of the albumin grade. The survival curves of all patients were stratified according to mALBI and albumin grades. The median survival times of patients with mALBI grades 1, 2a, 2b, and 3 were 7.8, 5.5, 3.2, and 1.2 years, and those of patients with albumin grades 1, 2a, 2b, and 3 were 8.3, 5.4, 3.3, and 1.5, respectively (Fig. 1). The AIC of the mALBI grade was lower than that of the albumin grade (64,506 and 64,529, respectively); the likelihood ratio of the mALBI grade was higher than that of the albumin grade (843.80 and 820.70, respectively); and the C-index of the mALBI grade was higher than that of the albumin grade (0.648 and 0.643, respectively) (Table 4). In other words, all three indices for the entire patient group showed better performance of the mALBI grade than the albumin grade; however, the differences were small.

Predictive ability of the albumin grade at different BCLC stages. The performance of the albumin grade and mALBI grade were next compared at each BCLC stage (Fig. 2 and Table 4). At BCLC stage 0, both the albumin and mALBI grades had the same AIC (5,229) and likelihood ratio (67.08). However, the albumin grade showed a higher C-index than the mALBI grade (0.620 and 0.618, respectively). In BCLC stage A, the albumin grade showed a lower AIC (24,208 vs. 24,224), a higher likelihood ratio (234.00 vs. 198.70), and a higher C-index (0.604 vs. 0.599) than the mALBI grade. These results suggest that the albumin grade has equivalent or better stratification ability than the mALBI grade at BCLC stages 0 and A. However, in BCLC stages B, C, and D, the mALBI grade had a lower AIC

Table 1 Characteristics of all patients

Variable	N = 7,645
Age, years	70 (63–77)
Gender, male (%)	5,672 (74.2)
HBV/HCV/HBV + HCV/NBNC	956/4,381/64/2,232
Child-Pugh grade, A/B/C	5,465/1,758/422
mALBI grade, 1/2a/2b/3	2,737/1,572/2,722/614
Albumin grade, 1/2a/2b/3	2,436/1,939/2,630/640
BCLC stage, 0/A/B/C/D	1,276/3,482/1,483/884/513
Treatment, surgery/ablation/TACE/MTA/others/BSC	1,879/2,634/1,905/115/284/828
Tumor number	1 (1–3)
Tumor size, cm	2.80 (1.80–5.00)
Platelet count, $\times 10^4/\mu L$	12.6 (8.6–17.8)
Prothrombin time, %	83.9 (0.7–95.0)
Albumin, g/dL	3.7 (3.2–4.1)
Total bilirubin, mg/dL	0.8 (0.6–1.2)
Alpha-fetoprotein, ng/mL	15.9 (5.5–132.7)
Des-gamma-carboxy prothrombin, mAU/mL	73.0 (23.0–962.3)

Data are expressed as the medians (interquartile range), or number (%).
BCLC, Barcelona Clinic Liver Cancer; BSC, best supportive care; HBV, hepatitis B virus; HCV, hepatitis C virus; mALBI, modified albumin-bilirubin; MTA, molecular targeted agent; NBNC, non-B and non-C; TACE, transcatheter arterial chemoembolization.

Table 2 Characteristics in each BCLC stage

BCLC stage	0	A	B	C	D	*P*-value
N	1,276	3,482	1,483	884	513	
Age	70 [62, 76]	71 [63, 77]	71 [64, 77]	71.00 [63, 79]	68 [60, 76]	<0.001
Gender, male (%)	864 (67.7)	2,550 (73.2)	1,189 (80.2)	698 (79.0)	365 (71.2)	<0.001
HBV/HCV/HBV+HCV/NBNC	192/840/8/236	388/2,045/35/1,006	185/788/11/499	137/436/4/304	53/269/6/184	<0.001
Child Pugh grade A/B/C	1,272/4/0	2,532/930/20	1,071/401/11	551/328/5	39/90/384	<0.001
mALBI grade 1/2a/2b/3	714/320/241/1	1,343/727/1,263/149	447/350/613/73	223/161/432/68	10/14/168/321	<0.001
Albumin grade 1/2a/2b/3	640/383/250/3	1,195/882/1,211/194	396/413/589/85	195/233/372/84	10/28/202/273	<0.001
Tumor number	1 [1, 1]	1 [1, 2]	4 [2, 6]	2 [1, 6]	2 [1, 5]	<0.001
Tumor size, cm	1.50 [1.20, 1.70]	2.50 [2.00, 3.60]	4.60 [3.30, 7.10]	6.50 [3.40, 10.00]	4.00 [2.10, 8.30]	<0.001
Platelet count, $\times 10^4/\mu L$	12.3 [8.9, 16.2]	12.2 [8.1, 17.2]	13.2 [9.2, 18.9]	15.7 [10.8, 22.2]	10.2 [6.6, 15.3]	<0.001
Prothrombin time, %	88.8 [80.0, 98.0]	84.0 [72.0, 96.0]	84.0 [73.0, 95.0]	83.0 [73.0, 95.4]	58.8 [46.5, 70.0]	<0.001
Albumin, g/dL	4.0 [3.6, 4.2]	3.7 [3.3, 4.1]	3.6 [3.3, 4.0]	3.5 [3.1, 3.9]	2.7 [2.4, 3.1]	<0.001
Total bilirubin, mg/dL	0.7 [0.5, 1.0]	0.8 [0.6, 1.1]	0.8 [0.6, 1.2]	0.9 [0.6, 1.4]	2.4 [1.4, 3.8]	<0.001
Alpha-fetoprotein, ng/mL	8.2 [3.8, 30.6]	12.0 [5.0, 65.3]	38.0 [9.6, 434.1]	156.0 [10.3, 5,283.2]	36.0 [8.1, 1,201.4]	<0.001
Des-gamma-carboxy prothrombin, mAU/mL	23.0 [17.0, 40.0]	51.5 [22.0, 326.3]	383.0 [51.0, 3,613.0]	2,117.0 [142.0, 23,091.0]	789.1 [76.5, 18,720.3]	<0.001

Data are expressed as the medians (interquartile range), or number (%).
BCLC, Barcelona Clinic Liver Cancer; BSC, best supportive care; HBV, hepatitis B virus; HCV, hepatitis C virus; mALBI, modified albumin-bilirubin; NBNC, non-B and non-C.

Table 3 Characteristics in each treatment

Treatment	Surgery	Ablation	TACE	MTA	others	BSC	*P*-value
N	1,879	2,634	1,905	115	284	828	
Age	69 [62, 75]	70 [63, 77]	71 [64, 78]	73 [67, 78]	66 [58, 73]	72 [64, 80]	<0.001
Gender, male (%)	1,498 (79.7)	1,797 (68.2)	1,449 (76.1)	93 (80.9)	231 (81.3)	604 (72.9)	<0.001
HBV/HCV/HBV+HCV/NBNC	324/925/14/615	307/1,691/20/611	147/1,177/21/556	15/35/2/63	74/106/0/103	89/447/7/284	<0.001
Child Pugh grade A/B/C	1,762/116/1	1,961/613/60	1,231/591/83	92/19/4	163/105/16	256/314/258	<0.001
mALBI grade 1/2a/2b/3	1,153/413/292/21	928/597/975/134	486/407/878/134	30/23/56/6	52/43/155/34	88/89/366/285	<0.001
Albumin grade 1/2a/2b/3	1,050/488/302/39	826/685/961/162	413/532/808/152	26/39/38/12	51/65/131/37	70/130/390/238	<0.001
BCLC stage 0/A/B/C/D	331/1,124/268/148/7	836/1,385/222/101/88	92/755/756/195/104	0/12/47/50/6	2/28/79/157/18	15/178/111/233/290	<0.001
Tumor number	1 [1, 1]	1 [1, 2]	2 [1, 4]	5 [1, 9]	5 [2, 10]	2 [1, 5]	<0.001
Tumor size, cm	3.30 [2.10, 5.20]	1.90 [1.50, 2.50]	3.50 [2.20, 5.90]	7.70 [5.00, 11.65]	8.00 [4.80, 10.53]	5.10 [2.90, 10.00]	<0.001
Platelet count, $\times 10^4/\mu L$	15.3 [11.2, 19.8]	11.0 [7.7, 15.2]	11.2 [7.8, 17.0]	17.3 [12.3, 23.8]	15.6 [10.1, 22.8]	13.4 [8.6, 20.1]	<0.001
Prothrombin time, %	91.0 [82.0, 100.0]	82.50 [71.00, 94.00]	81.00 [69.00, 93.00]	83.50 [75.00, 94.65]	81.00 [68.00, 93.25]	72.85 [56.48, 85.45]	<0.001
Albumin, g/dL	4.0 [3.7, 4.3]	3.7 [3.3, 4.1]	3.5 [3.1, 3.9]	3.6 [3.2, 3.9]	3.4 [3.1, 3.8]	3.1 [2.7, 3.5]	<0.001
Total bilirubin, mg/dL	0.7 [0.5, 0.9]	0.8 [0.6, 1.1]	0.9 [0.6, 1.3]	0.9 [0.7, 1.3]	1.0 [0.7, 1.5]	1.4 [0.8, 2.8]	<0.001
Alpha-fetoprotein, ng/mL	10.4 [4.0, 88.6]	10.7 [4.9, 44.1]	29.1 [8.0, 235.7]	85.5 [10.9, 3,418.5]	354.9 [27.0, 13,700.3]	74.9 [8.9, 3,218.6]	<0.001
Des-gamma-carboxy prothrombin, mAU/mL	74.5 [24.0, 727.8]	29.0 [18.0, 95.0]	237.0 [35.3, 2,216.0]	2,650.0 [234.5, 18,184.0]	7,397.0 [682.3, 41,078.5]	1,230.0 [112.0, 24,203.0]	<0.001

Data are expressed as the medians (interquartile range), or number (%).
BCLC, Barcelona Clinic Liver Cancer; BSC, best supportive care; HBV, hepatitis B virus; HCV, hepatitis C virus; mALBI, modified albumin-bilirubin; MTA, molecular targeted agent; NBNC, non-B and non-C; TACE, transcatheter arterial chemoembolization.

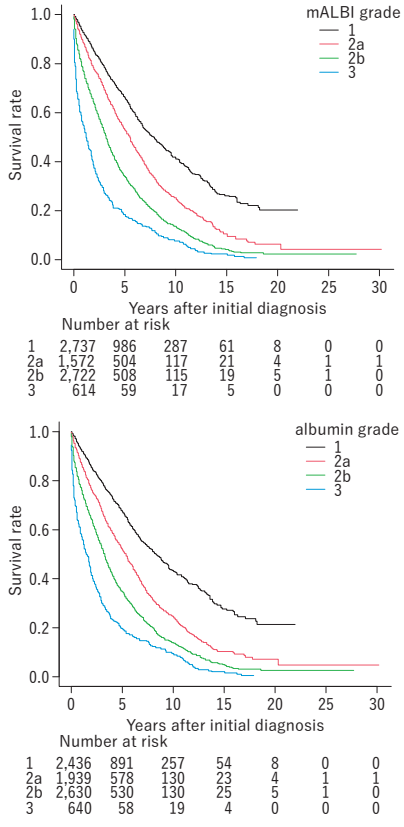

Fig. 1 Overall survival stratified by mALBI and albumin grades in all patients. Survival curves stratified by mALBI and albumin grades in all patients. The median survival times of patients with mALBI grades 1, 2a, 2b, and 3 were 7.8, 5.5, 3.2, and 1.2 years, and those of patients with the albumin grades 1, 2a, 2b, and 3 were 8.3, 5.4, 3.3, and 1.5 years, respectively. Both *p*-values were <0.001.
mALBI, modified albumin-bilirubin.

and higher likelihood ratio and C-index than the albumin grade, indicating the better performance of the mALBI grade than the albumin grade. Nevertheless, the differences in these three indices were small, and no clear difference in the Kaplan-Meier curves was observed between the mALBI and albumin grades in any of the BCLC stages.

The ability of the albumin grade in different treatments. In the analysis by treatment type (Fig. 3 and Table 5), the overall survival of patients treated with surgery was well stratified by the albumin grade, which had a lower AIC (10,036 vs. 10,067), a higher likelihood ratio (72.05 vs. 41.88), and a higher C-index (0.583 vs. 0.559) compared with the mALBI grade, indicating its superior performance to the mALBI grade. A similar relationship was observed in the ablation group, in which the albumin grade showed a lower AIC (16,175 vs. 16,178), a higher likelihood ratio (183.00 vs. 180.10), and a higher C-index (0.623 vs. 0.622) than the mALBI grade. Conversely, the overall survival of patients treated with TACE and BSC was poorly stratified by the albumin grade compared to the mALBI grade. The albumin grade showed a higher AIC and a lower likelihood ratio and C-index than the mALBI. The comparative stratification ability of the albumin grade in the MTA group showed mixed results. The AIC was high and the likelihood ratio was low for the albumin grade compared to the mALBI grade, but the C-index of the albumin grade was higher than that of the mALBI grade.

Table 4 Prognostic ability of mALBI grade and albumin grade in different BCLC stages

BCLC stage	Classification system	AIC	Likelihood ratio	C-index
0	mALBI grade	5,229	67.08	0.618
	Albumin grade	5,229	67.08	0.620
A	mALBI grade	24,244	198.70	0.599
	Albumin grade	24,208	234.00	0.604
B	mALBI grade	12,116	74.87	0.598
	Albumin grade	12,123	68.21	0.594
C	mALBI grade	6,821	55.92	0.602
	Albumin grade	6,833	43.99	0.595
D	mALBI grade	4,032	12.52	0.551
	Albumin grade	4,035	9.85	0.540
All	mALBI grade	64,506	843.80	0.648
	Albumin grade	64,529	820.70	0.643

AIC, Akaike information criterion; BCLC, Barcelona Clinic Liver Cancer; mALBI, modified albumin-bilirubin.

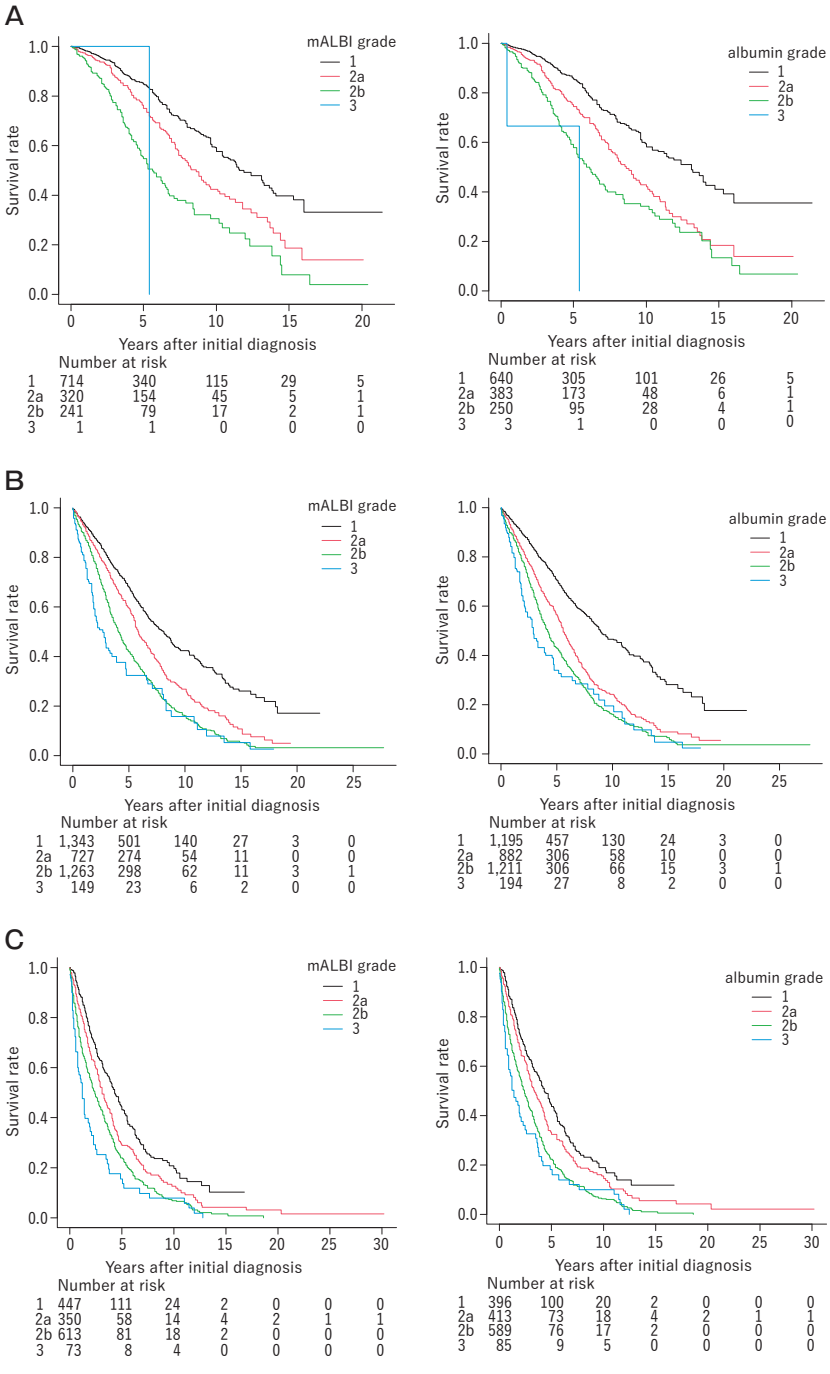

Fig. 2 Overall survival stratified by mALBI and albumin grades in different BCLC stages. Survival curves of patients at different BCLC stages stratified by the mALBI and albumin grades. Both mALBI and albumin grades showed similar curves for all BCLC stages. Analysis using the log-rank test showed that the differences were statistically significant at all stages ($p<0.05$). **A**, BCLC stage 0; **B**, BCLC stage A; **C**, BCLC stage B.
mALBI, modified albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer.

Discussion

We previously reported that the albumin grade, which relies on only one measure, the serum albumin level, was useful for predicting the outcome of LENHCC [9]. In this study, we examined the stratification ability of the albumin grade by the AIC, likelihood ratio, and C-index in patients with HCC by treatment modality and by BCLC stage. We found that the the albumin grade had better performance than mALBI grade at predicting overall survival prediction of patients at BCLC stages 0 and A HCC, while the

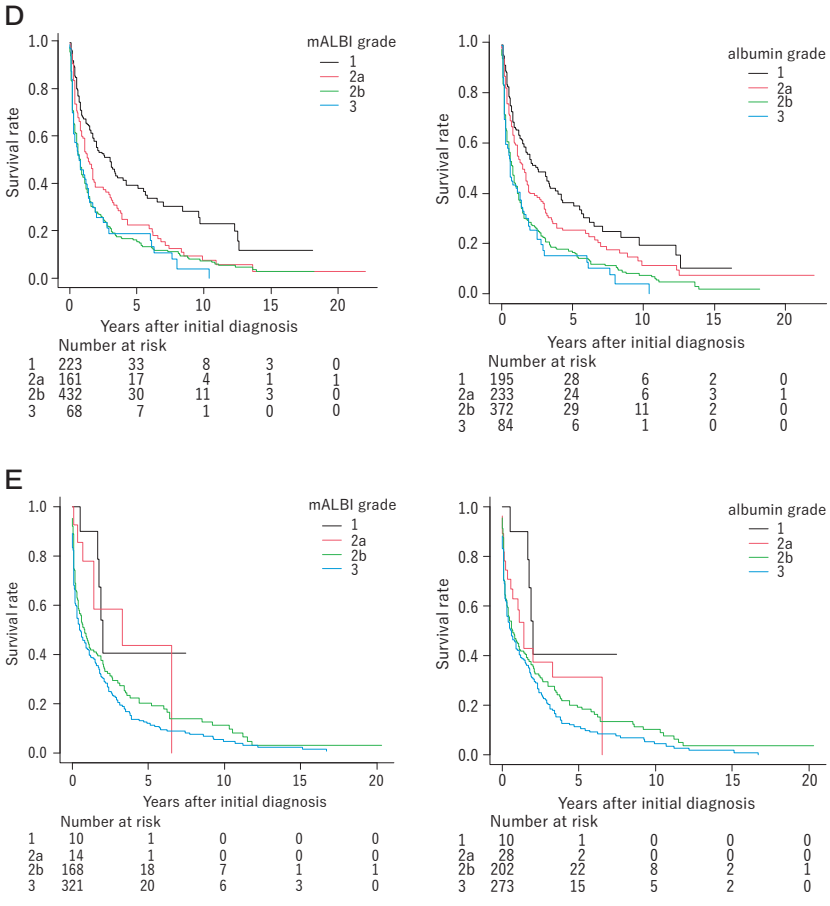

Fig. 2 Overall survival stratified by mALBI and albumin grades in different BCLC stages. Survival curves of patients at different BCLC stages stratified by the mALBI and albumin grades. Both mALBI and albumin grades showed similar curves for all BCLC stages. Analysis using the log-rank test showed that the differences were statistically significant at all stages ($p<0.05$). **D**, BCLC stage C; **E**, BCLC stage D. mALBI, modified albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer.

mALBI grade showed better stratification ability for BCLC stages B, C, and D. Additionally, the albumin grade performed better than the mALBI grade in patients who underwent surgery and ablation, whose liver function was generally good and whose T.Bil levels were still low. Although the ability of the albumin grade was lower in patients treated with TACE and BSC, whose liver function was generally poor, the differences in the three indices between the albumin grade and the mALBI grade were very small, indicating that the albumin grade is sufficient for predicting the outcome of HCC in most patients. The mALBI grade has been used based on the premise that both albumin and bilirubin are necessary factors for predicting prognosis. However, this study demonstrates that albumin alone can provide sufficient prognostic accuracy, depending on the patient profile.

Although both albumin and T.Bil are related to the prognosis of HCC, albumin has a greater impact. The interquartile range of albumin levels was 3.2-4.1, with a median of 3.7, and the interquartile range of bilirubin levels was 0.6-1.2, with a median of 0.8. Using these values, we compared the influence of albumin and T.Bil on the mALBI grade. When the albumin level was constant at the median value of 3.7 g/dL and the T.Bil levels were 0.6, 0.8, and 1.2 mg/dL, ALBI scores were −2.48, −2.40, and −2.28, respectively. All of them were classified as mALBI grade 2a, indicating that T.Bil level had a very minor influence on the mALBI grade in most patients. On the other hand, when the T.Bil level was constant at the median value of 0.8 mg/dL and the albumin levels were 3.2, 3.7, and 4.1 g/dL, the ALBI scores were −1.97, −2.40, and −2.74, and the corresponding mALBI grades were 2b, 2a, and 1, respectively. These results indicate that albumin has a greater impact on the calculated mALBI grade than T.Bil does. In particular, our clinical analysis found albumin to be a good prognostic measure in the surgery and ablation groups,

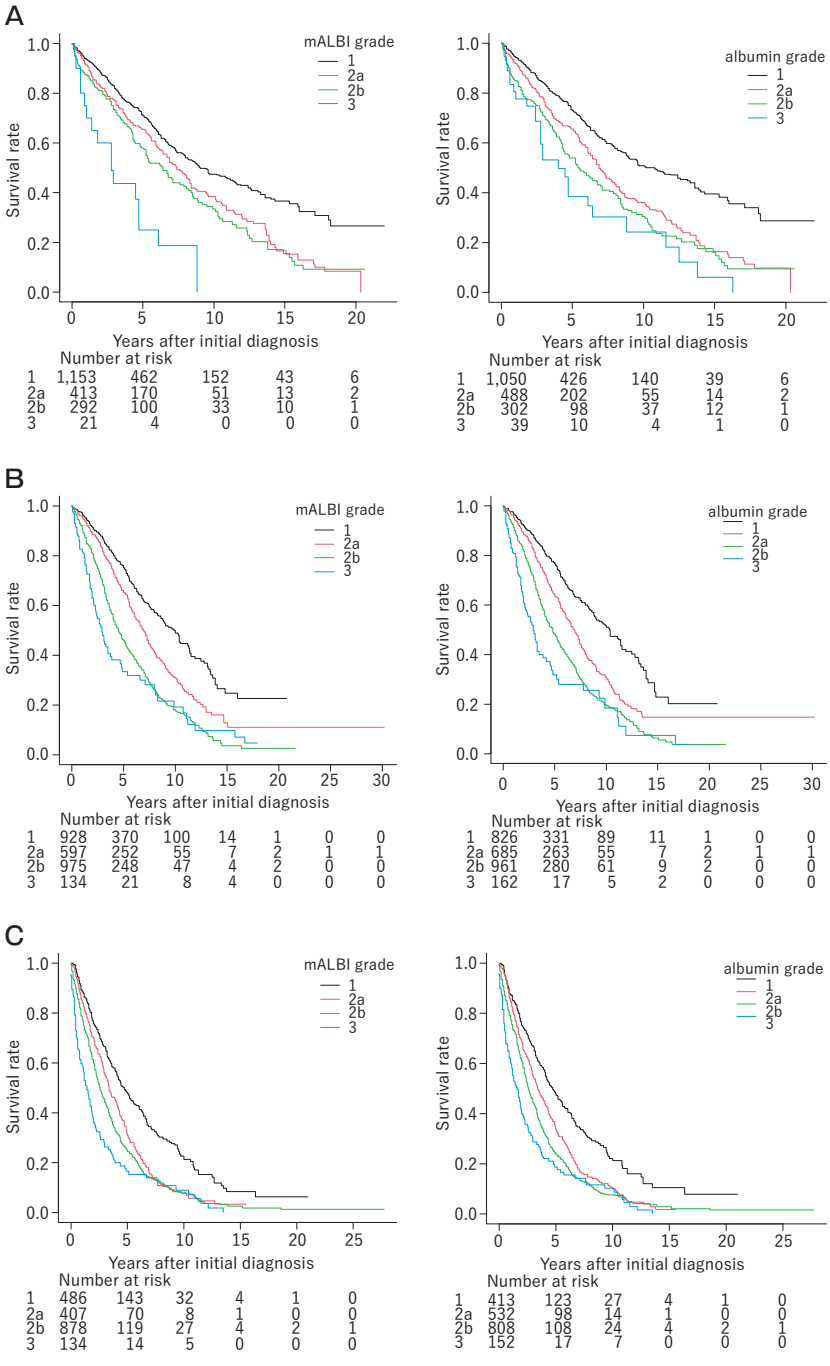

Fig. 3 Overall survival stratified by the mALBI and albumin grades in different treatment modalities. Survival curves stratified by mALBI and albumin grades for HCC patients by treatment modality. Both the mALBI and albumin grades showed similar curves for all treatments. Analysis using the log-rank test showed that the differences were statistically significant at all stages ($p<0.05$). **A**, surgery; **B**, ablation; **C**, transcatheter arterial chemoembolization.
mALBI, modified albumin-bilirubin.

whose frequencies of high-level T.Bil were low.

Elevated T.Bil levels are frequently observed in Gilbert's syndrome, particularly during fasting [13]. This level sometimes increases to 5 mg/dL. This syndrome affects 3-7% of the population, indicating that evaluating prognosis based on bilirubin levels is difficult for a considerable number of patients [14]. This is one of the reasons why the albumin grade is superior to the mALBI grade in BCLC stages 0 and A and in cases of surgery, ablation, and some MTA. In contrast, patients with HCC treated with TACE or BSC often have high T.Bil levels (Table 3). Therefore, the mALBI

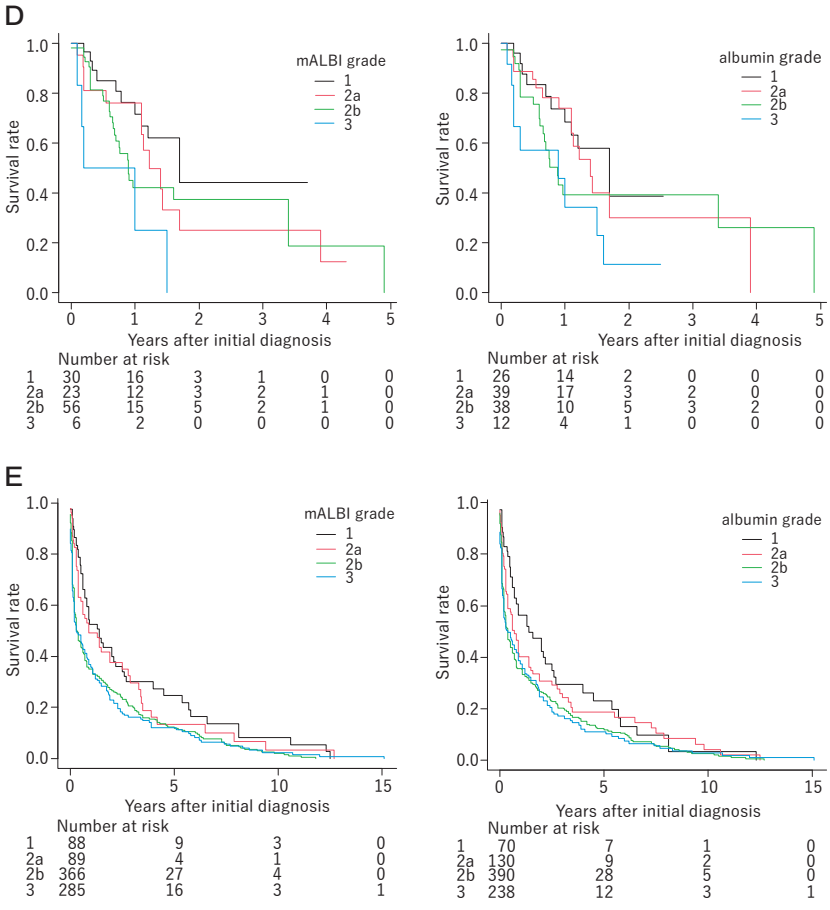

Fig. 3 Overall survival stratified by the mALBI and albumin grades in different treatment modalities. Survival curves stratified by mALBI and albumin grades for HCC patients by treatment modality. Both the mALBI and albumin grades showed similar curves for all treatments. Analysis using the log-rank test showed that the differences were statistically significant at all stages ($p<0.05$). **D**, molecular targeted agent; **E**, best supportive care. mALBI, modified albumin-bilirubin.

Table 5 Prognostic ability of mALBI grade and albumin grade in different treatments

Treatment	Classification system	AIC	Likelihood ratio	C-index
Surgery	mALBI grade	10,067	41.88	0.559
	Albumin grade	10,036	72.05	0.583
Ablation	mALBI grade	16,178	180.10	0.622
	Albumin grade	16,175	183.00	0.623
TACE	mALBI grade	16,254	103.10	0.597
	Albumin grade	16,264	93.69	0.591
MTA	mALBI grade	452	5.83	0.604
	Albumin grade	453	4.10	0.609
BSC	mALBI grade	6,689	19.57	0.574
	Albumin grade	6,697	11.39	0.558

AIC, Akaike information criteria; BSC, best supportive care; mALBI, modified albumin-bilirubin; MTA, molecular targeted agent; TACE, transcatheter arterial chemoembolization.

grade, which considers T.Bil, showed better stratification performance in patients treated with TACE and BSC than the albumin grade, although the differences were small. For evaluating the prognosis of patients with good liver reserve undergoing surgery or RFA, the bilirubin index is unnecessary, and the albumin grade alone is sufficient. However, for patients for whom TACE or chemotherapy are options, the mALBI grade,

which includes bilirubin, may be somewhat more useful for prognostic purposes.

This study had several limitations. First, this was a retrospective study that only used data from Japan. Second, the frequency of Child-Pugh grade C was only 5.5% (n = 422) in this study; therefore, it was insufficient to evaluate the ability of the albumin grade in patients with poor liver function, such as BSC. Furthermore, the stratification ability of the albumin grade in patients treated with molecular-targeted anticancer agents (atezolizumab and bevacizumab, durvalumab, tremelimumab, *etc.*) [15-18] was not sufficiently analyzed because this database only dealt with newly diagnosed HCC. Most patients receive more conventional treatments before using these drugs.

Nevertheless, our analysis of our large Japanese cohort suggests that HCC prognosis can be evaluated with the albumin grade alone in most scenarios, especially in patients with early-stage HCC who are candidates for curative treatment. An examination of the prognostic value of the albumin grade in an international cohort is desirable in the future.

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