LI-RADS Version 2018 Treatment Response Algorithm: The Evidence Is Accumulating

Richard K. Do, MD PhD • Mishal Mendiratta-Lala, MD

Dr Do is an associate attending physician in the body imaging service in the Department of Radiology at Memorial Sloan Kettering Cancer Center. He is the current chair of the ACR LI-RADS Treatment Response Working Group, and his research interests focus on hepatopancreatobiliary malignancies. Dr Do is a principle investigator for an NIH grant on prognostic radiomic markers for colorectal liver metastases.

Dr Mendiratta-Lala is an associate professor in abdominal and cross-sectional interventional radiology at the University of Michigan Health System. She is currently co-chair of both the ACR LI-RADS Treatment Response Working Group and the Society of Abdominal Radiology Hepatocellular Carcinoma Treatment Response panel. Her research interests are on hepatobiliary malignancies, including interventional therapy and translational research using animal models for new ablative technology. Dr Mendiratta-Lala is co-investigator on an NIH grant for adaptive radiotherapy for hepatocellular carcinoma.

In 2017, the Liver Imaging Reporting and Data Systems (LI-RADS) was updated to include a treatment response algorithm (TRA) (1), which did not undergo modification in the 2018 LI-RADS update (2,3). In patients with hepatocellular carcinoma (HCC), the TRA offers diagnostic radiologists a standardized approach to assess tumors and report their response after local-regional therapy (4).

According to the LI-RADS TRA, treated HCC can be classified as LI-RADS treatment response (LR-TR) viable, LR-TR equivocal, or LR-TR nonviable, based on the posttreatment enhancement pattern. The TRA is modeled after the modified Response Evaluation Criteria in Solid Tumors (mRECIST) (5), which is primarily based on the recognition of arterial phase hyperenhancement. However, the TRA differs by including an LR-TR equivocal category and an expansion of the imaging criteria for tumor viability, such as the inclusion of washout appearance. Unlike the patient-level response provided by mRECIST, the LI-RADS TRA aims to categorize individual lesion viability to help guide future local-regional interventions. However, as a newer algorithm for HCC treatment response, it needs further validation to ensure that the response

categories accurately reflect tumor viability after local-regional therapy.

In this issue of *Radiology*, Chaudhry et al assessed the performance of the LI-RADS TRA in 36 patients with 53 lesions who were undergoing ablative therapy prior to liver transplantation to predict complete necrosis as compared with a histopathologic reference standard (6). When LR-TR equivocal was treated as equivalent to LR-TR nonviable, sensitivity in the prediction of viable tumor ranged from 40% to 77% across readers. When LR-TR equivocal was treated as LR-TR viable, the sensitivity increased to 81%–87%. The specificity in the prediction of complete tumor necrosis ranged from 85% to 97% and from 81% to 85%, respectively, based on the same two scenarios. These results are comparable to those reported by two separate studies evaluating the LI-RADS TRA in patients with HCC undergoing predominantly transarterial embolization or chemoembolization (7,8).

The necessity of the LR-TR equivocal category has often been questioned, but its inclusion reflects the decision by the LI-RADS Tumor Response Working Group to allow some uncertainty in the assessment of treatment response. Chaudhry et al assessed a minority of the lesions as LR-TR equivocal after local ablative therapy by consensus reading (six of 53 lesions [11%]); of the six LR-TR equivocal lesions, five (83%) were incompletely necrotic at histopathology. On the other hand, Shropshire et al used the LR-TR equivocal category more frequently in patients treated with transarterial embolization (17 of 63 [27%]); of the 17 LR-TR equivocal lesions, 12 (71%) were incompletely necrotic at histopathology (7). Seo et al used the LR-TR equivocal category less frequently (59 of 287 [21%]), with most demonstrating some tumor viability at pathology (53 of 59 [90%]) (8). Taken together, these studies suggest that many treated lesions categorized as LR-TR equivocal harbor some viable tumor at histopathology, and the impact of folding the LR-TR equivocal category into the LR-TR viable category may yield higher sensitivity with a minimal loss in specificity. Whether the LR-TR equivocal category should be eliminated altogether requires further study, including an evaluation of its role in other local-regional therapies, such as radioembolization. In clinical practice, patients with treated HCC classified as LR-TR equivocal should be monitored closely for interval progression.

The ability of the LR-TR algorithm to allow us to predict complete tumor necrosis remains limited. In Chaudhry et al and Shropshire et al, less than half of

From the Department of Radiology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, C-278D, New York, NY 10065 (R.K.D.); and Department of Radiology, University of Michigan Medical Center, Ann Arbor, Mich (M.M.). Received November 7, 2019; revision requested November 14; revision received November 15; accepted November 18. **Address correspondence to R.D.** (e-mail: dok@mskcc.org).

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

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

Radiology 2020; 294:327–328 • <https://doi.org/10.1148/radiol.2020192484> • Content code: **GI** • ©RSNA, 2019

This copy is for personal use only. To order printed copies, contact reprints@rsna.org

the lesions categorized as LR-TR nonviable were completely necrotic at pathology after either ablative therapy (26 of 53 [49%]) (6) or transarterial embolization (range, 38%–46%) (7), respectively, whereas Seo et al reported that about two-thirds of the lesions were completely necrotic after chemoembolization (range, 60%–64%) (8). This is not surprising, given that the threshold for calling a lesion completely necrotic on pathology is 100% and any microscopic viability (<100% necrotic) is considered a failure in prediction. Thus, while an LR-TR nonviable category is desirable after local-regional therapy, the interval for imaging follow-up should initially remain the same given the potential of microscopic residual disease. The accuracy of LR-TR nonviable and LR-TR viable categories has not yet been directly compared against the volume of residual disease on pathology. It would be interesting to show whether LR-TR nonviable is a sufficient response, even in the presence of minimal residual disease, for patient outcomes, such as overall survival or progression-free survival.

In Chaudhry et al, the interreader agreement for LR-TR categories was substantial ($\kappa = 0.71$; 95% confidence interval: 0.59, 0.84) and higher than the interreader agreement for pretreatment LI-RADS categories ($\kappa = 0.40$). It was also comparable to interreader agreement in the two prior studies (Shropshire et al [7], Seo et al [8]) evaluating postembolization response ($\kappa = 0.55$ and $\kappa = 0.69$). One limitation acknowledged by Chaudhry and colleagues is that they evaluated only postablation imaging on MRI. Previously, Seo et al found a higher interreader agreement among readers when evaluating treated lesions on CT scans compared with treated lesions on MRI scans; however, the sensitivity for viable disease was higher for MRI than for CT (74.1% vs 39.2%) at the expense of some specificity (84.6% vs 95.8%) (8). A question to address in the future is whether eliminating the LR-TR equivocal category would potentially increase interreader agreement for the LI-RADS TRA in addition to increasing the sensitivity.

Although the study by Chaudhry et al is limited by the small sample size of patients and lesions, it adds to the emerging evidence that LI-RADS TRA should be used in clinical practice. The algorithm provides reasonable accuracy to predict residual viable tumor after either transarterial embolotherapy or locoablative therapy. Given the challenge in implementing mRECIST in daily clinical practice, LR-TR categories will be used increasingly in conjunction with LI-RADS diagnostic categories, such

as LI-RADS 5 or tumor in vein to report the response of individually treated lesions in patients with HCC. Further studies will help guide future refinements in the TRA and aid clinicians in understanding the probability of viable disease, similar to how the LI-RADS diagnostic categories have clarified communications between radiologists and our clinical colleagues (9). An important gap to address is the use of LI-RADS in assessing treatment response after radiation-based local-regional therapy (transarterial radioembolization or external beam radiation therapy), which is more challenging given the expected heterogeneity in spatial and temporal changes in enhancement patterns. Hence, patient-level response assessment in the clinical trial setting remains best assessed with mRECIST (10), until LI-RADS treatment response categories can be shown as potential surrogates for overall survival or progression-free survival.

Disclosures of Conflicts of Interest: R.K.D. disclosed no relevant relationships. M.M. disclosed no relevant relationships.

References

1. Elsayes KM, Hooker JC, Agrons MM, et al. 2017 Version of LI-RADS for CT and MR Imaging: An Update. *RadioGraphics* 2017;37(7):1994–2017.
2. Kielar AZ, Chernyak V, Bashir MR, et al. An update for LI-RADS: Version 2018. Why so soon after version 2017? *J Magn Reson Imaging* 2019;50(6):1990–1991.
3. Elsayes KM, Kielar AZ, Elmohr MM, et al. White paper of the Society of Abdominal Radiology hepatocellular carcinoma diagnosis disease-focused panel on LI-RADS v2018 for CT and MRI. *Abdom Radiol (NY)* 2018;43(10):2625–2642.
4. Kielar A, Fowler KJ, Lewis S, et al. Locoregional therapies for hepatocellular carcinoma and the new LI-RADS treatment response algorithm. *Abdom Radiol (NY)* 2018;43(1):218–230.
5. Lencioni R, Llovet JM. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. *Semin Liver Dis* 2010;30(1):52–60.
6. Chaudhry M, McGinty KA, Mervak B, et al. The LI-RADS version 2018 MRI treatment response algorithm: evaluation of ablated hepatocellular carcinoma. *Radiology* 2020;294:320–326.
7. Shropshire EL, Chaudhry M, Miller CM, et al. LI-RADS Treatment Response Algorithm: Performance and Diagnostic Accuracy. *Radiology* 2019;292(1):226–234.
8. Seo N, Kim MS, Park MS, et al. Evaluation of treatment response in hepatocellular carcinoma in the explanted liver with Liver Imaging Reporting and Data System version 2017. *Eur Radiol* 2019 Aug 15 [Epub ahead of print].
9. van der Pol CB, Lim CS, Sirlin CB, et al. Accuracy of the Liver Imaging Reporting and Data System in Computed Tomography and Magnetic Resonance Image Analysis of Hepatocellular Carcinoma or Overall Malignancy: A Systematic Review. *Gastroenterology* 2019;156(4):976–986.
10. Lencioni R, Montal R, Torres F, et al. Objective response by mRECIST as a predictor and potential surrogate end-point of overall survival in advanced HCC. *J Hepatol* 2017;66(6):1166–1172.