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US LI-RADS: Ultrasound liver imaging reporting and data system application for screening and surveillance of hepatocellular carcinoma during national mass screening campaign for patients with positive HCV serological test

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***Abstract*---**Purpose: We aimed to apply Ultrasound Liver Imaging Reporting and Data System (US LI-RADS) to the patients with positive serological HCV test surveyed during the national mass screening campaign. Methods: We conducted a cross-sectional study that recruited patients with positive serological test for HCV, who underwent the national mass screening campaign during the period from April 2019 to June 2020. Each operator was required to classify

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the patients into one of the following three categories according to the US visualization into: A, no or minimal limitations; (2) B, moderate limitations; and (3) C, severe limitations. Results: A total of 763 HCV patients were recruited in the present study. Conclusion: US is the modality of choice during mass screening for HCC, yet the presence of the human factor (being operator dependent) and the lack of unified reporting scheme were drawbacks; thus US- LI-RADS, overcome the latter drawback with ready to go plan according to the given score of each individual patient.

***Keywords*---**US LI-RADS, hepatocellular carcinoma, ultrasound, surveillance.

Introduction

Hepatocellular carcinoma (HCC) is one of the most prevalent cancers that causing an increasing number of cancer-related deaths (1). HCC is linked to long-term liver inflammation and, eventually, cirrhosis (2). Its prevalence varies by location, reflecting changes in risk factors such as hepatitis B (HBV) or C virus (HCV) infection (3). Early detection of HCC allows several management options, including radiotherapy, chemotherapy, surgical resection, and liver transplantation (4). The application of these options at an early stage can reduce the risk of mortality. However, only about a third of individuals are diagnosed early enough to benefit from such treatment (5). In case of late detection, the estimated survival time of HCC patients is less than a year (6). Therefore, effective screening and surveillance are critical to HCC patients' survival. Serial examination with ultrasound every six months is recommended for extensive screening and surveillance with serial ultrasound examinations at least every six months (7,8). Ultrasound provides essential anatomic and physiologic details in addition to detecting HCC in high-risk groups (9). At the time of screening ultrasound, imaging signs such as splenomegaly and elevated liver stiffness can indicate advanced fibrosis or cirrhosis (10).

The Ultrasound Liver Imaging Reporting and Data System (US LI-RADS) of the American College of Radiology (ACR) was developed in 2017 and provides criteria for consistent technique, interpretation, and reporting of surveillance ultrasound examinations (11). The ultrasound visualization score and category in the US LI-RADS technique are as follows: Visualization scores denote the expected sensitivity of the test, based on the adequacy of liver visualization with ultrasound; ultrasound categories define the test as negative, subthreshold, or positive and direct next steps in management (12,13) On the other hand, US LI-RADS does not address alternative screening or surveillance modalities or biomarkers. Therefore, in this study, we aimed to apply US LI-RADS to the patients with positive serological HCV test surveyed during the national mass screening campaign for the aid of clarification of management plans and improvement of the communication with the referring physician.

Materials and Methods

The present manuscript was approved by the local ethics committee of Faculty of Medicine, Cairo University and prepared in concordance with the recommendations of STrengthening the Reporting of OBservational studies in Epidemiology (STROBE)(14).

Study Design and Patients

We conducted a cross-sectional study that recruited patients with positive serological test for HCV, who underwent the national mass screening campaign during the period from April 2019 to June 2020. The examinations took place in different hospitals and radiology centers in Cairo and Giza, Egypt. We excluded patients with confirmed HCC diagnosis and patients who did not agree to sign the written informed consent.

Data Collection and US Procedure

Eligible patients underwent detailed history regarding the age, marital history, parental history and history of chronic illness, and surgical intervention or blood transfusions. Then all patients underwent trans-abdominal ultrasound and color Doppler examinations using high frequency endo-cavitary ultrasound transducers (3.5-7.5 MHZ). The following ultrasound machines were used: GE Logic P6 (SN: K073297, made in USA), P7 (SN: 252345YM6, made in USA), P9 (2294853-M10, made in USA) and S7 (SN: 205665- US-3, Made in USA); GE voluson P8 (SN: 286896-SU-6, Made in USA); and Toshiba Xario (Model USQ1 770*, made in Japan).

The assessment of the US LI-RADS score was done by two independent operator and any discrepancies were resolved by consensus. Each operator was required to classify the patients into one of the following three categories according to the US visualization into: A, no or minimal limitations; (2) B, moderate limitations; and (3) C, severe limitations (15).

Statistical Analysis

SPSS version 19 (SPSS Inc., Cary, NC) was used for the statistical analysis. We described the central tendency and variation of age using mean and standard deviation (SD). Frequency tables were used for gender, US LIRADS category, visualization score, and gall bladder disease. The association between visualization score and other parameters was assessed using Chi-squarer test. A P-value of less than 5% was considered statistically significant.

Results

A total of 763 HCV patients underwent the US screening and were recruited in the present study. The mean age of the patients was 51.14 ± 10.22 years, with slight male predominance (55.2%). Nearly 88.6% of the cases have US category 1 and 10.5% have category 2. Concerning the visualization score, 84 .3% of cases have visualization score category A, 13.9% has category B, and 1.8% has category. The examination revealed that 73.5% of the patients had gall bladder disease (Table 1).

Table 1: Characteristics of the study group

Variables		Study group (n=40)
Age (years)	Mean ± SD	51.14 ± 10.22
	Range	25-94
Male	N (%)	421 (55.2%)
US LIRADS category	US 1	676 (88.6%)
	US 2	80 (10.5%)
	US 3	7 (0.9%)
Visualization score	A	643 (84.3%)
	B	106 (13.9%)
	C	14 (1.8%)
Gall bladder disease	Yes	561 (73.5%)
	No	202 (26.5%)

There was statistically significant relation between US visualization score and sex; the majority of females (90.1%) had a score A, compared to 79.6% of male cases (P = 0.002). Likewise, there was statistically significant relation between US visualization score and gall bladder disease, as score A represents 91.9% of cases with gall bladder disease and 81.8% of cases without gall bladder disease. Score B represents 8.9% of cases with gall bladder disease and 15.7% of cases without gall bladder disease (P =0.0032). The association between US category and visualization score was not statistically significant, Table 2.

Table 2: The association between visualization score and other studied parameters

Variables		Visualization score						P-value
		A		B		C		
		N	%	N	%	N	%	
US LIRADS	US 1	576	89.6	89	84	11	78.6	0.119
	US 2	60	9.3	17	16	3	21.4	
	US 3	7	1.1	0	0	0	0	
Gender	Male	335	79.6	78	18.5	8	1.9	0.002
Gall bladder disease	Yes	184	91.1	18	8.9	0	0	0.0032

Discussion

Despite Hepatitis C virus (HCV) prevalence is the highest in Egypt. due to the mass anti-schistosomiasis treatment initiatives in the 1960s and 1970s (16). At that time, the source of HCV transmission is thought to be a lack of sterilization of the injecting equipment used during the mass treatment campaign (17). The most extensively utilized imaging method for HCC screening and surveillance is ultrasound. However, there were no established rules for interpretation, reporting, or management advice for this method until today (18). Ultrasound LI-RADS addresses the use of ultrasound for screening and/or surveillance. It does not address the possible use of other modalities or biomarkers for screening or surveillance (11,13). The objective of ultrasound LI-RADS is not limited to diagnosing hepatic focal lesions, nor is it especially concerned with it. However, its primary function is to assist the clinician in obtaining a standardized reporting scheme that can help him or her address the patient's proper state, the limitations of ultrasound examination, and the need to assess the liver further using other imaging methods (19).

During the national mass screening campaign, our study was carried out where the patients with positive serological HCV tests underwent ultrasound examination of the abdomen after regular preparation. No special techniques or patient preparation are needed. Seven hundred sixty-three patient data were randomly collected with their imaging criteria and examination results applied to the ultrasound LI-RADS reporting system. Our findings demonstrated a marked predominance of the US LI-RADS-Category 1 (88.6 %), followed by US LI-RADS-Category 2 (10.5 %) and US LI-RADS-Category 3 (0.9 %). The visualization score A was predominant with a total of 84.3 % compared to 13% for score B was 13.9%, and 1.8% for score C. Interestingly, there was no statistically significant association between the US LI-RADS category and the visualization score. In agreement with our findings, Rodgers et al. demonstrated that incorporating the US LI-RADS into the LI-RADS system improved communication and improved patient outcomes among hospitalized patients. In addition, they have reported that US LI-RADS improved the communication between radiologists, hepatologists, and transplant surgeons (20). During our study, when the algorithm was explained to other medical practitioners involved, they were more than welcoming and agreed that it provides better communication and more structurally sound conclusions. In addition, the clinicians had a more precise evaluation and more concise decisions leading their way. In the retrospective study of Choi and his colleagues, 43% of the included patients were cirrhotic. Similar to our findings, the visualization score A was detected in 75%, score B in 22%, and score C in 3%. Moreover, they found a significant ($p<0.001$) association between the poor visualization scores and spleen size, clinical fibrosis, and patient's age (5). Kang et al. included 208 patients with focal hepatic lesions; the US LI-RADS was able to detect 85.1% of them. The visualization score A was 70.2%, followed by 26.4% for score B and 3.4% for score C. The majority of these patients were affected with HBV (62%), and only 7.7% had HCV. Liver cirrhosis was reported in 76% of the included patients. Multivariate analysis showed that lesion size, visualization score, and high-risk needle pathway usage were the main predictors of non-diagnostic results (11).

Extrinsic and intrinsic liver factors can alter ultrasonography sensitivity for HCC diagnosis. Extrinsic factors such as overlying bandages or devices, obesity, and tenderness may alter over time or result from the ultrasound method. Intrinsic factors, such as hepatic steatosis, parenchymal heterogeneity, or liver atrophy, are inherent to the liver and are unlikely to change over time (21). According to recent studies, a US visualization score of C is linked to an 86 percent false-negative rate for the diagnosis of HCC in surveillance US examinations, and parenchymal macronodularity may make early-stage tumors challenging to detect during US monitoring (22). Therefore, exam optimization is essential for minimizing both types of limitations. This involves the performing sonographers' training and expertise and real-time modifications to technological settings (13,19,23). However, our study had some drawbacks that should be avoided in the upcoming studies; the lack of follow up protocol for most the patients with different results, the inability to communicate with all the referring physicians and get their feedback about using the US LI-RADS reporting algorithm as well as the lack of comparison with the other imaging modalities.

In conclusion, ultrasound is the modality of choice during mass screening, for being cheap, available, and non-invasive, yet the presence of the human factor (being operator dependent) and the lack of unified reporting scheme were drawbacks; thus US- LI-RADS, overcome the latter drawback with ready to go plan according to the given score of each individual patient. Furthermore, the algorithm is still relatively new, but radiologists/clinicians' interaction, feedback, and research, will provide better further refinements upon the already existing algorithm; thus, future versions may be able to clarify that the US LI-RADS category is the critical value of the reporting system within this algorithm and that the visualization score should not be an obstacle in the management way.

Conflict of interest
None.

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