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Evaluation of Treatment Response in Hepatocellular Carcinoma in the Explanted Liver with Liver Imaging Reporting and Data System version 2017

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Abstract

Objective—To investigate the performance of Liver Imaging Reporting and Data System (LI-RADS) v2017 treatment response algorithm for predicting hepatocellular carcinoma (HCC) viability after locoregional therapy (LRT) using the liver explant as reference.

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The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

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Institutional Review Board approval was obtained.
Methodology:

- Retrospective
- Diagnostic or prognostic study
- Performed at one institution

Methods—114 patients with 206 HCCs who underwent liver transplantation (LT) after LRT for HCCs were included in this retrospective study. Two radiologists independently evaluated tumor viability using LI-RADS and modified RECIST (mRECIST) with CT and MRI, respectively. The sensitivity and specificity of arterial phase hyperenhancement (APHE) and LR-TR viable criteria (any of three findings: APHE, washout, enhancement pattern similar to pre-treatment imaging) were compared using logistic regression. Receiver operating characteristics (ROC) analysis was used to compare the diagnostic performance between LI-RADS and mRECIST, and between CT and MRI.

Results—The sensitivity and specificity for diagnosing viable tumor were not significantly different between APHE alone and LR-TR viable criteria on CT ($P = 0.054$ and $P = 0.317$) and MRI ($P = 0.093$ and $P = 0.603$). On CT, the area under the ROC curve (AUC) of LI-RADS was significantly higher than that of mRECIST (0.733 vs. 0.657, $P < 0.001$). On MRI, there was no significant difference in AUCs between LI-RADS and mRECIST (0.802 vs. 0.791, $P = 0.500$). Intra-individual comparison of CT and MRI showed comparable AUCs using LI-RADS (0.783 vs. 0.795, $P = 0.776$).

Conclusions—LI-RADS v2017 treatment response algorithm showed better diagnostic performance than mRECIST on CT. With LI-RADS, CT and MRI were comparable to diagnose tumor viability of HCC after LRT.

Keywords

Liver transplantation; Hepatocellular Carcinoma; Multidetector Computed Tomography; Magnetic Resonance Imaging; Therapeutic Chemoembolization

Introduction

Liver-directed locoregional therapy (LRT), such as transarterial chemoembolization (TACE) or radiofrequency ablation (RFA), is widely used as curative or palliative treatment in patients with hepatocellular carcinoma (HCC). In patients with HCC who are scheduled to undergo liver transplantation (LT), the frequency of LRT as a bridging or downstaging procedure prior to LT is increasing. In these patients, LRT has capability to decrease the tumor burden beyond the selection criteria and select tumors with favorable biological features and prognosis for LT [1]. Objective and reliable evaluation of the treatment response after LRT is essential for selecting suitable candidates for LT and deciding patient management

There are several guidelines to assess treatment response in patients with HCC, including the World Health Organization (WHO), Response Evaluation Criteria in Solid Tumors (RECIST), European Association for the Study of the Liver (EASL), or modified RECST (mRECIST) criteria [2–5]. The WHO and RECIST criteria are solely based on the size of the tumor, while the EASL and mRECIST criteria are under consideration of the viable enhancing portion of the tumor [2–5]. Previous studies have demonstrated that enhancement methods based on assessment of the arterial phase, such as EASL and mRECIST criteria, are more reliable to assess tumor viability, and accurately predict survival than size-based criteria in patients with treated HCCs [6–9]. The Liver Imaging Reporting and Data System

(LI-RADS) has introduced a treatment response algorithm using CT and MRI in version 2017 [10]. The new LI-RADS treatment response algorithm differs from other criteria of the guidelines in use since it standardizes the reporting of treated observations, is a per-lesion criterion rather than per-patient criterion, and provides new imaging features for defining viable tumor in addition to arterial phase hyperenhancement (APHE) [10, 11]. Although there have been several imaging studies regarding application of LI-RADS for LT candidates before treatment [12, 13], to our knowledge, the diagnostic performance of the LI-RADS treatment response algorithm with CT or MRI scan has not been investigated yet in patients with HCC who have undergone LRT.

In this study, we aimed to validate the LI-RADS v2017 treatment response algorithm in patients with HCC who underwent LRT and subsequent LT, particularly in comparison with the mRECIST; in addition, we compared the diagnostic performance of computed tomography (CT) and magnetic resonance imaging (MRI) to evaluate tumor viability using these guidelines.

Materials and Methods

Patients

This study was approved by our Institutional Review Board, and requirement for informed consent was waived because of its retrospective design. From the prospectively maintained database at our institution's Department of Surgery, 493 adult patients who underwent LT between January 2007 and December 2014 were identified. A blinded study coordinator with 5 years' experience in liver MRI who did not participate in image analysis reviewed the database, electronic medical records, and radiologic studies to identify eligible patients. Inclusion criteria were the following: Patients who (a) underwent LT, (b) underwent LRT for HCC, and (c) underwent dynamic liver CT or MRI before and after LRT. Of 493 patients, 315 were excluded because of the absence of HCC in the explanted liver (n = 216), presence of other hepatic malignancy (n = 2, combined HCC and cholangiocarcinoma in both patients), lack of treatment (n = 76), with only surgical resection (n = 12), or systemic treatment (n = 9) prior to LT. Among 178 patients who underwent LRT for HCC, 64 were excluded based on the following criteria: Patients who (a) underwent radiotherapy for HCC (n = 4), (b) were without dynamic CT or MRI before LRT (n = 5), (c) without posttreatment dynamic CT or MRI (n = 9), (d) with interval between posttreatment imaging and LT of > 3 months (n = 25), and (e) with > five nodules per patient (n = 21) because strict radiologic-pathologic correlation is challenging in these patients. Finally, 114 patients with 206 HCCs were included in this study; among these, 113 patients with 203 HCCs had preoperative CT, 53 patients with 84 HCCs had MRI, and 52 patients with 81 HCCs had both CT and MRI (Fig. 1).

CT and MRI acquisition

CT scans were performed using 64-, or 128-channel multidetector (Siemens Medical Solutions; GE Healthcare) CT scanners. Routine dynamic liver CT includes the precontrast, late arterial, portal venous, and delayed phases. After precontrast scanning, 2.0 mL/kg of iodinated contrast medium was injected intravenously, followed by 20-mL saline bolus

injected during 30 s (fixed duration). Using the bolus-tracking method, the late arterial phase was scanned at 18–20 s after 100-HU attenuation of the abdominal aorta. The portal venous and delayed phases were obtained with delay time of 30 s and 150 s after the scanning of late arterial and portal venous phases, respectively. The CT parameters were as follows: 120 kV; 240 mAs; rotation time, 0.5 s; beam pitch, 2; and slice thickness, 3–5 mm.

Dynamic liver MRI was performed using a 3.0-T (MAGNETOM Tim Trio, Siemens Medical Solutions; Intera Achieva, Philips Medical Systems) or 1.5-T machine (Intera Achieva, Philips Medical Systems). Routine liver MRI included the following sequences: Dual-echo spoiled gradient-echo T1-weighted in-phase and opposed-phase images, multi-shot and single-shot turbo T2-weighted spin-echo images, and diffusion-weighted imaging with single-shot echo planar images. Dynamic fat-suppressed spoiled gradient-echo T1-weighted images were acquired before and after contrast medium injection (late arterial, portal venous, 3-min and 5-min delayed phases). Using the bolus-tracking method, the late arterial and portal venous phases were usually obtained at 20–30 s and 60–70 s after contrast injection. In the majority of the patients (86.8%, 46/53), gadoxetic acid disodium (Primovist, Bayer Schering Pharma) was used as contrast agent, and 0.1 mL/kg (0.025 mmol/kg) of gadoxetic acid disodium was administrated at a rate of 1 or 2 mL/s. The hepatobiliary phase was obtained at 15 or 20 min after contrast injection. In the remaining patients, 0.1 mmol/kg of gadoterate meglumine (Dotarem, Guerbet) was used, and routine sequences were the same as those of gadoxetic acid-enhanced MRI, except for the absence of hepatobiliary phase.

LI-RADS v2017 treatment response algorithm and modified RECIST

For assessment of HCC viability after LRT with LI-RADS [10, 14], LR-TR nonevaluable category is considered when treatment response cannot be reliably evaluated due to image degradation or omission; otherwise, one of the following categories is considered: LR-TR nonviable, LR-TR equivocal, or LR-TR viable. LR-TR nonviable is applied for the lesions with no enhancement or expected treatment-specific enhancement pattern. LR-TR viable is assigned for nodular or thick irregular tissue within or along the treated lesion with any of the following findings: APHE, washout, or enhancement pattern similar to pretreatment imaging. LR-TR equivocal category is assigned for those treated lesions that are atypical for treatment-specific enhancement patterns and do not meet the criteria for LR-TR nonviable or LR-TR viable category.

The mRECIST is based on the one-dimensional largest diameter of arterially enhancing viable tumor and lipiodolized lesion or nonenhancing portion is regarded as nonviable tumor [5]. Although mRECIST can be used for per-patient response evaluation, we used it only for per-lesion evaluation, because our study was focused on lesion-to-lesion radiologic-pathologic correlation of the treated lesion.

Image analysis

The study coordinator annotated target lesions on a picture archiving and communication system (PACS) to enable evaluation of the selected hepatic lesions by the reviewers. Two blinded board-certified abdominal radiologists with 16 and 17 years' experience in liver

MRI independently reviewed the CT and MR images using PACS. Both reviewers were informed that all patients had undergone LRT for HCC and subsequent LT. However, they were unaware of the final histopathological results in the explanted livers. Posttreatment CT and MRI were interpreted separately with 1-month washout period to avoid recall bias between reading sessions. The readers evaluated the following findings per definitions provided by each guideline [5, 10]: APHE, washout, enhancement similar to pretreatment, no lesional enhancement, and treatment-specific enhancement pattern. For evaluation of APHE, subtraction images were also reviewed. The evaluation of washout was performed in the portal venous phase for patients who underwent MRI with gadoxetic acid disodium, while it was performed in the portal venous and delayed phases when extracellular contrast agent was used [10]. Subsequently, they assigned the response category according to LI-RADS treatment response algorithm (nonviable, equivocal, viable) and mRECIST (nonviable, viable), respectively. For tumors rated as equivocal or viable tumor, the single longest dimension was measured.

Pathologic evaluation

An experienced hepatic pathologist with 25 years' experience in liver pathology performed histopathologic evaluation. The explanted liver specimens were routinely sectioned into 5–9-mm-thick slices in the axial plane. All suspected lesions on macroscopic examination were histopathologically evaluated and correlated with the preoperative images. The pathologist evaluated each hepatic lesion on hematoxylin and eosin-stained slides at the level of the largest tumor size. Finally, the pathologist reported the location and size of HCC, presence of any microvascular invasion, and differentiation of HCC according to Edmondson–Steiner grading system [15]. With regard to treated lesions, the percentage of necrosis and size of viable tumor was recorded. Totally necrotic lesion was considered as pathologically nonviable tumor.

Statistical analysis

The sensitivity and specificity of each LI-RADS criterion for viable tumor was calculated based on the explanted liver pathology. The sensitivity and specificity of APHE and LR-TR viable criteria (any of three findings: APHE, washout, enhancement pattern similar to pre-treatment imaging) were compared using logistic regression with generalized estimating equation (GEE). The sensitivity and specificity of LI-RADS criteria for viable tumor (LR-TR viable) were compared between CT and MRI using logistic regression with GEE.

Overall diagnostic performance of each guideline was evaluated with receiver operating characteristic (ROC) curve analysis. The areas under the ROC curve (AUCs) between LI-RADS and mRECIST were compared using multireader multicase ROC analysis with reader-averaged results [16]. Subgroup analyses according to the imaging modality (CT or MRI) and LRT type (TACE or RFA) were performed.

Inter-observer agreement for criteria of treated lesions was assessed using κ statistics as follows: κ values < 0.20, poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; and 0.81–1.00, excellent agreement [17]. All statistical analyses were performed using R version

3.4.2 (R Foundation for Statistical Computing). *P* values < 0.05 were considered to be statistically significant.

Results

Clinicopathologic features of study population

The patient demographics are summarized in Table 1. Of 114 patients, 96 (84.2%) patients were male individuals, and the mean age of patients was 54.0 years. The most common etiology of chronic liver disease was hepatitis B virus (HBV) infection (100/114, 87.7%). In total, 206 HCCs in 114 patients were analyzed. The most common type of LRT was TACE (162/206, 78.6%), followed by RFA (34/206, 16.5%), drug-eluting bead chemoembolization, and combined TACE and RFA. Among 206 HCCs, 84 lesions (40.8%) showed total necrosis in the explanted liver. The mean time interval between CT and LT, and that between MRI and LT was 21.5 days (0–82, SD 20.8 days) and 17.1 days (1–82, SD 18.6 days), respectively.

Diagnostic performance of each LI-RADS criterion for viable tumor (LR-TR viable)

The sensitivity and specificity of each criterion for the LR-TR viable are demonstrated in Table 2. The sensitivity of APHE was higher than the value of washout or enhancement pattern similar to pre-treatment imaging. Using CT, 5 and 2 lesions were additionally diagnosed as viable tumor based on “washout” in the absence of APHE, by reader 1 and reader 2, respectively (Fig. 2). Most lesions showing washout without APHE were confirmed as viable tumor, except one false positive lesion by reader 1. Similarly, only 1 and 2 viable lesions showed “similar enhancement pattern to pretreatment imaging” in the absence of APHE, by reader 1 and reader 2, respectively. The sensitivity and specificity of CT for viable tumor were not significantly different ($P = 0.054$, and $P = 0.317$, respectively) between APHE alone and LR-TR viable criteria (any of three findings). Using MRI, in the absence of APHE, one viable tumor was additionally diagnosed by “washout” in both readers, and one viable tumor was diagnosed by “similar enhancement pattern to pretreatment imaging” in reader 1 only. Also, on MRI, the sensitivity and specificity of APHE and LR-TR viable criteria were not significantly different ($P = 0.093$, and $P = 0.603$, respectively).

The reader-averaged sensitivity of APHE on MRI was significantly higher than that on CT (71.6% vs. 35.0%, $P < 0.001$). The sensitivity of washout on MRI was also significantly higher than that on CT (41.4% vs. 23.3%, $P = 0.005$). The sensitivity and specificity of the enhancement pattern similar to that at pretreatment imaging were not significantly different between CT and MRI. Applying criteria for viable tumor (at least one of three features), MRI showed significantly higher sensitivity than CT (74.1% vs. 39.2%, $P < 0.001$), but lower specificity than CT (84.6% vs. 95.8%, $P = 0.030$).

Comparison of overall diagnostic performance to assess tumor viability: LI-RADS treatment response algorithm versus mRECIST

In this study, there was no lesion which was assigned as LR-TR nonevaluable. The distribution of posttreatment LI-RADS category was summarized in Table 3, and the results

of ROC analysis are shown in Table 4. Both readers assigned equivocal category more frequently on CT rather than MRI (15.8% vs. 6.0% in reader 1, and 8.9% vs. 4.8% in reader 2, respectively; Fig. 3). Using CT, the AUC of LI-RADS treatment response algorithm (0.733) was significantly higher than that of mRECIST (0.657, $P < 0.001$). The sensitivity, specificity, and accuracy for predicting viable tumor were 54.2%, 94.6%, and 70.0% for LI-RADS, and 35.0%, 96.4%, and 59.1% for mRECIST, respectively. In subgroup analysis of CT according to the LRT type, AUC of LI-RADS (0.764) was significantly higher than that of mRECIST (0.671, $P < 0.001$) in patients who underwent TACE. On the other hand, for MRI, there was no significant difference in AUCs between LI-RADS and mRECIST in all patients and in any subgroups according to the LRT type.

Comparison of overall diagnostic performance to assess tumor viability: CT versus MRI

In terms of imaging modality, CT and MRI showed comparable AUCs using LI-RADS ($P = 0.272$). However, the AUC of MRI was significantly higher than that of CT when using mRECIST (0.791 vs. 0.657, $P = 0.003$) (Fig. 4). In addition, intra-individual comparison of 52 patients with 81 HCCs who underwent both CT and MRI showed similar results: AUCs were comparable between CT and MRI using LI-RADS (0.783 [95% CI, 0.721–0.845] for CT vs. 0.795 [0.718–0.872] for MRI, $P = 0.776$). However, using mRECIST, MRI showed significantly higher AUC than CT (0.792 [0.715–0.868] vs. 0.665 [0.607–0.723], $P = 0.005$).

Interobserver agreement

Interobserver agreement between two readers was good for all criteria using CT (κ, 0.667–0.800), and moderate to good using MRI (0.411–0.713) (Supplementary Table 1). The interobserver agreement was slightly higher on CT than MRI for all criteria except treatment specific enhancement pattern. The interobserver agreement for viability assessment using LI-RADS was lower than that using mRECIST (κ, 0.693 vs. 0.800 on CT, and 0.560 vs. 0.713 on MRI).

Discussion

In this study, the mRECIST and recently introduced LI-RADS v2017 treatment response algorithm were compared. The mRECIST defines viable tumor solely based on APHE, whereas the treatment response algorithm in LI-RADS v2017 includes washout and enhancement similar to that at pretreatment imaging, in addition to APHE [2–5, 10]. According to our results, with CT, the diagnostic performance of LI-RADS evaluated with AUCs considering three categories (viable, equivocal, nonviable) was superior to mRECIST, and the performance of CT to predict viable tumor was improved to similar level as that of MRI, using LI-RADS. However, sensitivity and specificity of LR-TR viable were not significantly different from APHE alone. Of 120 viable tumors, only 5 and 2 lesions (by reader 1 and reader 2) were additionally diagnosed as viable tumor based on washout in the absence of APHE, without significant increase in the sensitivity. Therefore, superior performance of LI-RADS to mRECIST on CT seems to be due to application of equivocal category rather than the addition of washout and enhancement similar to pre-treatment imaging as viable criteria. On the other hand, incorporation of the equivocal viable category in LI-RADS treatment response algorithm seems to increase the AUC of CT to detect viable

tumor. Equivocal category reflects the real-world challenge of difficulty in determining viability in some treated nodules. Both readers assigned the equivocal category more frequently on CT than on MRI. In addition, lesions assigned as equivocal category on CT were mostly viable tumor (93.8–100%), while those on MRI were with lower likelihood of viable tumor (50.0–60.0%) than CT. Therefore, the equivocal category in LI-RADS algorithm should be interpreted carefully considering the imaging modality. In particular, LI-RADS showed better diagnostic performance than mRECIST to assess tumor viability using CT in patients who underwent TACE. LI-RADS has strengths; it can improve the accuracy of CT to detect viable tumor and provide standardized reports, although application of LI-RADS is more complicated and the interobserver agreement is lower than that of mRECIST. As there is no difference in the treatment response algorithm between LI-RADS v2017 and recently released LI-RADS v2018 [18], our results may be valid also for the LI-RADS v2018.

CT and MRI have different characteristics for assessment of treated HCCs [19–23]. CT can visualize the accumulation of iodized oil itself, and is less costly and more widely available than MRI. However, beam hardening artifacts of lipiodolized nodule may obscure accurate evaluation of APHE, and hypervascular false-positive lesions such as the arterioportal shunt can mimic viable HCC [19–22]. In contrast, MRI has an advantage that iodized oil does not mask assessment of APHE, although it cannot visualize the iodized oil itself [20–22]. Several previous studies have reported conflicting results regarding optimal imaging modality to assess the viability of HCC after LRT [21, 22, 24, 25]. In our study, the overall diagnostic performance of both CT and MRI was similar using LI-RADS. Therefore, our results suggest that either CT or MRI could be used to assess the treatment response of HCC after LRT using LI-RADS. In contrast, with using mRECIST, MRI was better than CT to predict the viable tumor. Deposition of hyperdense embolic materials after TACE may limit the assessment of APHE with CT (Fig. 4).

Our study has several limitations. First, there was an unavoidable selection bias due to the retrospective design with explant correlation. Second, precise lesion-by-lesion matching in the explanted liver is quite challenging. However, the routine plane of histological sections is similar to the axial imaging plane used at our institution, and our study coordinator rigorously correlated imaging studies with the explanted livers, based on the lesion’s location and size. Third, the lack of delayed phases for the evaluation of the washout in patients who underwent MRI with gadoxetic acid disodium might have underestimated the sensitivity of MRI on these patients. Finally, we did not evaluate the overall response on per-patient basis, since our study’s primary purpose was to validate LI-RADS v2017 treatment response algorithm for treated observations with lesion-by-lesion radiologic-pathologic correlation. Further studies including per-patient analysis are warranted.

In conclusion, LI-RADS v2017 treatment response algorithm had better diagnostic performance than mRECIST using CT. With the LI-RADS, CT and MRI showed comparable performance to diagnose tumor viability of HCC after LRT.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

APHE	Arterial phase hyperenhancement
CT	Computed tomography
EASL	European Association for the Study of the Liver
GEE	Generalized estimating equation
HCC	Hepatocellular carcinoma
LI-RADS	Liver Imaging Reporting and Data System
LRT	Locoregional therapy
LT	Liver transplantation
mRECIST	Modified Response Criteria in Solid Tumors
MRI	Magnetic resonance imaging
PACS	Picture archiving and communication system
RFA	Radiofrequency ablation
TACE	Transarterial chemoembolization
WHO	World Health Organization

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Key points

- Using Liver Imaging Reporting and Data System (LI-RADS) v2017 treatment response algorithm, viability of hepatocellular carcinoma (HCC) after locoregional therapy (LRT) can be accurately diagnosed.
- LI-RADS v2017 treatment response algorithm is superior to modified Response Evaluation Criteria in Solid Tumors for evaluating HCC viability using CT.
- Either CT or MRI can be performed to assess tumor viability after LRT using LI-RADS v2017 treatment response algorithm.

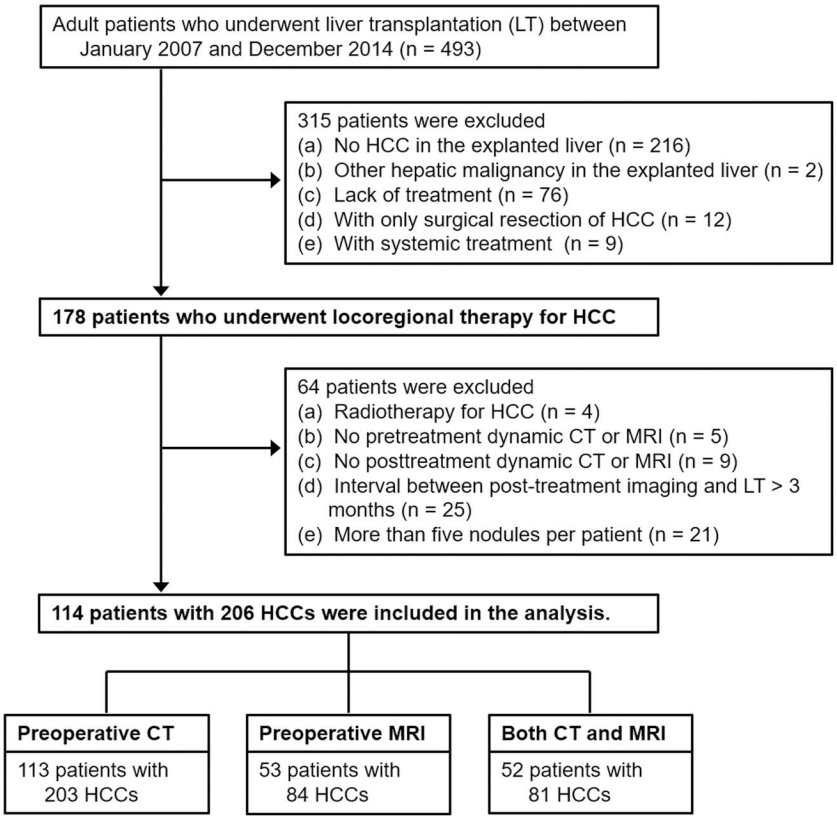

Figure 1.
Flow diagram of patients included in the study.

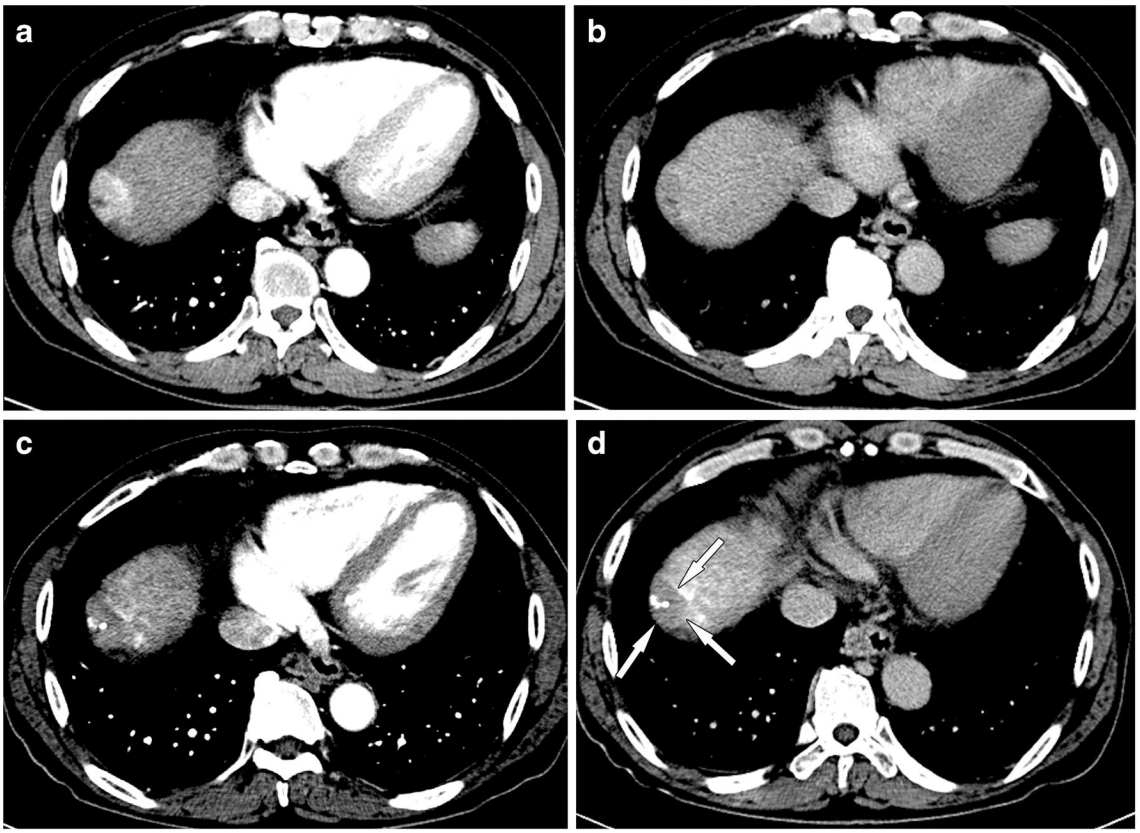

Figure 2.

A 56-year old man with hepatocellular carcinoma (HCC) who underwent transarterial chemoembolization (TACE). Pre-treatment axial CT images obtained during late arterial phase (A) and delayed phase (B) show a 3-cm arterial enhancing and washout mass in the liver dome, suggestive of HCC (LR-5). After TACE, axial CT images obtained during late arterial phase (C) and delayed phase (D) show washout (arrows) without definite arterial enhancement surrounding lipiodolized nodule in the liver dome. Liver Imaging Reporting and Data System (LI-RADS) v2017 treatment response algorithm revealed viable tumor (LR-TR viable), whereas modified Response Evaluation Criteria in Solid Tumors (mRECIST) revealed nonviable tumor. Based on pathology examination, the lesion was diagnosed as 2.8-cm sized HCC with 50% necrosis.

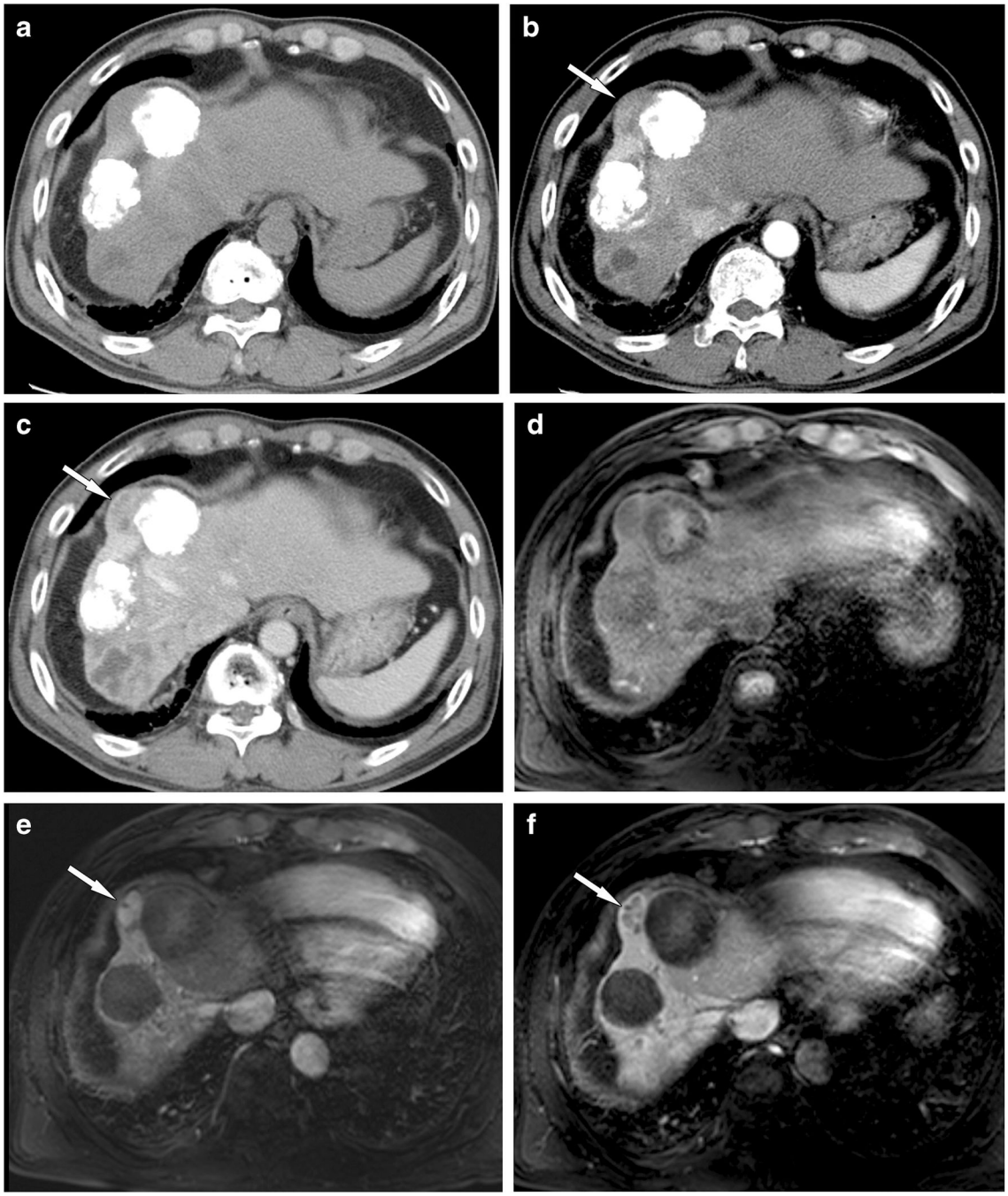

Figure 3.

A 56-year old man with hepatocellular carcinoma (HCC) who underwent transarterial chemoembolization (TACE). Post-TACE CT images obtained at precontrast (A), late arterial phase (B), and portal venous phase (C) show partial lipiodolized mass in the liver segment IV. Lipiodol-defect area (arrows) reveals questionable nodular arterial enhancement and washout. This lesion was categorized as LR-TR equivocal through LI-RADS v2017 treatment response algorithm, and nonviable tumor through mRECIST. On post-TACE T1-weighted MR images obtained at precontrast (D), late arterial phase (E), and portal venous

phase (F) show nodular arterial enhancement and washout (arrows) of the lipiodol-defect area. The lesion was considered as viable tumor through both LI-RADS and mRECIST. Based on pathology examination, the lesion was diagnosed as HCC with 70% necrosis.

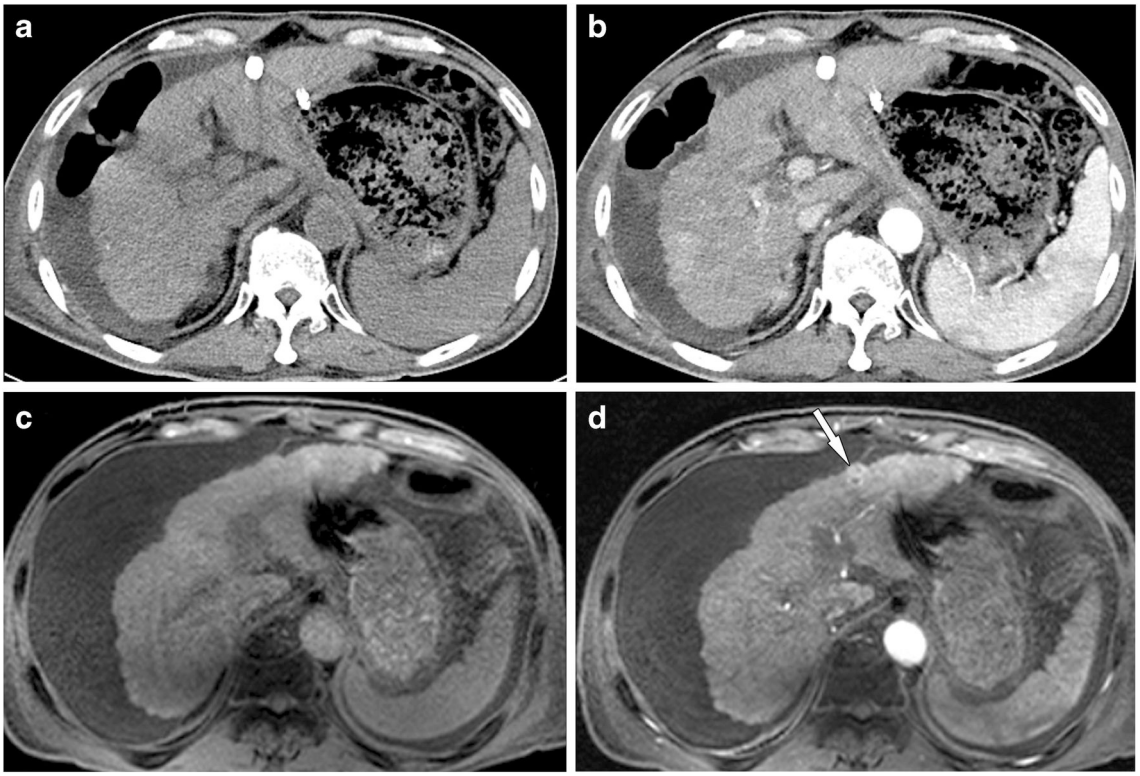

Figure 4.

A 52-year old man with hepatocellular carcinoma (HCC) who underwent transarterial chemoembolization (TACE). Post-TACE axial CT images obtained at precontrast (A) and the late arterial phase (B) demonstrate compact lipiodol uptake without residual arterial enhancing portion. Axial T1-weighted MR image at late arterial phase (D) shows remaining arterial enhancement (arrow) compared with that of precontrast scan (C). The lesion was categorized as nonviable tumor on CT, but viable tumor on MRI using both LI-RADS v2017 treatment response algorithm, and mRECIST. Based on pathology examination, the lesion was diagnosed as HCC with 80% necrosis.

Table 1.

Patient demographics

Variable	
Clinical factors (no. of patients = 114)	
Age (years)	54.0 ± 6.9
Male gender	96 (84.2)
Etiology of liver disease	
HBV	100 (87.7)
HCV	8 (7.0)
Alcoholic	2 (1.8)
Others	4 (3.5)
Serum AFP (ng/ml)	100.3 ± 320.6
Child-Pugh class	
A	60 (52.6)
B	40 (35.1)
C	14 (12.3)
Type of liver transplantation	
Living donor	72 (63.2)
Deceased donor	42 (36.8)
Pathologic factors (no. of HCCs = 206)	
Number of HCCs per patient	2.1 ± 1.5
Type of locoregional treatment	
TACE	162 (78.6)
RFA	34 (16.5)
TACE+RFA	4 (1.9)
Drug-eluting bead chemoembolization	6 (2.9)
Percent of necrosis (%)	
0–50%	63 (30.6)
51–99%	59 (28.6)
100%	84 (40.8)
Size of viable tumor (cm)	
Nonviable tumor	84 (40.8)
< 1	63 (30.6)
1 ≤ < 2	44 (21.4)
≥ 2	15 (7.3)
Edmondson-Steiner grading	
Nonviable tumor	84 (40.8)
I	22 (10.7)
II	73 (35.4)
III	27 (13.1)

Data are means ± standard deviations.

Data in parentheses are percentages. Percentages may not sum to 100% because of rounding off.

AFP, alpha-fetoprotein; HBV, hepatitis B virus; HCV, hepatitis C virus; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization; RFA, radiofrequency ablation

Table 2.

Sensitivity and specificity of LI-RADS criteria for viable tumor (LR-TR viable)

	CT (n = 203)		MRI (n = 84)			
	Sensitivity	**Specificity**	**Sensitivity**	**Specificity**	**†P value_ sensitivity**	**†P value_ specificity**
APHE						
Reader 1	34.2 (41/120)	95.2 (79/83)	72.4 (42/58)	84.6 (22/26)		
Reader 2	35.8 (43/120)	97.6 (81/83)	70.7 (41/58)	88.5 (23/26)		
Averaged (95% CI)	35.0 (26.4–44.7)	96.4 (88.8–98.9)	71.6 (59.2–81.3)	86.5 (73.0–93.9)	<0.001	0.063
Washout						
Reader 1	24.2 (29/120)	96.4 (80/83)	37.9 (22/58)	96.2 (25/26)		
Reader 2	22.5 (27/120)	98.8 (82/83)	44.8 (26/58)	92.3 (24/26)		
Averaged (95% CI)	23.3 (17.3–30.7)	97.6 (92.8–99.2)	41.4 (29.3–54.6)	94.2 (77.9–98.7)	0.005	0.368
Pre-treatment enhancement						
Reader 1	20.8 (25/120)	98.8 (82/83)	13.8 (8/58)	96.2 (25/26)		
Reader 2	22.5 (27/120)	97.6 (81/83)	13.8(8/58)	100 (26/26)		
Averaged (95% CI)	21.7 (15.3–29.7)	98.2 (92.8–99.6)	13.8 (7.4–24.2)	98.1 (87.5–99.7)	0.127	0.959
Any of three of these findings						
Reader 1	39.2 (47/120)	94.0 (78/83)	75.9 (44/58)	80.8 (21/26)		
Reader 2	39.2 (47/120)	97.6 (81/83)	72.4 (42/58)	88.5 (23/26)		
Averaged (95% CI)	39.2 (30.5–48.6)	95.8 (88.7–98.5)	74.1 (61.8–83.6)	84.6 (71.3–92.4)	<0.001	0.030
*P value	0.054	0.317	0.093	0.603		

APHE, arterial phase hyperenhancement; CI, confidence interval

*P values were obtained from comparison between APHE and LR-TR viable criteria (any of three findings).

†P values were obtained from comparison between CT and MRI.

Table 3.

Distribution of LI-RADS category with CT and MRI

	CT (n = 203)		MRI (n = 84)	
	Pathologically viable (n = 120)	**Pathologically nonviable (n = 83)**	**Pathologically viable (n = 58)**	**Pathologically nonviable (n = 26)**
LR-TR viable				
Reader 1	47 (39.2)	5 (6.0)	44 (75.9)	5 (19.2)
Reader 2	47 (39.2)	2 (2.4)	42 (72.4)	3 (11.5)
LR-TR equivocal				
Reader 1	30 (25.0)	2 (2.4)	3 (3.6)	2 (7.7)
Reader 2	18 (15.0)	0 (0.0)	2 (3.4)	2 (7.7)
LR-TR nonviable				
Reader 1	43 (35.8)	76 (91.6)	11 (19.0)	19 (73.1)
Reader 2	55 (45.8)	81 (97.6)	14 (24.1)	21 (80.8)

Data in parentheses are percentages. Percentages may not sum to 100% because of rounding off.

Table 4.

Comparison of AUCs between LI-RADS treatment response algorithm and mRECIST

	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	AUC (95% CI)	*P* value
CT					
Total					< 0.001
LI-RADS	54.2 (45.7, 62.4)	94.6 (87.9, 97.7)	70.0 (63.1, 76.0)	0.733 (0.696, 0.790)	
mRECIST	35.0 (26.4, 44.7)	96.4 (88.8, 98.9)	59.1 (51.9, 66.0)	0.657 (0.612, 0.701)	
TACE					< 0.001
LI-RADS	58.8 (48.2, 68.6)	92.1 (80.7, 97.0)	71.9 (64.4, 78.4)	0.764 (0.711, 0.816)	
mRECIST	36.1 (26.3, 47.2)	95.2 (82.2, 98.9)	59.4 (51.2, 67.0)	0.671 (0.620, 0.722)	
RFA					0.288
LI-RADS	29.4 (12.5, 54.8)	87.5 (71.0, 100.0)	57.6 (39.3, 74.0)	0.602 (0.488, 0.716)	
mRECIST	17.7 (5.716, 43.1)	93.8 (81.8, 100.0)	54.6 (36.3, 71.5)	0.558 (0.470, 0.646)	
MRI					
Total					0.500
LI-RADS	78.5 (67.4, 86.5)	76.9 (63.0, 86.7)	78.6 (68.8, 85.9)	0.802 (0.722, 0.877)	
mRECIST	71.6 (59.2, 81.3)	86.5 (73.0, 93.9)	76.2 (66.4, 83.8)	0.791 (0.715, 0.866)	
TACE					0.709
LI-RADS	82.4 (70.3, 90.2)	58.8 (32.1, 81.2)	76.5 (65.9, 84.5)	0.778 (0.685, 0.871)	
mRECIST	72.6 (59.8, 82.4)	76.5 (51.2, 91.0)	73.5 (63.0, 81.9)	0.770 (0.676, 0.863)	
RFA					0.507
LI-RADS	75.0 (23.8, 96.7)	100.0 (100.0, 100.0)	91.7 (58.3, 98.9)	0.836 (0.566, 1.000)	
mRECIST	75.0 (23.8, 96.7)	100.0 (100.0, 100.0)	91.7 (58.3, 98.9)	0.844 (0.566, 1.000)	

CI, confidence interval; LI-RADS, Liver Imaging Reporting and Data System; mRECIST, modified Response Evaluation Criteria in Solid Tumors; RFA, radiofrequency ablation; TACE, transarterial chemoembolization

P values are obtained from comparison of AUCs between LI-RADS and mRECIST.

The optimal cut-off value of LI-RADS was considered as equivocal category.