Intraprocedural Transcatheter Intra-arterial Perfusion MRI as a Predictor of Tumor Response to Chemoembolization for Hepatocellular Carcinoma

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Rationale and Objectives: To prospectively test the hypothesis that transcatheter intraarterial perfusion magnetic resonance imaging (TRIP-MRI) measured semiquantitative perfusion reductions during transcatheter arterial chemoembolization of hepatocellular carcinoma (HCC) are associated with tumor response.

Materials and Methods: Twenty-eight patients (mean age 63 years; range 47–87 years) with 29 tumors underwent chemoembolization in a combined magnetic resonance interventional radiology suite. Intraprocedural tumor perfusion reductions during chemoembolization were monitored using TRIP-MRI. Pre- and postchemoembolization semiquantitative area under the time-signal enhancement curve (AUC) tumor perfusion was measured. Mean tumor perfusion pre- and postchemoembolization were compared using a paired *t*-test. Imaging follow-up was performed 1–3 months after chemoembolization. We studied the relationship between short-term tumor imaging response and intraprocedural perfusion reductions using univariate and multivariate analysis.

Results: Intraprocedural AUC perfusion value decreased significantly after chemoembolization (342.1 vs. 158.6 arbitrary unit, $P < .001$). Twenty-six patients with 27 HCCs ($n = 27$) had follow-up imaging at mean 39 days postchemoembolization. Favorable response was present in 67% of these treated tumors according to necrosis criteria. Fifteen of 16 (94%) tumors with 25%–75% perfusion reductions showed necrosis treatment response compared to only 3 of 11 (27%) tumors with perfusion reductions outside the above range ($P = .001$). Multivariate logistic regression indicated that intraprocedural tumor perfusion reduction and Child-Pugh class were independent factors associated significantly with tumor response ($P = .012$ and .047, respectively).

Conclusion: TRIP-MRI can successfully measure semiquantitative changes in HCC perfusion during chemoembolization. Intraprocedural tumor perfusion reductions are associated with future tumor response.

Key Words: Transcatheter intraarterial perfusion magnetic resonance imaging (TRIP-MRI); transcatheter arterial chemoembolization; hepatocellular carcinoma (HCC); tumor response; functional embolic endpoint.

Early identification of tumor response to transcatheter arterial chemoembolization may facilitate efficient assessment of treatment efficacy, timing of repeat therapy, and patient prognosis. Radiological hepatocellular carcinoma (HCC) response assessment by conventional computed tomography (CT) or magnetic resonance imaging (MRI) typically occurs 1–3 months after chemoembolization. Although several studies have identified early vascular and cellular changes using dynamic-contrast enhanced (DCE) and diffusion-weighted (DW) MRI as potential markers for early tumor response assessment (1–4), few studies have explored intraprocedural functional imaging biomarkers that may objectively predict future tumor response at the time of chemoembolization procedures.

Intraprocedural MRI allows objective assessment of tumor functions during transcatheter liver-directed embolotherapies (5). We previously demonstrated that transcatheter intraarterial

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perfusion (TRIP)-MRI, which uses direct catheter-based intraarterial injections of gadolinium (Gd) contrast, may be clinically employed for intraprocedural monitoring and quantification of tumor perfusion changes during chemoembolization when performed in a combined MRI/digital subtraction angiography (DSA) unit (termed MR-IR suite) (6–9). TRIP-MRI serially monitors tumor contrast uptake during chemoembolization, providing reliable objective measurement of tumor perfusion before and after therapy (7–9).

In this study, we aimed to investigate the relationship between intraprocedural tumor perfusion reductions and tumor response to chemoembolization. We prospectively tested the hypothesis that changes in semiquantitative TRIP-MRI tumor perfusion obtained during chemoembolization may be used to predict future tumor response.

MATERIALS AND METHODS

This prospective study was approved by our hospital's Institutional Review Board, and was in compliance with the Health Insurance Portability and Accountability Act. All patients provided written informed consent for procedures.

Clinical Setting and Patients Characteristics

Between February 2006 and January 2010, 28 patients with surgically unresectable HCC presenting for MR-IR monitored chemoembolization at a single university-affiliated hospital in a large metropolitan area were prospectively enrolled for this study. Inclusion criteria consisted of 1) age >18 years, 2) surgically unresectable HCC, 3) Eastern Cooperative Oncology Group (ECOG) performance status ≤2, 4) Child-Pugh class A or B liver disease, 5) focal or multifocal measurable HCC, 6) <50% overall liver tumor burden, 7) ability to maintain adequate breath hold (30 seconds), 8) ability to lay supine greater than 30 minutes, (h) ability to undergo angiography and selective visceral catheterization, 9) ability to provide informed consent, and 10) no contraindications to MRI. Exclusion criteria consisted of 1) life expectancy <6 months, 2) uncorrectable coagulopathy (international normalized ratio greater than 1.5), 3) total bilirubin >4.0 mg/dL, 4) serum creatinine >2.0 mg/dL, and 5) uncorrectable thrombocytopenia (platelet count less than 50,000/μL). Patients with portal vein thrombosis were included if superselective segmental chemoembolization was technically feasible. The HCC study sample was limited to tumor treated in a single chemoembolization session to reduce bias related to differences in treatment session number in the same tumor.

The diagnosis of HCC was established by percutaneous biopsy or noninvasively based on the presence of a hepatic mass >2 cm diameter with characteristic imaging findings in the setting of liver cirrhosis (10). Surgical unresectability was determined by multidisciplinary consensus at tumor conference comprised of surgical and medical oncology, transplant surgery, hepatology, and interventional radiology.

Patient demographic and tumor characteristic information is presented in Table 1.

MR-IR Suite

All chemoembolization procedures were performed in a dedicated MR-IR suite (Miyabi, Siemens AG Healthcare Sector, Erlangen, Germany) that contains a flat panel Artis dTA DSA unit integrated with a 1.5 T Magnetom Espree MR imager (Siemens AG Healthcare Sector, Erlangen, Germany) via a moving table. Patients were transferred between the IR angiography table and MRI scanner according to an institutional safe transfer protocol that accounted for all ferromagnetic devices.

Chemoembolization Procedures

Chemoembolization was performed by a single Certificate of Added Qualification certified interventional radiologist with more than 15 years of clinical experience. Patients were prepared and draped in standard sterile fashion while supine on the angiographic procedure table; routine arterial access was gained via the right common femoral artery. Initial mapping visceral angiography was then performed using a 5 French visceral catheter (cobra catheter [Terumo Medical, Somerset, NJ], or Simmons [Cook Medical, Bloomington, IN], or Sos [AngioDynamics, Latham, NY]). Subsequent lobar or segmental angiography in the tumor vascular distribution was performed using a coaxially placed 2.8 French microcatheter (Renegade Hi-Flo; Boston Scientific, Natick MA) after vessel selection with a 0.016-inch-diameter guidewire (Headliner; Terumo Medical, Aliso Viejo CA). Catheter position was confirmed using DSA with iohexol (Omnipaque-300; Amersham Health, Princeton, NJ) injection. After selecting the appropriate catheter position for chemoembolization, patients were transferred to the adjacent MRI on a moving table. Vascular catheters were covered using a sterile drape to allow for placement of an MRI torso array coil. Prechemoembolization MRI was then performed.

After MRI, patients were transferred back to the IR angiography table for chemoembolization. Chemoembolization was performed via the coaxially placed microcatheter with a 1:1, 20 mL volume solution of chemotherapy agents (100 mg cisplatin, 30 mg mitomycin C, and 30 mg doxorubicin) and emulsifying contrast (Ethiodol; Savage Laboratories, Melville, NY). The chemotherapy suspension was injected under direct fluoroscopic observation. Chemoembolization was then concluded by injecting 300–700 μm diameter tris-acryl gelatin microspheres (Embosphere; Biosphere Medical, Rockland, MA) mixed with iohexol. Completion angiography was performed after microsphere embolization. Angiographic endpoint was graded based upon the subjective chemoembolization endpoint classification (6) and determined at the discretion of the attending interventional radiologist.

After chemoembolization, patients were again transferred to the MRI scanner for postchemoembolization completion MRI. After scanning, all catheters and vascular access devices were removed, and hemostasis was achieved with manual compression or a vascular closure device (Angio-Seal, St. Jude