CLINICAL STUDY

Progression of Treated versus Untreated Liver Imaging Reporting and Data System Category 4 Masses after Transcatheter Arterial Embolization Therapy

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ABSTRACT

Purpose: To compare outcomes of treated vs untreated Liver Imaging Reporting and Data System category 4 (LR-4) masses after transcatheter arterial embolization.

Materials and Methods: In 167 patients undergoing embolization for HCC from January 2005 to December 2012, LR-4 masses were retrospectively identified on CT and MR imaging examinations performed before embolization. In 149 patients undergoing embolization from January 2013 to December 2016, masses prospectively classified as LR-4 were identified. In total, there were 81 LR-4 masses in 62 patients (16 women; mean age 62 y; range 29-83 y). Procedures were reviewed to determine whether LR-4 masses were within or outside the liver volume that received embolization during treatment of dominant masses. Time to progression to LR-5 and by modified Response Evaluation Criteria in Solid Tumors (mRECIST) was estimated for treated vs untreated LR-4 masses using the Kaplan-Meier method and compared using the log rank test.

Results: LR-4 masses averaged 1.8 cm; 88%, 60%, 14%, and 14% demonstrated arterial phase hyperenhancement, washout, a capsule, and growth. Of LR-4 masses, 62 were within the liver volume that received embolization and considered treated, and 19 were outside and considered untreated. Response rates according to mRECIST were 37% vs 21% for treated vs untreated masses ($P = .27$). The 6- and 12-month rates of progression to LR-5 were 7% and 26% for treated masses vs 27% and 75% for untreated masses ($P = .001$). According to mRECIST, 7% and 27% of treated masses progressed vs 30% and 65% of untreated masses ($P = .001$).

Conclusions: LR-4 masses that receive embolization in the setting of dominant masses elsewhere show lower rates of progression compared with untreated masses.

ABBREVIATIONS

APHE = arterial phase hyperenhancing, CI = confidence interval, HCC = hepatocellular carcinoma, LI-RADS = Liver Imaging Reporting and Data System, LR = LI-RADS category, mRECIST = modified Response Evaluation Criteria in Solid Tumors

The American College of Radiology Liver Imaging Reporting and Data System (LI-RADS) is a widely used standard for classifying liver lesions in patients at risk for hepatocellular carcinoma (HCC) (1). LI-RADS category 5 (LR-5) masses are considered definite HCC, whereas LR-4 masses are considered probable HCC. LR-4 masses represent a heterogeneous group, including arterial phase isoenhancing or hypoenhancing masses; arterial phase hyperenhancing (APHE) masses with classic features of HCC such as washout, a capsule, and interval growth but that are small in size; and larger APHE masses without classic features of HCC (2). Although > 90% of LR-4

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masses are reported to be HCC at biopsy (3), there are currently few data on outcomes of LR-4 masses treated with liver-directed locoregional therapy. As LR-4 masses do not meet Organ Procurement and Transplantation Network 5 criteria (4), it may be desirable to preemptively treat LR-4 masses in patients with coexisting LR-5 masses who are candidates for liver transplantation to prevent progression outside Milan criteria (5). On one hand, of LR-4 masses that progress to LR-5, most do so within 6 months (6), a relevant time frame given the required 6-month waiting period for Model for End-Stage Liver Disease exception points for HCC. On the other hand, previous studies have suggested that one third of LR-4 masses may spontaneously downgrade without treatment (6–8). The purpose of the present study was to compare outcomes of treated versus untreated LR-4 masses in patients undergoing transcatheter arterial embolization for a dominant HCC elsewhere in the liver.

MATERIALS AND METHODS

Patient Population

Approval for this retrospective study was obtained from the Committee on Human Research of the Institutional Review Board. A waiver for consent was obtained. A search of the interventional radiology (IR) electronic procedural database from January 1, 2005, to December 31, 2016, for patients undergoing bland embolization as initial transcatheter liver-directed intra-arterial therapy for HCC revealed 316 patients. Patients were referred for embolization as either palliative therapy or bridge to liver transplant based on the recommendation of a multidisciplinary tumor board that included hepatologists; medical, surgical, and radiation oncologists; diagnostic and interventional radiologists; and transplant surgeons. Patients who were Barcelona Clinic Liver Cancer stage C solely based on Eastern Cooperative Oncology Group performance status of 1 or 2 were considered candidates for embolization. Patients who were Child-Pugh class C or Barcelona Clinic Liver Cancer stage D were offered treatment only if deemed appropriate based on multidisciplinary consensus. Demographics of patients included in the study are shown in **Table 1**.

Identification of LR-4 Masses

For patients undergoing embolization from January 1, 2005, through December 31, 2012, baseline multiphase contrast-enhanced computed tomography (CT) or magnetic resonance (MR) imaging scans obtained immediately before embolization were retrospectively screened to identify observations meeting LR-4 criteria according to LI-RADS version 2014, the latest release at the time of data collection for this article (2). Screening was done by a single fellowship-trained board-certified IR attending physician with 1 year of experience (J.R.). Only masses meeting LR-4 criteria based on major features (APHE, diameter, washout, capsule, and threshold growth) were included. Masses meeting LR-3 or LR-5 criteria were not adjusted to LR-4 based on ancillary features. Masses in close proximity (< 2 cm) of a larger dominant LR-5 mass were excluded because they were considered to represent satellite nodules rather than distinct observations. After initial screening, all potential LR-4 masses on baseline imaging were independently verified by fellowship-trained board-certified abdominal imaging attending radiologists with 5 and 8 years of experience (D.M., R.T.G., respectively). For patients undergoing embolization from January 1, 2013, to December 31, 2016, corresponding to the time at which LI-RADS entered routine clinical use, all observations that were prospectively classified as LR-4 by fellowship-trained board-certified abdominal imaging attending radiologists in the official report generated at the time of the original interpretation of baseline imaging were included. Among these prospectively identified LR-4 masses, 1 met LR-3 based on major criteria but was upgraded to LR-4 based on the ancillary features. The remaining masses met LR-4 criteria based on major criteria. Masses without at least 1 follow-up multiphase contrast-enhanced CT or MR imaging examination following embolization were excluded. The final study population was composed of 81 masses in 62 patients (**Fig 1**).

Transcatheter Arterial Embolization Procedures

All embolization procedures were performed under the supervision of fellowship-trained board-certified IR attending physicians with 8–26 years of experience. All patients received moderate sedation and antibiotic prophylaxis with ceftriaxone (1 g) or clindamycin (600 mg). Via common femoral artery access, celiac and superior mesenteric angiography was performed to delineate hepatic arterial anatomy and the arterial supply of the tumor. The right phrenic artery was interrogated for tumors located at the hepatic dome. Tumor embolization was performed via a microcatheter using Contour polyvinyl alcohol (Boston Scientific, Marlborough, Massachusetts) or Embozene (Boston Scientific) particles. Based on institutional practice, patients undergoing embolization of 1 or 2 liver segments were treated with 40–150 μm particles, and patients undergoing embolization of > 2 segments were treated with 150–250 μm particles. Embolization was performed to 5 beats of stasis of arterial blood flow. The degree of selectivity and the decision to treat other masses, including LR-4 masses, in addition to the dominant HCC, either by performing a lobar embolization to increase the volume of liver treated or by performing separate selective embolization of masses, were at the discretion of the IR attending physician.

The embolization procedure report and the angiographic images obtained during the procedure were reviewed in correlation with the CT or MR imaging scan performed before embolization by 2 fellowship-trained board-certified IR attending physicians with 8 and 26 years of experience (C.Y.K., P.V.S.) to determine the location of LR-4 masses