

ALBI-RT: A Novel Radiation Therapy Specific Hepatotoxicity Prediction Model for Hepatocellular Carcinoma Patients

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Abstract

Objectives: An unmet need in radiation treatment (RT) of hepatocellular cancer (HCC) is objective prediction models that aid in appropriate patient selection for safe treatment. Recent studies have suggested the albumin-bilirubin (ALBI) grade system may predict for hepatotoxicity; however, the original ALBI grades were not optimized to predict survival after RT. We propose a novel analysis of the ALBI equation, designated ALBI-RT, to assess hepatotoxicity risk in HCC patients after RT.

Methods: We retrospectively reviewed the charts of 47 consecutive HCC patients treated with SBRT (n = 21) and hypofractionated proton therapy (n = 26) from 2013-2016. Raw ALBI values and Child-Pugh (CP) scores were calculated from albumin and bilirubin data. Any patient deaths were recorded, and assessed for association with radiation induced liver disease (RILD). Raw ALBI was assessed as a continuous variable to perform ROC analyses to identify cutoffs for overall survival (OS) and RILD-specific survival (RILD-SS) that maximized the Youden index of ROC accuracy. Dichotomization of the ROC for RILD-SS resulted in ALBI-RT. Univariate predictors of OS and RILD-SS were evaluated using Cox proportional hazard regression to determine hazard ratios (HR) and Chi-squared p values.

Results: Patient cohort median age was 67 years (43-89) with 62% CP-A and 38% CP-B/C. Median follow-up and OS was 13 months and 10 months, respectively. There were 18 deaths with 6 ascribed to RILD. ROC analysis based on raw ALBI identified an OS cutoff at -2.00 (AUC=0.68, p=0.04) with a sensitivity and specificity of 67%. ROC analysis for RILD-SS had an increased sensitivity to 100% and specificity of 71% with an identified raw ALBI cutoff at -1.70 (AUC=0.94,

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p=0.008). We defined ALBI-RT grades as: A < -1.70 (n=29) and B = -1.70 (n=18). On univariate analysis for OS, raw ALBI as a continuous variable (HR 3.0, p=0.02) and to a lesser degree ALBI-RT

Grade B (HR 2.4, p=0.06) performed similarly to traditional ALBI grade (HR 3.0, p=0.01), and CP score (HR 1.4, p=0.03). Conversely, for RILD-SS, univariate analysis revealed that raw ALBI as a continuous variable (HR 25.1, p=0.01) and ALBI-RT Grade B (HR 9.9, p=0.04) were associated with

higher average increases in relative risk of radiation-related hepatotoxicity than traditional ALBI

grade (HR 5.8, p=0.02) and CP score (HR 2.3, p=0.003).

Conclusions: ALBI-RT is a promising novel metric that may have a larger effect size when predicting RILD related death after RT for HCC than both CP and conventional ALBI grades in this

patient cohort. It has potential utility in the pre-treatment assessment of HCC patients, with a cutoff of = -1.70 predicting death from RILD. Future prospective evaluation and validation in independent data sets will strengthen the generalizability and utility of ALBI-RT.