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Title: Disease control and hepatotoxicity following stereotactic body radiotherapy for hepatocellular carcinoma

Purpose/Objectives: Stereotactic body radiotherapy (SBRT) is increasingly utilized in the definitive management of patients with hepatocellular carcinoma (HCC), but long-term data regarding treatment efficacy and hepatotoxicity are lacking. We present our experience with SBRT and analyze patient and tumor characteristics associated with local control (LC), overall survival (OS), worsening of Child-Pugh (CP) score, and albumin-bilirubin grade (ALBI).

Materials/Methods: Patients with HCC treated with SBRT at a large referral center were included in this IRB-approved retrospective institutional database. Baseline patient characteristics, SBRT dose and fractionation, and laboratory data were collected by chart review. LC and OS were calculated using the Kaplan-Meier method starting from the date of the cross-sectional imaging study diagnosing the HCC lesion treated with SBRT. LC (at lesion level) was computed with a cumulative incidence function censoring for death. Local progression was defined by the interpreting radiologist, interdisciplinary review, or any decision to intervene with salvage therapy. A mixed-effects multivariable analysis (MVA) using a Cox proportional hazards model was performed using patient age, performance status, gender, HCC diameter (maximum length per-lesion), biological effective dose (alpha/beta = 10), number of prior treatments to the target lesion, and pre-treatment CP score as regression variables. CP score and ALBI were used to quantify hepatotoxicity following SBRT.

Results: A total of 130 HCC lesions in 104 patients (69% male) were included and median follow up was 1.6 years (range 0.3 – 6.8). Hepatitis C was the most common etiology for underlying liver disease (n = 44, 42%). The medians for MVA variables were age = 65 years, ECOG performance status = 1, maximum lesion diameter = 2.4 cm, BED₁₀ = 112.5 Gy, CP = A6, and ALBI = grade 1. LC and OS for the entire cohort were 92% and 80% at 1-year, and 89% and 46% at 3-years, respectively. On MVA, no variables were significantly associated with either LC or OS (all p-values > 0.05). At 3-months post-SBRT, the number of patients with a worsening in CP score of 2 and 3+ points were 7 (7%) and 4 (4%), respectively, while the number of patients with a decline in ALBI score of 1 and 2 grades was 27 (26%) and 2 (2%), respectively. Of 12 lesions with local progression following radiation, salvage therapy was delivered in 11 with the most common technique being thermal ablation (n = 7, 64%). There was one documented local failure after salvage treatment.

Conclusion: SBRT with an ablative dose is associated with excellent LC with little hepatotoxicity in well-selected patients. High rates of LC after SBRT appear maintained with longer follow up, but overall survival remains limited.