CLINICAL STUDY

Is a Technetium-99m Macroaggregated Albumin Scan Essential in the Workup for Selective Internal Radiation Therapy with Yttrium-90? An Analysis of 532 Patients

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ABSTRACT

Purpose: To determine if baseline patient, tumor, and pretreatment evaluation characteristics could help identify patients who require technetium-99m (^{99m}Tc) macroaggregated albumin (^{99m}Tc MAA) imaging before selective internal radiation therapy (SIRT).

Materials and Methods: In this retrospective analysis, 532 consecutive patients with primary (n = 248) or metastatic (n = 284) liver tumors were evaluated between 2006 and 2015. Variables were compared between patients in whom ^{99m}Tc MAA imaging results contraindicated/modified SIRT administration with yttrium-90 (^{90}Y) resin microspheres and those who were treated as initially planned. The ^{99m}Tc MAA findings that contraindicated/modified SIRT were a lung shunt fraction (LSF) > 20%, gastrointestinal ^{99m}Tc MAA uptake, or a mismatch between ^{99m}Tc MAA uptake and intrahepatic tumor distribution.

Results: LSF > 20% and gastrointestinal MAA uptake were observed in 7.5% and 3.9% of patients, respectively, and 11% presented a mismatch. Presence of a single lesion (odds ratio [OR] = 2.4) and vascular invasion (OR = 5.5) predicted LSF > 20%, and GI MAA uptake was predicted by the presence of liver metastases (OR = 3.7) and ^{99m}Tc MAA injection through the common/proper hepatic artery (OR = 4.7). Vascular invasion (OR = 4.1) was the only predictor of LSF > 20% and/or GI MAA uptake (sensitivity = 49.2%, specificity = 80.3%, negative predictive value = 92.4%). Previous antiangiogenic treatment (OR = 2.4) and presence of a single lesion (OR = 2.6) predicted mismatch.

Conclusions: Imaging with ^{99m}Tc MAA is essential in SIRT workup because baseline characteristics may not adequately predict ^{99m}Tc MAA results. Nevertheless, the absence of vascular invasion potentially identifies a group of patients at low risk of SIRT contraindication/modification in whom performing SIRT in a single session (ie, pretreatment evaluation and SIRT on the same day) should be explored.

ABBREVIATIONS

CI = confidence interval, GI = gastrointestinal, LSF = lung shunt fraction, MAA = macroaggregated albumin, OR = odds ratio, PET = positron emission tomography, SIRT = selective internal radiation therapy, SPECT = single-photon emission CT

In the pretreatment evaluation of patients with liver tumors for their candidacy to undergo selective internal radiation therapy (SIRT), technetium-99m (^{99m}Tc) macroaggregated albumin (MAA) imaging is part of the workup, with the aim to simulate yttrium-90 (^{90}Y) microsphere distribution during SIRT. One of the main purposes of ^{99m}Tc MAA imaging is to enable calculation of the lung shunt fraction (LSF), as a high LSF value is indicative of an increased risk of radiation

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pneumonitis (1). According to the manufacturer's recommendations for ^{90}Y resin microspheres (SIR-Spheres; Sirtex Medical, North Sydney, Australia), SIRT is contraindicated for patients with a LSF > 20%, and a reduction in prescribed activity is recommended for those with a LSF between 10% and 20% (SIR-Spheres Microspheres [package insert]. North Sydney, Australia: Sirtex Medical; 2016). Baseline patient and tumor characteristics associated with a high LSF have been recently described (2–6), and it has been suggested that there is a group of patients at such low risk of a high LSF that the ^{99m}Tc MAA scan could be omitted from the pretreatment workup, leading to reductions in treatment time and costs (7,8).

However, in addition to the LSF calculation, ^{99m}Tc MAA imaging provides valuable information that may allow safer and more effective SIRT. The detection of ^{99m}Tc MAA in the organs of the gastrointestinal (GI) tract as a result of shunting through collateral blood vessels may help to identify the risk of radiation-induced GI ulceration (9–11). On the contrary, the relative distribution of ^{99m}Tc MAA particles in the tumor and nontumoral compartment of the liver may also help guide pretreatment dosimetry (2,12). Although the presence of GI MAA uptake or a significant mismatch between ^{99m}Tc MAA uptake and tumor distribution in the liver are not absolute contraindications to SIRT in most cases, they may indicate that a modification to the initial treatment plan is required. Characteristics associated with GI MAA uptake or mismatch between ^{99m}Tc MAA uptake and tumor distribution have not been fully characterized, and omitting ^{99m}Tc MAA scans from the pretreatment evaluation of such patients could result in an increased risk of complications and in poorer treatment efficacy.

The purpose of the present study was to determine patient, tumor, and pretreatment evaluation characteristics that could identify patients for whom ^{99m}Tc MAA imaging cannot be excluded when planning SIRT, as ^{99m}Tc MAA findings (including high LSF, GI MAA uptake, or mismatch between ^{99m}Tc MAA uptake and tumor distribution) would contraindicate or prompt modification of SIRT as initially planned.

MATERIALS AND METHODS

The study was a retrospective review of the records of 532 consecutive patients with liver tumors evaluated for SIRT by hepatic angiography and ^{99m}Tc MAA scanning between 2006 and 2015 at a single institution. SIRT was performed with the use of ^{90}Y resin microspheres in all patients.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the institutional review board, and the need for written informed consent was waived (registration no. 31/2015). All patients gave written consent for the ^{90}Y radioembolization procedure.

Baseline characteristics are shown in **Table 1**. Almost half of the patients (46.2%) had primary liver tumors, mostly hepatocellular carcinoma (40.8%). The cohort of patients with liver metastases was a heterogeneous group, with colorectal cancer being the predominant type of primary disease. A whole-liver approach was the most common injection strategy for ^{99m}Tc MAA imaging (47.2%), but lobar extended (4.5%), lobar (38.9%), and segmental (9.4%) procedures were also performed.

Table 1. Baseline Characteristics (N = 532)

Characteristic	Incidence
Male sex	365 (68.6)
Type of tumor	
Primary liver tumors	
Hepatocellular carcinoma	217 (40.8)
Cholangiocellular carcinoma	31 (5.8)
Liver metastases	
Colorectal cancer	142 (26.7)
Neuroendocrine tumors	49 (9.2)
Breast cancer	20 (3.8)
Other tumors	73 (13.7)
Previous therapies	
Hepatic resection	92 (17.3)
Radiofrequency ablation	28 (5.3)
(Chemo)embolization	41 (7.7)
Previous intravenous chemotherapy	303 (57.0)
Intraarterial chemotherapy	44 (8.3)
Antiangiogenic drugs (≤ 3 mo before SIRT)	156 (29.3)
Vascular invasion (portal and/or hepatic venous)	123 (23.1)
Portal venous invasion only	78 (14.7)
Hepatic venous invasion only	14 (2.6)
Portal and hepatic venous invasion	31 (5.8)
Disease distribution	
Uninodular	95 (17.9)
Multinodular	437 (82.1)
Unilobar	63 (11.8)
Bilobar	374 (70.3)
Cirrhosis	176 (33.1)
Liver volume targeted by ^{99m}Tc-MAA	
Total	251 (47.2)
Single injection (proper/common hepatic artery)	136 (25.6)
Double injection (right and left hepatic arteries)	115 (21.6)
Lobar extended	24 (4.5)
Lobar	207 (38.9)
Segmental	50 (9.4)

MAA = macroaggregated albumin; SIRT = selective internal radiation therapy.

Pretreatment Imaging Evaluation

Hepatic angiography was performed to assess the suitability of the patient to undergo SIRT by confirming that the hepatic tumor(s) could be targeted without the risk of ^{90}Y resin microspheres reaching extrahepatic tissues. Coil