HCC IN FOCUS

Current Developments in the Management of Hepatocellular Carcinoma

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Use of the Liver Imaging Reporting and Data System in Hepatocellular Carcinoma

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G&H Why was the Liver Imaging Reporting and Data System created?

CS A colleague and I decided to create the Liver Imaging Reporting and Data System (LI-RADS) to standardize and clarify the language used in radiologic reports when describing computed tomography (CT) and magnetic resonance imaging (MRI) examinations for hepatocellular carcinoma (HCC). Several years later, the American College of Radiology (ACR) accepted our application to form a committee to develop an ACR-sponsored guideline based on our system as well as other systems being developed independently at other institutions. Thus, in 2008, a committee of radiologists from the United States was convened, and the first version of the system was released in 2011.

G&H What is the current use of this system?

CS Initially, LI-RADS applied only to CT and MRI examinations with extracellular agents. Over the years, it has expanded to include MRI examinations with hepatobiliary agents, and further expansions are expected soon. For now, LI-RADS remains restricted to the evaluation of HCC in adult patients with cirrhosis or patients with other risk factors for HCC. In the future, this system will likely be expanded to include children as well as benign liver lesions in noncirrhotic patients.

G&H When is the next update expected, and what is its goal?

CS The next update will likely be released this summer. It was submitted to the steering committee in February, but several changes were made and a revote is needed.

The goal of this update is to expand LI-RADS from covering only CT and MRI to also including conventional ultrasound and contrast-enhanced ultrasound. In addition, LI-RADS will soon have a system for assessing treatment response. In other words, LI-RADS will expand from not only being a diagnostic system to being a screening and treatment response system. Some of this update is essentially new content, and some is expanded content designed to address prior ambiguities or unnecessary complexities. In addition, some of the update involves responses to user feedback or emerging scientific evidence.

G&H What are the most important LI-RADS categories?

CS LI-RADS has several categories to describe the probability of malignancy, in a general sense, based on imaging features. LI-RADS 5 indicates a lesion for which the radiologist has 100% certainty that it is diagnostic of HCC. Thus, the lesion should be treated as HCC without a biopsy. Depending on the burden of HCC in the liver (ie, the number and size of LI-RADS 5 lesions), the patient may be eligible for liver transplantation without a biopsy.

Another important category is LI-RADS M. This category is used when the radiologist is 100% or close to 100% certain that a lesion is malignant but not 100%

certain that it is HCC. This distinction is important because the presence of HCC enables the patient to be eligible for liver transplant, but the presence of other malignancies in the liver does not. Other cancers have different prognoses and treatments. Although LI-RADS should not be used to determine when a biopsy is needed, many lesions may benefit from biopsy because it can reveal the type of cancer.

In addition, it should be clarified that, based on preliminary evidence, probably approximately half of LI-RADS M lesions end up being HCC that did not look like classic HCC on imaging (and, therefore, were not designated as LI-RADS 5), and approximately half end up being other cancers, such as cholangiocarcinomas, which can also occur in the cirrhotic liver.

Another important category is LI-RADS TIV (tumor in vein), which means that the patient has a malignancy in which the cancer is invading 1 or more veins. This category is important because the cancer has entered into the lumen of the vein, and it is likely that at least some of the cells have escaped the liver and have metastasized elsewhere in the body. These lesions are a contraindication for liver transplantation in nearly all cases.

The other important category is LI-RADS 4, which indicates a lesion that is probably HCC but cannot be proven to be HCC based on imaging. For example, if a radiologist sees a lesion and is 95% certain (but not 100%) that it is HCC, the lesion can be categorized as LI-RADS 4. This category is important because these lesions need to be managed very carefully because they may be cancers. Depending on the patient and the clinical context, appropriate management may be to examine the lesion with a different modality or contrast agent, to perform a liver biopsy, or, occasionally, to choose to treat the lesion as presumptive HCC without a biopsy. With so many complex considerations, multidisciplinary discussion is required to determine the best course of action for these lesions.

G&H How well does LI-RADS correlate with criteria from the Organ Procurement and Transplantation Network for listing patients?

CS Over the years, LI-RADS has tried to become congruent with the Organ Procurement and Transplantation Network (OPTN), and with the upcoming 2017 update, LI-RADS will enable unambiguous translation to OPTN. This update will provide instructions on how to convert from LI-RADS to OPTN. The vast majority of the time, the conversion is straightforward, requiring simply a tabulation of the number and size of observations fitting the LI-RADS 5 and 5g categories as well as pathology-proven HCCs. However, there are rare occasions in which straightforward conversion will not be the case, mainly due to ambiguities and internal inconsistencies with the OPTN system, which LI-RADS cannot change. This is not meant to be a criticism of OPTN; this system was a major advance, but it was developed over a short period of time almost 10 years ago and has not been modified since, in part because it does not have a standing committee to refine it over time.

G&H Does LI-RADS allow for integrated interpretation of multiple imaging modalities, such as ultrasound, MRI, and CT?

CS Integration is a complicated issue, mainly because there is very little scientific evidence currently available. With the exception of ultrasound, LI-RADS does not formally allow integration across modalities in the 2017 update, although this issue will likely be addressed in the subsequent update (scheduled for 2020 or 2021). Currently, only integration with ultrasound is allowed. If, for example, a nodule is seen on ultrasound, and a CT or MRI is performed to further evaluate the nodule, the knowledge that the nodule is visible on ultrasound can help its categorization using LI-RADS. There is scientific evidence that nodules visible on ultrasound are intrinsically more likely to be cancerous in a patient with cirrhosis than nodules not visible on ultrasound. Therefore, if a nodule is seen on CT or MRI as well as on ultrasound, there is more reason for concern. The category assigned to a nodule on CT and MRI can be changed based on whether it was also visible on ultrasound.

However, if a nodule is seen on CT as well as on MRI, the imaging information gleaned from one modality cannot be combined with the information gleaned from the other, at least not in 2017. For example, if a 20-mm nodule is identified with arterial phase hyperenhancement on CT and washout appearance on MRI, it may be tempting to combine the features across modalities and thereby assign a category of LI-RADS 5; however, there are not yet rigorous scientific data to inform how, or even if, features across modalities should be combined.

G&H Does LI-RADS address when MRI should be used and when CT should?

CS The system provides a little information on the advantages and disadvantages of different modalities, but it does not tell people which modality to use for 2 reasons. First, the scientific evidence supporting one modality over another is fairly weak. Second, and more importantly, the scientific data there might be about one modality being better than another may not be generalizable to every imaging center, particularly community centers. For

example, several studies have shown that MRI is slightly more accurate than CT. However, all of these studies have been conducted in academic centers, and almost all have been single-center studies. Proving that MRI is better than CT in an academic center does not demonstrate that MRI is better than CT in a community center or even in an academic center that does not have expertise in MRI.

G&H Does LI-RADS have any role in determining when a patient should be biopsied?

CS Not directly. A management committee comprising radiologists and hepatologists from the United States, Europe, and Asia was established several years ago to address this issue. The overwhelming consensus of the hepatology members was that radiologists, and therefore LI-RADS, should not determine who should and should not undergo a liver biopsy; that decision should be left to the clinician taking care of the patient. Radiologists often do not have enough clinical information with which to make that decision. In other words, radiologists might see a lesion that looks suspicious, but do not usually know the whole picture: whether the patient has relevant comorbidities, whether the patient is risk-adverse and would never want to undergo a biopsy, and so on. There are a number of psychological and physical conditions that a patient may or may not have that influence whether a biopsy should be performed.

Thus, LI-RADS cannot determine whether a patient should undergo a biopsy. Instead, LI-RADS can provide guidance to radiologists for when they may suggest consideration for biopsy, but radiologic reports should avoid wording that might compel a clinician to perform a biopsy.

G&H Does LI-RADS play a role in HCC that is multifocal?

CS Yes. This is another challenging area. Historically, LI-RADS was used to examine each individual observation or lesion in the liver. Thus, if multiple lesions, all of which are diagnostic of HCC, are seen in the liver, then by definition the patient has multifocal HCC. The challenge with multifocal disease is that when too many details are given in a report, the referring clinician and the patient might lose sight of the overall picture. One of the reasons that the 2017 update is necessary is to provide better guidance to radiologists in terms of how to report multifocal cancer. In general, radiologists should use their judgment in deciding when to report lesions individually and when to report lesions in aggregate. The reporting of multifocal HCC is such an area of complexity in LI-RADS that it will still likely need improvement in future updates.

G&H What limitations or challenges are associated with the use of LI-RADS?

CS The strength of LI-RADS, rigor, is also its main weakness. It is faster not to use LI-RADS than to methodically characterize a lesion using this system. Computer systems that can help radiologists apply LI-RADS rapidly and properly are needed, and are now in development.

Dr Sirlin is the chair of the LI-RADS Steering Committee and of the v2017 Writing Group.

Suggested Reading

Elsayes KM, Kielar AZ, Agrons MM, et al. Liver Imaging Reporting and Data System: an expert consensus statement. *J Hepatocell Carcinoma*. 2017;4:29-39.

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