Scientific Article

Stereotactic Body Radiation Therapy for Hepatocellular Carcinoma in Patients With Child-Pugh B or C Cirrhosis

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Abstract

Purpose: Our purpose was to report outcomes in patients with Child-Pugh B or C (CP B/C) hepatocellular carcinoma (HCC) treated with stereotactic body radiation therapy (SBRT).

Methods and Materials: Patients with HCC suitable for SBRT were prospectively enrolled in the study from 2012 to 2018. Outcomes in patients with CP B/C were analyzed. Cox proportional hazard models were used to compare survival outcomes between baseline CP score and post-SBRT CP score.

Results: Twenty-three patients with CP B/C with a total of 29 HCC tumors were treated with SBRT. Eighty-seven percent of patients were CP B8-C10. Median tumor size was 3.1 cm (range, 1-10 cm). Median dose delivered was 40 Gy in a median of 5 fractions. Eighteen of 23 patients (78.3%) had been previously treated with transarterial chemoembolization. Median follow-up was 14.5 months. Rates of 6- and 12-month local control were 100% and 92.3%, respectively. Six- and 12-month survival rates were 73.9% and 56.5%, respectively. Median survival was 14.5 months overall and 9.2, 22.5, 14.5, and 14.4 months for patients with CP B7, B8, B9, and C10, respectively. No patients exhibited symptoms of classic radiation-induced liver disease. However, 10 patients had CP score progression, with 4 patients (17%) having a $\geq$2-point increase in CP score by 6 months (or time of censor). There were 7 liver-related deaths, and based on independent review by a hepatologist, 1 of these deaths may have been attributable to SBRT-related liver injury. Fifteen of 23 patients were listed for liver transplant (LT) at the time of SBRT and 9 went on to receive LT with a pathologic complete response rate of 63.6%. Median survival, excluding patients who received LT, was 7.3 months.

Conclusions: SBRT is a reasonable treatment option for carefully selected patients with CP B7-C10. In our small cohort, there was no detectable difference between local control or overall survival and baseline CP score.

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Introduction

There is emerging evidence establishing stereotactic body radiation therapy (SBRT) as a safe and efficacious local treatment option for patients with localized hepatocellular carcinoma (HCC).[1-3] Local control (LC) ranges from 84% to 100%.[4,5] However, the majority of the published reports on SBRT for HCC have focused on patients with well-compensated Child-Pugh (CP) A liver function. A few reports have included patients with CP B, and most of these patients had CP B7.[3,6,7] There are also reports that suggest increased risk of toxicity in patients with CP B (vs A) and prescription dose reduction and tighter liver dose constraints have been recommended.[3,6-8]

Treatment options for patients with CP B/C impaired liver function are limited owing to concerns for toxicity, and many patients are treated with best supportive care as the risk of dying from their underlying liver disease or treatment-related toxicity may outweigh the risk of dying from HCC progression. The Barcelona Clinic Liver Cancer staging system deems all patients with CP C as stage D and recommends only best supportive care with a life expectancy of ≤ 3 months regardless of HCC size or extent.[9] The purpose of this study was to address the current gap in the literature regarding the tolerability and efficacy of SBRT in early stage HCC with CP B/C disease.

Methods and Materials

Study design

In 2012, our institution at the UMass Memorial Medical Center established a weekly multidisciplinary HCC clinic and simultaneously launched a SBRT for HCC program. All new and established patients with HCC were presented at our institution's weekly multidisciplinary HCC conference attended by the following disciplines: radiology, hepatology, transplant surgery, interventional radiology, medical oncology, and radiation oncology. Pathologic confirmation of HCC was not required as long as radiographic and clinical criteria were met.[10] All nonmetastatic patients were evaluated regarding suitability for locoregional therapies including resection, radiofrequency ablation, microwave ablation, transarterial chemoembolization (TACE), transarterial radioembolization, and SBRT. Patients with tumors amenable to SBRT that were not eligible for other local treatment options were referred for SBRT. Prior liver-directed therapy was allowed. Patients listed for liver transplant (LT) were also eligible. In 2012, our institutional review board approved database of all HCC patients treated with SBRT was created, and in 2014 it was converted to a prospective database requiring informed consent for participation from all patients.

Radiation treatment

Patients were simulated with customized vacuum cushion and wing board for immobilization in the supine position with arms extended overhead. A 3-dimensional CT followed by 4-dimensional gated CT scan was obtained for motion awareness and treatment planning. Contrast enhanced diagnostic imaging was fused to CT simulation scan for target delineation. The 4-dimensional gated CT scan was used to define the internal target volume and a minimum of a 3-mm margin expansion was used for the planning target volume.

All patients were treated by volumetric modulated arc therapy in the form of RapidArc with 6 MV or 6 MV flattening filter free photon beam generated by Varian Trilogy or STX linear accelerator equipped with high definition multileaf collimators. Maximum allowed dose rate was set to 1400 MU/min. Individualized optimization was performed using multiple coplanar or noncoplanar, monoisocentric arcs. Patients were treated with free breathing. Cone beam CT was performed before each treatment to verify target and normal tissue localization and was reviewed by the treating radiation oncologist. Patients were treated with SBRT 30 to 50 Gy in 4 to 6 fractions over a 2 to 3 week period. The goal was to keep the mean liver dose <8.8 Gy for CP B and <6 Gy for CP C. An additional liver planning objective was to spare a minimum of 700 cm^3 of liver to <15 Gy.[11] Maximum dose to 0.5 cm^3 of stomach, esophagus, and duodenum was 30 Gy and 32 Gy for large bowel. Chest/abdominal wall V30 was limited to 30 cm^3.

Follow-up

Patients were seen weekly during SBRT, 1 and 3 months post-SBRT, and then every 3 months thereafter. Blood work was obtained at every visit post-SBRT and imaging was obtained every 3 months. Blood work included a complete blood count, comprehensive metabolic panel, alpha fetalprotein, and international normalized ratio. Imaging was either a 4 phase liver CT or magnetic resonance imaging. All imaging was reviewed by a body radiologist on the HCC multidisciplinary team. Radiographic response was assessed based on modified Response Evaluation Criteria in Solid Tumors (mRECIST) for enhancing tumors, RECIST v1.1 for tumors lacking classic enhancement pattern, alpha fetalprotein trend, and overall impression of the radiologist.[10] Treatment-related adverse events were defined by the multidisciplinary HCC team as those judged to be due to SBRT and not worsening of the underlying cirrhosis or progression of disease. All patients with liver-related mortality were independently reviewed by a single hepatologist to determine whether the cause of death was most likely attributable to cancer progression, SBRT-related complications, or the natural history of cirrhosis.

The hepatologist took into consideration each patient's pretreatment liver function trajectory, including data such as model for end-stage liver disease score trend over time, tolerance of other therapeutic interventions in the past, and history and frequency of liver-related decompensations. Importantly, the hepatologist also evaluated time course between SBRT treatment, liver function decline, and ultimately death as well as other potentially contributing factors to the patient's decline in liver function.

Endpoints

Primary endpoints were survival, LC, and toxicity within 6 months of treatment. LC was defined as complete response, partial response, or stable disease within the irradiated region of the liver. Local recurrence (LR) was defined as progression of disease within the irradiated region of the liver. Elsewhere liver recurrence (ELR) was defined as appearance of disease beyond the region of irradiated liver. Secondary endpoint was cause of death.

Statistical analysis

Overall survival (OS) was calculated from completion of SBRT. OS and LC were evaluated using the Kaplan-Meier method. Survival is reported including and excluding LT patients. Cox proportional hazards models were used to compare survival outcomes between baseline CP score and post-SBRT CP score. All analyses were performed using Stata version 11.1 software (College Station, TX).

Results

Sixty-five consecutive patients with HCC treated with SBRT at our institution have been enrolled into the database. Twenty-three CP B/C patients with 29 tumors were identified. Baseline patient and tumor characteristics are shown in Table 1. Three, 6, 9, and 5 had CP B7, B8, B9, and C10 scores, respectively. Most patients had underlying liver disease related to alcohol consumption (35%), hepatitis C (13%), or both (35%). Median age at time of SBRT was 62 years (range, 41-82 years), and 83% were men. Median size of lesion treated was 3.1 cm (range, 1-10 cm). Eighteen patients had been previously treated with TACE; 10 patients were referred for salvage SBRT after LR post-TACE and 8 were referred for combined modality treatment. Median time interval between TACE and SBRT was 178 days and 46 days for salvage and combined modality treatment, respectively. Only 1 patient had portal vein tumor thrombus.

Treatment details are shown in Table 2. Median dose delivered was 40 Gy in a median of 5 fractions. Mean uninvolved liver dose was constrained to a median dose of 7 Gy (3.1-10.4 Gy) overall and 4.8 Gy for patients with CP C. Median treatment interval was 14 days.

Treatment results are shown in Table 3. Median follow-up (FU) was 14.5 months (1-67.1) with a median FU for all living patients of 34.3 months (24.2-67.1). LC was 100% at 6 months and 92.3% at 1 year. The 1 LR was a marginal failure (new focus of enhancement just inferior to the treated area) in a patient with B9 with biopsy-proven HCC with only noncontrast imaging before SBRT due to diminished kidney function. In retrospect, the lack of contrast-enhanced imaging limited the ability to clearly define the SBRT target volume. She received 44 Gy in 4 fractions with a coplanar volumetric modulated arc therapy plan. Ten months after SBRT, her kidney and liver function had significantly improved (glomerular filtration rate improved from 36-55 and CP score improved from B9 to B7), and she was able to undergo a 4-phase contrast enhanced liver CT. She was successfully salvaged with TACE and is still alive with no evidence of disease at the time of this study. Six patients had LC while developing ELR.

Median OS was 14.5 months with 6- and 12-month survival rates of 73.9% and 56.5%, respectively. When excluding patients who received liver transplant from the survival analysis, median OS was 7.3 months (Fig 1a). Median OS for CP B7, B8, B9, and C10 groups were 9.2, 22.5, 14.5, and 14.4 months. One-year OS for the patients with CP C10 was 60%. There was no statistical difference in all-cause mortality or liver-related mortality based on baseline CP score 7 to 8 versus 9 to 10, $P = .88$ and $P = .22$, respectively (Fig 1b).

Of the 15 patients listed for transplant, 9 went on to receive LT with a median time interval between SBRT and LT of 7 months (9-680 days). The pathologic complete response rate is 63.6%. Seven of the 9 LT patients are alive and without HCC recurrence at the time of this analysis with a median FU of 34.3 months (9.1-67.1). The 2-year OS for LT patients is 88.9%. One LT patient died of postoperative complications that were not related to SBRT. Another LT patient passed away at home from unknown causes. Five patients died while awaiting LT and 1 patient was delisted owing to a diagnosis of oropharyngeal cancer, resulting in a dropout rate of 33.3%. No patients were delisted owing to HCC disease progression.

Toxicity

The most common acute toxicity was grade 1 to 2 fatigue in 43% and nausea in 30%. There was no grade 3 or higher toxicity seen during treatment. In the subacute period, defined as 1 to 6 months posttreatment, no patients developed classic radiation-induced liver disease. Two patients developed an increase in baseline ascites requiring increased frequency of paracenteses, and 1 patient developed bland right portal vein thrombus 1 month after completing SBRT. The area of the portal vein that

Table 1   Baseline patient and tumor characteristics: Patient information including starting CP score, age, tumor size, etiology of liver disease, and therapies before SBRT

Baseline patient and tumor characteristics	All patients	CP 7	CP 8	CP 9	CP 10	
No patients	23	3	6	9	5	
Median age (range)	62 (41-82)	62	61.5	56	65	
Median tumor size (range)	3.1 cm (1-10)	4 cm	2.7 cm	2.6 cm	3.2 cm	
Etiology of liver disease						
EtOH	8	1	1	3	3	
HCV	3	1	1	1	0	
HBV	1	0	0	1	0	
NASH	2	1	1	0	0	
PBC	1	0	1	0	0	
EtOH + HCV	8	0	2	4	2	
	All patients					Median interval
Total no. previous TACE	18	3	5	5	5	75.5 days
Salvage	10	1	3	4	2	178 days
CMT	8	2	2	1	3	46 days

Abbreviations: CMT = combined modality treatment; CP = Child-Pugh; EtOH = ethanol; HBV = hepatitis B; HCV = hepatitis C; NASH = nonalcoholic steatohepatitis; PBC = primary biliary cirrhosis; SBRT = stereotactic body radiation therapy; TACE = transarterial chemoembolization.

developed thrombus received a maximum dose of 12 Gy. His CP score increased from B7 to B9 at the time of developing the PVT, and 6 months after SBRT he received orthotopic liver transplant (OLT) with a pathologic complete response in the treated tumor.

The effect of SBRT on liver function is shown in Table 4 with regard to effect on CP score and liver enzymes. The following changes in CP score at 6 months after SBRT (or time of censor) were noted: 5 improved, 7 remained stable, and 10 progressed with a median CP score change of 0. Of those who had CP improvement, all 5 had improvement by 1 point. Of those with CP score progression, 6 progressed by 1 point, 3 progressed by 2 points, and 1 progressed by 3 points. Of the 10 patients who had CP progression, 8 have died and 5 of the deaths

Table 2   Treatment information: SBRT details stratified by starting CP score, including tumor size, prescribed dose, MLD, and treatment interval between first and last doses

Treatment information	All patients	CP 7	CP 8	CP 9	CP 10
No patients	23	3	6	9	5
Median tumor size (range)	3.1 cm (1-10)	4 cm	2.7 cm	2.6 cm	3.2 cm
Prescribed dose (range)	40 Gy (30-50)	40 Gy	40 Gy	35 Gy	40 Gy
MLD (range)	7 Gy (3.1-10.4)	8.8 Gy	8 Gy	5.4 Gy	4.8 Gy
Median treatment interval	14 d	15 d	13.5 d	14 d	12 d

Abbreviations: CP = Child-Pugh; MLD = mean liver dose; SBRT = stereotactic body radiation therapy.

were liver related. CP progression post-SBRT was significantly correlated with decreased OS ($P = .04$; hazard ratio [HR], 3.29; 95% confidence interval [CI], 1.06-10.18) and a trend toward increased liver-related mortality ($P = .06$; HR 4.78; 95% CI, 92-24.95) (Fig 1c). Median mean liver dose (MLD) was not statistically different between patients who had CP progression versus CP stability/improvement (6.5 Gy compared with 6.8 respectively; $P = .76$). The median MLD was also not statistically different between patients who experienced a liver-related mortality and those who did not (6.1 Gy and 6.9 Gy; $P = .45$).

Of the Common Terminology Criteria for Adverse Events v5.0 liver enzyme parameters, 1 patient had grade 2 increase in aspartate aminotransferase and 1 patient had grade 3 increase in alkaline phosphatase within 6 months of radiation therapy. All other patients saw grade 0 to 1 Common Terminology Criteria for Adverse Events parameter changes in aspartate aminotransferase, alkaline phosphatase, and alanine aminotransferase levels.

Seven patients died of liver-related issues. Based on independent review by a hepatologist, it was determined that of the 7 deaths, 1 may have been partially attributable to SBRT-related liver injury. The other 6 deaths were either related to HCC progression (ELR, portal vein tumor thrombus, or distant metastasis) or the natural progression of cirrhosis (Table 5). Six of the 7 liver-related mortalities had more advanced cirrhosis with a baseline CP score of B9 or C10, whereas 1 had a baseline CP of B7 but progressed rapidly to C10 within 1 month of SBRT. There was no statistically significant difference in risk of developing a liver-related mortality and baseline CP score when comparing CP 9-10 patients with CP 7-8 patients (HR, 3.7; $P = .225$; 95% CI, 446-30.85). For this subset

Table 3 Treatment results: Results after SBRT stratified by starting CP score, including 1-year survival rate, median overall survival, patients who underwent transplant, and tumor response

Treatment results	All patients	CP 7	CP 8	CP 9	CP 10
1-year survival	52.10%	33%	66%	44.40%	60%
OS	14.5 mo (1-67.1)	9.2 mo	22.5 mo	14.5 mo	14.4 mo
OLT	9	2	3	2	2
CR	13	1	4	4	4
PR	6	1	1	3	1
SD	1	0	1	0	0
LR	1	0	0	1	0
N/A	2	1	0	1	0
Total	23	3	6	9	5

Abbreviations: CP = Child-Pugh; CR = complete response; LR = local recurrence; OLT = orthotopic liver transplant; OS = overall survival; PR = partial response; SBRT = stereotactic body radiation therapy; SD = stable disease.
N/A − data unavailable.

of 7 patients who died of liver-related issues, the median survival was 7.3 months after SBRT and the 6- and 12-month OS rates were 57.1% and 14.3%, respectively.

Discussion

CP class was initially designed to predict survival after porto-systemic shunting in patients with cirrhosis.[12] It was later found to be predictive of survival after surgery and was then extrapolated to predict outcomes after other liver-directed therapies.[13-15] The CP scoring system is fraught with subjectivity (degree of encephalopathy or ascites), and small variations in laboratory values can result in score or even class changes. Despite these limitations, it remains the most-studied measure of liver function in the SBRT literature. Current guidelines still use CP score to determine eligibility for SBRT, prescription dose, fractionation, and mean liver dose constraints. Although baseline CP score did not correlate with risk of all-cause or liver-related mortality, an increase in CP score within 6 months of SBRT did correlate with all-
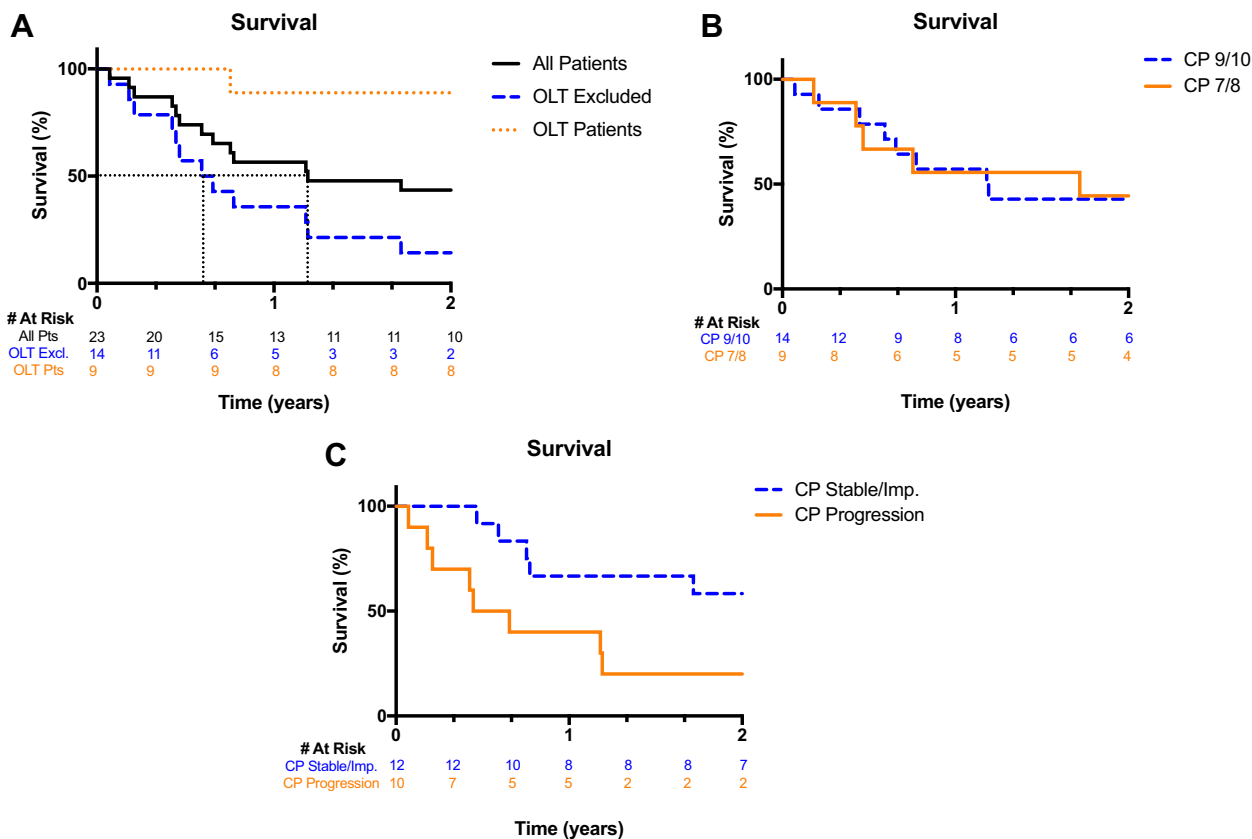

Figure 1 Survival curves: (a) Kaplan-Meier survival curves of all patients, orthotopic liver transplant (OLT) patients excluded, and only OLT patients. Median overall survival (OS) = 14.5 months. Median OS excluding OLT = 7.3 months. (b) Patients with starting Child-Pugh (CP) score of 7/8 and CP 9/10. There was no significant difference of survival rates between CP 7/8 vs 9/10. (c) Patients with stable or improved CP score after stereotactic body radiation therapy (SBRT) and patients with CP score progression. Patients with CP progression had significantly decreased OS rate ($P = .039$).

Table 4 CP score and adverse events: Change in CP score at 6 months or at time of censor and severe (grade 2 or higher) adverse events

CP score and adverse events	All patients	CP 7	CP 8	CP 9	CP 10
No patients	23	3	6	9	5
CP progression	10 (43%)	2	1	3	4
CP stability	7 (30 %)	1	3	3	0
CP improvement	5 (22 %)	0	1	3	1
Gr2 + adverse events	6	2	1	2	1
N/V	3	0	0	2	1
Encephalopathy	1	0	0	1	0
Ascites	2	0	1	1	0

Abbreviations: CP = Child-Pugh; N/V = nausea or vomiting.

cause mortality and a trend toward liver-related mortality. However, there was no clear correlation between baseline CP score and risk of CP progression after SBRT; 37.5% of patients with a starting CP of 7 or 8 saw progression of their score, while 50% of those with a starting CP of 9 or 10 saw progression ($P = .675$). Thus, it appears that among patients with CP B7-C10, change in CP after SBRT is prognostic while baseline CP by itself is not; however, a strong statistical conclusion here is limited by the small sample size of this study. It is important to note

that while a statistically significant correlation to starting CP score was not found, the majority of patients who suffered from a liver-related death did have a starting CP score of B9 or C10. Overall, the utility of baseline CP score to determine eligibility for SBRT should be re-evaluated and patients with more advanced CP scores should not automatically be deemed ineligible.

At our institution's HCC multidisciplinary conference, we use a more comprehensive approach to measure liver function that includes CP score as well as performance status, comorbidities, model for end-stage liver disease score, other decompensations like thrombocytopenia and history of upper gastrointestinal bleed, and tolerance to previous liver-directed therapies. Feedback from a hepatologist who knows a patient's liver history intimately and from interventional radiologists regarding how a patient has tolerated previous treatments factors critically into selecting which patients with CP B/C disease would benefit from treatment with SBRT.

Culleton et al[6] represents another institution with a comprehensive multidisciplinary team approach to the management of HCC, and their outcomes of SBRT in patients with CP B/C were published in 2014. Compared with our cohort, their series had more advanced HCC (76% had tumor thrombus, 24% had extrahepatic HCC, the median number of tumors treated was 2, and the median sum of the largest diameter was 8.6 cm) but less

Table 5 Patients with liver-related deaths: Details of post-SBRT complications in the 7 patients who were identified to have liver-related deaths

Baseline CP	Baseline decompensations	LC	CP change post-SBRT	Post-SBRT decompensations	Interval between SBRT and death	Cause of liver-related death
B9	Encephalopathy, diuretic refractory edema	Y	1	Progression of encephalopathy, edema	435 d	Progression of HCC elsewhere in the liver and progression of cirrhosis
B9	Encephalopathy	Y	−1	Encephalopathy stable	282 d	Progression of HCC elsewhere in the liver
B9	ESRD, ascites	Y	0	SBP/sepsis	216 d	Progression of cirrhosis
C10	GI bleed, ascites, encephalopathy	Y	2	Volume overload, progression of encephalopathy	239 d	Progression of cirrhosis and SBRT-related liver injury (MLD = 5.6 Gy)
B7	None	Y	3	None	66 d	Progression of HCC elsewhere in the liver (PVTT and IVC tumor thrombus)
C10	None	Y	1	Cholecystitis	163 d	Progression of HCC elsewhere (peritoneal carcinomatosis)
B9	Refractory ascites	Y	2	Peritonitis	26 d	Progression of cirrhosis

Abbreviations: CP = Child-Pugh; ESRD = end-stage renal disease; GI = gastrointestinal; HCC = hepatocellular carcinoma; IVC = inferior vena cava; LC = local control; MLD = mean liver dose; PVTT = portal vein tumor thrombosis; SBP = spontaneous bacterial peritonitis; SBRT = stereotactic body radiation therapy.

advanced cirrhosis (69% CP B7), and they excluded patients with OLT from their analysis. They also had a lower prescription dose of 30 Gy in 6 fractions. Despite these differences in patient population, tumor characteristics, and treatment parameters, our median survivals were similar when we excluded our patients with OLT (7.3 vs 7.9 months). Given the expected natural history of progression in patients with HCC and severe baseline liver disease, it is important to evaluate the cost-benefit of treating these patients with the goal of LC. Although HCC does seem to respond quite well to radiation therapy, it is reasonable to question whether or not LC truly benefits these patients because they generally have poor overall survival rates (unless they receive transplant).

The effort by Chapman et al[16] to define clinically relevant endpoints in liver toxicity after SBRT was inspirational to our study. Although we did not identify any correlation between starting CP score and most laboratory value-based posttreatment hepatotoxicity metrics proposed by Chapman et al, the posttreatment CP progression parameters did correlate with all-cause mortality and trended toward correlation with liver-related mortality. Further study into progression of CP and its correlation with negative outcomes is warranted.[16,17] We made similar efforts as Chapman and colleagues to define causes of liver-related mortality. We agree that we need to continue to move toward a consensus on how to report liver toxicity after SBRT in patients with cirrhosis. Toxicity rates depend on how one defines toxicity,[16,18] and in this cohort of patients with decompensated livers, it's a challenge to distinguish treatment-related toxicity from the natural progression of cirrhosis and disease progression.

Owing to the paucity of liver SBRT outcome data in CP B/C patients and aforementioned challenges in defining SBRT-related liver toxicity, the appropriate dose-volume parameters for cirrhotic livers are not well understood. Many dose-volume parameters have been studied including MLD V1, V2.5, V5, V7.5, V10, V12.5, V15, dose to 1/3 of the liver, volume of liver spared to <15 Gy, and volume of uninvolved liver. MLD has been well studied in CP A patients with guidelines recommending MLD of 13 to 18 Gy in 3 to 6 fractions, but there are very limited data on appropriate MLD objectives for patients with CP B8 or higher.[11,19] A conservative and unsubstantiated MLD < 6 Gy in 4 to 6 fractions has been recommended for patients with more advanced cirrhosis but is frequently not feasible without significantly compromising prescription dose. Thus, in our study we allowed a more liberal CP-based adaptive approach to MLD such that the lower the CP score the higher the allowed MLD, ranging from 6 to 8.8 Gy. We extrapolated the MLD threshold of 8.8 Gy from Lasley et al,[20] who reported the mean MLD was 8.8 Gy among CP B patients who did not develop liver toxicity after SBRT. However, the majority of patients in their cohort were CP B7, with

only 4 patients with CP $\geq$ B8. Our MLD was 8.8, 8, 5.4, and 4.8 Gy for CP B7, B8, B9, and C10 patients, respectively, and there was no correlation between MLD and CP progression, all-cause mortality, or liver-related mortality. Thus, it appears that using a CP-based adaptive approach to MLD with a constraint of ~8 Gy for CP B7-8 and ~5 Gy for CP B9-C10 is reasonable.

The small number of subjects in our study limits the statistical power to detect differences, and thus our outcomes need to be validated in a larger study with subsequent improvement in definition of SBRT-related liver toxicity and dose-volume parameters to limit liver toxicity.

Conclusion

Results from our study suggest that SBRT is a potentially safe and efficacious local modality for carefully selected patients with CP B7-C10 with HCC with excellent LC. Distinguishing late SBRT-related liver toxicity from natural progression of cirrhosis and progressive HCC is a challenge, but from our analysis, it does not appear that baseline CP score correlated with liver-related mortality or OS.

Acknowledgments

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