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LI-RADS Treatment Response Algorithm: Performance and Diagnostic Accuracy

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Conflicts of interest are listed at the end of this article.

See also the article by Shropshire et al in this issue.

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The Liver Imaging Reporting and Data System (LI-RADS) is a comprehensive system aiming to standardize performance, interpretation, and reporting of liver imaging findings, with prevailing emphasis on the imaging diagnosis of hepatocellular carcinoma (HCC) in patients at risk (1). In 2017, LI-RADS added an interpretation and reporting scheme for assessing the response of HCCs after local-regional therapies—a scheme that was based on existing understanding of imaging features after tumor ablation or embolization. Imaging findings after local-regional therapies guide clinical decision making by determining the likelihood of the presence or absence of viable tumor in a targeted tumor, which may require additional treatment. As a new algorithm, the LI-RADS Treatment Response, or LR-TR, algorithm has not been independently evaluated to determine its performance characteristics (2). In this issue of *Radiology*, Shropshire and colleagues report on the performance characteristics of the LI-RADS Treatment Response algorithm. These characteristics include a high positive predictive value, a high negative predictive value, and moderate interreader agreement based on retrospectively evaluated imaging findings in a cohort of patients with HCC treated with bland embolization prior to liver transplantation (3).

The LI-RADS Treatment Response algorithm replaces the LR-Treated category introduced in 2014 to categorize tumors treated with local-regional therapies without providing guidance on interpreting the likelihood of viable tumor. For technically adequate multiphase CT or MRI examinations, treated tumors are categorized as follows: The LR-TR Nonviable category indicates that the tumor is probably or definitely not viable (showing no tumor enhancement or showing a treatment-specific expected enhancement pattern); the LR-TR Equivocal category, that the tumor is equivocally viable (showing enhancement atypical for a treatment-specific expected enhancement pattern and not meeting the criteria for being probably or definitely viable); and the LR-TR Viable category, that the tumor is probably or definitely viable (1) (showing enhancement from nodular, mass-like, or thick irregular tissue in or along the treated tumor with arterial enhancement, washout, or enhancement similar to that before treatment).

If the radiologist is unsure between two categories, a tie-breaking rule is incorporated into the interpretation scheme that favors the category of lower certainty. Because there are only three tumor categories for imaging studies deemed technically adequate, the tie-breaking rule effectively renders cases with reader uncertainty as LR-TR Equivocal. LI-RADS–based treatment suggestions are identical for LR-TR Nonviable and LR-TR Equivocal tumors—namely, short-term (≤3 months) imaging. For LR-TR Viable tumors, multidisciplinary discussion is recommended for consensus management, which often includes repeat treatment.

Shropshire and colleagues report 45 patients with 63 tumors who underwent transcatheter bland arterial embolization for HCC between 2006 and 2016 with subsequent liver transplantation (3). Three experienced radiologists who were blinded to clinical information, including radiology reports, retrospectively evaluated the pre- and postembolization images. They evaluated all lesions according to LI-RADS 2017. Imaging findings were compared with findings at explant pathologic examination to determine LI-RADS Treatment Response performance characteristics.

For the practicing radiologist, the most clinically useful findings reported in this article are the high positive predictive value of the LI-RADS Treatment Response algorithm (the TR-Viable category [viable tumor at histopathologic examination]), which ranged from 86% to 96%, and the high negative predictive value (the TR-Nonviable category [no viable tumor at histopathologic examination]), which ranged from 81% to 87%. The high positive predictive value for the presence of viable tumor in a patient with LR-TR Viable findings is useful in guiding clinical decision making with respect to the performance and timing of additional treatment. Likewise, the high negative predictive value in patients with LR-TR Nonviable findings supports continued imaging surveillance without necessitating additional treatment. In contrast, the accuracy was moderate at 60%–65% for predicting incomplete necrosis and at 67%–71% for predicting complete necrosis. The interobserver agreement was moderate, with a κ statistic of 0.55 (95% confidence interval: 0.47, 0.67), and was similar to pretreatment LI-RADS interobserver performance (3).

Investigators from transplant centers are in a distinct position to assess the performance characteristics of new imaging assessment criteria such as the LI-RADS Treatment Response algorithm. In liver transplant candidates with HCC and long wait times for organs, local-regional therapies are often used as a bridge to transplantation. The goal is to treat the tumor(s), or, at a minimum, limit tumor growth while the patient waits for a transplant to minimize

the likelihood that the tumor growth results in the patient dropping off the waiting list because the tumor burden exceeds the Milan criteria (ie, one HCC 5 cm or smaller or up to three HCCs, none larger than 3 cm). For these patients to remain on the transplant list, imaging is required at 3-month intervals. For patients who exceed the Milan criteria at presentation, downstaging with local-regional therapies may be attempted, with the goal of treating HCC so that it becomes smaller and meets Milan criteria. Hence, centers with patient cohorts with pretransplant local-regional therapy for HCC often perform posttreatment imaging and correlative explant pathologic examination within a 90-day window, allowing evaluation of imaging assessment criteria. Such centers are fertile grounds for additional research evaluating the performance characteristics of the LI-RADS Treatment Response algorithm.

Of importance for clinical practice, the experience reported by Shropshire et al brings to light existing challenges with cases with uncertainty, whether there is viable tumor or no viable tumor. The very existence of the LR-TR Equivocal category is evidence of the frequency with which radiologists encounter treated tumors that do not show arterial enhancement or washout but do show enhancement in a pattern not expected after the treatment. By consensus, Shropshire et al found that 27% (17 of 63) of the tumors were categorized as LR-TR Equivocal, with 71% (12 of 17) of them showing incomplete necrosis at histopathologic examination (3). The authors comment that at consensus readings of the LR-TR Equivocal lesions, a small number of lesions had features of the LR-TR Viable or LR-TR Nonviable categories, and categorization of some lesions as LR-TR Equivocal may have reflected reader uncertainty with the application of the criteria for LR-TR Viable and Nonviable tumors. They speculate that in the face of uncertainty, readers applied the tiebreaking rule in the LI-RADS algorithm, which resulted in assignment of these tumors to the LR-TR Equivocal category. If in future studies the LR-TR Equivocal category is shown to include a consistently high rate of lesions with incomplete necrosis, then many patients with LR-TR Equivocal findings might benefit from additional local-regional treatment following multidisciplinary discussion. Current LI-RADS–based management suggestions are short-term (≤3 months) imaging follow-up for LR-TR Equivocal tumors and multidisciplinary discussion, often with repeat treatment, for LR-TR Viable tumors. In clinical practice, multidisciplinary discussion is often initiated with imaging reports that are indeterminate or uncertain with respect to the presence or absence of viable tumor. Which patients with LR-TR Equivocal tumors would benefit from which local-regional therapy or therapies and at what time interval remain questions for further investigation.

The study by Shropshire and colleagues had limitations that provide opportunities for further research. The study is from a single transplant center. LI-RADS Treatment Response performance characteristics could conceivably be different outside of transplant centers or tertiary hospitals or could even differ between transplant centers. The cohort demonstrated heterogeneity of imaging modalities in that both CT and MRI multiphase imaging were included, though in insufficient numbers to compare the LI-RADS Treatment Response performance of CT and MRI. It is possible that adherence to a single imaging modality may result in different performance characteristics, even for examinations performed according to LI-RADS technical specifications. Only a single local-regional therapy, transcatheter bland embolization, was studied. Although this focus on a single treatment modality reflects a strength of the study in that it provides evaluation for this specific treatment, the performance characteristics of LI-RADS Treatment Response were not evaluated for different treatments, including percutaneous ablation or other transcatheter therapies. The majority of tumors were treated with a single session of bland embolization, and only nine of the 63 tumors were treated with a second session (3). In clinical practice, patients may undergo multiple different treatment sessions with varying combinations of percutaneous ablation and transcatheter embolization to treat different tumors or areas of viable tumor in previously targeted tumors. Conceivably, session multiplicity, varying treatments, and/or varying the order of treatments may result in different LI-RADS Treatment Response performance characteristics. The median tumor size before treatment was small, at 25 mm (range, 10–90 mm) (3). LI-RADS Treatment Response performance characteristics could prove different for larger tumors than for smaller tumors.

LI-RADS self-defines in part as "a dynamic document to be expanded and refined as knowledge accrues..." (1). Shropshire and colleagues have provided an important contribution to the dynamic and evolving LI-RADS endeavor in evaluating the performance characteristics of the first iteration of a LI-RADS Treatment Response algorithm.

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