Yttrium-90 Glass-Based Microsphere Radioembolization in the Treatment of Hepatocellular Carcinoma Secondary to the Hepatitis B Virus: Safety, Efficacy, and Survival

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ABSTRACT

Purpose: To evaluate outcomes of yttrium-90 radioembolization performed with glass-based microspheres in the treatment of hepatocellular carcinoma (HCC) secondary to the hepatitis B virus (HBV).

Materials and Methods: A total of 675 patients treated between January 2006 and July 2014 were reviewed, of which 45 (age 62 y ± 10; 91% male) received glass-based radioembolization for HCC secondary to HBV. All patients were stratified according to previous therapy (naive, n = 14; 31.1%), Child–Pugh class (class A, n = 41; 91%), Eastern Cooperative Oncology Group (ECOG) performance status (PS; < 1, n = 21; 47%), solitary (n = 26; 58%) and unilobar (n = 37; 82%) tumor distribution, tumor size < 5 cm (n = 29; 64%), portal vein thrombosis (n = 14; 31%), α-fetoprotein level > 400 ng/mL (n = 17; 38%), and Barcelona Clinic Liver Cancer stage (A, n = 8; B, n = 9; C, n = 28).

Results: A total of 50 radioembolization treatments were performed, with a 100% technical success rate (median target dose, 120 Gy). Clinical toxicities included pain (16%), fatigue (12%), and nausea (4%). Grade 3/4 laboratory toxicities included bilirubin (8%) and aspartate aminotransferase (4%) toxicities. Observed toxicities were independent of treatment dose. The objective response rates were 55% per modified Response Evaluation Criteria In Solid Tumors and 21% per World Health Organization criteria, and the disease control rate was 63%. Disease progression was secondary to new, nontarget HCC in 45% of cases. Median time to progression and overall survival were 6.0 mo (95% confidence interval [CI], 4.4–8.0 mo) and 19.3 mo (95% CI, 11.2–22.7 mo), respectively. Multivariate analysis demonstrated ECOG PS ≥ 1 and AFP level > 400 ng/mL to be independent predictors of inferior overall survival.

Conclusions: Glass-based radioembolization for HCC secondary to HBV can be safely performed, with favorable target lesion response and overall survival.

ABBREVIATIONS

AFP = α-fetoprotein, BCLC = Barcelona Clinic Liver Cancer, CI = confidence interval, ECOG = Eastern Cooperative Oncology Group, HBV = hepatitis B virus, HBV-HCC = hepatocellular carcinoma resulting from hepatitis B virus etiology, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, HCV-HCC = hepatocellular carcinoma resulting from hepatitis C virus etiology, HR = hazard ratio, mRECIST = modified Response Evaluation Criteria In Solid Tumors, PS = performance status, TTP = time to progression, WHO = World Health Organization

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Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and the second most common cause of cancer mortality worldwide (1,2). A heterogeneous array of different HCC etiologies have been described, including chronic hepatitis caused by viruses, alcohol, or inflammatory disease states (1). The hepatitis B virus (HBV) causes the majority of cases in Asia and worldwide but accounts for only a small percentage of HCC cases in the United States and Europe, where HCC secondary to the hepatitis C virus (HCV) and alcohol predominate (1,3). Differences in the molecular pathogenesis of HCC resulting from HBV etiology (HBV-HCC) and HCC resulting from HCV etiology (HCV-HCC) have incited a considerable amount of study on the differences in clinical outcomes between these two distinct HCC entities (4,5).

The large retrospective and prospective studies on the clinical outcomes, survival, and prognostic factors in patients with HCC treated with yttrium-90 (^{90}Y) radioembolization have been conducted in Western patient cohorts (in Europe and the United States) with very low incidences of HBV-HCC (6–9). The distinct tumor biology of HBV-HCC creates uncertainty surrounding the extrapolation of radioembolization outcomes in Western-based cohorts of patients with HCC that is largely HCV-related. Recently, a study by Khor et al (10) on HCC treated with resin-based radioembolization in an Asian population (48% HBV-HCC) demonstrated similar outcomes to a large multicenter study on resin-based RE in an European population (13% HBV-HCC) (7). Although the study of Khor et al (10) supports resin-based radioembolization as a safe and efficacious treatment for HBV-HCC, significant differences between resin- and glass-based radioembolization makes extension of these findings to the latter form of radioembolization dubious (11). As such, specific questions remain regarding the clinical outcomes of patients with HBV-HCC treated with glass-based radioembolization. The aim of the present study was to determine the safety, efficacy, and overall survival following glass-based radioembolization in patients with HCC secondary to HBV.

MATERIALS AND METHODS

This retrospective, single-center study was Health Insurance Portability and Accountability Act–compliant and approved by the local institutional review board. Data were obtained by searching the electronic medical record system (EPIC, Verona, Wisconsin). From January 2006 to July 2014, a total of 675 cases of patients treated with radioembolization were reviewed. Patients included in the study had unresectable HCC and serology compatible with chronic HBV infection (ie, positive for surface antigen of HBV) and underwent glass-microsphere radioembolization treatment. HCC was diagnosed based on American Association for the Study of Liver Disease guidelines in all cases (12,13). Patients who had undergone radioembolization previously were excluded. Patients with portal vein thrombosis (n = 14) and extrahepatic disease (n = 1) were included. Decisions regarding which patients to treat, as well the decision to use glass-based radioembolization, were reached by consensus at a weekly multidisciplinary conference of hepatologists, oncologists, transplant surgeons, and interventional radiologists.

Patients

Forty-five patients met the inclusion criteria for the study. All patients were stratified according to previous locoregional therapy, previous sorafenib therapy, Child–Pugh class, Eastern Cooperative Oncology Group (ECOG) performance status (PS), tumor characteristics, presence or absence of portal vein thrombosis, pretreatment α-fetoprotein (AFP) levels, and Barcelona Clinic Liver Cancer (BCLC) stage (14). Patient demographic characteristics are displayed in **Table 1**.

Radioembolization Treatment

All patients underwent a standardized pretreatment workup that comprised clinical evaluation, laboratory and imaging assessment, and a mapping procedure with technetium-99 macroaggregated albumin (6,15,16). Radioembolization therapy was administered via a glass-based device in all cases (TheraSphere; BTG, West Conshohocken, Pennsylvania), with a target dose of dose of 80–150 Gy calculated with a noncompartmental Medical Internal Radiation Dose Committee method (17). Radiation therapy was administered as selectively as possible to limit radioembolization of nontarget hepatic parenchyma. Segmental radioembolization therapy was defined as ^{90}Y infusion to two or fewer hepatic segments (18). Lobar injection was performed when segmental feeding vessels were not clearly identified. Treatment-naive patients with bilobar disease were treated with a staged approach, defined as delivery of radiation therapy to the contralateral lobe 4–6 weeks after treatment of the initial lobe (15). Pretreatment antiviral therapy with tenofovir and entecavir was initiated in all cases. A standard postprocedural protocol including the use of antiemetic agents, pain medication, intravenous hydration, and prophylactic proton-pump inhibitors was administered in all cases (15).

Clinical or Laboratory Toxicities

Patients were followed at regular 4–6-week intervals. All clinical and laboratory toxicities occurring within 90 days were recorded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03 (19). Posttreatment toxicities were documented independently of pretreatment toxicities and were included as toxicities at follow-up irrespective of whether they were present before radioembolization. Toxicities for staged treatments were calculated independently