Assessment and Validation of Ultrasound liver Imaging Reporting and Data System Version 2017 (US-LI-RADS V 2017) in Patients at High Risk of Hepatocellular Carcinoma

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ABSTRACT

Background: Improvement of patient-centered outcomes through standardization of ultrasound reporting in patients at high risk of developing Hepatocellular Carcinoma (HCC).

Objective: To assess the role of US-LI-RADS in the detection of HCC in high-risk patients.

Patients and Methods: Fifty patients of both sexes referred from Tropical and Internal Medicine Departments with cirrhosis due to chronic viral hepatitis (C&B) with a mean age of 58 years were included in this comprehensive study, at the Radiodiagnosis Department, Faculty of Medicine, Zagazig University Hospital. All patients were subjected to conventional B-mode ultrasound. **Results:** Out of the 50 cirrhotic patients, 13 patients (26%) had positive findings by the US. Using US-3 as a positive finding had a high specificity and negative predictive value (100 percent). Instead of being high, the sensitivity and positive predictive value (PPV) were poor when a positive observation was classified as US-3 (43.3 percent). **Conclusion:** It was found that the LI-RADS US-3 category had a high specificity for hepatocellular carcinoma diagnoses, however, it had a low sensitivity.

Keywords: Ultrasound liver Imaging Reporting and Data System Version 2017, Hepatocellular Carcinoma.

INTRODUCTION

Hepatocellular carcinoma is the third most prevalent cause of cancer-related death worldwide, and it is the sixth most common type of cancer [(1)]. HCC is a public health issue in Egypt, where it accounts for 33.63 percent of male malignancies and 13.54 percent of female cancers (2) Hepatitis C and B, alcoholic and nonalcoholic cirrhosis, and hepatocellular carcinoma are all risk factors for hepatocellular carcinoma. Once it is discovered, which is usually at a late stage of the disease, the prognosis is bad [(2)]. Overall survival improves when a patient is diagnosed at an early stage and given a curative treatment plan [(3)].

For HCC surveillance, ultrasound (US) is a commonly utilized imaging technique since it is widely available and inexpensive, noninvasive, and doesn't involve radiation exposure [(4)] When it was first developed, this test had no established criteria for interpreting the results and making management decisions. The (US-LIRADS®) algorithm has been created by the ACR to address this issue [(5)]. A detection score and a visualization score are part of this algorithm. US-detection LIRADS's score is broken down into three areas to help managers make decisions.

US-1: Negative. (There was either no observation or benign observations). like, calcified granuloma, focal parenchymal sparing from steatosis, as well as a simple cyst. US-2: Sub-threshold. (Uncertainty about the benignity of observations smaller than 10 mm in diameter), Keeping an eye on them could be warranted in the short term by the US. US-3: Positive. (Multiphase contrast-enhanced imaging may be warranted if the diameter of the thrombus is more than or equal to 10 mm, or if the thrombus is a fresh thrombus), and the visualization score also has three categories and informs the expected sensitivity of the US examination [(5)].

Visualization A: Minimal or no restrictions. Sensitivity is unlikely to be affected by any limitations. Visualization B: With some limits. Small masses can be obscured by limitations. Visualization C: Sensitivity to focal liver lesions is greatly reduced as a result of severe restrictions. In patients at high risk of developing HCC, Improved communication with patients, referring physicians and improved patient-centered outcomes can be achieved by standardizing ultrasound reporting [(5)].

The present study aimed to assess the role of US-LIRADS in the detection of HCC in high-risk patients.

PATIENTS AND METHODS

This study was undertaken in the period between October 2020 to June 2021, at the Radiodiagnosis Department; Zagazig university hospitals as a comprehensive study, It included 50 cirrhotic patients of both sexes (27 males and 23 females) referred from the Tropical and Internal Medicine Departments due to chronic viral hepatitis (C&B) with a mean age of 58 years.

Ethical consent:

Approval of the study was obtained from Zagazig University Academic and Ethical Committee (ZU-IRB#6829). Every patient signed informed written consent for the acceptance of participation in the study. This work has been carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Radiologic diagnosis of liver cirrhosis of any etiology, and >18 years old.
Exclusion criteria: Creatinine level > or = 2.0 mg/dl.

All patients were subjected to:

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Full history: Name, age, sex, residence, medical history of chronic and metabolic diseases, date of examination and/or admission, contact information, and other habits of medical interest.

Clinical examination: Patients were assessed by the tropical and internal medicine physicians and then redirected to the radiology unit.

Imaging studies: All patients were subjected to a Conventional B-mode ultrasound examination of the liver in different positions and acoustic windows were used to maximize liver vision. Among the methods employed were the following: (a) The patient should be lying on their back with their arms at their sides, with their legs slightly bent; (to properly visualize the hepatic dome and posterior superior regions of the liver, deep suspended inspiration is required; (c) acoustic windows in the subcostal and intercostal regions; and (d) maintaining a sufficient amount of abdominal transducer pressure, and US category score (1,2 or 3), and the US visualization score (A, B or C).

The US-LI-RADS detection score has three categories and guides management:

US-1: Negative. (There was either no observation or benign observations), as calcified granuloma, focal parenchymal sparing from steatosis, as well as a simple cyst.

US-2: Sub-threshold. (Uncertainty about the benignity of observations smaller than 10 mm in diameter), Keeping an eye on them could be warranted in the short term by the US.

US-3: Positive. (Multiphase contrast-enhanced imaging may be warranted if the diameter of the thrombus is more than or equal to 10 mm, or if the thrombus is a fresh thrombus).

And the visualization score also has three categories and informs the expected sensitivity of the US examination. Visualization A: Minimal or no restrictions. Sensitivity is unlikely to be affected by any limitations. Visualization B: With some limits. Small masses can be obscured by limitations. Visualization C: Sensitivity to focal liver lesions is greatly reduced as a result of severe restrictions.

Triphasic CT imaging: These were the major criteria for diagnosing a patient with HCC by triphasic CT.

Arterial phase hyperenhancement: The arterial phase's improvement is unquestionably bigger than the background liver's.

Portal and delayed phase washout: visual comparison of the lesion's relative hypodensity compared to the background liver in the portal venous and delayed phases.

Statistical analysis

The collected data were coded, processed, and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi-square test ($\chi 2$) to calculate the difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare the two independent groups of normally distributed variables (parametric data). P-value < 0.05 was considered significant.

RESULTS

Among the studied cases there were 27 (54%) were males, 23 (46%) were females, 28 (56%) were <60 years old, 22 (44%) were >60 years old, the mean of age was 58.20 (± 7.04 SD) **(Table 1).**

Table (1): Demographic data (n = 50):

Demographic data	No.	%
Gender		
Male	27	54.0
Female	23	46.0
Age (years)		
<60	28	56.0
≥60	22	44.0
Min. – Max.	45.0 – 73.0	
Mean ± SD.	58.20 ± 7.04	
Median (IQR)	58.50 (53.0 – 63.0)	

According to US category, there were 37 (74%) were US-1, 2 (4%) were US-2, 11 (22%) were US-3 **(Table 2).**

Table (2): US category (n = 50):

US category	No.	%
US – 1	37	74.0
US – 2	2	4.0
US - 3	11	22.0

According to US visualization Score, 19 (38%) were A, 19 (38%) were B, 12 (24%) were C **(Table 3).**

Table (3): US visualization score (n = 50)

US visualization score	No.	%
A	19	38.0
B	19	38.0
C	12	24.0

According to the cause of cirrhosis, 15 (30%) were hepatitis B, 35 (70%) hepatitis C **(Table 4).**

Table (4): Cause of cirrhosis (n = 50):

Cause of cirrhosis	No.	%
Hepatitis B	15	30.0
Hepatitis C	35	70.0

Among the studied cases there were 2 (4%) had portal vein thrombosis, and 3 (6%) had ascites **(Table 5).**

Table (5): Portal vein thrombosis and ascites (n = 50):

	No.	%
Portal vein thrombosis	2	4.0
Ascites	3	6.0

There is a significant difference between the (A and B US visualization score) group and the (C US visualization score) group with regards to US category,

size and location of the lesion, and triphasic imaging findings **(Table 6).**

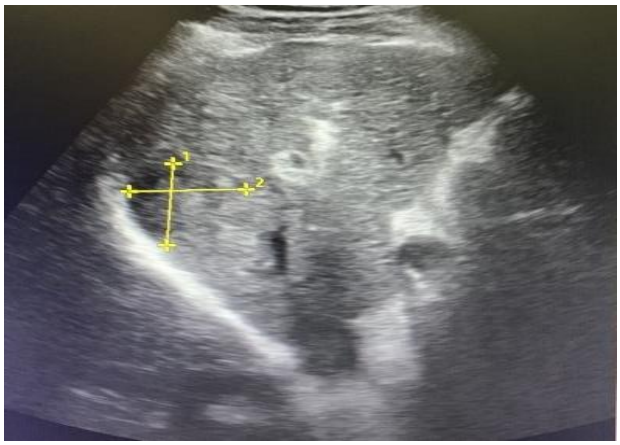
Table (6): Relation between US visualization score and different parameters :

	US visualization score				χ^2	P
	A and B (n = 38)		C (n = 12)			
	No.	%	No.	%		
Age (years)						
<60	24	63.2	4	33.3	3.292	0.070
≥60	14	36.8	8	66.7		
Gender						
Male	17	44.7	10	83.3	5.469*	0.019*
Female	21	55.3	2	16.7		
US category						
US – 1	31	81.6	6	50.0	6.393*	MCp=0.025*
US – 2	2	5.3	0	0.0		
US - 3	5	13.2	6	50.0		
US – 1	31	81.6	6	50.0	4.727	FEp = 0.055
US – 2 + 3	7	18.4	6	50.0		
Size of the lesion by ultrasound						
No lesion	31	81.6	6	50.0	8.779*	MCp=0.007*
Yes lesion	7	18.4	3	25.0		
Multiple Focal Lesions	0	0.0	3	25.0		
No lesion	31	81.6	6	50.0	4.727	FEp = 0.055
Lesions	7	18.4	6	50.0		
Location of the lesion						
NA	32	84.2	6	50.0	11.475*	MCp=0.030*
Segment II	2	5.3	1	8.3		
Segment III	0	0.0	2	16.7		
Segment IV	1	2.6	0	0.0		
Segment V	1	2.6	0	0.0		
Segment VI	1	2.6	2	16.7		
Segment VII	1	2.6	1	8.3		
NA	32	84.2	6	50.0	5.852*	FEp=0.025*
Segment	6	15.8	6	50.0		
Triphasic imaging findings						
No lesion	28	73.7	2	16.7	18.630*	MCp<0.001*
Yes lesion	10	26.3	7	58.3		
Multiple focal lesions	0	0.0	3	25.0		
No lesion	28	73.7	2	16.7	17.125*	FEp<0.001*
Lesions	10	26.3	10	83.3		
Cause of cirrhosis						
Hepatitis b	14	36.8	1	8.3	3.530	FEp=0.079
Hepatitis c	24	63.2	11	91.7		
Portal vein thrombosis	0	0.0	2	16.7	6.597	FEp=0.054
Ascites	2	5.3	1	8.3	0.152	FEp=1.000

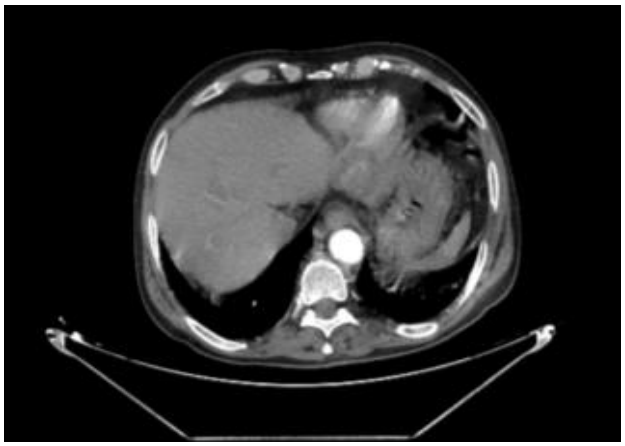
There is a significant association between visualization score C and (Gender, US category, size of lesion, location of lesion, and triphasic imaging findings). The results show that US category A is associated with the highest sensitivity while US category C is associated with the lowest sensitivity **(Table 7).**

Table (7): Univariate and multivariate binary logistic regression for the parameters affecting (C) (visualization score)

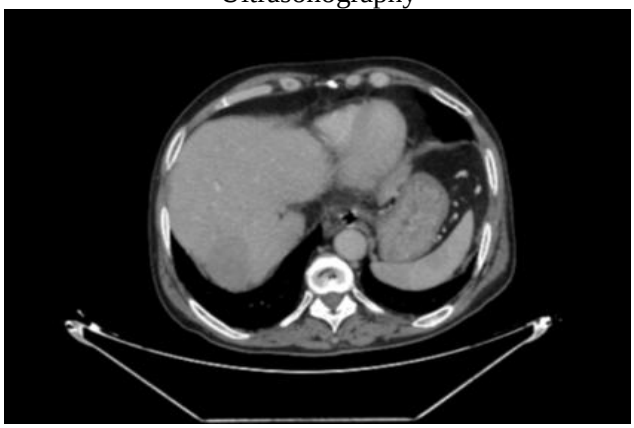
	Univariate		Multivariate	
	P	**B (95%C.I)**	**p**	**B (95%C.I)**
Age (years)	**0.078**	3.429 (0.872 – 13.48)		
Gender	**0.030***	0.162* (0.031 – 0.841)	**0.080**	–1.550 (0.037 – 1.201)
US category (US – 1(R) vs 2 + 3)	**0.037***	4.429* (1.095 – 17.915)	**0.329**	0.916 (0.398 – 15.681)
Size of the lesion by ultrasound (No(R) vs lesions)	**0.037***	4.429* (1.095 – 17.915)	**0.329**	0.916 (0.398 – 15.681)
Location of the lesion (no(R) vs segment)	**0.022***	5.333* (1.278 – 22.254)	**0.461**	2.022 (0.311 – 13.129)
Triphasic imaging findings (No(R) vs lesions)	**<0.001***	22.143* (3.943 – 124.34)	**–**	–
Cause of cirrhosis (Hepatitis b(R) vs c)	**0.090**	6.417 (0.747 – 55.120)		
Portal vein thrombosis	**0.999**	–		
Ascites	**0.699**	1.636 (0.135 – 19.808)		



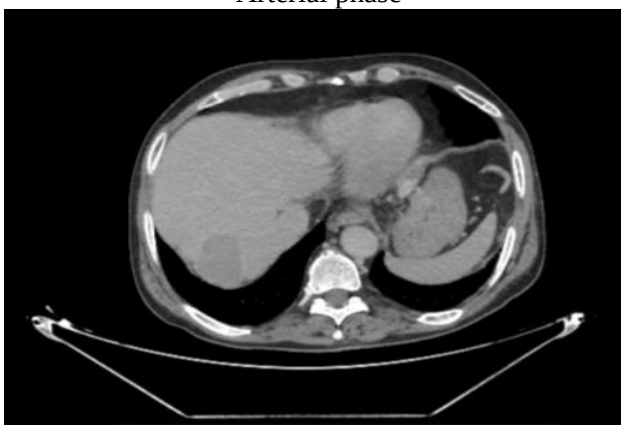
Ultrasonography



Arterial phase



Portal phase



Delayed phase

Figure (1): A male patient 70 years old with hepatitis C has average size, cirrhotic texture liver with prominent caudate lobe, there is well defined Rt. liver lobe focal mass lesion involving posterior subcapsular aspect of segment VII measuring about 41x35 mm shows a faint heterogeneous enhanced pattern in the arterial phase with rapid fade out in portal & delayed phases with an enhanced capsule. No intra-hepatic biliary dilatations. US-LI-RADS category: 3 US-3. US visualization score C

DISCUSSION

HCC is the most common kind of primary liver cancer in adults. The third greatest cause of cancer-related fatalities globally is hepatocellular carcinoma (HCC). As a result, early detection of HCC is critical for improving patient survival [3].

US LI-RADS® was created to standardize the reporting and data collection of ULTRASOUND imaging for hepatocellular carcinoma (HCC) [6].

According to age, the age range of the involved patients was from 45 to 73 years with a mean age of 58 which is in agreement with **Liu *et al.*** [7] who reported a median age of 52.

According to sex, there was a slight male predominance of 54% males vs 46% females which is in disagreement with **Ajayi *et al.*** [8] who reported a male predominance of up to 6 times that of females.

According to the cause of cirrhosis in our study, 70% of the patients had hepatitis c cirrhosis and 30% had hepatitis b cirrhosis which is in disagreement with **Hiotis *et al.*** [9] who reported 60% hepatitis b cirrhosis predominance in patients diagnosed with HCC versus 25% for hepatitis c predominance but in agreement with **Yang *et al.*** [10] who reported 84% prevalence of hepatitis C cirrhosis among patients diagnosed with HCC in Egypt.

For the detection of hepatocellular carcinoma, the LI-RADS US-3 category showed a high specificity (100%) but a low sensitivity (43.3%), as shown by our findings. The sensitivity of the US LI-RADS for the detection of HCC is frequently below average.

In earlier research, the sensitivity of the US for HCC diagnosis ranges from 20.5 to 94% [11, 12].

Our findings are in line with a meta-analysis that found a sensitivity of 47% for detecting early-stage HCC [12].

Of recent studies which utilized the US-LI-RADS, our results are similar to **Tillman *et al.*** [13] who found US sensitivity of about 47% but is in contrast with **Millet *et al.*** [5] in this study US LI-RADS was found to have a high sensitivity for detection of HCC (82.4%).

HCC was diagnosed incorrectly 60 percent of the time in one trial, which is greater than the 30 percent false-negative rate for A or B visual scores, according to the researchers CT scans found all of the false-negative results. It is therefore possible to stratify false-negative outcomes in US surveillance by using the US LI-RADS visualization score. Patients with a high failure risk could be identified and an alternative screening technique could be recommended to improve the ultrasound surveillance outcome [8].

There have recently been discussions on the possibility of using US in conjunction with alpha-fetoprotein or MRI to monitor patients. Recent research suggests that shorter MRI scans, which use fewer picture sequences and do not involve dynamic imaging, may have advantages over standard MRI scans since they are more sensitive (82.6–85.2%) and can be completed in as little as five minutes [13].

In our research, moderate to severe fatty liver was the most common risk factor for having a low vision score.

The limitations of this study are the low sample size and the small number of research papers that examined US-LI-RADS because it is a relatively new algorithm.

With regards to the frequency of surveillance, a randomized prospective trial at many centers found that trimestral surveillance in cirrhotic patients was no better than a typical 6-month program. We may therefore say that an ultrasound examination should be performed every six months without increasing or decreasing its frequency [14].

Triphasic CT recognized all of the false-negative results. It may be possible to use the US LI-RADS visualization score to stratify the danger of false-negative outcomes in US surveillance. Other surveillance methods, such as the use of alpha-fetoprotein in the United States, have recently been introduced. or MRI-based surveillance**,** could be considered[15, 16].

Recent research suggests that shorter MRI scans, which use fewer picture sequences and do not involve dynamic imaging, may have advantages over standard MRI scans since they are more sensitive (82.6–85.2%) and can be completed in as little as five minutes[15, 16].

CONCLUSION

The US Liver Imaging Reporting and Data System US-3 category showed a good specificity but a low sensitivity for the identification of hepatocellular carcinoma (HCC) in the surveillance of patients at high risk. There was a greater false-negative rate for HCC detection in patients with visualization scores C compared to those with visualization scores A or B.

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