2018

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HHS Public Access

Author manuscript

Am J Clin Oncol. Author manuscript; available in PMC 2018 September 01.

Published in final edited form as:

Am J Clin Oncol. 2018 September ; 41(9): 861–866. doi:10.1097/COC.0000000000000384.

Assessment of the Albumin-Bilirubin (ALBI) Grade as a Prognostic Indicator for Hepatocellular Carcinoma Patients Treated With Radioembolization

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Abstract

Objective—As the utility of Child-Pugh (C-P) class is limited by the subjectivity of ascites and encephalopathy, we evaluated a previously established objective method, the albumin-bilirubin (ALBI) grade, as a prognosticator for yttrium-90 radioembolization (RE) treatment for patients with hepatocellular carcinoma (HCC).

Materials and Methods—A total of 117 patients who received RE for HCC from 2 academic centers were reviewed and stratified by ALBI grade, C-P class, and Barcelona Clinic Liver Cancer stage. The overall survival (OS) according to these 3 criteria was evaluated by Kaplan-Meier survival analysis. The utilities of C-P class and ALBI grade as prognostic indicators were compared using the log-rank test. Multivariate Cox regression analysis was performed to identify additional predictive factors.

Results—Patients with ALBI grade 1 (n = 49) had superior OS than those with ALBI grade 2 (n = 65) ($P = 0.01$). Meanwhile, no significant difference was observed in OS between C-P class A (n = 100) and C-P class B (n = 14) ($P = 0.11$). For C-P class A patients, the ALBI grade (1 vs. 2) was able to stratify 2 clear and nonoverlapping subgroups with differing OS curves ($P = 0.03$).

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Multivariate Cox regression test identified alanine transaminase, Barcelona Clinic Liver Cancer stage, and ALBI grade as the strongest prognostic factors for OS ($P < 0.10$).

Conclusions—ALBI grade as a prognosticator has demonstrated clear survival discrimination that is superior to C-P class among HCC patients treated with RE, particularly within the subgroup of C-P class A patients. ALBI grade is useful for clinicians to make decisions as to whether RE should be recommended to patients with HCC.

Keywords

hepatocellular carcinoma; yttrium-90 radioembolization; prognostic indicator; albumin-bilirubin (ALBI) grade

The clinical prognosis and therapeutic options of patients with hepatocellular carcinoma (HCC) depends on both tumor burden and underlying hepatic dysfunction.[1–3] The Child-Pugh (C-P) scoring system has been widely used to measure the latter. This system was originally proposed to assess surgical risk in patients with portal hypertension by Child and Turcotte in 1964.[4] In 1972, the score was modified by Pugh et al[5] to include the current 5 parameters: albumin, bilirubin, ascites, encephalopathy, and prothrombin time or international normalized ratio (INR). The C-P scoring system is limited due to subjectivity of factors including ascites and encephalopathy. In medical practice, the clinical experience ranges widely between novices and experienced health care providers, which affects the judgment of ascites and encephalopathy.[6] In addition, factors including ascites and serum albumin levels are confounded by their interrelationship.

Johnson and colleagues introduced a new model for liver function assessment only based on albumin and bilirubin and termed the albumin-bilirubin (ALBI) grade. The formula for this scoring system relies on the following equation: ALBI score = ($\log_{10}$ bilirubin [μmol/L] × 0.66) + (albumin [g/L] × −0.0852). As a result, ALBI grades 1, 2, and 3 were developed as follows: ALBI score ≤ −2.60 (ALBI grade 1), > −2.60 to ≤ −1.39 (ALBI grade 2), and > −1.39 (ALBI grade 3).[7] This simple and objective model demonstrated its usefulness for evaluation of prognosis of HCC patients who underwent liver resection for early stage HCC or who were treated with sorafenib in advanced stage HCC.[8–10] Patients with intermediate stage (eg, those treated with chemoembolization or radioembolization [RE]) were a small subset of the patients included in the Johnson and colleagues study.

RE is an effective therapy with a favorable toxicity profile in intermediate-stage and advanced-stage HCC patients.[11–15] Previous studies on the prognosis of HCC patients receiving RE primarily focused on Okuda, C-P, Barcelona Clinic Liver Cancer (BCLC), Cancer of the Liver Italian Program (CLIP) score, or the TNM Staging System. The present study was designed to evaluate the prognostic value of ALBI grade in patients with HCC undergoing RE. We hypothesized that the ALBI prognostic index would serve as a better discriminator of overall survival (OS) for RE compared with C-P score.

MATERIALS AND METHODS

Study Design and Eligibility Criteria

Our patient database was reviewed for patients with HCC treated with RE from June 2007 to January 2015 at 2 separate institutes. Pretherapeutic baseline medical history, laboratory values, treatment method and dosage, and survival were obtained retrospectively. All patients were scheduled for routine follow-up on site every month in first 3 months then every 3 months afterwards, including laboratory values, computed tomography/magnetic resonance imaging, and performance status. Patients' date of death and cause of death were reported to the institutes. Death from noncancer cause was considered to be censored in the survival analysis.

Patients were selected to receive RE if they demonstrated an ECOG performance status from 0 to 3, alanine transaminase (ALT) < 400 IU/L, AST < 400 IU/L, total bilirubin < 2 mg/dL. Two patients whose total bilirubin values were more than 2 mg/dL (2.2 and 2.6 mg/dL) also received RE under the clinicians' decision. Before RE delivery, multidisciplinary consensus was reached to evaluate the patients' conditions and make therapeutic decisions. Included patients were not operative candidates. All patients were first-time treated with yttrium-90 resin microspheres when enrolled. This retrospective study received institutional review board authorization and was compliant with the Health Insurance Portability and Accountability Act.

Patients and Evaluation

A total of 122 patients received RE, and 5 patients were excluded because of missing baseline albumin or total bilirubin and according to the criteria introduced above. Baseline characteristics were collected within 1 week before radiation therapy. Baseline laboratory tests including complete blood count, liver function tests, INR, and α-fetoprotein level (AFP) were collected. Baseline computed tomography scans of the abdomen and chest were analyzed to evaluate tumor burden, volume, and vascular invasion. Baseline functional performance status was evaluated according to ECOG criteria.

Radiation Treatment

Patients were treated with resin-based microsphere beads (SIR-Spheres; Sirtex Medical, Lane Cove, Australia) or glass microspheres loaded with yttrium-90 (TheraSpheres; MDS Nordion, Kanata, ON, Canada). Pretreatment mesenteric angiography and technetium-99m macroaggregated albumin scanning (99mTC-MAA) were performed before RE to assess for gastrointestinal arterial supply (with identification of anatomic variants and prophylactic embolization of vessels if necessary) and for lung shunting. RE was performed 2 to 4 weeks following 99mTC-MAA scan using the methods outlined by Salem and Thurston.[16] Resin-based yttrium-90 microspheres were dosed based on tumor volumetry and total body surface area (BSA): activity (GBq) = (BSA − 0.2) + tumor volume/total liver volume, where BSA (m^2) = 0.20247 × height (m)$^{0.725}$ × weight (kg)$^{0.425}$; whereas glass yttrium-90 microspheres were dosed based on infused liver volume: activity (GBq) = nominal target dose (Gy) × liver mass for planning target volume (kg)/50.[17] The prescribed dose was administered into the

proper hepatic artery for bilobar treatment, left or right hepatic artery for unilobar. Two consecutive treatments within 8 weeks were considered as sequential treatment.[16,18]

Postradiation Treatments

The subsequent treatments patients received after RE were recorded, including sorafenib, transarterial chemoradioembolization, bland embolization, and liver transplantation.

Postradiation Toxicities

Clinical and laboratory adverse events were noted either during regular visits or through patient reports within 90 days after RE treatment. Toxicities were graded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) v4.0.[19]

Statistics

Patients were stratified into 3 classes according to the ALBI formula previously described: ALBI score = ($\log_{10}$ bilirubin [μmol/L] × 0.66) + (albumin [g/L] × −0.0852). ALBI grades 1, 2, and 3 were stratified as follows: ALBI score ≤ − 2.60 (ALBI grade 1), > −2.60 to ≤ −1.39 (ALBI grade 2), and > −1.39 (ALBI grade 3).[7] Patients' baseline characteristics among 3 ALBI groups were presented. Owing to baseline characteristics required for receipt of RE (eg, most patients' total bilirubin < 2 mg/dL), only 3 patients were ALBI grade 3 and were excluded from the following statistical analysis. We compared patients' baseline characteristics between ALBI grade 1 and 2 groups using Wilcoxon rank sum test for continuous variables and χ^2 test for categorical variables. Toxicities among different ALBI grades were listed and compared using Fisher exact test. OS was evaluated by Kaplan-Meier survival analysis. Medians and 95% confidence intervals (CI) were also presented. Utilities of C-P class and ALBI grade as prognostic indicators were compared using log-rank test and C-index which is, when outcome is time-event, a generalization of the area under the receiver-operating characteristic curve. C-index measures the degree of discrimination: the higher C-index, the higher discrimination.[20] P value < 0.05 was considered statistically significant. Univariate and multivariate Cox regression analyses were performed to look for potential prognosticators cooperating with ALBI grade. Significant factors in univariate regression analysis (P < 0.05) and factors of interest (ALBI grade, BCLC, and C-P class) were taken into backward multivariate regression analysis (elimination level = 0.10). Only factors with P values < 0.10 would stay in the final model because the sample size was small. To better interpret their influence on mortality in univariate and multivariate Cox regression analyses, certain continuous variables (AST, ALT, and AFP) were dichotomized into low levels and higher levels according to their medians as cutoffs. All statistical analyses were performed using SAS University Edition for Windows version (SAS Institute Inc., Cary, NC) and R packages survival and compare C available on CRAN at http://cran.r-project.org.

RESULTS

Descriptive Characteristics

A total of 117 HCC patients (median age 65.6 y old, 24 females, 93 males) who underwent RE were included. According to ALBI grade classification, patients were divided into 3 groups: ALBI grade 1 (n = 49, 41.9%), ALBI grade 2 (n = 65, 55.6%), and ALBI grade 3 (n = 3, 2.6%). All patients had similar baseline characteristics except ALT, AST, albumin, bilirubin, ascites, INR, and C-P class (Table 1). According to C-P classification, patients were classified as C-P class A (n = 100, 85.5%) and C-P class B (n = 17, 14.5%). According to BCLC classification, patients were classified as BCLC stage A (n = 15, 12.8%), BCLC stage B (n = 53, 45.3%), and BCLC stage C (n = 49, 41.9%).

Grade 2/3 and Grade 4/5 Toxicities

Toxicities among 3 ALBI grades are listed in Table 2. There were 9 (7.7%) grade 2/3 adverse events and 8 (6.8%) grade 4/5 adverse events overall. Among those 8 grade 4/5 adverse events, 4 patients died from corresponding adverse events with 90 days (2 from hepatic bleeding, 2 from hepatic failure). Among 3 ALBI grades, there was no significant difference of grade 2/3 adverse events ($P = 0.79$), grade 4/5 adverse events ($P = 0.57$), or total adverse events ($P = 0.63$).

OS

ALBI revealed 2 classes with different prognoses for patients treated with RE. Patients with ALBI grade 1 had an improved survival over ALBI grade 2 ($P = 0.01$, Kaplan-Meier curves shown in Fig. 1) with median survival time of 16.7 months (95% CI, 12.3–56.9 mo) compared with those with ALBI grade 2 who demonstrated a median survival of 9.8 months (95% CI, 7.3–13.2 mo). The C-index for ALBI was 0.581. Meanwhile, no significant difference in OS was observed between C-P class A and C-P class B ($P = 0.11$, Kaplan-Meier curves shown in Fig. 1) for which C-P class A demonstrated a median survival time of 13.2 months (95% CI, 9.7–15.7 mo) and C-P class B had a median survival of 10.4 months (95% CI, 3.1–14.0 mo). The C-index for C-P was 0.545. There were significant differences observed in OS between BCLC stage A and B ($P = 0.02$) and between BCLC stage A and C ($P < 0.01$), but no significant differences observed in OS between BCLC stage B and C (BCLC stage B: 13.0 mo; 95% CI, 8.1–15.6 mo; BCLC stage C: 10.4 mo; 95% CI, 7.2–13.8 mo; $P = 0.28$; C-index for BCLC 0.575). However, the median survival time of BCLC stage A was not reached because of its low patient number and highly censored observation number.

Survival was stratified stepwise by C-P class, and then by ALBI grade or C-P score. For C-P class A patients, 2 non-overlapping groups of ALBI grade 1 and 2 were revealed ($P = 0.03$; C-index 0.572; Kaplan-Meier curves shown in Fig. 2). Median survival for ALBI grade 1 was 16.7 months; 95% CI, 12.3–56.9 months; whereas median survival for ALBI grade 2 was 10.8 months; 95% CI, 7.6–13.8 months. In contrast, C-P score 5 versus 6 had no significant difference in terms of OS ($P = 0.11$; C-index = 0.545; Kaplan-Meier curves shown in Fig. 2). Median survival for C-P score 5 was 14.5 months; 95% CI, 11.9–25.0 months; whereas C-P score 6 was 9.8 months; 95% CI, 7.6–15.0 months. For C-P class B

patients, neither ALBI grade nor C-P score was able to discriminate subgroups with different OS (P= 0.57 and 0.17, respectively).

Patients were stratified by BCLC stage first, then survival was compared between C-P class and ALBI grade. Within each BCLC stage, neither C-P class nor ALBI grade distinguished the survival time except that OS of C-P class A and B revealed a significant difference in patients with BCLC stage C (P = 0.01; median of C-P class A: 12.3 mo, median of C-P class B: 4.0 mo).

Univariate Cox regression analysis suggested that ALBI grade, BCLC, AFP, ALT, AST, tumor volume percentage, and portal vein invasion were correlated with OS (P values < 0.05) (Table 3). On multivariate analysis, ALBI grade, BCLC, and ALT remained survival prognosticators (P values < 0.10) (Table 4).

DISCUSSION

Our data revealed that ALBI grade had a superior ability to discriminate the prognosis of HCC patients treated with RE, whereas C-P class was not able to clearly predict for OS. The degree of discrimination by ALBI grade was better than C-P class both graphically and on formal statistical analysis. The C-index for ALBI grade was slightly greater than that for C-P class.

In a recent study by Hickey et al,[21] 765 HCC patients treated with RE and chemoembolization were independently divided into ALBI grade 2 and grade 3 with a significant survival difference. The majority of patients in the study were C-P class B and were stratified into 2 groups according to ALBI grade. In contrast, our patients generally had preserved hepatic function with a normal total bilirubin and C-P class A classification at the onset of treatment. Most of patients in the present study were successfully stratified by ALBI grade within C-P class A. This demonstrates the versatility of ALBI grade discrimination across both C-P class A and C-P class B patients. On the basis of our outcome and the Hickey et al, outcome together, ALBI grade is a promising prognostic factor that can be used widely in HCC patients treated with RE.

C-P class includes 3 parameters that do not directly contribute to ALBI grade—INR, ascites, and encephalopathy. However, distributions of INR and ascites were correlated with ALBI grade. The relationship of ALBI grade with encephalopathy was limited by the low rates of encephalopathy in this study; all 5 patients with encephalopathy had an ALBI score of 2 but this did not reach statistical significance (P = 0.07). These results attest to the overlap of hepatic function parameters (ascites, INR, encephalopathy) as prognosticators. Although ALBI grade is composed only of albumin and bilirubin, it had a good capacity to reveal the impact of liver function on survival time. It therefore may be preferred to avoid the subjectivity of characterizing ascites and encephalopathy, which are sources of potential error in the C-P system.

Liver function and tumor burden are 2 different factors that impact OS. These 2 factors are also correlated, and patients with high tumor burden may have resulting decline in liver function in excess of baseline hepatic dysfunction. In the multivariate analysis, tumor

volume failed to independently predict OS. On the contrary, ALT which also suggests liver function demonstrated its prognostic ability. Further studies with detailed causes of death might uncover whether the mortality is associated with liver function failure or tumor burden.

Another prognostic factor is BCLC stage which has been commonly used to stratify and select HCC patients for different therapeutic strategies.[22] BCLC staging consists of performance status, C-P score, tumor size, number of tumors, vascular invasion, nodal spread, and extrahepatic metastases. BCLC stage includes both liver function and tumor burden simultaneously, and helps to define treatments that are indicated for the patient. By the definition, BCLC stage A (early stage), stage B (intermediate stage), and stage C (advanced stage) share the same live function characteristic—C-P class A or B. However, as we reported earlier, C-P class was not able to clearly predict for OS. ALBI grade might be a promising substitute of C-P class in BCLC stage.

Patients with ALBI grade 2 had the highest rate of adverse events (18.4%). Even though no statistically significant difference of overall adverse events was found between different ALBI grades, a higher ALBI grade seemed to show a higher number of liver-related complications. As for CTCAE grade 2/3 liver-related complications, patients with ALBI grade 1 presented fewer than ALBI grade 2 complications (n = 1 encephalopathy vs. n = 4 total including encephalopathy and ascites). High-grade liver-related complications (CTCAE grade 4/5) were less frequent in patients with ALBI grade 1 than ALBI grade 2 (n = 1 hepatic failure vs. n = 6 total including hyperbilirubinemia, hepatic failure, and hepatic bleeding). A larger population with a more robust analytical power to examine the relationship between ALBI grade and liver-related complications would be useful for future study.

This study included patients receiving health care in 2 large medical centers, which ensured high quality of follow-up, comprehensiveness of analysis factors, and consensus of data (tested in Table 1). We analyzed a novel and promising predictor that is more objective than the conventional C-P class. Our data provided a supplement to the results reported by Hickey and colleagues who stratified between ALBI grade 2 and 3, but were unable to illustrate differences between survivals for ALBI grade 1 and 2, and between these 2 groups within C-P class A. Our finding of 2 distinct subpopulations (ALBI grade 1 and 2) within C-P class A with different OS correlates with the findings of Johnson et al in their initial discussion of the ALBI grade. More importantly, we addressed how the ALBI grade performs in comparison with C-P score within a given C-P class. Johnson and colleagues did not have access to C-P scores, and therefore could not answer this question. We found that even though C-P score 5 and 6 seemed to graphically stratify the survival curves of C-P class A, this difference was not statistically significant. However, ALBI grade successfully demonstrated this capacity and revealed a higher discrimination degree than C-P score did within C-P class A patients.

Because of the criteria of patients inclusion for RE (total bilirubin < 2 mg/dL), this study was limited by the small proportion of C-P class B patents (n = 17, 14.5%) and ALBI grade 3 patients (n = 3, 2.6%), which set a barrier for the analysis of patients with poor liver

function. Patients mostly had well-compensated cirrhosis (C-P class A, n = 100, 85.5%) which might compromise the discrimination ability of C-P class. In addition, as a consequence of a small sample size in each category, ALBI grade failed to break down the survival in any subgroups stratified by BCLC stage. The same reason was considered to explain why ALBI failed to demonstrate a *P* value < 0.05 (*P* value = 0.06) in multivariate analysis.

In summary, ALBI grade is an objective prognosticator for liver function and has shown survival discrimination of HCC patients treated with RE that is superior to C-P class. Our study delineates the ability of ALBI grade to discriminate 2 subpopulations within C-P class A. ALBI grade is a promising indicator for predicting the prognosis of patients with HCC; therefore, it can play a role in guiding treatment options including RE. Further research incorporating ALBI grade into an existing staging system might give rise to a more concise and robust prediction system.

Acknowledgments

The authors thank the patients who participated in this study, Dr Neil Newman, and the research administrative nurse Donna Normann who allowed us to achieve a high-quality database with comprehensive factors.

P.J.P. has received grants from Sirtex. The grants are only for radiation dosimetry, not related to the submitted work. He has grants from Philips Healthcare, personal fees from Johnson & Johnson, grants and other financial support from Varian Medical System, Holaira Inc., and Medtronic/Covidien, outside the submitted work; J.R.O. reports grants and personal fees from Viewray Inc., outside the submitted work; D.C. reports personal fees from Z53 Therapeutics, outside the submitted work. None of these grants, personal fees, or other financial fees mentioned above is related to the submitted work. Other authors of this paper have no financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

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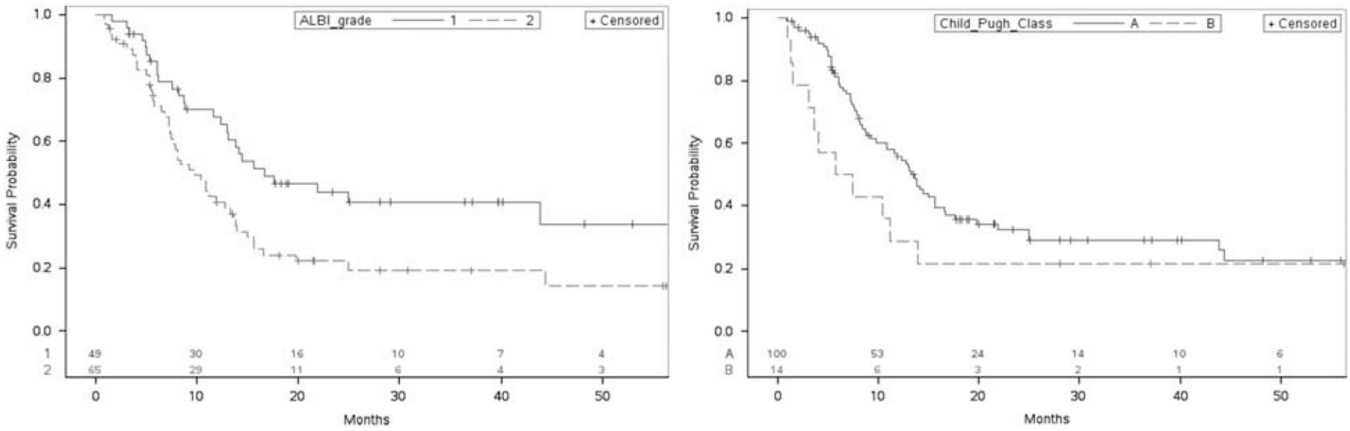

FIGURE 1.

Overall survival in months after radioembolization stratified by albumin-bilirubin (ALBI) grade ($P = 0.01$; C-index between ALBI grade 1 and 2 = 0.581) and Child-Pugh class ($P = 0.11$; C-index = 0.545).

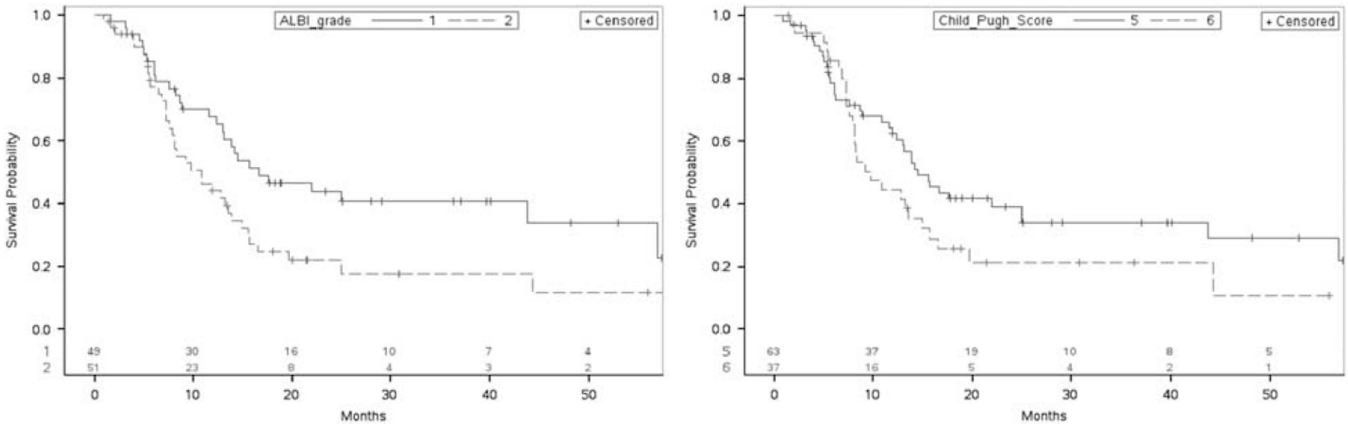

FIGURE 2.

Child-Pugh (C-P) class A patient survival in months for radioembolization according albumin-bilirubin (ALBI) ($P = 0.03$; C-index = 0.572) and C-P score ($P = 0.11$; C-index = 0.545).

Am J Clin Oncol. Author manuscript; available in PMC 2018 September 01.

TABLE 1

Baseline Characteristics

Characteristics	Parameter	ALBI Grade 1	ALBI Grade 2	ALBI Grade 3	*P**
Sex (n [%])	Female	13 (26.5)	11 (16.9)	0	0.21
	Male	36 (73.5)	54 (83.1)	3 (100)	
Site (n [%])	Medical center 1	9 (18.4)	15 (23.1)	0	0.54
	Medical center 2	40 (81.6)	50 (76.9)	3 (100)	
Age (y)	Median	69	63	64	0.057
	Range	38–85	36–90	60–69	
AFP (ng/mL)	Median	42.0	190.9	18.6	0.08
	Range	2.6–205,981.3	4.7–151,806.0	8.1–921.1	
ALT (IU/L)	Median	44	69	128	0.04
	Range	8–223	15–287	41–165	
AST (IU/L)	Median	52	88	156	< 0.01
	Range	16–201	25–365	45–235	
Albumin (g/dL)	Median	4.1	3.5	2.4	< 0.0001
	Range	3.7–4.8	2.6–4.1	1.9–2.6	
Bilirubin (mg/dL)	Median	0.5	0.9	1.6	0.0001
	Range	0.2–1.8	0.2–2.2	1.5–2.6	
INR	Median	1.09	1.15	1.35	0.02
	Range	0.95–1.36	0.80–1.77	1.25–1.65	
Ascites (n [%])	Yes	2 (4.1)	19 (29.2)	2 (66.7)	< 0.001
Encephalopathy (n [%])	Yes	0	5 (7.7)	2 (66.7)	0.07
Cirrhosis (n [%])	Yes	33 (67.4)	53 (81.5)	3 (100)	0.08
Tumor volume (%)	Median	16	21	6	0.38
Percentage	Range	1–74	1–84	1–11	
Bilobar (n [%])	Yes	19 (38.8)	34 (52.3)	1 (33.3)	0.15
Vascular invasion (n [%])	Yes	17 (34.7)	26 (40.0)	0	0.56
Metastases (n [%])	Yes	7 (14.3)	8 (12.5)	0	0.78
Biopsy-proven (n [%])	Yes	28 (58.3)	36 (56.3)	0	0.86
SIRT type (n [%])	Resin-based microspheres	15 (30.6)	20 (30.8)	0	0.99

Characteristics	Parameter	ALBI Grade 1	ALBI Grade 2	ALBI Grade 3	*P**
	Glass microspheres	34 (69.4)	45 (69.2)	3 (100)	
Treatment approach (n [%])	Sequential administration	25 (51.0)	23 (35.4)	0	0.09
	Single administration	24 (49.0)	42 (64.6)	3 (100)	
Subsequent treatment after radioembolization (n [%])	Sorafenib	9 (18.4)	12 (18.5)	0	0.99
	TACE	7 (14.3)	7 (10.8)	0	0.57
	Bland embolization	1 (2.0)	1 (1.5)	0	1.00
	Liver transplant	4 (8.2)	6 (9.2)	1 (33.3)	1.00
Radiation activity (GBq)	Median	2.38	3.24	3.31	0.18
	Range	0.87–7.73	0.77–8.80	1.75–3.91	
BCLC stage (n [%])	A	8 (16.3)	6 (9.2)	1 (33.3)	0.49
	B	20 (40.8)	31 (47.7)	2 (66.7)	
	C	21 (42.9)	28 (43.1)	0	
C-P class (n [%])	A	49 (100)	51 (78.5)	0	< 0.001
	B	0	14 (21.5)	3 (100)	

**P*-values was computed by comparing ALBI grade 1 and grade 2 only, while grade 3 was removed due to limited number (n = 3).

AFP indicates a-fetoprotein; ALBI, albumin-bilirubin; ALT, alanine transaminase; AST, aspartate transaminase; BCLC, Barcelona Clinic Liver Cancer; C-P, Child-Pugh; INR, international normalized ratio; SIRT, selective internal radiation therapy; TACE, transarterial chemoembolization.

Am J Clin Oncol. Author manuscript; available in PMC 2018 September 01.

TABLE 2

Toxicity Event

Adverse Event	ALBI Grade 1	ALBI Grade 2	ALBI Grade 3	Total	*P*
Grade 2/3					
Ascites	0	3	0	3	
Gastric antrum ulcer	1	1	0	2	
Groin hematoma	1	1	0	2	
Mild encephalopathy	1	1	0	2	
Grade 2/3 total (n [%])	3 (6.1)	6 (9.2)	0	9 (7.7)	0.79
Grade 4/5					
Bilirubin > 10	0	2	0	2	
AST	0	0	0	0	
Lymphopenia	1	0	0	1	
Hepatic bleeding	0	2	0	2	
Hepatic failure (encephalopathy)	1	2	0	3	
Grade 4/5 total (n [%])	2 (4.1)	6 (9.2)	0	8 (6.8)	0.57
Total (n [%])	5 (10.2)	12 (18.4)	0	17 (14.5)	0.63

ALBI indicates albumin-bilirubin; AST, aspartate transaminase.

TABLE 3

Univariate Cox Regression Analysis

Characteristics	Hazard Ratio	95% Confidence Interval	*P*
Sex	0.72	0.40–1.29	0.27
Age (y)	1.01	0.99–1.03	0.43
ALBI grade 2 vs. 1	1.78	1.12–2.84	0.01
BCLC stage B vs. A	2.85	1.10–7.35	0.03
BCLC stage C vs. A	3.72	1.46–9.48	< 0.01
Child-Pugh class	1.68	0.89–3.19	0.11
Tumor volume (%)	4.87	1.57–15.04	< 0.01
Portal vein invasion yes vs. no	1.63	1.02–2.57	0.04
AST > 80 vs. ≤ 80 (IU/L)	1.91	1.21–3.03	< 0.01
ALT > 63 vs. ≤ 63 (IU/L)	1.72	1.10–2.72	0.02
AFP > 144 vs. ≤ 144 (ng/mL)	1.79	1.14–2.83	0.01

AFP indicates α-fetoprotein level; ALBI, albumin-bilirubin; ALT, alanine transaminase; AST, aspartate transaminase; BCLC, Barcelona Clinic Liver Cancer.

TABLE 4

Multivariate Backward Cox Regression

Analysis Characteristics	Hazard Ratio	*P*
ALBI grade 2 vs. 1	1.62	0.06
BCLC B vs. A	3.17	0.03
BCLC C vs. A	4.10	0.01
ALT > 63 vs. ≤ 63 (IU/L)	1.67	0.046

Elimination level = 0.10.

AFP indicates a-fetoprotein level; ALBI, albumin-bilirubin; ALT, alanine transaminase; AST, aspartate transaminase; BCLC, Barcelona Clinic Liver Cancer.