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RESEARCH

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Diagnostic performance of US LI-RADS in hepatocellular carcinoma surveillance

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Abstract

Background Liver cirrhosis and chronic infection with hepatitis B virus are major risk factors for hepatocellular carcinoma (HCC). Guidelines recommend ultrasound (US) surveillance for population at risk of HCC. The US Liver Imaging Reporting and Data System (LI-RADS) aims at standardization of interpretation, reporting, and management recommendations for US surveillance examinations. The aim of this study is to assess the diagnostic accuracy of US LI-RADS in early HCC detection in patients at risk.

Results This retrospective study included patients with surveillance US between January 2018 and January 2020 who had a contrast-enhanced CT or MRI of the liver within 1 month from the date of US examination. Visualization scores and US categories were assigned according to the US LI-RADS lexicon. A total of 264 participants were eligible for the study. HCC was diagnosed in 33 participants. The US-3 category had a 39.4% sensitivity and 93.5% specificity for HCC detection. The US-2 category had a 45.4% sensitivity and 87% specificity for HCC detection. The visualization score C showed the highest number of HCC (19/33) and had the highest false-negative rate (76%, 13 of 17).

Conclusions Both US-2 and US-3 categories showed high specificity and low sensitivity for HCC detection in the setting of surveillance of patients at high risk. Visualization score C had the highest risk for HCC and the highest rate of false-negative results. Intense surveillance by contrast-enhanced CT or MRI might be beneficial for patients with limited visualization scores B and C.

Keywords Hepatocellular carcinoma, Surveillance, Liver cirrhosis, Ultrasound, Ultrasound LI-RADS

Background

The most frequent primary liver cancer is hepatocellular carcinoma (HCC), which is also the second cause of cancer-related death globally. The stage at the time of diagnosis affects the prognosis for HCC. The typical survival time for patients with advanced cancer is less than 1 year, whereas patients with early disease are responsive to curative therapy and have a 5-year survival rate of roughly 60–80%. Consequently, it is critical to identify HCC early on [1, 2].

For surveilling patients with cirrhosis, the American Association for the Study of Liver Disease (AASLD) recommendation suggests US monitoring every 6 months [3]. Ultrasound is widely available, affordable, and non-invasive. On the other hand, there are some patients with significant liver surface nodularity or morbid obesity in whom the diagnostic accuracy of US for early-stage HCC is reduced [4–6]. Another restriction on US surveillance is the absence of uniform rules for interpretation, reporting, and management recommendations [7, 8]. In order to improve the quality and sufficiency of the ultrasound surveillance, the Ultrasound Liver Imaging Reporting and Data System (US LI-RADS) algorithm was developed in 2017 by the American College of Radiology. The algorithm describes three categories that summarize the

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findings and guide the most appropriate follow-up (US-1 negative, US-2 subthreshold, and US-3 positive). To assess the technical adequacy of the examination, three visualization scores are described to communicate the expected level of sensitivity for the screening/surveillance examination (A no limitation, B moderate limitations, and C severe limitations) [9, 10].

Recent studies showed that moderate-to-severe limitations are observed in approximately one-third to half of surveillance US examinations [11, 12]. An earlier study by Son et al. [13] evaluated the diagnostic performance of US LI-RADS and found that category US-3 has a good specificity and low sensitivity for HCC detection. However, the diagnostic performance of US-2 category was not assessed and compared to US-3 category.

Therefore, the aim of this study is to assess the diagnostic accuracy of US LI-RADS in HCC surveillance and to compare the accuracy of US-2 and US-3 as a positive finding.

Methods

Participants

Patients who underwent US surveillance between January 2018 and January 2020 were eligible for this retrospective analysis if they had cirrhosis of any etiology, chronic HBV, or HCV infections. For CT and MRI scans as well as biopsy results, if any were available, the medical records were checked. Patients were considered if their CT or MRI was performed within a month of the ultrasound examination date. Patients with extrahepatic cancer or a prior diagnosis of HCC were excluded.

The study was approved by the research ethics committee, and the requirement of written informed consent was waived.

Imaging analysis

One of the four board-certified radiologists with 6, 8, 9, or 10 years of experience in abdominal imaging performed the US studies. Philips EPIQ or Philips Iu22 US machines (Philips health care) were used for the examinations. The US examinations were performed in accordance with institution protocol using a curvilinear transducer (1–5 MHz) and included a series of static grayscale images of the left and right liver lobes taken while the patient was lying supine and in the left lateral decubitus position, as well as colored Doppler images of the portal and hepatic veins.

US images were retrospectively analyzed by one radiologist with 10 years of experience in hepatic imaging who was blinded to the final diagnosis.

The US LI-RADS category was assigned according to the US imaging findings. Lesions were assessed as US-3 (positive) when lesions not definitely benign measuring at least 10 mm in diameter or a new thrombus in a vein were noted. Subthreshold observations (US-2) were assigned for lesions smaller than 10 mm in diameter and not definitely benign. When no focal lesions or definitely benign observations were detected, the US-1 category (negative) was assigned.

Visualization scores were assigned as follows; score A, no or minimal limitations (limitations unlikely to meaningfully affect sensitivity); score B, moderate limitations (limitations that may obscure small masses); and score C, severe limitations (limitations significantly lowering the sensitivity for focal liver lesions).

Reference standard

The diagnosis of HCC was based on CT and/or MRI findings and biopsy results of indetermined observations. The Liver Imaging and Reporting Data System (LI-RADS) v2018 [10] criteria were used for CT and MRI interpretation. If no observations or definitely benign lesions were detected on CT and/or MRI, the results were defined as negative.

Statistical analysis

For continuous data, the mean and standard deviation were used, while categorical data were reported as percentages and frequencies. Comparing categorical data was done using the Chi-square test, while comparing continuous data was done using the independent samples t-test. For the assessment of the US LI-RADS diagnostic performance in HCC diagnosis, calculations of the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were done for both categories US-2 and US-3 when each was considered as a positive finding. Statistical significance was defined as a p value 0.05. For the analysis, SPSS (version 24) was employed.

Results

Study participants

The characteristics of 264 participants are summarized in Table 1. Thirty-three patients were diagnosed with HCC. A total of 207 patients had CT scans, 23 received MRI scans, and 34 received both CT and MRI. Biopsy was performed for seven patients due to indeterminate observations, and the results were HCC in all of them.

Results of US LI-RADS category and visualization score

A total of 147 examinations were given a visualization score A, of which six HCCs were diagnosed. Fifty-three were scored as B, of which eight HCCs were diagnosed. Sixty-four were scored C, among them 19 HCCs were diagnosed.

Table 1 Baseline characteristics of study participants

	All participants 264	No HCC 231	HCC 33	*P* **
Age* (years)	58.5 [15]	56 [15.6]	65.5 [7]	< 0.001
Gender				0.02
Male	126	104	22	
Female	138	127	11	
Hepatitis				0.07
Negative	110	101	9	
Hepatitis B	50	46	4	
Hepatitis C	104	84	20	
Cirrhosis				< 0.001
Negative	53	53	0	
Positive	211	178	33	

Data represent number of participants

*Age is displayed as mean [standard deviation]

***P* is the p value for the comparison of variables between the two groups

Table 2 US LI-RADS category assessment and visualization scores

		Visualization score			
		A	B	C	Total
US LI-RADS categories	US-1	136	42	41	219
	US-2	5	8	4	17
	US-3	6	3	19	28
Total		147	53	64	264

Twenty-eight observations were classified as US-3, of which there were 13 HCCs. Seventeen observations were US-2, of which two HCCs were diagnosed. US-1 category was assigned in 219 examinations of them 18 HCCs were founded. Visualization score C showed the highest false-negative rate, 76% (13/17). Table 2 summarizes the distribution of US LI-RADS categories and visualization scores.

Diagnostic performance of US LI-RADS

Table 3 shows the diagnostic accuracy parameters of US LI-RADS. When US-3 was considered as a positive finding, the specificity and NPV were high (specificity, 93.5% [216 of 231]; NPV, 91.5% [216 of 236]), while the sensitivity and PPV value were low (sensitivity, 39.4% [13 of 33]; PPV, 46.4% [13 of 28]).

When US-2 was considered as a positive finding, no significant change was observed in the diagnostic performance. The specificity and PPV were slightly decreased, and the sensitivity and NPV slightly increased (specificity, 87% [201 of 231]; PPV, 33.3% [15 of 45], sensitivity, 45.4% [15 of 33]; NPV, 92% [201 of 219]). Overall accuracy was higher for US-3 category (86.7% vs. 81.8%).

Discussion

The results of this retrospective study showed that the US LI-RADS US-3 category had a low sensitivity and high specificity for diagnosis of hepatocellular carcinoma (HCC) (39.4% [13 of 33] and 93.5% [216 of 231], respectively). When US-2 category was defined as a positive finding, only slight increase in the sensitivity and decrease in the specificity were observed (45.4% [15 of 33] and 87% [201 of 231], respectively).

The previous studies reported a wide range for the sensitivity of US in diagnosing HCC (20–94%) [7, 8, 14–17]. Our results are similar to the results of the study by Son et al. [13], which reported a sensitivity of 34% and specificity of 92% for US-3 category in early HCC detection. However, in their study, they did not evaluate the performance of US-2 category as a positive finding, probably because of the small number of US-2 observations encountered in their study (six observations), while in our study, there was 16 observations labeled as US-2.

The accuracy of US in the screening or surveillance of early HCC is significantly decreased when limited visualization scores exist. In our study, 24% of examinations showed visualization score C, and 20% was graded visualization score B. The previous studies reported percentages of visualization scores B and C ranging between

Table 3 Diagnostic accuracy of US Liver Imaging Reporting and Data System

Diagnostic accuracy of US LI-RADS for HCC diagnosis		
Parameter	**US-3 as positive finding**	**US-2 as positive finding**
Sensitivity	13/33 [39.4] (22.9–57.9)	15/33 [45.4] (28–66.6)
Specificity	216/231 [93.5] (89.5–96.2)	201/231 [87] (82–91)
Positive predictive value	13/28 [46.4] (31–62.3)	15/45 [33.3] (23.2–45.2)
Negative predictive value	216/236 [91.5] (89–93.4)	201/219 [92] (89–94.2)
Accuracy	[86.7] (82–90.6)	[81.8] (76.6–86.3)

Data are number of observations. Numbers between brackets are % percentages. Numbers between parentheses are 95% confidence intervals

19–30% and 4–20%, respectively [11, 13, 18]. In our study, 57% (19/33) of HCCs were associated with visualization score C, and 24% (8/33) were associated with visualization score B. Similar findings were reported by a recent study in which visualization scores B and C had a higher risk of HCC and higher odds of false-negative rates of US for HCC detection [12]. We found a 76% false-negative rate for diagnosing HCC in the case of a visualization score C, this is also similar to the study by Son et al. [13] which reported an 86% false-negative rate in visualization score C.

Due to these limitations associated with the US, other alternative surveillance strategies were warranted. These include US in combination with alpha-fetoprotein [19–24] and MRI-based surveillance [9, 15, 25, 26]. Recently, abbreviated MRI has emerged as a potential surveillance test with reported sensitivity ranging between 82.6 and 85.2% [27–29].

Our study has some limitations to be acknowledged. First, study participants were retrospectively recruited based on the availability of confirmatory cross-sectional studies. This may have caused selection bias with larger percentage of US-2 and US-3 categories. However, this design was selected to correctly evaluate the false-negative rates of US with confirmatory CT or MRI available for all patients. Second, we did not perform inter-reader agreement analysis. Recent studies reported moderate-to-good inter-reader agreement in US LI-RADS visualization scores and category assignment [30, 31]. Therefore, we think that this did not negatively affect our results.

Third, the visualization scores were assigned retrospectively from the previously obtained images, not at the time of examination. Further prospective studies incorporating visualization score assessment by the sonographers and radiologists at the time of performing ultrasound examinations are required. Fourth, we had a relatively small number of participants and HCC cases.

Conclusions

The US Liver Imaging Reporting and Data System US-2 and US-3 categories demonstrated a high specificity and low sensitivity for diagnosis of HCC in the setting of surveillance of patients at high risk. Visualization score C had the highest risk for HCC and the highest rate of false-negative results. Intense surveillance by contrast-enhanced CT or MRI might be beneficial for patients with limited visualization scores B and C.

Abbreviations

AASLD	American Association for the Study of Liver Disease
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
US LI-RADS	Ultrasound Liver Imaging Reporting and Data System
US	Ultrasound

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Author contributions

AHJ helped in data collection, analysis, and writing. MAW contributed to analysis and writing. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The research ethics committee at Faculty of Medicine, King AbdulAziz University, approved this retrospective study. The requirement of written informed consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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