Radiology

Does Hepatocellular Carcinoma Screening with US Work? Using the US LI-RADS Algorithm

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

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

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Hepatocellular carcinoma (HCC) is a common disease occurring in patients with known risk factors. Because its prognosis varies with its stage, large screening programs have been developed with the hope of finding the disease as early as possible, when it can be cured either with local therapy or transplantation (1). For economical and practical reasons, imaging screening of HCC relies on US, with cross-sectional imaging (CT and MRI) being used in case of suspicious findings at US. However, uncertainty exists regarding the sensitivity of the technique, especially in the detection of early HCC (2).

Since 2011, the Liver Imaging Reporting and Data System (LI-RADS) has been proposed and updated by the American College of Radiology, with a specific focus on the imaging diagnosis of HCC (3). In 2017, the American College of Radiology added a new component, the US LI-RADS algorithm, which focused on screening and surveillance US. The US LI-RADS included standardized guidelines for interpretation, reporting, and management recommendation (4). The algorithm suggested the reporting of two separate scores, one regarding the likelihood of HCC during the examination (US-1 = negative, US-2 = subthreshold, and US-3 = positive) and one regarding the quality of the examination (visualization score A = no or minimal limitations, visualization score B = moderate limitations, and visualization score C = severe limitations) (4).

Because this algorithm is new, US LI-RADS has not yet been independently evaluated. In this issue of Radiology (5), Son and colleagues evaluate the performance of the US LI-RADS algorithm and the clinical factors affecting the visualization. The key findings include a low sensitivity of US, especially in patients with a visualization score of C.

Son et al evaluated 407 participants with an annual risk of developing HCC of more than 5%. There were 32 HCCs in 28 participants. Two experienced radiologists, blinded to the final diagnosis, independently reviewed the images from screening US. A consensus review was performed in cases of disagreement. The US LI-RADS category was assessed according to the US findings. When lesions measuring at least 10 mm in diameter and not definitely benign or a new thrombus in a vein were noted, lesions were assessed as US-3 (positive). When lesions smaller than 10 mm in diameter that were not definitely benign were noted, they were assessed as US-2 (subthreshold). An absence of lesions or only definitely benign observations were assessed as US-1 (negative). The visualization score was also determined during the same review. The reference standard for most patients was multiphasic CT (at 3 months in the case of a positive US and at 6 months when the US was negative), with some participants undergoing biopsy. Sensitivity analysis was performed taking a US LI-RADS score 3 as a positive finding.

For the practicing radiologist, the most clinically useful findings reported in this article are the low sensitivity of US LI-RADS score 3 (39% in the per-patient analysis) and the high rate of false-negative findings, especially in cases of poor visualization, in which situation six out of seven HCCs were missed (86%). It must be noted that even in cases of optimal visualization (visualization score A), the rate of false-negative findings was still high, with eight of 14 HCCs being missed (57%). The other findings of note were the factors leading to poor visualization, including a high body weight, moderate to severe fatty infiltration of the liver, and Child-Pugh class B disease. The high negative predictive value of US LI-RADS score 3 found in this study is of lesser value and should not reassure the reader, because the prevalence of HCC was low in this population (only 7% of patients had HCC). This means that a negative study had a high likelihood of being a true negative even if this meant missing most of the HCC.

There are limitations to the study from Son and colleagues, providing opportunities for further research. The study is from a single center, with a relatively low prevalence of HCC in this population, most of whom have early HCC, limiting the generalization of the results. Studies from larger multicenter cohorts could be of interest. In that regard, it must be noted that one goal of the US LI-RADS algorithm is to facilitate standardization between institutions, which should in turn permit better data extraction for future evaluation (4).

Despite prospective collection of a cohort of participants, retrospective review of the US images can generate some observation biases. However, this is similar to a situation where a radiologist reviews images acquired by a sonographer, so this remains valuable in many settings. Examinations were performed with an Aixplorer system (SuperSonic Imagine; Aix-en-Provence, France), which is not widely used in the United States. Thus, the reader could question the applicability of the results on studies performed with other systems. Studies comparing the performances of different US machines may be of interest in the future to exclude a possible technological limitation explaining at least in part the poor sensitivity of US in this context.

Despite these limitations, the findings of this article are important for the practicing radiologist. They show that US has substantial limitations in the detection of HCC in patients at high risk for HCC, especially a low sensitivity. The 39% sensitivity found in this study is well in line with the low sensitivity (47%) of US in detecting early HCC as established in a recent meta-analysis (2). This sensitivity is even lower in patients with a low visualization score. What this means in practice is likely twofold. First, the radiologist should spend a substantial amount of time determining whether the study was of sufficient quality, covering the entire liver without too many artifacts and/or regions of marked attenuation. This is why the visualization score proposed in the US LI-RADS algorithm is key. If Son et al evaluated US scans obtained and reviewed by radiologists, we can assume that this could be especially important in busy practices where US scans are acquired by technologists and reviewed by radiologists; however, this would need to be specifically evaluated. The study gives some clues on some patient characteristics requiring special scrutiny, such as obesity and fatty infiltration. These factors may be very important problems in some parts of the world.

Second, radiologists and other clinicians treating these patients must be aware of the limitations of the technique itself and should not shy away from using cross-sectional imaging if they feel it is appropriate. However, this specific point is not addressed in the US LI-RADS algorithm, with no specific recommendations based on visualization scores (4). Another consequence is that novel screening paradigms should also be developed and evaluated, and some of them are already proposed, using some variants of fast MRI protocols (6,7). If they seem efficient based on early reports, their value must be assessed in large cohorts and should include cost-effectiveness analyses, as screening numerous patients with MRI may lead to unmanageable cost (1). Other strategies would be to improve the preprobability test by adding some biomarkers to imaging to narrow the selection of patients to be included in screening programs (2).

While the medical community is waiting for the results of such studies, US will most likely remain the initial imaging modality of choice in the screening of patients at risk for hepatocellular carcinoma. In this setting, it is very important for the practicing radiologists to be made aware of the limitations of the techniques, and the current study by Son and colleagues (5) provides an important contribution in that regard.

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References

1. Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology 2018;68(2):723–750.
2. Tzartzeva K, Obi J, Rich NE, et al. Surveillance imaging and alpha fetoprotein for early detection of hepatocellular carcinoma in patients with cirrhosis: a meta-analysis. Gastroenterology 2018;154(6):1706–1718.e1.
3. Chernyak V, Fowler KJ, Kamaya A, et al. Liver Imaging Reporting and Data System (LI-RADS) Version 2018: Imaging of Hepatocellular Carcinoma in At-Risk Patients. Radiology 2018;289(3):816–830.
4. Morgan TA, Maturen KE, Dahiya N, Sun MRM, Kamaya A; American College of Radiology Ultrasound Liver Imaging and Reporting Data System (US LI-RADS) Working Group. US LI-RADS: ultrasound liver imaging reporting and data system for screening and surveillance of hepatocellular carcinoma. Abdom Radiol (NY) 2018;43(1):41–55.
5. Son HG, Choi SH, Kim SY, et al. Validation of US Liver Imaging Reporting and Data System version 2017 in patients at high risk of hepatocellular carcinoma. Radiology 2019;292:390–397.
6. Kim HA, Kim KA, Choi JI, et al. Comparison of biannual ultrasonography and annual non-contrast liver magnetic resonance imaging as surveillance tools for hepatocellular carcinoma in patients with liver cirrhosis (MAGNUS-HCC): a study protocol. BMC Cancer 2017;17(1):877.
7. Kim SY, An J, Lim YS, et al. MRI with liver-specific contrast for surveillance of patients with cirrhosis at high risk of hepatocellular carcinoma. JAMA Oncol 2017;3(4):456–463.