Intrahepatic Cholangiocarcinoma Treated with Transarterial Yttrium-90 Glass Microsphere Radioembolization: Results of a Single Institution Retrospective Study

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ABSTRACT

Purpose: To evaluate the efficacy and safety of transarterial yttrium-90 glass microsphere radioembolization in patients with unresectable intrahepatic cholangiocarcinoma (ICC).

Materials and Methods: Retrospective review of 85 consecutive patients (41 men and 44 women; age, 73.4 ± 9.3 years) was performed. Survival data were analyzed by the Kaplan-Meier method, Cox regression models, and the log-rank test.

Results: Median overall survival (OS) from diagnosis was 21.4 months (95% confidence interval [CI]: 16.6–28.4); median OS from radioembolization was 12.0 months (95% CI: 8.0–15.2). Seven episodes of severe toxicity occurred. At 3 months, 6.2% of patients had partial response, 64.2% had stable disease, and 29.6% had progressive disease. Median OS from radioembolization was significantly longer in patients with Eastern Cooperative Oncology Group (ECOG) scores of 0 and 1 than patients with an ECOG score of 2 (18.5 vs 5.5 months, $P = .0012$), and median OS from radioembolization was significantly longer in patients with well-differentiated histology than patients with poorly differentiated histology (18.6 vs 9.7 months, $P = .012$). Patients with solitary tumors had significantly longer median OS from radioembolization than patients with multifocal disease (25 vs. 6.1 months, $P = .006$). The absence of extrahepatic metastasis was associated with significantly increased median OS (15.2 vs. 6.8 months, $P = .003$). Increased time from diagnosis to radioembolization was a negative predictor of OS. The morphology of the tumor (mass-forming or infiltrative, hyper- or hypo-enhancing) had no effect on survival. Post-treatment increased cancer antigen 19-9 level, increased international normalized ratio, decreased albumin, increased bilirubin, increased aspartate aminotransferase, and increased Model for End-Stage Liver Disease score were significant predictors of decreased OS.

Conclusions: These data support the therapeutic role of radioembolization for the treatment of unresectable ICC with good efficacy and an acceptable safety profile.

ABBREVIATIONS

CA = cancer antigen, CI = confidence interval, ECOG = Eastern Cooperative Oncology Group, ICC = intrahepatic cholangiocarcinoma, INR = international normalized ratio, MELD = Model for End-Stage Liver Disease, OS = overall survival, RECIST = Response Evaluation Criteria in Solid Tumors, ^{90}Y = yttrium-90

Cholangiocarcinoma is the second most common primary liver malignancy, and its incidence is increasing, currently being 2.1 per 100,000 population [1]. Compared to hilar and distal bile duct cholangiocarcinoma, intrahepatic cholangiocarcinoma (ICC) is often asymptomatic and is frequently found incidentally [2]. For this reason, many patients present with locally advanced tumors. Although surgical resection offers the highest curative potential, almost 90% of tumors are deemed unresectable at diagnosis [3]. In addition, the recurrence rate is approximately 70% after attempted curative resection [4]. ICC has a poor prognosis. Patients who receive palliative treatment alone have a median overall survival (OS) of 3 months [5], and less than 10% of all patients survive more than 5 years regardless of treatment [6]. Patients who are not surgical candidates may receive palliative systemic chemotherapy, but the available systemic chemotherapies and newer targeted therapies have limited success, with only a modest increase in OS (8.1–11.7 months) [7,8].

Transarterial radioembolization with yttrium-90 (^{90}Y) microspheres has been included in the armamentarium of treatment options for ICC. Published studies have reported a wide range of survival outcomes after radioembolization treatment (6.1–22 months), which is likely due in part to the small number of patients (18–46 patients) included in those studies and the heterogeneity of selection criteria in the different protocols [9–19]. The aim of this retrospective study was to evaluate the safety and efficacy of transarterial radioembolization treatment of patients with ICC using ^{90}Y-labeled glass microspheres.

MATERIALS AND METHODS

Patients

This study was approved by the institutional review board. Medical records of 85 consecutive patients with biopsy-proven ICC who underwent radioembolization treatment between May 2009 and May 2016 in a single institution were retrospectively reviewed and analyzed. Criteria for receiving radioembolization treatment included Eastern Cooperative Oncology Group (ECOG) performance status score ≤ 2, total serum bilirubin ≤ 2 mg/dl, serum creatinine ≤ 2 mg/dl, international normalized ratio (INR) ≤ 1.5, and platelet count $\geq 50,000/\mu l$. Patients were not excluded if they had received previous liver-directed therapy or multiple lines of chemotherapy before the radioembolization treatment.

Patient demographics are summarized in Table 1. The study included 41 men and 44 women, aged 73.4 ± 9.3 years (mean ± standard deviation [SD]), who underwent a total of 140 radioembolization treatments. The median interval between the diagnosis of ICC and initial radioembolization treatment was 4.4 months (range, 0.5–58.5 months). At the time of the radioembolization, 36 (42%) patients had extrahepatic disease. Sixty-one (71.8%) patients received chemotherapy before the first radioembolization, and 18 (21.2%) patients had prior liver-directed therapy (14 had surgical resection and 4 had external-beam radiation). Nineteen (22.3%) patients

Table 1. Demographic Characteristics of Patients

	n	%
Age (years)		
<70	35	41.2
≥70	50	58.8
Sex		
Men	41	48.2
Women	44	51.8
ECOG score		
0	35	41.2
1	22	25.9
2	28	32.9
Tumor grade		
Well differentiated	8	9.4
Moderately differentiated	30	35.3
Poorly differentiated	34	40.0
Not reported	13	15.3
Distribution		
Unilobar	54	63.5
Bilobar	31	36.5
Number of tumors		
Solitary	52	61.2
Multiple	33	38.8
Tumor morphology		
Mass-forming	32	37.6
Infiltrative	53	62.4
Tumor enhancement		
Nonenhancing	33	38.8
Enhancing	49	57.7
Contrast study not available	3	3.5
Extrahepatic metastasis		
No	49	57.6
Yes	36	42.4
Previous chemotherapy		
None	24	28.2
Yes	61	71.8
Previous liver-directed therapy		
None	67	78.8
Resection	14	16.5
Radiation	4	4.7

ECOG = Eastern Cooperative Oncology Group.

received radioembolization as first-line treatment. Six (7.1%) patients received systemic chemotherapy after the radioembolization treatment.

Radioembolization Procedure

All patients underwent a treatment planning angiogram before the radioembolization treatment as previously described [20]. During the planning angiography, the tumor-feeding vessels and anatomic variants were identified, and technetium-99-labeled macroaggregated albumin was injected into the hepatic arteries to determine the magnitude of hepatopulmonary shunting. Radioembolization was performed using ^{90}Y-labeled glass microspheres (TheraSphere;