CLINICAL STUDY

Single-Center Comparison of Overall Survival and Toxicities in Patients with Infiltrative Hepatocellular Carcinoma Treated with Yttrium-90 Radioembolization or Drug-Eluting Embolic Transarterial Chemoembolization

Joseph L. McDevitt, MD, MBA, Ali Alian, MD, Baljendra Kapoor, MD, Stacy Bennett, RN, Amanjit Gill, MD, Abraham Levitin, MD, Mark Sands, MD, K.V. Narayanan Menon, MD, Federico N. Aucejo, MD, Bassam Estfan, MD, Anil K. Pillai, MD, Sanjeeva P. Kalva, MD, and Gordon McLennan, MD

ABSTRACT

Purpose: To compare overall survival and toxicities after yttrium-90 (^{90}Y) radioembolization and chemoembolization with drug-eluting embolics (DEE) in patients with infiltrative hepatocellular carcinoma (HCC).

Materials and Methods: Retrospective review of 50 patients with infiltrative HCC without main portal vein invasion who were treated with ^{90}Y radioembolization (n = 26) or DEE chemoembolization (n = 24) between March 2007 and August 2012 was completed. Infiltrative tumors were defined by cross-sectional imaging as masses that lacked well-demarcated boundaries, and treatment allocations were made by a multidisciplinary tumor board. Median age was 63 years; median tumor diameter was 9.0 cm; and there were no significant differences between groups in performance status, severity of liver disease, or HCC stage. Toxicities were graded by Common Terminology Criteria for Adverse Events v4.03. Overall survival from treatment was assessed by Kaplan-Meier analysis, with analysis of potential predictors of survival with log-rank test.

Results: There was no difference in the average number of procedures performed in each treatment group (DEE, 1.5 ± 1.1; ^{90}Y, 1.6 ± 0.5; $P = .97$), and technical success was achieved in all cases. Abdominal pain (73% vs 33%; $P = .004$) and fever (38% vs 8%; $P = .01$) were more frequent after DEE chemoembolization. There was no significant difference in median overall survival between treatment groups after treatment (DEE, 9.9 months; ^{90}Y, 8.1 months; $P = .11$).

Conclusions: ^{90}Y radioembolization and DEE chemoembolization provided similar overall survival in the treatment of infiltrative HCC without main portal vein invasion. Abdominal pain and fever were more frequent after DEE chemoembolization.

ABBREVIATIONS

BCLC = Barcelona Clinic Liver Cancer, DEE = drug-eluting embolics, HCC = hepatocellular carcinoma, ^{90}Y = yttrium-90

From the Division of Vascular and Interventional Radiology (A.K.P., S.P.K.), Department of Radiology (J.L.M., A.A.), University of Texas Southwestern Medical Center, 5959 Harry Hines Boulevard, Dallas, TX 75235; and Vascular and Interventional Radiology (B.K., S.B., A.G., A.L., M.S., G.M.), Gastroenterology and Hepatology (K.V.N.M.), Transplant Surgery (F.N.A.), and Solid Tumor Oncology (B.E.), Cleveland Clinic, Cleveland, Ohio. Received February 5, 2017; final revision received May 12, 2017; accepted May 20, 2017. **Address correspondence to** J.L.M.; E-mail: josephlmcdevitt@icloud.com

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Infiltrative hepatocellular carcinoma (HCC) is a subtype of HCC that represents 7%–15% of cases. It is associated with hepatitis B infection, often manifests at an advanced stage because of difficulty in diagnosis, and has a worse prognosis than the more typical nodular subtype (1–5). The roles of specific locoregional treatment options, such as conventional chemoembolization, chemoembolization with drug-eluting embolics (DEE) and yttrium-90 (^{90}Y) radioembolization, are not well defined for infiltrative tumors, as major HCC trials have assessed cohorts comprised predominately or exclusively of patients with nodular HCC (1).

The original series evaluating conventional chemoembolization in infiltrative HCC showed no survival benefit (6), but more recent series evaluating DEE chemoembolization (7) and conventional chemoembolization (8,9) have shown improved survival relative to supportive care. ^{90}Y radioembolization has been associated with reduced toxicity (10,11) and longer time to progression relative to conventional chemoembolization in the treatment of nodular HCC (11,12), particularly in the treatment of Barcelona Clinic Liver Cancer (BCLC) stage C disease, similar to many patients with infiltrative HCC (13). One small study consisting primarily of patients with BCLC stage C HCC showed no difference in median overall survival between nodular and infiltrative subtypes after treatment with ^{90}Y radioembolization (14). However, data directly comparing DEE chemoembolization and ^{90}Y radioembolization in infiltrative HCC are limited. Therefore, this study was undertaken to compare overall survival after these 2 therapies in patients with infiltrative HCC without main portal vein invasion.

MATERIALS AND METHODS

Patient Evaluation and Treatment Selection

This single-center, retrospective study was conducted and this article was written in accordance with the most up-to-date Society of Interventional Radiology (SIR) guidelines on terminology and reporting for transcatheter hepatic locoregional therapies (15,16). The study was approved by the institutional review board and was compliant with the Health Insurance Portability and Accountability Act of 1996. Consecutive patients who underwent transarterial hepatic therapy between March 2007 (when the institution began performing DEE chemoembolization) and August 2012 were included for review, with follow-up through August 1, 2014.

Patients were determined to have infiltrative HCC if masses lacked well-demarcated boundaries on cross-sectional imaging (either 4-phase computed tomography or gadolinium-enhanced magnetic resonance with diffusion-weighted imaging) (**Fig 1a–d**). Biopsy was performed if imaging demonstrated the largest tumor dimension to be < 2 cm or if other standard diagnostic criteria were not present (17). Biopsy was performed in 20 (40%) patients for diagnosis (10 [42%] patients who were treated with DEE chemoembolization and 10 [38%] patients who were treated with ^{90}Y radioembolization). Patients with infiltrative HCC with the following conditions were excluded from the study: concurrent nonhepatic malignancy, prior transarterial therapy, prior radiofrequency or microwave ablation, crossover between transarterial modalities during the course of treatment, and main portal vein invasion (all patients with main portal vein invasion were treated with ^{90}Y radioembolization) (18).

Underlying hepatic disease was staged using the Child-Pugh classification (16), and HCC was staged using the BCLC classification (19). The following guidelines were considered to determine if a patient was a suitable candidate for transarterial therapy: total bilirubin ≤ 2.0 mg/dL, tumor burden $< 50\%$ of liver volume on cross-sectional imaging, and Eastern Cooperative Oncology Group grade ≤ 3. Five patients with total bilirubin > 2 mg/dL who had tumors amenable to segmental transarterial therapy were deemed appropriate candidates for locoregional therapy. Choice of transarterial therapy was made by consensus at a multidisciplinary tumor board that included representatives from transplant surgery, solid tumor medical oncology, radiation oncology, diagnostic radiology, hepatology, and interventional radiology. Final treatment selection was determined by discussion between the patient and attending interventional radiologist.

Inclusion criteria were met by 50 patients (26 treated with DEE chemoembolization and 24 treated with ^{90}Y radioembolization). The treatment groups did not differ in demographics, etiology of cirrhosis, severity of underlying liver disease, stage of HCC, performance status, prior therapies, or hepatic function (**Table 1**). Levels of total bilirubin and albumin before the procedure were stratified based on thresholds used for Child-Pugh scoring (16), and alpha fetoprotein level before the procedure was stratified based on levels previously associated with poor prognosis (20). Most patients had bilobar disease with median tumor diameter of 9.0 cm. No patients underwent subsequent liver transplant.

Treatment Protocols

Antibiotics, antacids, antiemetics, and analgesics were given before all transarterial interventions. Procedures were performed by 4 attending interventional radiologists with 10–20 years of experience. Tumor targeting was accomplished via subselective catheterization of feeding arteries using iodinated contrast material under fluoroscopic guidance. In patients with segmental portal venous invasion, the embolization territory was chosen to avoid segments with invasion. Bilobar disease was preferentially treated in multiple treatment sessions separated by 2–4 weeks.

DEE Chemoembolization. DEE chemoembolization was performed as described previously (21). Briefly, vials containing 50 mg of doxorubicin loaded in 100–300 μm, 300–500 μm, or 700–900 μm LC beads (Biocompatibles UK Ltd, Farnham, United Kingdom) were employed after