

Predictors of Survival after Yttrium-90 Radioembolization for Colorectal Cancer Liver Metastases

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ABSTRACT

Purpose: To identify clinical parameters that are prognostic for improved overall survival (OS) after yttrium-90 radioembolization (RE) in patients with liver metastases from colorectal cancer (CRC).

Materials and Methods: A total of 131 patients who underwent RE for liver metastases from CRC, treated at 2 academic centers, were reviewed. Twenty-one baseline pretreatment clinical factors were analyzed in relation to OS by the Kaplan-Meier method along with log-rank tests and univariate and multivariate Cox regression analyses.

Results: The median OS from first RE procedure was 10.7 months (95% confidence interval [CI], 9.4–12.7 months). Several pretreatment factors, including lower carcinoembryonic antigen (CEA; ≤ 20 ng/mL), lower aspartate transaminase (AST; ≤ 40 IU/L), neutrophil-lymphocyte ratio (NLR) < 5 , and absence of extrahepatic disease at baseline were associated with significantly improved OS after RE, compared with high CEA (> 20 ng/mL), high AST (> 40 IU/L), NLR ≥ 5 , and extrahepatic metastases (P values of $< .001$, $< .001$, $.0001$, and $.04$, respectively). On multivariate analysis, higher CEA, higher AST, NLR ≥ 5 , extrahepatic disease, and larger volume of liver metastases remained independently associated with risk of death (hazard ratios of 1.63, 2.06, 2.22, 1.48, and 1.02, respectively).

Conclusions: The prognosis of patients with metastases from CRC is impacted by a complex set of clinical parameters. This analysis of pretreatment factors identified lower AST, lower CEA, lower NLR, and lower tumor burden (intra- or extrahepatic) to be independently associated with higher survival after hepatic RE. Optimal selection of patients with CRC liver metastases may improve survival rates after administration of yttrium-90.

ABBREVIATIONS

AST = aspartate transaminase, CEA = carcinoembryonic antigen, CRC = colorectal cancer, NLR = neutrophil-lymphocyte ratio, OS = overall survival, RE = radioembolization, ^{90}Y = yttrium-90

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Colorectal cancer (CRC) is the third most common cancer diagnosis in the United States (1). More than one-half of patients with CRC present with or develop liver metastases during the course of the disease (2). Although surgical resection is a potentially curative treatment for hepatic metastases, this approach is feasible in only 20% of patients owing to medical comorbidities, underlying hepatic dysfunction, or extent of tumor burden (3,4). Radiofrequency ablation (RFA) has been investigated as a potentially curative and less invasive alternative to surgical resection, but tumor size and location can limit its feasibility (3,5). A number of other locoregional therapies are available, including stereotactic body radiation therapy, cryotherapy, hepatic intra-arterial pump chemotherapy, transarterial chemoembolization, and transarterial radioembolization (RE). RE with yttrium-90 (⁹⁰Y) resin microspheres is approved by the Food and Drug Administration for treatment of liver metastases from CRC (6–11). The treatment has been shown in multiple institutional studies to be safe and has been used and compared with transarterial chemoembolization in patients with a greater hepatic disease burden (12–14).

It is difficult to predict which patients have the best outcomes after RE. Previous studies identified lung shunt fraction and markers of hepatic function as having prognostic implications in patients both with primary hepatic malignancies and with hepatic metastases treated by RE (15,16). Similarly, elevated bilirubin, high alkaline phosphatase, high tumor volume, increased number of previous therapies, low albumin, and presence of extrahepatic disease have been correlated with poor prognosis after RE in patients with metastatic CRC (12,13). The purpose of the present report was to elucidate and further identify prognostic factors in a patient population with metastatic CRC treated with RE at 2 different academic centers.

MATERIALS AND METHODS

Patients

Institutional Review Board approval was obtained before data collection, and owing to the retrospective nature requirement of informed consent was waived. One hundred thirty-one patients undergoing RE at 2 separate institutions from 2007 to 2014 were identified and included in the analysis. Patients were not operative candidates (because of patient- or tumor-related factors) and had failed multiple previous chemotherapy regimens. All patients were treated with ⁹⁰Y resin microspheres. The study population included 84 men (64.1%) and 47 women (35.9%) with an overall mean age of 59 years. All patient baseline characteristics are summarized in Table 1. Most patients (71.8%) had hepatic metastases at the time of their initial CRC diagnosis, 68% of the patients had received greater than 2 lines of chemotherapy, and 79% had undergone resection of their primary colorectal tumor. The colorectal primary tumor was right-sided in 19% of patients, left sided-in 68% of patients, and unknown in 16% of patients. Right-sided

Table 1. Baseline Characteristics

Characteristic	Parameter	Value
Sex	Female	47 (35.9%)
	Male	84 (64.1%)
Age, y		59 ± 1
ECOG performance status	0	74 (64.9%)
	1	33 (29.0%)
	2	6 (5.3%)
	3	1 (0.9%)
Site	Medical center 1	43 (32.8%)
	Medical center 2	88 (67.2%)
CEA, ng/mL		37.3 (0–7690.5)
ALT, IU/L		33.5 (10–291)
AST, IU/L		39 (13–207)
ALP, IU/L		138 (43–1,554)
Albumin, g/dL		3.9 (2.6–4.7)
Bilirubin, mg/dL		0.5 (0.2–2.9)
NLR class	1	81 (64.3%)
	2	45 (35.7%)
Extrahepatic metastases	Yes	59 (46.1%)
	No	69 (53.9%)
Lesion size, cm		<5 (1.5–20.8)
Tumor volume, %		12.6 (0.8–76.0)
Metastasis to liver	Synchronous	94 (71.8%)
	Metachronous	37 (28.2%)
Lesion category	Dominant	35 (27.1%)
	Diffuse	94 (72.9%)
Previous chemotherapy lines	0	2 (1.6%)
	1	39 (30.5%)
	2	50 (39.1%)
	3	22 (17.2%)
	≥4	15 (11.7%)
Hepatic local therapy	Yes	34 (26.0%)
	No	97 (74.0%)
Hepatic regional therapy	Yes	43 (32.8%)
	No	88 (67.2%)
Type of hepatic locoregional therapy*	Resection	18 (13.7%)
	Transarterial chemoembolization	10 (7.6%)
	Cryoablation	2 (1.5%)
	HAIP	2 (1.5%)
	RFA	16 (12.2%)
	SBRT	4 (3.0%)
Primary colorectal cancer removal	Yes	104 (79.4%)
	No	27 (20.6%)
Side of origin of primary colorectal tumor	Left	89 (67.9%)
	Right	25 (19.1%)
	Unknown	21 (16.0%)
Lung shunting, %		4 (0–18)
Treatment approach	Sequential lobar	67 (51.1%)
	Single administration	64 (48.9%)
Radiation activity, GBq		1.51 ± 0.04

Note—Values are presented as n (%), mean ± SD, or median (range). ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate transaminase; CEA = carcinoembryonic antigen; ECOG = Eastern Cooperative Oncology Group; HAIP = hepatic artery infusion pump; NLR = neutrophil-lymphocyte ratio; RFA = radiofrequency ablation; SBRT = stereotactic body radiotherapy. *Some patients underwent more than one type of hepatic locoregional therapy.

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