

Response and Overall Survival for Yttrium-90 Radioembolization of Hepatic Sarcoma: A Multicenter Retrospective Study

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ABSTRACT

Purpose: To evaluate the effectiveness and safety of yttrium-90 transarterial radioembolization (TARE) for the treatment of primary and metastatic soft tissue sarcoma (STS) of the liver.

Materials and Methods: A retrospective review of 39 patients with primary ($n = 2$) and metastatic ($n = 37$) hepatic STS treated with TARE at 4 institutions was performed. Fourteen STS subtypes were included, with leiomyosarcoma being the most common (51%). TARE with glass (22 patients) or resin (17 patients) microspheres was performed, with single lobe (17 patients) or bilobar treatment (22 patients) based on disease burden. Adverse events of treatment, overall survival (OS), and tumor response at 3, 6, and 12 months after TARE were assessed per the Response Evaluation Criteria in Solid Tumors.

Results: Fourteen patients demonstrated either partial or complete response to therapy, with an objective response rate of 36%. Thirty patients (77%) demonstrated disease control (DC)—either stable disease or response to treatment. Median OS was 30 months (95% confidence interval 12–43 months) for all patients. DC at 3 months was associated with an increased median OS (44 months) compared with progressive disease (PD) (7.5 months; $P < .0001$). Patients with DC at 6 months also demonstrated an increased median OS (38 months) compared to patients with PD (17 months; $P = .0443$). Substantial adverse events included 1 liver abscess, 1 gastric ulceration, and 1 pneumonitis.

Conclusions: Patients with hepatic STS treated with TARE demonstrated a high rate of DC and a median OS of 30 months, which suggests a role for TARE in the palliation of hepatic STS.

ABBREVIATIONS

CI = confidence interval, CR = complete response, DC = disease control, OS = overall survival, PD = progressive disease, PR = partial response, RECIST = Response Evaluation Criteria in Solid Tumors, SD = stable disease, STS = soft tissue sarcoma, TARE = transarterial radioembolization

Soft tissue sarcoma (STS) is a rare and diverse group of cancers consisting of over 50 separate subtypes, which comprises less than 1% of the malignancies diagnosed in the United States annually. STS has a 60% 5-year metastasis-free survival rate for early-stage disease (1,2). Metastases from STS, however, frequently occur despite aggressive local treatment. Of the 85%–88% of STS patients diagnosed with intermediate- to high-grade tumors, up to half will

develop metastatic disease (1,3). Additionally, 8% of patients with STS initially present with metastatic disease (1,2). Prognosis for patients with metastatic STS is much poorer, with a median overall survival (OS) ranging from 12 to 17.4 months (2–7). Within this group, of the 18%–19% of patients affected with liver metastases, the prognosis is even poorer, with a median OS of 11 months and a poorer response to chemotherapy (4,8). Primary hepatic STS

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EDITORS' RESEARCH HIGHLIGHTS

- Radioembolization in patients with hepatic sarcoma is safe and effective, with the majority of patients (77%) demonstrating disease control at 6 months.
- 3-month imaging may underestimate response to treatment; 42% of patients with objective response (6 of 14) at 6 months had stable disease at 3 months.
- Survival was significantly worse in patients with progressed disease at 3 months compared with those with disease control (7.5 months versus 44 months, $p < .0001$).
- Treatment with glass microspheres was associated with increased radiation dose and increased median overall survival.

demonstrates a similar prognosis for resectable disease, with 5-year survival ranging from 36% to 72%. This survival decreases precipitously with nonresectable disease, with a median OS of less than 12 months (9,10).

Yttrium-90 transarterial radioembolization (TARE) is an effective treatment for hepatocellular carcinoma (11) and for metastatic disease to the liver (12,13). Few reports in the literature describe TARE for hepatic STS, with only a few case studies or mentions in multiple tumor type studies (11,12). The purpose of this multicenter study was to assess the safety and effectiveness of TARE for hepatic STS.

MATERIALS AND METHODS

Patients

This multi-institutional study was approved by the respective institutional review boards of 4 participating institutions and conducted in compliance with the Health Insurance Portability and Accountability Act. The need for informed consent was waived given the retrospective nature of the study. All patients with hepatic STS who underwent TARE from the date that radioembolic agents became available at the participating institutions were included. From 2006 to 2015, 39 patients with primary liver sarcoma ($n = 2$) or metastatic liver sarcoma ($n = 37$) underwent TARE. A total of 14 different subtypes of STS were included in the study. Gastrointestinal stromal tumors, due to their response to imatinib and resulting improved OS, were excluded from the study. Patient characteristics are summarized in Table 1. Prior to TARE, 95% (37/39) of the patients had received at least 1 course of chemotherapy. The most common first-line therapies were doxorubicin monotherapy ($n = 5$) and docetaxel and gemcitabine ($n = 5$). Second- and third-line chemotherapy regimens were variable but most commonly included docetaxel and gemcitabine ($n = 7$), pazopanib ($n = 6$), and doxorubicin ($n = 4$).

Embolization Procedures

TARE procedures were performed by multiple interventional radiologists at their corresponding institutions, with proceduralist experience levels ranging from 11 to 23 years.

Table 1. Baseline Patient Characteristics

	N (%)
Sex	
Women	20 (51)
Men	19 (49)
Age	
Median (years)	59
Interquartile range	(48–70)
Bilirubin	
Median	.6
Range	.2–2.6
Albumin	
Median	3.6
Range	2.20–4.50
INR	
Median	1.005
Range	.80–1.23
Sarcoma Subtype	
Leiomyosarcoma	20 (51)
Hemangiopericytoma	4 (10)
Other	15 (38)
Primary Site	
Retroperitoneum	6 (15)
Uterus	4 (10)
Extremity	4 (10)
Extrahepatic Metastatic Disease	
Lungs	17 (44)
Bones	10 (26)
Solid organs	10 (26)
Peritoneum	5 (13)
Hypervascular Lesions on Cross-Sectional Imaging	
Yes	9 (23)
No	30 (77)
Institution	
Stanford University	15 (38)
Indiana University	13 (33)
University of Washington	7 (18)
Northwestern University	4 (10)
Prior Systemic Chemotherapy	
Yes	37 (95)
No	2 (5)
Prior Radiotherapy	
Yes	9 (23)
No	30 (77)
Prior Liver Resection	
Yes	3 (8)
No	36 (92)

INR = international normalized ratio.

At all institutions, patients underwent visceral arteriography with the administration of technetium-99^m-macro-aggregated albumin, to estimate hepatopulmonary shunting and to simulate dose to target liver. During subsequent TARE procedures, either glass (TheraSphere, BTG International,

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