CLINICAL STUDY

Radioembolization for Hepatocellular Carcinoma: A Nationwide 10-Year Experience

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ABSTRACT

Purpose: To examine the US nationwide experience with transarterial radioembolization (TARE) for hepatocellular carcinoma (HCC) in the years 2003–2012 and the prognostic factors associated with overall survival.

Materials and Methods: A retrospective cohort study from the National Cancer Database included 110,139 adult patients with HCC between 2003 and 2012, of whom 1,222 received TARE. Primary outcome of interest was mortality after treatment. Univariate and multivariate analyses for factors predicting mortality were performed for 961 patients treated between 2003 and 2011. Overall survival was estimated by Kaplan-Meier method.

Results: There was a steady increase in utilization of TARE in the past decade. Most patients were white men with median age of 64 years. Of those patients, 67% received treatment at an academic institution, 42% were American Joint Committee on Cancer stage I or II, and 10% had metastatic disease at the time of treatment. Median overall survival was 13.3 months. Overall survival varied by patient and tumor characteristics. Female patients with tumors < 5 cm or stage I or II disease benefited the most from treatment. Outcomes were the same across all age groups. Patients who were African American or had metastatic disease tended to have worse outcomes.

Conclusions: Use of TARE in patients with HCC has been increasing. Several factors are significantly associated with a less favorable outcome after TARE, including male sex, large tumors, and extrahepatic disease. These data can be used for designing future radioembolization trials.

ABBREVIATIONS

AJCC = American Joint Committee on Cancer, HCC = hepatocellular carcinoma, NCDB = National Cancer Database, TARE = transarterial radioembolization

Deaths resulting from hepatocellular carcinoma (HCC) have been increasing, and HCC had the highest mortality rate of all common cancers between 2003 and 2012 (1). Although surgical resection and liver transplantation are considered potentially curative treatments, there are several other treatment options, including locoregional therapies, which can offer benefits of slowing disease progression and prolonging survival for patients with advanced or unresectable disease (2). One of these treatments is transarterial radioembolization (TARE), a minimally invasive therapy that delivers radioactive microbeads containing β-emitting yttrium-90 isotopes directly to the tumor via hepatic artery branches (3). TARE exploits the pathophysiology of HCC, which derives almost all of its blood supply from hepatic arteries as opposed to the native liver parenchyma, which depends predominantly on portal venous supply (4). This dissimilarity in perfusion pattern allows tumoricidal doses of radiation to be locally administered with relative sparing of healthy liver and minimal toxicity to the patient.

Over the past decade, there has been increasing evidence supporting the role of TARE in treating HCC, particularly in patients with unresectable, intermediate-stage disease.

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Tables E1 and E2 are available online at *www.jvir.org*.

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Table 1. Characteristics of Patients Receiving Radioembolization for Hepatocellular Cancer

Characteristics	All Patients (N = 1,222)
Age at diagnosis, years, median (IQR)	63 (56, 72)
Age, years, n (%)	
≤ 65	717 (58.7)
66–70	164 (13.4)
71–74	141 (11.5)
> 75	200 (16.4)
Sex, n (%)	
Male	949 (77.7)
Female	273 (22.3)
Race, n (%)	
White	942 (77.1)
African American	165 (13.5)
Asian/Pacific Islander	85 (7.0)
Other/unknown	30 (2.5)
Insurance type, n (%)	
Private	481 (39.4)
Medicaid	101 (8.3)
Medicare	574 (47.0)
Not insured/unknown	66 (5.4)
Income, n (%)	
< $38,000	243 (20.2)
$38,000–$47,999	317 (26.4)
$48,000–$62,999	309 (25.7)
> $63,000	332 (27.6)
No high school diploma, n (%)	
> 21%	230 (19.2)
13%–20.9%	331 (27.6)
7%–12.9%	384 (32.0)
< 7%	256 (21.3)
Patient urban/rural location, n (%)	
Metro areas	1,011 (86.1)
Urban metro-adjacent	103 (8.8)
Urban not metro-adjacent	43 (3.7)
Rural	17 (1.4)
Miles to hospital, median (IQR)	21.3 (7.6, 58.5)
Tumor size, n (%)	
< 2 cm	86 (7.0)
2–5 cm	382 (31.3)
> 5 cm	754 (61.7)
AJCC stage	
I	267 (21.8)
II	263 (21.5)
III	368 (30.1)
IV	118 (9.7)
Unknown	205 (16.8)
Charlson-Deyo score, n (%)	
0	672 (55.0)
1	314 (25.7)
2	236 (19.3)
Hospital type, n (%)	
Community cancer program*	396 (32.4)
Academic/research program	826 (67.6)
Facility location, n (%)	
New England	29 (2.4)
Middle Atlantic	193 (15.8)
South Atlantic	201 (16.4)
East North Central	308 (25.2)
East South Central	46 (3.8)
West North Central	60 (4.9)
West South Central	95 (7.8)
Mountain	114 (9.3)
Pacific	176 (14.4)

AJCC = American Joint Committee on Cancer; IQR = interquartile range.
*This category includes community programs and comprehensive community programs.

Multiple single-center cohort studies have shown that TARE is efficacious and very well tolerated in selected patients and has been found to delay disease progression with only minimal transient side effects, such as fatigue, abdominal pain, and nausea and vomiting (5,6). Furthermore, TARE may be effective for tumor downstaging, possibly serving as a bridge to transplantation or resection, and is suspected to cause contralateral lobe hypertrophy, which helps compensate for the declining functional capacity of the cirrhotic liver (7–10). Despite this encouraging research, the sample sizes of the studies have not been powered to detect any possible discrepancies in treatment efficacy among various patient populations. Factors such as age, sex, race, or tumor burden may be associated with significant differences in mortality following this procedure. Therefore, a large population-based study is indicated to identify and characterize any patient factors that affect outcome of TARE therapy and could direct the selection of patients in future prospective randomized studies.

MATERIALS AND METHODS

Participants and Variables

A retrospective cohort study using data from the National Cancer Database (NCDB) was conducted. All patients ≥ 18 years of age who with a diagnosis of HCC between 2003 and 2012 were included in the analysis. Cases treated before 2003 represented < 5% of the total cases and were excluded from the analysis because they may represent early isolated experiences with TARE. Of primary interest for analysis in this study were patients who received radioembolization, defined as patients who received liver-directed radioisotopes during the above-specified period. Between 2003 and 2012, 110,139 patients received a diagnosis of HCC. Liver-directed radioembolization was performed in 1,342 (1.2%)