CLINICAL STUDY

Albumin-Bilirubin and Platelet-Albumin-Bilirubin Grades Accurately Predict Overall Survival in High-Risk Patients Undergoing Conventional Transarterial Chemoembolization for Hepatocellular Carcinoma

Jan Hansmann, MD, Maximilian J. Evers, BS, James T. Bui, MD, R. Peter Lokken, MD, MPH, Andrew J. Lipnik, MD, Ron C. Gaba, MD, and Charles E. Ray, Jr, MD, PhD

ABSTRACT

Purpose: To evaluate albumin-bilirubin (ALBI) and platelet-albumin-bilirubin (PALBI) grades in predicting overall survival in high-risk patients undergoing conventional transarterial chemoembolization for hepatocellular carcinoma (HCC).

Materials and Methods: This single-center retrospective study included 180 high-risk patients (142 men, 59 y ± 9) between April 2007 and January 2015. Patients were considered high-risk based on laboratory abnormalities before the procedure (bilirubin > 2.0 mg/dL, albumin < 3.5 mg/dL, platelet count < 60,000/mL, creatinine > 1.2 mg/dL); presence of ascites, encephalopathy, portal vein thrombus, or transjugular intrahepatic portosystemic shunt; or Model for End-Stage Liver Disease score > 15. Serum albumin, bilirubin, and platelet values were used to determine ALBI and PALBI grades. Overall survival was stratified by ALBI and PALBI grades with substratification by Child-Pugh class (CPC) and Barcelona Liver Clinic Cancer (BCLC) stage using Kaplan-Meier analysis. C-index was used to determine discriminatory ability and survival prediction accuracy.

Results: Median survival for 79 ALBI grade 2 patients and 101 ALBI grade 3 patients was 20.3 and 10.7 months, respectively ($P < .0001$). Median survival for 30 PALBI grade 2 and 144 PALBI grade 3 patients was 20.3 and 12.9 months, respectively ($P = .0667$). Substratification yielded distinct ALBI grade survival curves for CPC B ($P = .0022$, C-index 0.892), BCLC A ($P = .0308$, C-index 0.887), and BCLC C ($P = .0287$, C-index 0.839). PALBI grade demonstrated distinct survival curves for BCLC A ($P = 0.0229$, C-index 0.869). CPC yielded distinct survival curves for the entire cohort ($P = .0019$) but not when substratified by BCLC stage (all $P > .05$).

Conclusions: ALBI and PALBI grades are accurate survival metrics in high-risk patients undergoing conventional transarterial chemoembolization for HCC. Use of these scores allows for more refined survival stratification within CPC and BCLC stage.

ABBREVIATIONS

ALBI = albumin-bilirubin, BCLC = Barcelona Liver Clinic Cancer, CI = confidence interval, CPC = Child-Pugh class, HCC = hepatocellular carcinoma, N/A = not applicable, PALBI = platelet-bilirubin-albumin, ^{90}Y = yttrium-90

From the Division of Interventional Radiology, Department of Radiology, University of Illinois Hospital and Health Sciences System, 1740 West Taylor Street, Chicago, IL 60612. Received March 27, 2017; final revision received May 18, 2017; accepted May 25, 2017. Address correspondence to C.E.R.; E-mail: chray@uic.edu

None of the authors have identified a conflict of interest.

Figures E1–E4 are available online at www.jvir.org.

J Vasc Interv Radiol 2017; ■:1–8

http://dx.doi.org/10.1016/j.jvir.2017.05.020

Risk stratification of patients with hepatocellular carcinoma (HCC) before locoregional therapy is paramount owing to the varying severity of underlying liver disease. A commonly used metric is the Child-Pugh scoring system. The use of interrelated and subjective variables, such as ascites and encephalopathy, limits the prognostic ability of the Child-Pugh score, particularly in patients with advanced cirrhosis and HCC. In 2015, Johnson et al (1) introduced a new tool to assess liver function, the albumin-bilirubin (ALBI) grade. This evidence-based model is solely based on laboratory parameters and has been validated in an

international cohort of Child-Pugh class (CPC) A patients with HCC from Asia, Europe, and the United States. Several other groups have since provided external validation of the ALBI grade (2,3). Further modification of the ALBI grade resulted in the platelet-bilirubin-albumin (PALBI) grade, which incorporates the blood platelet count as a surrogate marker for portal hypertension (4). ALBI and PALBI grades assess the degree of underlying liver dysfunction in patients with HCC and may be helpful in predicting mortality related to liver failure rather than tumor progression. Despite numerous external validations of the ALBI and PALBI grades, there is a paucity of data regarding their use in high-risk patients undergoing transarterial chemoembolization, and their utility in this population has not been well characterized. The purpose of this study was to assess the performance of ALBI and PALBI grades in predicting overall survival outcomes in high-risk patients undergoing conventional transarterial chemoembolization for treatment of HCC.

MATERIALS AND METHODS

Institutional review board approval was obtained for this study, which was compliant with the Health Insurance Portability and Accountability Act. This retrospective study identified patients who underwent conventional transarterial chemoembolization for HCC between April 2007 and January 2015 at a tertiary care referral center using the department of radiology picture archiving and communication system and the interventional radiology case log book. Demographic, laboratory, and imaging data were reviewed to collect baseline demographic and disease information. Diagnosis of HCC was made by established imaging criteria using National Comprehensive Cancer Network (5) and American Association for the Study of Liver Disease criteria (6) (n = 137) or biopsy (n = 43). Biopsy was performed for atypical imaging presentations to confirm the diagnosis before treatment. Patients who underwent conventional transarterial chemoembolization for HCC were included if they met at least 1 of the following risk factors previously described in the literature (7,8) before transarterial chemoembolization: serum bilirubin level > 2 mg/dL; albumin level < 3.5 mg/dL; serum platelet count < 60,000 mL; serum creatinine > 1.2 mg/dL; portal vein thrombus diagnosed on computed tomography or magnetic resonance imaging performed before the procedure; presence of ascites established on abdominal ultrasound, computed tomography, or magnetic resonance imaging; presence of hepatic encephalopathy, defined as brain dysfunction caused by liver insufficiency and/or portosystemic shunting (9); presence of transjugular intrahepatic portosystemic shunt; or Model for End-Stage Liver Disease score > 15. **Figure 1** outlines eligibility criteria for study inclusion and patient allocation, and the features of the study cohort are presented in **Table 1**. A serum albumin level < 3.5 mg/dL was used based on previously published data on high-risk patients undergoing transarterial chemoembolization (8). Using an albumin level < 3.5 mg/dL preserves the full range of abnormal albumin levels (as the 3.5 mg/dL threshold delineates the lower limit of normal albumin level), which is useful given that albumin level is an integral component in calculating both the ALBI and the PALBI scores.

Transarterial Chemoembolization

The decision to treat with conventional transarterial chemoembolization was made by an interdisciplinary tumor board consisting of hepatologists, transplant surgeons,

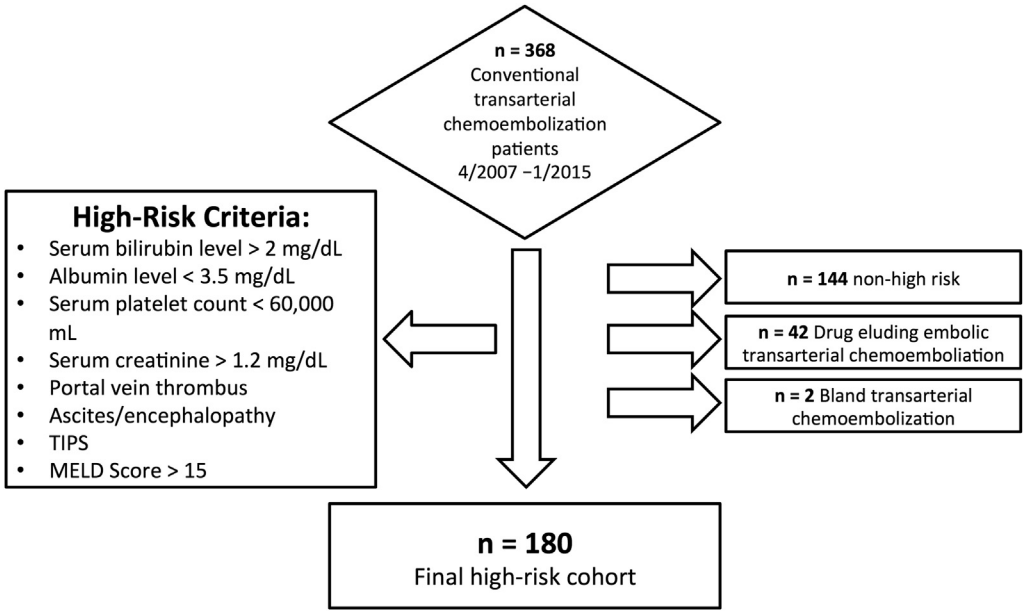

Figure 1. Flow diagram highlighting the process of patient selection and inclusion criteria for retrospective analysis. DEE = drug-eluting embolic; MELD = Model for End-Stage Liver Disease; TIPS = transjugular intrahepatic portosystemic shunt.

Table 1. Patient Baseline Characteristics

Characteristic	Value
Age, y, mean ± SD	59 ± 9
Sex, n	
Male	142
Female	38
Total	180
ECOG status, n (%)	
Grade 0	165 (92)
Grade 1	15 (8)
Risk factor, n (%)	
Bilirubin > 2 mg/dL	72 (40)
Bilirubin > 3 mg/dL	30 (17)
Albumin < 3.5 mg/dL	170 (94)
Platelet count < 60,000	39 (22)
INR > 1.5	37 (21)
Creatinine > 1.2 mg/dL	34 (19)
Ascites	34 (19)
Encephalopathy	8 (5)
TIPS	10 (6)
Portal vein thrombus	16 (9)
MELD score > 15	35 (19)
CPC, n (%)	
A	44 (24)
B	105 (58)
C	31 (18)
BCLC stage, n (%)	
0/A	68 (38)
B	53 (29)
C	27 (15)
D	32 (18)
ALBI grade, n (%)	
1	0
2	79 (44)
3	101 (56)
PALBI grade, n (%)	
1	6 (3)
2	30 (17)
3	144 (80)

ALBI = albumin-bilirubin; BCLC = Barcelona Clinic Liver Cancer; CPC = Child-Pugh class; ECOG = Eastern Cooperative Oncology Group; INR = international normalized ratio; MELD = Model for End-Stage Liver Disease; PALBI = platelet-albumin-bilirubin; TIPS = transjugular intrahepatic portosystemic shunt.

medical oncologists, and interventional radiologists based on considerations such as liver reserve, performance status, tumor size, number, stage, morphology, distribution, burden, vascularity, presence of portal vein invasion, and operator expertise and/or preference. Specifically, patients with Barcelona Liver Clinic Cancer (BCLC) stages A and C were allocated to treatment with transarterial chemoembolization if the multidisciplinary consensus deemed it reasonable as either the best treatment option given the individual patient's comorbidities or as a bridge to liver transplantation. Procedures were performed by 5 Certificate of Added Qualification–licensed interventional radiologists with a range of 2–20 years of experience. Chemoembolization was performed using combinations of cisplatin (100 mg), doxorubicin (50 mg), and mitomycin C (10 mg) with ethiodized oil (Lipiodol; Guerbet LLC, Bloomington, Indiana) using previously described technique (10,11). There were 33 procedures performed with lobar infusion. The remaining procedures (n = 147) were performed using selective or subselective catheterization.

Data Collection and Evaluation

Serum bilirubin and albumin values obtained before the procedure were used to calculate the ALBI grade using previously published criteria with linear predictor as follows: linear predictor = ($\log_{10}$ bilirubin × 0.66) + (albumin × −0.085), where bilirubin is in μmol/L and albumin is in g/L. ALBI grade was assigned using the following described ranges: ≤ −2.60 (ALBI 1), > −2.60 to ≤ −1.39 (ALBI 2), and > −1.39 (ALBI 3) (1). Serum platelet, bilirubin, and albumin values obtained before the procedure were used to calculate the PALBI grade using previously published criteria as follows: (2.02 × $\log_{10}$ bilirubin) + (−0.37 × [$\log_{10}$ bilirubin]^2) + (−0.04 × albumin) + (−3.48 × $\log_{10}$ platelets) + (1.01 × [$\log_{10}$ platelets]^2). PALBI grade was assigned using previously published ranges: ≤ −2.53 (PALBI 1), > −2.53 to −2.09 (PALBI 2), and > −2.09 (PALBI 3) (4). Laboratory values before the procedure were predominantly obtained on the day of the procedure (mean/median 0.7/0 d ± 2.7, range 0–21 d). Survival was analyzed on a per-patient basis based on the initial conventional transarterial chemoembolization procedure. Patients who underwent liver transplantation were censored at the time of orthotopic liver transplant for the purposes of survival analysis. Survival was determined by electronic medical record review and use of the US Social Security Death Index. If the date of death could not be confirmed by medical record review or use of the Social Security Death Index at the time of study truncation, patient survival was censored at the last clinic follow-up. At the time of study truncation, 41 patients (23%) had no confirmed date of death. There were 34 patients (83%) with at least a 6-month clinic follow-up and 26 patients (63%) with a 12-month clinic follow-up.

Statistical Analysis

Descriptive statistics were used to summarize data. Survival analyses were performed using log-rank and Cox regression method to compare the survival months from the date of first transarterial chemoembolization between different staging indices. ALBI and PALBI grades were calculated at baseline before the index conventional transarterial chemoembolization procedure, and survival months were measured from the time of first transarterial chemoembolization. Substratification by CPC, BCLC stage, ALBI grade, and PALBI grade was performed. The C-index, testing the concordance rate of the estimated and observed

survival results, was used to compare several survival regression models with different staging systems. Analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, North Carolina). A P value of $< .05$ was considered significant.

RESULTS

Stratification by ALBI grade identified 79 patients with ALBI grade 2 (44%), 101 patients with ALBI grade 3 (56%), and no patients with ALBI grade 1. Stratification by PALBI grade identified 6 patients with PALBI grade 1 (3%), 30 patients with PALBI grade 2 (17%), and 144 patients with PALBI grade 3 (80%). **Table 1** summarizes these findings and provides further risk factor differentiation.

Survival Outcomes by ALBI Grade

Distinct survival curves were demonstrated for ALBI grades 2 and 3 ($P < .0001$), with median survival for ALBI grade 2 patients of 20.3 months (95% confidence interval [CI], 10.5 to not applicable [N/A]), and median survival for ALBI grade 3 patients of 10.7 months (95% CI, 3.5 to 21.6 months). Survival curves are shown in **Figure 2**. Patients were then stratified by CPC and BCLC stage, with survival outcomes calculated based on ALBI grade.

Child-Pugh Class

For CPC A, all patients were ALBI grade 2, prohibiting a comparison of survival differences between ALBI grades 2 and 3. For CPC B patients, median survival was 14.7 months for ALBI grade 2 (95% CI, 9.6 to N/A) and 12.2 months (95% CI, 3.5 to 22.7 months) for ALBI grade 3 ($P = .002$, C-index 0.892) (**Fig E1** [available online at *www.jvir.org*]). For CPC C patients, median survival differences were not compared between ALBI grades because only 1 patient was stratified as ALBI grade 2, with most patients (n = 30) in ALBI grade 3, prohibiting a meaningful comparison. Median survival for CPC C, ALBI grade 3 patients was 6.9 months (95% CI, 2.9 to 10.7 months).

BCLC Stage

Patients were stratified by BCLC stage, with survival outcomes calculated based on ALBI grade. For BCLC stage A, median survival time could not be calculated for ALBI grade 2 because of the large number of patients still alive at the time of analysis (16 of 35; 46%); median survival was 21.6 months for ALBI grade 3 (95% CI, 8.4 to 29.1 months; $P = .031$, C-index 0.887) (**Fig E2** [available online at *www.jvir.org*]). For BCLC stage B, median survival was 20.1 months for ALBI grade 2 (95% CI, 11.2 to 33.9) and 12.2 months for ALBI grade 3 (95% CI, 3.5 to 17.9; $P = .079$, C-index 0.917). For BCLC stage C, median survival was 12.9 months for ALBI grade 2 (95% CI, 4.2 to N/A) and 3.5 months for ALBI grade 3 (95% CI, 2.4 to 5.2; $P = .029$, C-index 0.839) (**Fig E3** [available online at *www.jvir.org*]). For BCLC stage D, only 1 patient was stratified as ALBI grade 2, with 31 patients ALBI grade 3, prohibiting a meaningful comparison between stages.

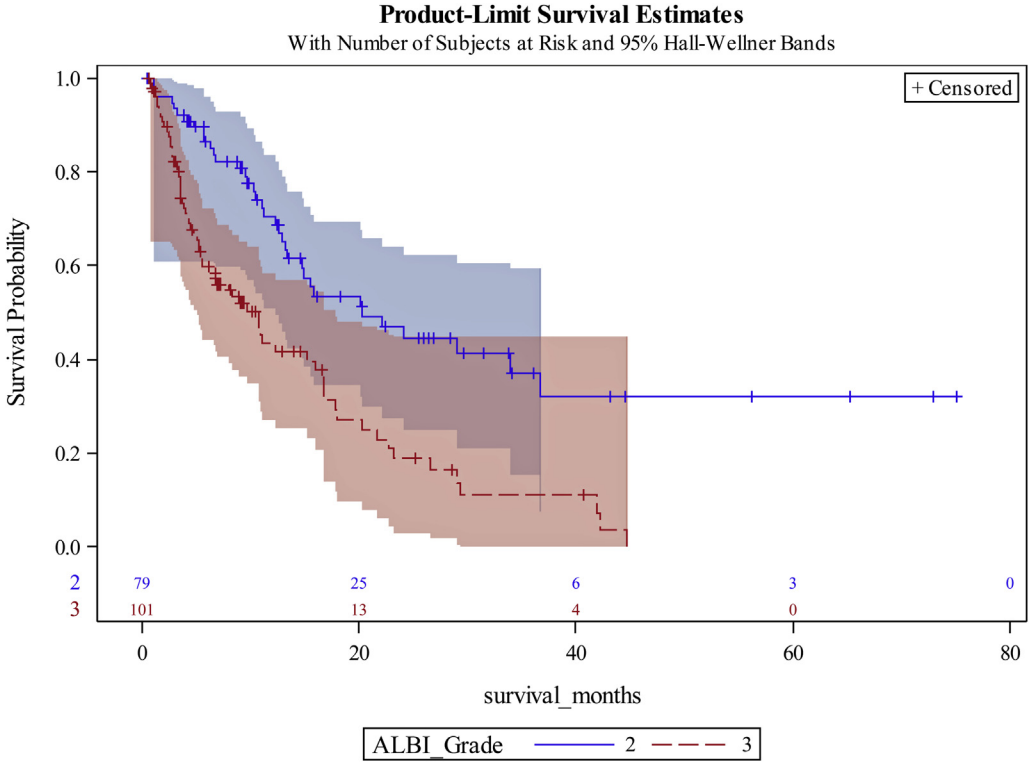

Figure 2. Overall survival after conventional transarterial chemoembolization stratified by ALBI grade ($P < .0001$).

Median survival for BCLC stage D ALBI grade 3 was 7.9 months (95% CI, 3.7 to 10.9).

Survival Outcomes by PALBI Grade

Distinct survival curves were demonstrated for all PALBI grades when the entire cohort was analyzed, although this finding did not reach statistical significance ($P = .067$) (Fig 3). Median survival for PALBI grade 1 patients was not calculated owing to the small number of patients. Median survival for PALBI grade 2 patients was 20.3 months (95% CI, 10.4 to N/A), and median survival for PALBI grade 3 patients was 12.9 months (95% CI, 4.8 to 26.6). Patients were then stratified by CPC and BCLC stage, with survival outcomes calculated based on PALBI grade.

Child-Pugh Class

Survival outcomes were not calculated for PALBI grade 1 because of the low number of patients (n = 6). For CPC A patients, median survival was 20.1 months (95% CI, 10.4 to 33.9) for PALBI grade 2 and 22.1 months (95% CI, 15.0 to 36.7) for PALBI grade 3 ($P = .632$, C-index 0.94). For CPC B patients, most patients (n = 97) were PALBI grade 3, with 6 patients in PALBI grade 2, prohibiting a meaningful comparison. Median survival for CPC B PALBI grade 3 patients was 13.3 months (95% CI, 4.8 to 26.6). For CPC C patients, all patients were PALBI grade 3 (n = 31), with a median survival of 7.9 months (95% CI, 2.9 to 10.7).

BCLC Stage

Patients were stratified by BCLC stage, with survival outcomes calculated based on PALBI grade. For BCLC stage A, median survival could not be calculated for PALBI grades 1 and 2 owing to the large number of patients still alive at the time of analysis (BCLC A, PALBI grade 1, 1 of 5 patients (20%); BCLC A, PALBI grade 2, 6 of 11 patients, 55%). Median survival was 16.8 months for PALBI grade 3 (95% CI, 9.0 to 42.3; $P = .023$, C-index 0.869) (Fig E4 [available online at www.jvir.org]). For BCLC stage B, no patients were PALBI grade 1. Median survival was 13.4 months for PALBI grade 2 (95% CI, 10.4 to 29.0) and 16.7 months for PALBI grade 3 (95% CI, 5.1 to 36.7; $P = .436$, C-index 0.968). For BCLC stage C, 1 patient with PALBI grade 1 survived 6.7 months, median survival for PALBI grade 2 was 11.1 months (95% CI, 4.2 to N/A), and median survival for PALBI grade 3 was 3.8 months (95% CI, 2.8 to 13.3; $P = .774$, C-index 0.938). For BCLC stage D, all patients were PALBI grade 3 with a median survival of 9.7 months (95% CI, 3.7 to 16.7).

Survival Outcomes by CPC

Patients were stratified by CPC, and survival outcomes were calculated. For CPC A patients, median survival was 20.3 months (95% CI, 11.1 to 36.7); for CPC B patients, median survival was 14.7 months (95% CI, 5.1 to 29.4); and for CPC C patients, median survival was 7.9 months (95% CI, 2.9 to 10.7; $P = .002$). Survival curves are shown in Figure 4.

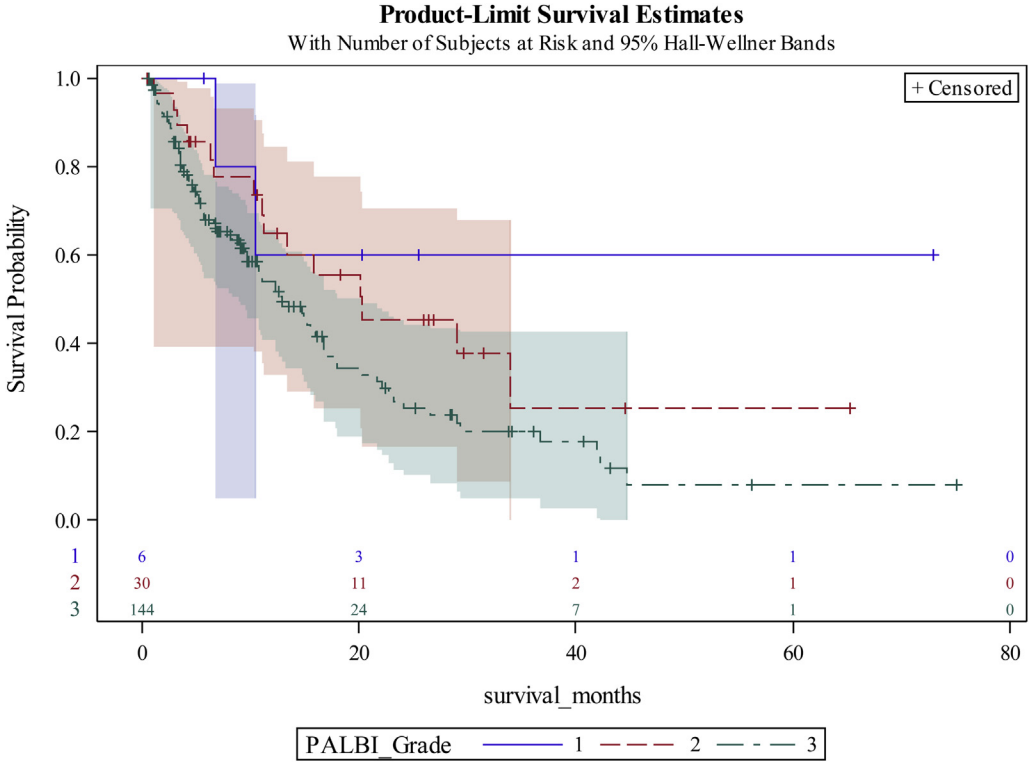

Figure 3. Overall survival after conventional transarterial chemoembolization stratified by PALBI grade ($P = .0667$).

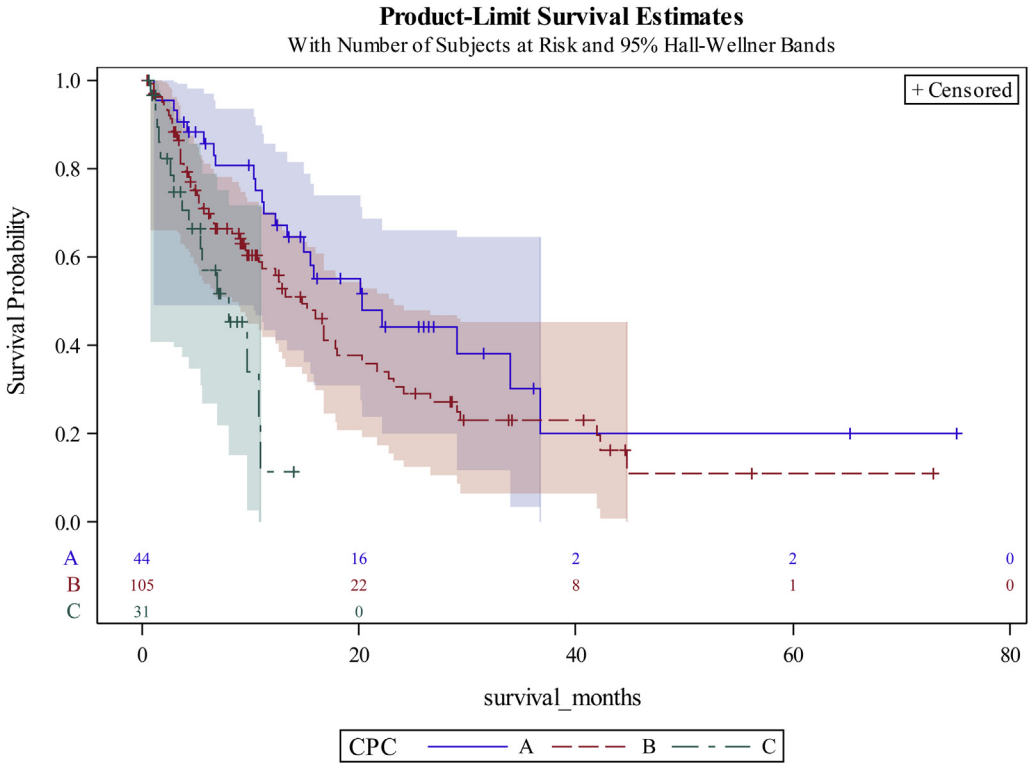

Figure 4. Overall survival after conventional transarterial chemoembolization stratified by CPC ($P = .0019$).

Patients were stratified by BCLC stage, with survival outcomes calculated based on CPC. For BCLC stage A, median survival for CPC A could not be calculated owing to the large number of patients still alive at the time of analysis; median survival for CPC B was 22.7 months (95% CI, 9.1 to 44.7; $P = .414$). For BCLC stage B, median survival for CPC A was 20.1 months (95% CI, 13.4 to 36.7), and median survival for CPC B was 14.7 months (95% CI, 4.0 to 20.3; $P = .157$). For BCLC stage C, median survival for CPC A was 6.8 months (95% CI, 4.2 to 11.1), and median survival for CPC B was 3.7 months (95% CI, 2.6 to 13.3; $P = .349$). For BCLC stage D, no patients were CPC A, 2 patients were CPC B, and 30 patients were CPC C, prohibiting a meaningful comparison of survival times. Tables 2 and 3 provide a comprehensive summary of these findings.

Table 2. Albumin-Bilirubin and Platelet-Albumin-Bilirubin Grades Stratified by Child-Pugh Class

	CPC			Total
	A	B	C	
ALBI grade				
1	0	0	0	0
2	44	34	1	79
3	0	71	30	101
P	N/A	.002*	N/A	
Total	44	105	31	180
PALBI grade				
1	4	2	0	6
2	24	6	0	30
3	16	97	31	144
P	.632	N/A	N/A	
Total	44	105	31	180

ALBI = albumin-bilirubin; CPC = Child-Pugh class; N/A = not applicable; PALBI = platelet-albumin-bilirubin.
*Denotes statistical significance.

DISCUSSION

The results indicate that in high-risk patients undergoing conventional transarterial chemoembolization for HCC, ALBI and PALBI grade are accurate metrics of survival. ALBI grade yielded distinct survival curves for the entire cohort and for the CPC B and BCLC stage A and C subgroups, whereas PALBI grade yielded distinct survival curves for the entire cohort and the subgroup of BCLC A patients. The overall survival prediction accuracy as tested by the C-index was similar between the ALBI and PALBI grades, indicating that both scores can be considered good survival indicators in high-risk patients. Both scoring systems primarily predict the risk of death related to underlying liver dysfunction and should not be considered primary markers for tumor progression. The ALBI grade primarily differentiated the high-risk cohort into ALBI grades 2 and 3, whereas the PALBI grade predominantly allocated patients to PALBI grade 3 (80%). This may imply that the ALBI grade allows for a more refined differentiation among high-risk patients, which warrants further investigation.

Table 3. Albumin-Bilirubin and Platelet-Albumin-Bilirubin Grades and Child-Pugh Class Stratified by Barcelona Clinic Liver Cancer Stage

	BCLC Stage				Total
	A	B	C	D	
ALBI grade					
1	0	0	0	0	0
2	35	31	12	1	79
3	32	22	15	32	101
P	.031*	.079	.029*	N/A	
Total	67	53	27	33	180
PALBI grade					
1	5	0	1	0	6
2	11	14	5	0	30
3	51	39	21	33	144
P	.023*	.436	.774	N/A	
Total	67	53	27	33	180
CPC					
A	17	20	7	0	44
B	50	33	20	2	105
C	0	0	0	31	31
P	.414	.157	.349	N/A	180

ALBI = albumin-bilirubin; BCLC = Barcelona Clinic Liver Cancer; CPC = Child-Pugh class; N/A = not applicable; PALBI = platelet-albumin-bilirubin.
*Denotes statistical significance.

The results in high-risk patients are in line with previously reported results using the ALBI grade in retrospective analyses to determine overall survival in non–high-risk patients undergoing locoregional treatment with both transarterial chemoembolization and yttrium-90 (^{90}Y) radioembolization. Hickey et al (12) reported a cohort of 337 patients undergoing transarterial chemoembolization and 428 patients undergoing ^{90}Y radioembolization. Patients were predominantly in CPC A and B for both the transarterial chemoembolization cohort (n = 186 and 146, respectively) and the ^{90}Y cohort (n = 201 and 215, respectively). Their analysis confirmed the utility of the ALBI grade for both locoregional treatment modalities, yielding distinct survival curves for both cohorts. For the ^{90}Y cohort, distinct survival outcomes by ALBI grade were observed for patients in CPC B, BCLC A, BCLC B, and BCLC C, and ALBI grade yielded different survival curves for patients undergoing transarterial chemoembolization in the CPC B, BCLC B, and BCLC C subgroups (12). Pinato et al (13) retrospectively evaluated the ALBI grade as a predictor of survival in a multicenter cohort of 1,461 patients with HCC from Europe, Asia, and the United States treated with transarterial chemoembolization. Patients were predominantly CPC A and BCLC stage B, and ALBI grade was found to be a significant predictor of overall survival, with comparable accuracy to CPC.

Modification of the ALBI grade resulted in the PALBI grade, which incorporates serum platelet counts as a surrogate marker of portal hypertension (4). In the initial description of the PALBI grade by Roayaie et al (4), most of the 3,992 patients (3,166; 79%) were CPC A, and PALBI grades 1–3 yielded distinct survival curves for the entire cohort as well as for the subgroup of 1,755 CPC A patients undergoing curative therapy. Liu et al (14) evaluated the utility of ALBI and PALBI grade compared with the Model for End-Stage Liver Disease score to evaluate the severity of liver dysfunction in 3,182 Asian patients with HCC, predominantly (73%) with CPC A liver disease. Both PALBI and ALBI grades were able to differentiate each BCLC stage into 3 distinct survival groups for the entire cohort. A higher C-index was observed for the PALBI grade over the ALBI grade, indicating its utility as a statistical model providing improved discriminatory power. In the subgroup of patients undergoing transarterial chemoembolization, ALBI grade discerned 2 prognostic groups, whereas PALBI grade differentiated patients into 3 prognostic groups (14).

In contrast to the above-mentioned studies, the present cohort included only patients considered to be at high-risk (8,9). The findings corroborate a high C-index for both the ALBI and the PALBI grades, indicating that the scores provide good discriminatory power. In this sample of high-risk patients, PALBI grade was unable to differentiate distinct survival groups for most BCLC stages, although the diagnostic performance was likely limited by small sample sizes for each group. Both ALBI and PALBI grades performed well in their ability to accurately predict overall survival. In addition, both grades address the well-known limitations of the CPC, including the use of interrelated variables such as albumin and ascites; use of subjective variables such as ascites and encephalopathy; and arbitrary selection of cutoff values for continuous variables such as bilirubin, albumin, and prothrombin time, leading to "ceiling" and "floor" effects. Although previously described scores have incorporated bilirubin and albumin levels obtained before treatment to guide administration of transarterial chemoembolization in HCC (15,16), differences in cutoff values including bilirubin according to local practice patterns limit performance of these algorithms. By using continuous variables, the ALBI and PALBI grades preserve diagnostic accuracy over the full spectrum of variables. Therefore, the ALBI and PALBI grades represent evidence-based and objective tools that eliminate the subjective components of the CPC and allow for stratification of patients with HCC into distinct risk categories based on laboratory values obtained from routine blood tests performed before treatment.

This study has several limitations. Retrospective single-center studies are inherently limited, and the relatively small sample size of the cohort may have contributed to the PALBI grade not demonstrating distinct survival differences for certain disease stages. The small proportion of ALBI and PALBI grade 1 patients limited the ability to evaluate this particular group compared with previous publications (1,4,14). A relatively large proportion of BCLC A patients was still alive at the time of study truncation, limiting evaluation of

overall survival in this subgroup of patients. The results are applicable only to conventional transarterial chemoembolization procedures, and variability in the degree of selectivity of catheter position during embolization and variations in transarterial chemoembolization technique across institutions (17) subtract from the overall generalizability of the results. Findings should not be extrapolated to drug-eluding bead transarterial chemoembolization or radioembolization procedures. Further investigation and comparison among locoregional therapies including radioembolization and ablation, systemic therapy, and supportive therapy should be considered in prospective trials to further evaluate the predictive qualities of the ALBI and PALBI grades.

In conclusion, ALBI and PALBI grades are accurate survival metrics in high-risk patients undergoing conventional transarterial chemoembolization for treatment of HCC. Use of these scores in clinical practice may allow for improved risk stratification in this patient group; however, confirmation in larger scale prospective studies is warranted.

ACKNOWLEDGMENTS

The authors thank Hajwa Kim, M.S., M.A., for her assistance and support with the statistical analysis for this study, and the Center for Clinical and Translational Science at the University of Illinois at Chicago. The project described was supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant No. UL1TR002003. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

REFERENCES

1. Johnson PJ, Berhane S, Kagebayashi C, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach—the ALBI grade. J Clin Oncol 2015; 33:550–558.
2. Chan AW, Leung HH, Chong CC, Chan SL. Validating the ALBI grade: its current and future use in HCC prognostication. J Hepatol 2017; 66: 661–663.
3. Hiraoka A, Kumada T, Michitaka K, et al. Usefulness of albumin-bilirubin grade for evaluation of prognosis of 2584 Japanese patients with hepatocellular carcinoma. J Gastroenterol Hepatol 2016; 31: 1031–1036.
4. Roayaie S, Jibara G, Berhane S, et al. PALBI—an objective score based on platelets, albumin & bilirubin stratifies HCC patients undergoing resection & ablation better than Child's classification. AASLD LiverLearning, 2015;110095. Available at: https://liverlearning.aasld.org/aasld/2015/thelivermeeting/110095/sasan.roayaie.palbi-an.objective.score.based.on.platelets.albumin.26.bilirubin.html. Accessed March 14, 2017.
5. National Cancer Comprehensive Network. NCCN clinical practice guidelines in oncology (NCCN guidelines): hepatobiliary cancers, version 2. 2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed February 20, 2017.
6. Bruix J, Sherman M; American Association for the Study of Liver Disease. Management of hepatocellular carcinoma: an update. Hepatology 2011; 53:1020–1022.
7. Garwood ER, Fidelman N, Hoch SE, Kerlan RK Jr, Yao FY. Morbidity and mortality following transarterial liver chemoembolization in patients with hepatocellular carcinoma and synthetic hepatic dysfunction. Liver Transpl 2013; 19:164–173.
8. Kothary N, Weintraub JL, Susman J, Rundback JH. Transarterial chemoembolization for primary hepatocellular carcinoma in patients at high risk. J Vasc Interv Radiol 2007; 18:1517–1526; quiz 1527.
9. Vilstrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. Hepatology 2014; 60:715–735.
10. Casadaban LC, Minocha J, Bui JT, Knuttinen MG, Ray CE Jr, Gaba RC. Conventional ethiodized oil transarterial chemoembolization for treatment of hepatocellular carcinoma: contemporary single-center review of clinical outcomes. AJR Am J Roentgenol 2016; 206:645–654.
11. Gaba RC, Zivin SP, Dikopf MS, et al. Characteristics of primary and secondary hepatic malignancies associated with hepatopulmonary shunting. Radiology 2014; 271:602–612.
12. Hickey R, Mouli S, Kulik L, et al. Independent analysis of albumin-bilirubin grade in a 765-patient cohort treated with transarterial locoregional therapy for hepatocellular carcinoma. J Vasc Interv Radiol 2016; 27:795–802.
13. Pinato DJ, Sharma R, Allara E, et al. The ALBI grade provides objective hepatic reserve estimation across each BCLC stage of hepatocellular carcinoma. J Hepatol 2017; 66:338–346.
14. Liu PH, Hsu CY, Hsia CY, et al. ALBI and PALBI grade predict survival for HCC across treatment modalities and BCLC stages in the MELD era. J Gastroenterol Hepatol 2017; 32:879–886.
15. Kadalayil L, Benini R, Pallan L, et al. A simple prognostic scoring system for patients receiving transarterial embolisation for hepatocellular cancer. Ann Oncol 2013; 24:2565–2570.
16. Pinato DJ, Arizumi T, Allara E, et al. Validation of the hepatoma arterial embolization prognostic score in European and Asian populations and proposed modification. Clin Gastroenterol Hepatol 2015; 13:1204–1208.e2.
17. Gaba RC. Chemoembolization practice patterns and technical methods among interventional radiologists: results of an online survey. AJR Am J Roentgenol 2012; 198:692–699.

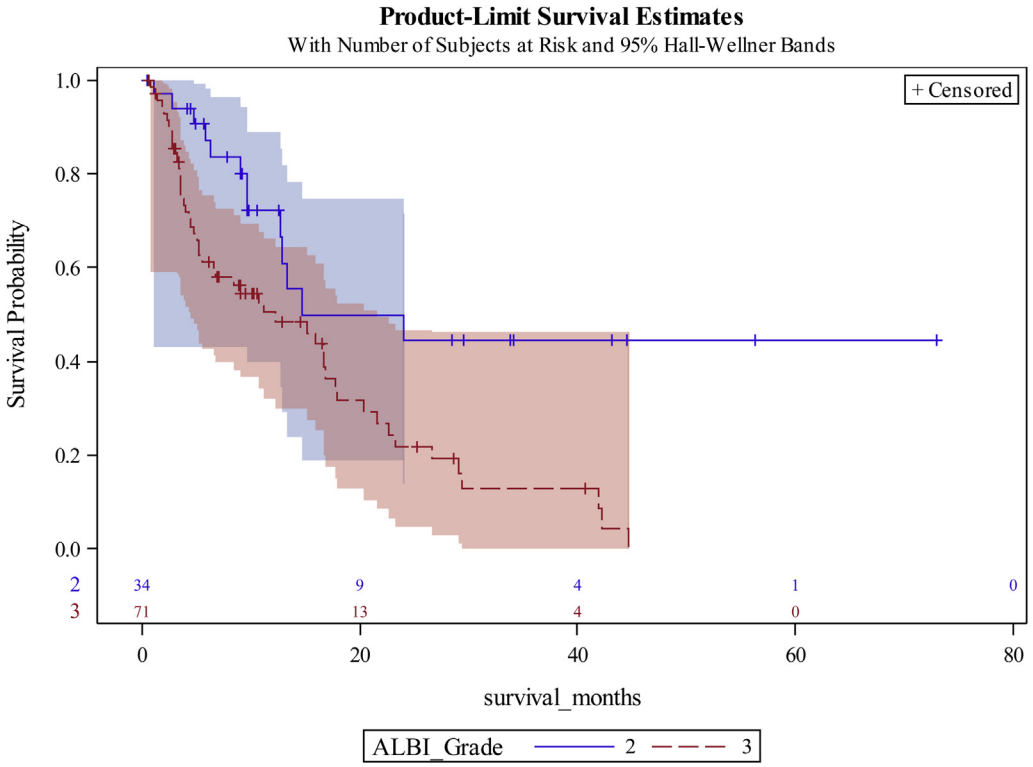

Figure E1. CPC B overall survival after conventional transarterial chemoembolization stratified by ALBI grade ($P = .0022$).

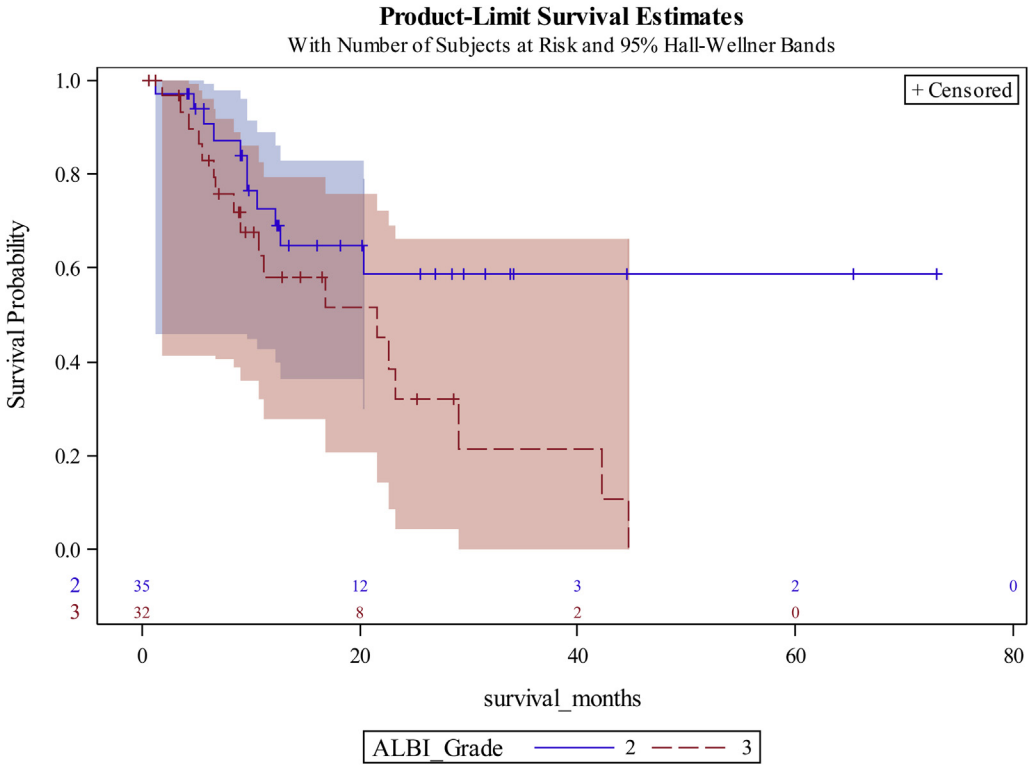

Figure E2. BCLC stage A overall survival after conventional transarterial chemoembolization stratified by ALBI grade ($P = .0308$).

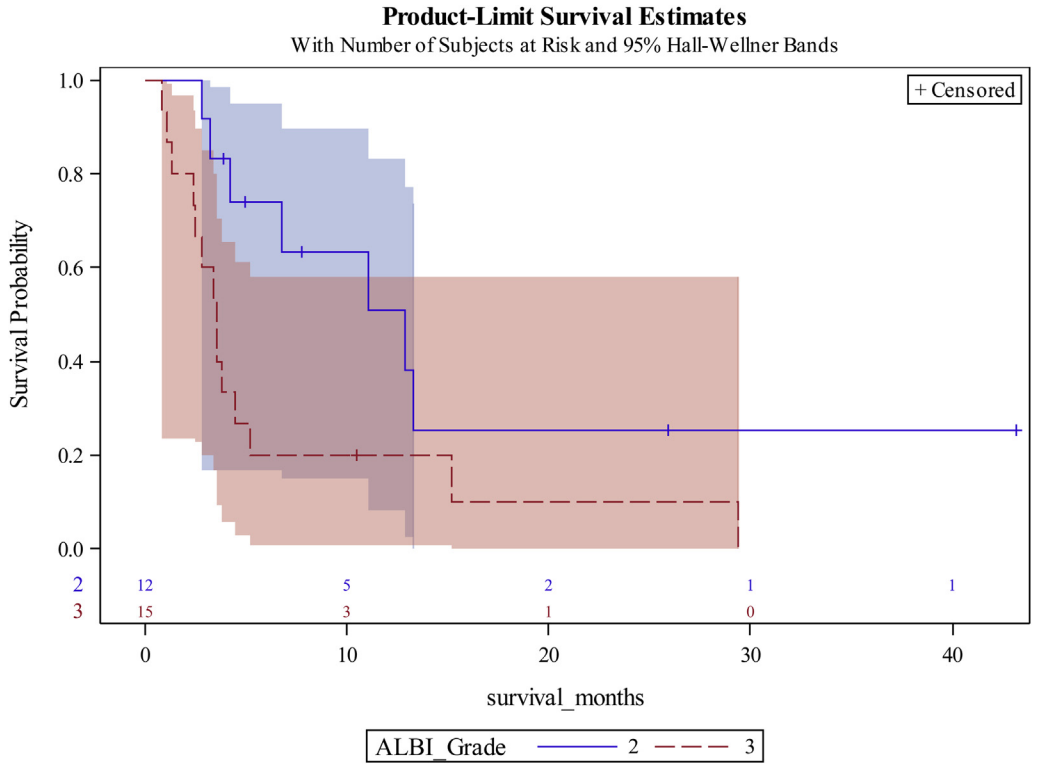

Figure E3. BCLC stage C overall survival after conventional transarterial chemoembolization stratified by ALBI grade ($P = .0287$).

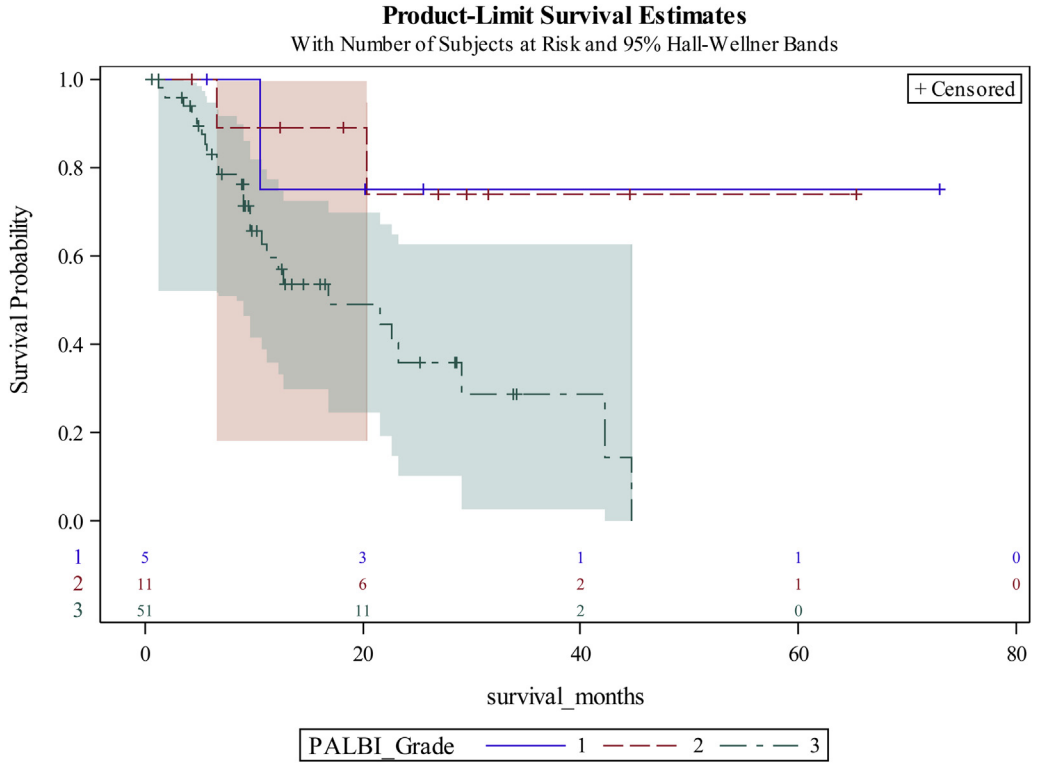

Figure E4. BCLC stage A overall survival after conventional transarterial chemoembolization stratified by PALBI grade ($P = .0229$).