Review

Newly Proposed ALBI Grade and ALBI-T Score as Tools for Assessment of Hepatic Function and Prognosis in Hepatocellular Carcinoma Patients

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Keywords

Hepatocellular carcinoma · Albumin-bilirubin grade · ALBI-T score · Child-Pugh classification · Prognosis · Modified ALBI grade

Abstract

Background: Because of the rapid progression of antiviral treatment options and the increasing frequency of nonviral-related hepatocellular carcinoma (HCC) due to the aging of society, the number of HCC patients with good hepatic function has been increasing and a more detailed method of assessment of hepatic function is needed. The Child-Pugh classification (CP) is used worldwide as an assessment tool for hepatic reserve function, even though it has some weaknesses. Recently, the albumin-bilirubin (ALBI) grade, calculated based on only albumin and total bilirubin, was proposed, and recent investigations have suggested that ALBI grade instead of CP can be used as an assessment tool for hepatic function as part of therapeutic strategies such as Barcelona Clinic Liver Cancer staging and a practical guideline presented by the Japan Society of Hepatology as well for total staging scoring systems. There has been an increasing number of reports showing that it has better capability than CP for HCC patients who undergo not only curative but also palliative treatments. Transcatheter arterial chemo-embolization (TACE) is a major palliative treatment used for unresectable HCC, and the idea of TACE-refractory status has been proposed to indicate the possibility of switching to a tyrosine kinase inhibitor (TKI). However, TKI administration requires a maintained hepatic reserve function, thus the importance of assessment of hepatic function in patients undergoing TACE treatments has increased. We consider that ALBI grade might also play a significant role as part of a detailed assessment of relative changes in hepatic function during treatment. In

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this review, we evaluate the practical usefulness of ALBI grade for assessing hepatic function and HCC prognosis. **Key Message:** A detailed assessment of hepatic function is required for recent HCC therapeutic strategies. ALBI grade may be a powerful tool to improve treatment options for affected patients.

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Introduction

Liver cancer, which is nearly always hepatocellular carcinoma (HCC), has been reported to be the sixth-most common cancer and third-most common cause of cancer death worldwide [1]. It is well known that the prognosis of affected patients is dependent on tumor burden and hepatic reserve function [2]. With recent progress in the development of antiviral therapies (e.g., direct-acting antivirals against hepatitis C virus [3, 4], nucleoside analogs against hepatitis B virus [5–8]) and the increase in cases of nonviral HCC associated with the aging of society [9], hepatic reserve function in HCC patients has steadily improved [10–14]. In addition, the development of imaging (e.g., contrast-enhanced ultrasonography [15] and gadolinium ethoxybenzyl diethylenetriamine penta-acetic acid-enhanced MRI [EOB-MRI] [16]) and treatment modalities (e.g., radiofrequency ablation [RFA] [17, 18], and the administration of sorafenib [19, 20], regorafenib [21], and lenvatinib [22]) have made it possible to diagnose HCC at an earlier stage, resulting in improved prognosis. On the other hand, though the Child-Pugh classification (CP) [23] has become a standard evaluation tool used for hepatic reserve function worldwide, a more effective method is required according to the recent clinical trend.

The CP has some weaknesses including subjective factors (ascites and encephalopathy) as well as interrelated factors (serum albumin and ascites), and it was not established statistically. On the other hand, a simple and statistical evaluation method for hepatic function, the albumin-bilirubin (ALBI) grade, which is calculated using only serum albumin and total bilirubin [$(\log_{10} \text{bilirubin (in } \mu\text{mol/L)} \times 0.66) + (\text{albumin (in g/L)} \times -0.085)$: grades 1, 2, 3 = ≤ -2.60 , < -2.60 to ≤ -1.39 , > -1.39 , respectively] was recently proposed [24].

Several treatment algorithms and total scoring systems for HCC have been proposed to improve patient outcome, many of which use CP (Table 1). This study was conducted to review the evidence supporting the use of ALBI grade for such algorithms and systems and the treatment of HCC patients.

ALBI Grade for Treatment Algorithms

Various studies that attempted to use ALBI grade with existing HCC treatment algorithms have been reported (Table 2). Along with the Barcelona Clinic Liver Cancer staging (BCLC) [25, 26], used as a treatment algorithm for HCC in western countries, CP is utilized for assessing hepatic reserve function. Chan et al. [27] demonstrated that the overall prognostic performance of ALBI grade-based and CP-based BCLC was similar, as they were highly concordant with a weighted κ value of 0.917, as noted in a multicenter cohort ($n = 3,696$). Pinato et al. [28] reported that the prognostic performance of ALBI grade is particularly appealing for intermediate-stage disease (BCLC-B), in which it is a widely generalizable biomarker able to overcome the survival heterogeneity of BCLC-B cases. Other recent studies have proposed subgrading for BCLC-B, because of its heterogeneous characteristic [29, 30]. The modified intermediate liver cancer criteria (MICAN), a subgrading for BCLC-B using the ALBI grade, have also been proposed; compared to the other systems examined, they show a good ability

Table 1. Previously proposed treatment algorithms and total scoring systems for HCC

	Liver factors	HCC factors	Other factors	First author [Ref.]	Year
Treatment algorithm					
BCLC	CP/portal hypertension	tumor size and number, PVTT	PS	Llovet [25] Forner [26]	1999 2018
Bolondi's BCLC-B subgrading	CP score	up to 7 criteria	PS	Bolondi [29]	2012
Kinki criteria for BCLC-B subgrading	CP score	up to 7 criteria	none	Kudo [30]	2015
MICAN criteria for BCLC-B subgrading	ALBI	up to 7 criteria	none	Hiraoka [31]	2016
JSH guidelines	CP/LD	tumor size and number (intrahepatic venous invasion and EHM)	none	Kokudo [32]	2015
APASL guidelines	CP	tumor size and number, macrovascular invasion, EHM	none	Omata [91]	2017
HKLC	CP	tumor size and number, intrahepatic venous invasion	PS	Yau [92]	2014
Total scoring system					
Okuda	albumin, bilirubin, ascites	tumor morphology (uninodular and extension ≤50%, multinodular and extension ≤50%, massive or extension >50%), PVTT	none	Okuda [35]	1985
CLIP	CP	tumor size (</≥50% of liver), PVTT	AFP	CLIP [36]	1998
JIS	CP	TNM of LCSGJ	none	Kudo [2]	2003
m-JIS	LD	TNM of LCSGJ	none	Nanashima [39] Ikai [40]	2004 2006
bm-JIS	CP	TNM of LCSGJ	AFP, AFP-L3, DCP	Kitai [38]	2008
Tokyo	albumin, bilirubin	tumor size and number	none	Tateishi [37]	2005
BALAD	albumin, bilirubin	none	AFP, AFP-L3, DCP	Toyoda [41, 43]	2006, 2017
BALAD-2	albumin, bilirubin	none	AFP, AFP-L3, DCP	Berhane [42] Toyoda [43]	2016 2017
GALAD	none	none	AFP, AFP-L3, DCP, age, sex	Caviglia [44]	2016
ALBI-T	ALBI	TNM of LCSGJ	none	Hiraoka [49]	2016
m-ALBI-T	m-ALBI	TNM of LCSGJ	none	Hiraoka [14, 50]	2018, 2017

HCC, hepatocellular carcinoma; BCLC, Barcelona Clinic Liver Cancer staging; PS, ECOG performance status; CP, Child-Pugh classification; PVTT, portal-vein tumor thrombosis; MICAN, modified intermediate stage of liver cancer criteria; JSH, Japan Society of Hepatology; LD, liver damage classification; APASL, Asia-Pacific Association for the Study of the Liver; HKLC, Hong Kong Liver Cancer classification system; CLIP, Cancer of the Liver Italian Program; JIS, Japan Integrated Staging score; EHM, extrahepatic metastasis; LSCGJ, Liver Cancer Study Group of Japan; m-JIS, modified JIS; bm-JIS, biomarker combined JIS; AFP, α -fetoprotein; AFP-L3, fucosylated AFP; DCP, des- γ -carboxy prothrombin; BALAD, bilirubin, albumin, AFP-L3, AFP, and DCP model; ALBI, albumin-bilirubin grade; ALBI-T, ALBI-TNM of LSCGJ score; m-ALBI, modified ALBI grade; m-ALBI-T, mALBI-TNM of LSCGJ score.

Table 2. Reports comparing ALBI grade and CP using the existing HCC treatment algorithm

	Study area	Patients, <i>n</i>	Outcome	First author [Ref.]	Year
BCLC	China	3,696	C index ALBI vs. CP: 0.750 vs. 0.750	Chan [27]	2016
BCLC	International research	2,426	C index ALBI vs. CP: 0.68 vs. 0.56	Pinato [28]	2017
BCLC-B subgrade	Japan	754 (all patients) 396 (treated with TACE)	AIC MICAN [31] vs. Bolondi [29] vs. Kinki [30]: 990.5 vs. 993.0 vs. 1,001.4 MICAN vs. Bolondi vs. Kinki: 508.7 vs. 512.0 vs. 514.1	Hiraoka [31]	2016
JSH guideline	Japan	3,495	AIC ALBI vs. LD vs. CP: 22,291.8 vs. 22,379.6 vs. 22,392.1	Hiraoka [34]	2017

HCC, hepatocellular carcinoma; ALBI, albumin-bilirubin grade; BCLC, Barcelona Clinic Liver Cancer staging; CP, Child-Pugh classification; MICAN, modified intermediate stage of liver cancer criteria; AIC, Akaike's information criterion; JSH, Japan Society of Hepatology; LD, liver damage classification.

to stratify the prognoses of all BCLC-B patients including those treated with transcatheter arterial chemoembolization (TACE) [31].

On the other hand, the evidence-based clinical practice guideline for HCC developed by the Japan Society of Hepatology (JSH) [32] uses CP and the liver damage classification (LD) based on the rate of indocyanine green retention at 15 min (ICG-R15) [33]. A recent report noted that the assessment ability of hepatic reserve function shown by ALBI grade was adequate for use in the JSH guideline instead of CP and LD [34]. Nevertheless, a prospective validation study to confirm the possibility of ALBI as a tool for assessing hepatic reserve function should be performed.

ALBI Grade for Total Prognostic Scoring System and Prognostic Value with Each Therapeutic Modality

Various total scoring systems have been proposed to predict the prognosis of HCC and have been found useful for comparing therapeutic results from different institutions as well as therapeutic modalities. The first system introduced to combine tumor burden and hepatic function was the Okuda staging system [35], which had become accepted worldwide. Subsequently, Cancer of the Liver Italian Program score (CLIP) [36], Japan Integrated Staging score (JIS) [2], Tokyo score [37], biomarker JIS (bm-JIS) [38], and modified JIS (m-JIS) with LD [39, 40] were proposed, and include similar factors like tumor burden and hepatic function. On the other hand, some unique systems that do not use tumor or hepatic function factors have also been reported, including BALAD [41], BALAD-2 [42, 43], and GALAD [44] (Table 1). Of these, CLIP is widely used in western countries and the JIS in Japan. HCC is often a smaller tumor when diagnosed in Japan than in other countries, due to the good performance of HCC surveillance. As a result, the tumor node metastasis (TNM) staging presented by the Liver Cancer Study Group of Japan (LCSGJ) [45] is suitable for HCC practice in Japan. The reason

Table 3. Prognostic scoring systems using ALBI grade

Original scoring system	Study area	Patients, <i>n</i>	Outcome	First author [Ref.]	Year
CLIP	Taiwan	142	AIC ALBI vs. CP: 995.0 vs. 1,001.1	Shao [47]	2016
CLIP	China	1,973	AIC ALBI vs. CP: 15,493.47 vs. 15,534.28	Chan [48]	2017
JIS	Japan	2,584	OS of ALBI-T superior to that of JIS for each corresponding score (≤ 3)	Hiraoka [49]	2016
JIS	China	1,222 (HBV-related HCC)	AIC ALBI vs. CP: 9,836.57 vs. 9,880.23	Chan [51]	2016
JIS	Japan	46,681 (all patients) 18,886 (patients treated curatively)	AIC ALBI vs. CP vs. m-ALBI: 256,952.4 vs. 256,356.7 vs. 256,955.5 ALBI vs. CP vs. m-ALBI: 57,365.5 vs. 57,416.3 vs. 57,133.3	Hiraoka [50]	2017

CLIP, Cancer of the Liver Italian Program; ALBI, albumin-bilirubin grade; CP, Child-Pugh classification; AIC, Akaike's information criterion; JIS, Japan Integrated Staging score; m-ALBI, modified ALBI grade; HBV, hepatitis B virus; HCC, hepatocellular carcinoma.

for the good acceptance of the JIS (which uses the TNM staging of LCSGJ) by Japanese institutions is because of its stratification ability and prognostic predictive power, which are considered better than for CLIP score and more suitable for Japanese HCC patients [46]. Although the m-JIS, which uses LD, was initially expected to have greater prognostic predictive power, opportunities for its use have been limited when compared to JIS due to a weakness, i.e., the requirement of an ICG injection for obtaining ICG-R15 results. A more detailed evaluation method for patients with good hepatic function is needed, as the frequency of patients with better hepatic reserve function has recently shown an increasing trend in Japan [10–14].

Based on such clinical needs, the ALBI score/grade was developed by an international study group [24]. It has been reported that the concordance index for a modification of CLIP with ALBI grade (ALBI-CLIP) was higher than CLIP alone, so ALBI-CLIP might provide improved prognosis prediction for advanced HCC cases [47, 48]. On the other hand, an m-JIS with ALBI grade (ALBI-T score) has also been proposed [49]. Analysis of nationwide survey data obtained in Japan showed that median survival time (MST) determined with ALBI-T score was always superior to that obtained with the corresponding scores of JIS and m-JIS, while Akaike's information criterion (AIC) for ALBI-T score was superior to JIS and m-JIS with LD, especially in early stage HCC cases treated in a curative manner (41,054.6, 41,107.9, and 41,094.1, respectively) [50]. Chan et al. [51] also reported the results of a validation study of ALBI-T score for patients infected with hepatitis B virus (Table 3). It is considered that ALBI grade may have a good performance for assessing hepatic reserve function when used in total staging scoring systems.

Table 4. Prognostic predictive power of ALBI grade compared with others for overall survival

Therapeutic modality	Study area	Patients	Outcome	First author [Ref.]	Year
Resection	China	1,242	3-year survival rate CP-A vs. CP-B: 63.0 vs. 53.0% ($p = 0.055$); ALBI 1 vs. ALBI 2: 68.0 vs. 52.5% ($p < 0.001$)	Wang [52]	2016
Resection	Taiwan	491	MST ALBI 1 vs. ALBI 2: 62 vs. 37 months ($p = 0.001$); CP score 5 vs. CP score 6: 57 vs. 36 months ($p = 0.235$) AIC ALBI vs. CP: 4,768.84 vs. 4,778.16	Li [53]	2017
Resection	China	318	AUC for predicting OS ALBI vs. CP: 0.650 vs. 0.511 ($p = 0.009$)	Ma [54]	2016
RFA	Korea	368	HR of multivariate analysis for OS ALBI 2: 2.32 (95% CI 1.35–3.99, $p = 0.002$); CP-B: 1.14 (95% CI 0.63–2.06, $p = 0.66$)	Oh [58]	2017
TACE	International team	3,030	C-index and AIC ALBI vs. CP: 0.5661 vs. 0.5586 and 26,963.33 vs. 26,548.21, respectively	Waked [63]	2017
TACE	Taiwan	881	AIC ALBI vs. CP: 8,094.296 vs. 8,111.090	Ho [64]	2017
Sorafenib	Japan	282 (CP score 5) 77 (BCLC-B)	MST ALBI 1 vs. ALBI 2: 17.5 vs. 9.9 months ($p = 0.010$) ALBI 1 vs. ALBI 2: 17.5 vs. 10.0 months ($p = 0.039$)	Hiraoka [65]	2017

ALBI, albumin-bilirubin grade; CP, Child-Pugh classification; MST, median survival time; AIC, Akaike's information criterion; AUC, area under the curve; OS, overall survival; RFA, radiofrequency ablation; HR, hazard ratio; CI, confidence interval; TACE, transcatheter arterial chemoembolization; BCLC-B, Barcelona Clinic Liver Cancer stage B.

Prognosis Prediction Ability of ALBI Grade in Curative and Palliative Treatment

Curative Treatment

ALBI grade predicts overall survival (OS) more accurately than CP in patients with HCC who undergo hepatic resection [52–54]. Moreover, some studies have reported that it had a better performance than CP, the model for end-stage liver disease (MELD) score, and the ICG-R15 for the prediction of posthepatectomy liver failure [52, 55–57]. Similarly, the prognostic predictive value of ALBI grade has been reported as being better than CP in cases that receive RFA [58]. Other studies have proposed the development of a nomogram based on ALBI grade and other clinical data for predicting the 2- and 5-year survival of patients with recurrence after a hepatectomy [59] as well as assess the long-term outcomes of RFA for early-stage HCC [60].

Palliative Treatment

In patients who receive palliative treatment, such as transarterial locoregional therapy (transcatheter arterial chemoembolization [TACE] or radioembolization), ALBI grade has

also shown a good prognostic predictive ability [61, 62] and been used to categorize patients receiving TACE for BCLC-B HCC [63]. Furthermore, Ho et al. [64] reported that ALBI grade showed a higher level of homogeneity and the lowest AIC value when compared to CP and MELD in patients who underwent TACE. In sorafenib-treated HCC patients, it was shown to be a better tool than CP for assessing hepatic function [65]. In fact, with each type of treatment, ALBI grade has been shown to be superior for the assessment of hepatic function (Table 4).

ALBI Grade for Treatment Selection in Curative Treatment

A few studies have investigated whether ALBI grade can be used for patient selection for available treatment modalities. Chong et al. [66] compared hepatic resection and RFA after propensity score-matching in BCLC-0/A HCC patients with an ALBI grade of 1 and reported that hepatic resection showed superior OS and disease-free survival of patients who underwent RFA ($p < 0.001$, respectively). In another study that compared hepatic resection with microwave ablation (MWA), patients with ALBI grade 1 who underwent the former had better overall and disease-free survival rates, while the latter resulted in significantly better OS in those with ALBI $\geq$ grade 2 [67].

Based on these findings, it is considered that ALBI grade might be able to identify patients with better hepatic function who would obtain a survival benefit by undergoing resection as well as those who would not benefit due to worse hepatic function. In a retrospective analysis of the indicators of RFA for HCC (<3 cm and ≤ 3 tumors), there was only a slight therapeutic efficacy for improving prognosis following RFA in ALBI grade 3 cases [68]. Furthermore, Ogasawara et al. [69] noted that sorafenib may be indicated for all patients with unresectable HCC and classified ALBI grade 1, and for some with ALBI grade 2. On the other hand, King et al. [70] reported that patients with ALBI $\geq$ grade 2 or CP-B seemed to derive limited therapeutic benefit from sorafenib treatment. Thus, ALBI grade may play a considerable role in determining treatment modality in current HCC practice, when considering the risks and benefits of the various treatments available.

ALBI Grade for the Assessment of Hepatic Reserve Function in the Era of Multiple Tyrosine Kinase Inhibitors

TACE is performed worldwide as a standard therapy for BCLC-B HCC [26, 71]. Recently, tyrosine kinase inhibitors (TKIs) were developed [19, 21, 22, 72], and the criteria for determining TACE-refractory status used to judge the efficacy of switching to a TKI [73, 74] hypothesized that it would prolong the prognosis of unresectable HCC patients, but the maintenance of hepatic reserve function is also important for the safe use of TKIs. Although some prognostic prediction methods for patients treated with TACE have been presented [75–80], no study has examined TACE-refractory strategies from the view of a relative decline in hepatic reserve function during repeated TACE. A recent report noted that a negative relative change in hepatic reserve function during repeated TACE procedures for BCLC-B HCC was more easily detected with ALBI grade than with CP [65]. Of course, adequate determination of TACE-refractory status is recognized as important for improving the prognosis of patients with unresectable HCC.

Although the TACE-refractory criteria items used in Japan include imaging findings and tumor markers, most clinicians ($>80\%$) judge TACE-refractory patients based on response shown by imaging findings, while only a small percentage (10.3%) use tumor marker findings as a reference [73]. The clinical items included in the Japanese criteria for TACE-refractory

Fig. 1. TACE-refractory with ALBI grade, tumor markers, and imaging findings algorithm. Possibility of complementary therapeutic strategy using ALBI grade so as to not lose the chance for switching to a TKI in BCLC-B HCC patients treated with TACE. ALBI, albumin-bilirubin; TKI, tyrosine-kinase inhibitor; BCLC-B, intermediate stage of Barcelona Clinic Liver Cancer; TACE, transcatheter arterial chemoembolization; TTTP, time to TACE progression; HAIC, hepatic arterial infusion chemotherapy; SD, stable disease; PD, progressive disease.

status have ambiguities, including some with no cut-off value of tumor markers. In examinations prior to treatment and after starting TACE, tumor marker score derived from marker levels has been reported to be predictive of a poor response and prognosis in BCLC-B patients with CP-A undergoing treatment with TACE (positive for each of α -fetoprotein [AFP] ≥ 100 ng/mL, fucosylated AFP [AFP-L3] $\geq 10\%$, and des- γ -carboxy prothrombin [DCP] ≥ 100 mAU/mL = a “tumor marker score” of 1 point; the response to TACE is expected to be very poor in patients with ≥ 2 points) [78, 81].

After starting TACE, even a slight enlargement noted from imaging findings (contrast-enhanced computed tomography [CECT] or EOB-MRI) is indicative of a risk of a rapid decline in OS (sum of maximum diameters of each viable area of the 5 largest tumors on follow-up imaging after the 1st TACE as baseline is compared to imaging findings [CECT or EOB-MRI] obtained after each TACE; a ratio >1.2 is considered as “time to TACE progression [TTTP]”) [79, 80]. Indeed, we have often encountered cases in which therapeutic response noted from imaging findings is recognized as stable disease (SD), in spite of no decline in tumor marker levels, and rapid progression as a result of additional TACE procedures has been observed [78]. An additional procedure after attaining a TACE-refractory status is not only less effective for preventing tumor progression but also has a harmful influence on hepatic reserve function.

Although CP-A status is an indispensable condition with TKI treatment, the hazard ratio (HR) for ALBI grade 2 is higher than grade 1, with regard to OS, in CP-A patients treated with sorafenib (HR 1.68, 95% CI 1.43–1.97, $p < 0.001$) [82]. Moreover, for those treated with sorafenib with a CP score of 5, the prognosis for ALBI grade 1 (among all patients) and BCLC-B patients was better than for ALBI grade 2 patients (MST: 17.5 vs. 9.9 months and 17.5 vs. 10.0

months, respectively; $p = 0.01$ and $p = 0.039$, respectively) [65]. Kuo et al. [83] reported that patients with ALBI grade 1 at the start of sorafenib treatment had a better prognosis than those with ALBI grade 2 (MST 8.5 vs. 4.4 months, $p = 0.003$). ALBI grade 2 at the start of sorafenib therapy and a worsening ALBI grade during treatment were strong prognostic factors for mortality ($p < 0.001$). In this era of multiple TKI options, second-line treatment is available when sorafenib treatment fails, and the importance of a detailed assessment of hepatic reserve function has grown. Indeed, ALBI grade has been reported to play a significant prognostic role in OS after sorafenib therapy in patients eligible for second-line therapy (MST for ALBI grades 1, 2, and 3: 17.5, 7.5, and 1.9 months, respectively; $p < 0.001$) [84].

In addition to evaluating imaging findings [79, 80] and tumor marker levels [78], a detailed assessment of a negative change in hepatic reserve function while undergoing TACE procedures is also important for judging TACE-refractory status adequately, so as to not miss the opportunity to switch to a TKI and gain its possible therapeutic efficacy (Fig. 1). Recently, Lee et al. [85] proposed ALBI progressive disease (PD) criteria for BCLC-C patients treated with sorafenib by using 3 factors to consider a second-line trial or salvage therapy (ALBI grade 3 at PD, a new extrahepatic lesion, and early PD within 4 months). It is important for attending physicians to keep in mind the importance of maintaining hepatic reserve function during TACE for unresectable HCC in order to widen the possibility of additional therapeutic options.

Weaknesses and Potential of ALBI Grades and Perspectives for the Near Future

A weakness of ALBI grades may be that involving the prognostic predictive power of decompensated cirrhosis status. A comparison between ALBI grade and MELD performed by Khabbaz et al. [86] in patients undergoing creation of a transjugular intrahepatic portosystemic shunt due to portal hypertension complications (variceal bleeding, 55%; ascites, 35%; other, 10%), only MELD was associated with transplant-free survival, while Ronald et al. [87] reported that MELD was a better predictor than ALBI grade of both 30-day mortality and OS (C-index: 0.74 vs. 0.64 and 0.63 vs. 0.59, respectively).

On the other hand, Lo et al. [88] reported the utility of the complementary use of CP and ALBI scores to predict the risk of liver toxicity after stereotactic ablative radiation therapy against HCC (2.4% for CP-A/ALBI score < -2.76 and 15.1% for CP-A/ALBI score ≥ -2.76). Moreover, compared to CP following HCC treatment, an advantage of ALBI grade is that it is calculated by using a continuous variable (ALBI score). For example, an ALBI grade of 2 has a very wide range, similar to CP-B and should be divided into subgrades for more detailed assessment of hepatic reserve function.

Since ALBI score has a good correlation with ICG-R15 ($r = 0.563$; 95% CI 0.550–0.570; $p < 0.0001$), it could be modified to 4 grades, m-ALBI 1, 2a, 2b, and 3, using ICG-R15 results as 30% (cut-off value for ALBI score = -2.270 , AUC 0.828, 95% CI 0.823–0.833), as noted in a previous study [50]. The results of that study also showed that for each TNM stage of LCSGJ, the prognosis according to m-ALBI grade was well stratified ($p < 0.001$, respectively). As a result, it was found that m-ALBI-T score using m-ALBI grade and TNM had a better prognostic predictive ability for early-stage HCC patients who underwent curative treatment. A recent validation analysis of m-ALBI-T also showed that it had better prognostic predictive value than ALBI-T and JIS [14]. In addition, Na et al. [89] reported that ALBI grade showed better discriminative performance than CP in patients receiving curative treatment (C index: 0.667 vs. 0.624), and Dong et al. [90] showed that preoperative ALBI score was significantly related to the OS of solitary HCC patients according to the Milan criteria and CP-A status. Therefore, ALBI/m-ALBI grade may provide a more accurate assessment than CP of HCC patients, especially those treated with a curative intent.

Conclusion

There is no doubt that ALBI grade can play an important complementary role in cases of both curative and palliative treatment. Moreover, it is expected that suitable therapeutic strategies can be supplied by determining ALBI/m-ALBI grade, which comply with recent trends of care of HCC patients, especially those scheduled to undergo curative treatment. Although additional prospective analyses are needed, the newly proposed ALBI grade and ALBI-T, including m-ALBI grade and m-ALBI-T, might become powerful tools for improving the prognosis of HCC patients.

Disclosure Statement

There are no financial disclosures, grants from any organizations, conflicts of interest, and/or acknowledgements for the authors to disclose.

Author Contributions

A. Hiraoka drafted and wrote the manuscript. T. Kumada and M. Kudo reviewed and approved the final version.

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