Independent Analysis of Albumin-Bilirubin Grade in a 765-Patient Cohort Treated with Transarterial Locoregional Therapy for Hepatocellular Carcinoma

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ABSTRACT

Purpose: To assess validity of albumin-bilirubin (ALBI) grade as a predictor of survival in patients undergoing transarterial embolization for hepatocellular carcinoma.

Materials and Methods: Baseline albumin and bilirubin values of 765 consecutive patients treated with conventional transarterial chemoembolization or yttrium-90 (^{90}Y) radioembolization at a single institution were used to determine liver function according to ALBI grade. Survival outcomes were stratified by ALBI grade using Kaplan-Meier and stratified by Child-Pugh (C-P) class and Barcelona Clinic Liver Cancer (BCLC) stage. Discriminatory ability was assessed by C-index.

Results: For 428 patients receiving ^{90}Y radioembolization, ALBI grade yielded distinct survival curves ($P < .001$). When stratified by C-P class and BCLC stage, ALBI grade revealed different survival outcomes for C-P B ($P = .001$), BCLC A ($P < .001$), BCLC B ($P = .001$), and BCLC C ($P < .001$). When substratified by BCLC stage, ALBI grade was a better discriminator of survival than C-P class (C-index 0.792, 0.763, respectively). For 337 patients receiving transarterial chemoembolization, ALBI grade yielded distinct survival curves ($P < .001$). When stratified by C-P class and BCLC stage, ALBI grade provided distinct survival curves for C-P B ($P = .02$), BCLC B ($P = .001$), and BCLC C ($P = .02$). When substratified by BCLC stage, ALBI grade was a better discriminator of survival than C-P class (C-index 0.739, 0.735, respectively).

Conclusions: ALBI grade outperforms C-P class at discriminating survival in patients receiving transarterial chemoembolization or ^{90}Y radioembolization. ALBI grade is also valuable in patients with moderate liver dysfunction and BCLC B disease.

ABBREVIATIONS

ALBI = albumin-bilirubin, BCLC = Barcelona Clinic Liver Cancer, C-P = Child-Pugh, CI = confidence interval, ECOG = Eastern Cooperative Oncology Group, HCC = hepatocellular carcinoma, OS = median overall survival, ^{90}Y = yttrium-90

The Child-Pugh (C-P) classification system is routinely used to assess the severity and prognosis of chronic liver disease in patients with hepatocellular carcinoma (HCC). C-P class has played a central role in determining patient eligibility for and allocation to HCC treatment; it is a cornerstone of the Barcelona Clinic Liver Cancer (BCLC) staging system (1,2). In this capacity, C-P class is not only used beyond its initial purpose but it also introduces subjectivity into the assessment of liver disease (ascites, encephalopathy) (3–5).

Johnson et al (6) recently introduced a new model for assessing liver function based on albumin and bilirubin. Referred to as albumin-bilirubin (ALBI) grade, this assessment tool has been shown to be a powerful and

objective discriminator of liver function able to distinguish survival outcomes among C-P A patients with HCC. It was validated in patients from Asia, Europe, and the United States, underscoring its universal applicability.

Candidates for HCC treatment comprise a heterogeneous population. According to the BCLC algorithm, transarterial chemoembolization is recommended for BCLC B patients, specifically C-P A or B patients with multinodular HCC and preserved performance status. Radioembolization is an alternative option with less toxicity (7). In practice, however, many BCLC A and C patients also receive transarterial therapy, often with other treatments. In each circumstance, the severity of liver disease is the critical component for predicting patient survival, with regard to both treatment tolerance and the likelihood of receiving an oncologic benefit not undermined by poor liver function. The C-P classification has served to assess severity of liver disease in determining patient candidacy for transarterial therapy. This study assesses the validity of ALBI grade as a powerful predictor of survival in patients with HCC undergoing transarterial therapy.

MATERIALS AND METHODS

This study was compliant with the Health Insurance Portability and Accountability Act and approved by the institutional review board. A prospectively acquired database of consecutive patients with HCC who received treatment was used to calculate ALBI grade using albumin and bilirubin values obtained on the day of chemoembolization or radioembolization using published methods (6). Patients with HCC treated with conventional transarterial chemoembolization or ^{90}Y radioembolization during the years 2005–2014 were studied. Patients with unresectable HCC and bilirubin $\leq$ 3.0 mg/dL as determined by multidisciplinary consensus were considered eligible.

Evaluation and Staging

Diagnostic HCC criteria have been defined by previously published guidelines (1,2,8). Baseline staging was performed by C-P class (liver function) and BCLC stage (liver function, tumor size and number, cancer symptoms). Patients without vascular invasion or extrahepatic metastases were classified as BCLC C only if they exhibited specific HCC-related symptoms. ALBI grade was applied 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 in g/L. ALBI grade was determined using the following ranges: $\leq$ −2.60 (ALBI 1), > −2.60 to $\leq$ −1.39 (ALBI 2), and > −1.39 (ALBI 3) (6).

Locoregional Therapies

Chemoembolization was performed using a doxorubicin-based regimen with ethiodized oil (Lipiodol; Guerbet LLC, Bloomington, Indiana), followed by particle embolization (9). Radioembolization was performed using glass microspheres (10,11).

Statistical Analyses and Survival

Baseline patient characteristics between groups were compared using t test (means) or Mann-Whitney U test (median) for continuous variables and χ^2 or Fisher exact test (small number, highly imbalanced cells) for categorical data. Data were summarized using descriptive statistics. Overall survival (OS) analyses were performed from the date of first locoregional therapy using Kaplan-Meier method censored to curative therapy (log-rank test). Substratification by ALBI grade, C-P class, C-P score, Eastern Cooperative Oncology Group (ECOG) status, presence or absence of ascites, and BCLC stage was also performed. Finally, model validation of different staging systems was compared using the C-index as a measure of discrimination. The C-index for the survival analysis model is defined as the probability of concordance given that the pairs considered are usable in which at least one had an event. It can be interpreted as the probability that a subject from the event group has a higher predicted probability of having an event than a subject from the nonevent group. Therefore, it tests the ability of a predictive model to separate subjects who develop an event from subjects who do not (higher C-index indicates higher predictive discrimination). Analyses were performed using IBM SPSS statistics for Windows version 22.0 (IBM Corporation, Armonk, New York). A P value < .05 was significant.

RESULTS

Of 765 patients who underwent transarterial treatment for HCC, 428 received ^{90}Y radioembolization, and 337 received conventional transarterial chemoembolization. The Table summarizes demographics, ALBI grade, C-P class, and BCLC stage. Baseline index lesion size was 5.4 cm (range, 1.2–22 cm) for ^{90}Y radioembolization and 3.6 cm (range, 1.8–20.2) for conventional transarterial chemoembolization.

^{90}Y Radioembolization

Of patients who underwent ^{90}Y radioembolization, four were identified with ALBI 1, 253 with ALBI 2, and 171 with ALBI 3 liver function. ALBI grade revealed different survival outcomes for ALBI 2 and 3 after ^{90}Y radioembolization. OS for ALBI 2 was 14.9 months (95% confidence interval [CI], 12.6–17.2 mo); for ALBI 3, it was 6.5 months (95% CI, 5.2–7.8 mo; P < .001; C-index 0.588). OS for ALBI 1 was not reached because