CLINICAL STUDY

Transarterial Yttrium-90 Radioembolization Treatment of Patients with Liver-Dominant Metastatic Renal Cell Carcinoma

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ABSTRACT

Purpose: To evaluate safety and efficacy of transarterial hepatic radioembolization treatment of patients with liver-dominant metastatic renal cell carcinoma (RCC).

Materials and Methods: From July 2010 to December 2014, 18 patients with liver-dominant metastatic RCC were treated with yttrium-90 glass microsphere radioembolization. Retrospective review of medical records and imaging studies was performed to evaluate toxicities, treatment response, and overall survival. The median follow-up period from radioembolization treatment was 17.8 months (range, 3–54.4 months).

Results: Median overall survival from RCC diagnosis was 64 months (95% confidence interval [CI], 0–144.1 months), from diagnosis of liver metastasis was 29 months (95% CI, 7.2–50.8 months), and from radioembolization treatment was 22.8 months (95% CI, 13.2–32.3 months). After treatment, 10 patients reported grade 1 clinical toxicities, and 8 patients had grade 1 or 2 biochemical toxicities. The best radiographic responses of 17 patients who underwent contrast-enhanced cross-sectional imaging showed complete response in 16 patients and partial response in 1 patient evaluated by modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria. The last available imaging of these 17 patients demonstrated complete response in 14 patients, partial response in 1 patient, and progression of disease in 2 patients. Images of a patient who underwent noncontrast CT showed stable disease as best response and stable disease on the last available imaging evaluated by RECIST.

Conclusions: Radioembolization is safe and effective and led to improved hepatic disease control and overall survival in patients with liver-dominant metastatic RCC.

ABBREVIATIONS

CI = confidence interval, mRECIST = modified Response Evaluation Criteria in Solid Tumors, RCC = renal cell carcinoma, ^{90}Y = yttrium-90

Metastasis develops in approximately 60% of patients with renal cell carcinoma (RCC) (1). Liver metastasis from RCC is uncommon; the rate has been reported to be up to 18% (2). Development of liver metastasis portends a poor prognosis with a median overall survival of 7.6 months, which is shorter compared with survival of patients with other metastases in whom the median overall survival time was 21.4 months (3). Once a tumor metastasizes to the liver, it is often the limiting factor for survival. RCC liver metastasis is relatively resistant to systemic chemotherapy, cytokine therapy, and external radiation (4,5). Hepatic metastasectomy in patients with RCC significantly improved survival (6,7), but $<$ 5% of patients are candidates for resection (8).

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Transarterial liver-directed embolization treatment of patients with liver-dominant metastatic disease is increasing worldwide because of the severe prognostic implications of the presence of liver metastasis regardless of the type of primary tumor. Transarterial embolization has lower comorbid risk compared with partial hepatectomy, and a higher fraction of tumors is accessible to transarterial treatment than to resection (9). Transarterial radioembolization with yttrium-90 (^{90}Y)-labeled microspheres improved overall survival of patients with liver-dominant metastatic diseases and has a favorable tolerability profile (9,10). Metastatic RCC is an attractive target for transarterial embolization therapies because of its hypervascularity, which ensures efficient delivery of the embolization microspheres to the tumor parenchyma. There is only 1 case series reporting the use of hepatic radioembolization in 6 patients with liver-dominant metastatic RCC (11). The purpose of this study was to evaluate the safety and efficacy of transarterial hepatic radioembolization treatment of patients with metastatic RCC to the liver.

MATERIALS AND METHODS

Patients

This study was approved by the institutional review board. Medical records of 20 consecutive patients with liver-dominant metastatic RCC who underwent radioembolization treatment between July 2010 and December 2014 in a single institution were retrospectively reviewed and analyzed. Criteria for receiving ^{90}Y radioembolization treatment included liver-dominant metastases, Eastern Cooperative Oncology Group performance status of $\leq$ 2, total serum bilirubin $\leq$ 2 mg/dL, serum creatinine $\leq$ 2 mg/dL, and international normalized ratio and platelet count correctable to $\leq$ 1.5 and $\geq$ 50,000/μL, respectively. Patients were not excluded if they had received previous liver-directed therapy or multiple lines of chemotherapy before radioembolization treatment.

There were 2 patients lost to follow-up; these patients were excluded from the study. Patient demographics are summarized in the **Table**. The study included 13 men and 5 women with a mean age of 66.1 years ± 9.6. All patients had biopsy-proven RCC; 15 patients had clear cell RCC, 2 patients had papillary RCC, and 1 patient had chromophobe RCC. Four patients presented with synchronous liver metastasis, and the remaining 14 patients developed liver metastasis later during the course of the disease. At the time of radioembolization treatment, 6 patients had hepatic-only metastatic disease, and 12 patients had both hepatic and extrahepatic metastases. Four patients had a solitary liver lesion, but none of the patients was amenable to percutaneous ablation because of the size of the metastasis. Seven patients received systemic treatment before radioembolization, and 13 patients received systemic treatment after radioembolization. One patient underwent intraoperative radiofrequency ablation of 2 liver metastases 23 months before radioembolization, and 1 patient had been treated with transarterial chemoembolization with doxorubicin-loaded drug-eluting beads 7 months after radioembolization.

Radioembolization Procedure

All patients underwent treatment planning angiography 1–2 weeks before radioembolization treatment according to previously published guidelines (12). During planning angiography, the tumor feeding vessels and anatomic variants were identified, and technetium-99m-labeled macroaggregated albumin was injected into the hepatic arteries to determine the magnitude of hepatopulmonary shunting. The average lung shunt was 7.2% ± 3.3% (range, 3.2%–12.7%). Radioembolization was performed using ^{90}Y-labeled glass microspheres (TheraSphere; BTG International Ltd, London, United Kingdom). In patients with bilobar disease, the left and right lobes were treated separately, approximately 5–7 weeks apart. Repeat radioembolization treatment to the same lobe or segment was not performed. The delivered hepatic dose was calculated based on the treated liver volume, the administered activity, and the lung shunt fraction. The average delivered dose was 137.6 Gy ± 27.6.

Clinical Outcome Measures

Overall survival was calculated from the date of the RCC diagnosis, from the date of the diagnosis of liver metastasis, and from the date of liver-directed therapy to last encounter/follow-up or death. Hepatic progression–free survival was calculated from date of radioembolization therapy until death, last follow-up, or date of first liver progression.

Clinical and laboratory toxicities were assessed at follow-up visits at 1 month, 3 months, and every 3–6 months after radioembolization treatment. Clinical toxicity was defined as subjective reporting by the patient of pain, fatigue, gastrointestinal symptoms (anorexia, nausea, vomiting), or other. Toxicities were defined according to the Common Terminology Criteria for Adverse Events Version 4.03 scoring system. Tumor response was evaluated using modified Response Evaluation Criteria in Solid Tumors (mRECIST) (13). At follow-up visits at 1 month, 3 months, and every 3–6 months after treatment, 17 patients underwent baseline and follow-up contrast-enhanced cross-sectional imaging (computed tomography [CT] or magnetic resonance imaging). RECIST (14) was used to evaluate tumor response in 1 patient who did not receive an intravenous contrast agent for imaging.

Statistical Analysis

Statistical analysis was performed with IBM SPSS Statistics for Windows version 22 (IBM Corporation, Armonk, New York). Data are presented as mean ± SD. The probabilities of survival and hepatic