International Journal of Radiology and Diagnostic Imaging

E-ISSN: 2664-4444
P-ISSN: 2664-4436
www.radiologypaper.com
IJRDI 2024; 7(2): 60-66
Received: 27-02-2024
Accepted: 02-04-2024

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Liver imaging reporting and data system (LI-RADs) of computed tomography in suspected hepatocellular carcinoma

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DOI: https://doi.org/10.33545/26644436.2024.v7.i2a.387

Abstract
Background: The results of imaging analysis of high-risk people are classified by the liver imaging reporting and data system (LI-RADS) according to the level of suspicion for hepatocellular carcinoma (HCC) and overall malignancy. This research aimed to evaluate the role of LI-RADS in creating a standardized reporting and data collection system for computed tomography (CT) scans of patients at risk of HCC.
Methods: This research was conducted on a sample of 40 adult patients, including both males and females, who presented with hepatic focal lesions thought to be HCC. These patients exhibited elevated alpha fetoprotein levels and had sonographically identified focal lesions that suggested malignancy. All patients had a triphasic CT scan of the liver with contrast.
Results: ROC curve for LI-RADS categorization according to the major imaging features give sensitivity, specificity, and accuracy of 100%, 84.6% and 93.5% respectively. The major imaging features of LI-RADS, the included focal lesions were categorized as follow: 9 (14.52%) focal lesions were LI-RADS 1, 5(8.06%) focal lesions were LI-RADS 2, 3(4.84%) focal lesions were LI-RADS 3, 3(4.84%) focal lesions were LI-RADS 4, 34(54.84%) focal lesions were LI-RADS 5 and 8(12.90%) focal lesions were LI-RADS M with significant difference. The two groups showed substantially different arterial phase hyper-enhancement, washout, and capsule appearance (p<0.05).
Conclusion: The primary characteristics of LI-RADS play a crucial role in the classification of hepatic focal lesions for the purpose of diagnosing HCC. The use of supplementary characteristics on CT altered the ultimate classification of a limited number of instances.

Keywords: LI-RADs, CT, HCC, arterial phase hyper-enhancement, washout appearance, capsule

Introduction
Globally, liver cancer is the second greatest cause of cancer-related death and the fifth most common kind of cancer. HCC is a major global health concern since it accounts for over 90% of all primary liver malignancies [1].
Chronic hepatitis B and C, alcohol addiction, metabolic liver disease (specifically, nonalcoholic fatty liver disease), and exposure to dietary toxins such aflatoxins and aristolochic acid are among the risk factors for HCC that have been discovered. Since each of these risk factors could be prevented, it is important to highlight how effective risk prevention may be in reducing the global burden of HCC [2].
Curative therapy modalities for HCC including surgical resection, liver transplantation, and ablation therapies such as radiofrequency and chemoembolization. These interventions have shown efficacy in the treatment of early-stage HCC. It is important to emphasize the significance of rapid diagnosis and early intervention in the management of HCC patients [3].
Non-invasive imaging tests are used to detect hepatocellular carinoma, and imaging-based staging is crucial for selecting the appropriate therapy. Therefore, imaging plays a vital role in the management of HCC [4].
Proposals for image-based diagnostic systems that standardize the acquisition, analysis, and reporting of liver imaging tests have been made by several scientific organizations. In the context of HCC, these technologies are meant to make surveillance, diagnosis, staging, therapy, and treatment response monitoring easier [5].
The designs of HCC imaging systems have shown variations across various geographic

regions in order to adapt to diverse target populations, resources, and treatment methodologies [6].

The primary aim of the Liver Imaging Reporting and Data System (LI-RADS) was to provide a standard methodology for the recording and collection of information related to CT and magnetic resonance (MR) imaging in patients at risk of HCC [7].

A multinational team of radiologists and other experts with specific training in liver cancer imaging developed the LI-RADS method. It was included by the American Association for the Study of Liver Diseases (AASLD) into their most recent clinical practice recommendations for HCC [8].

The AASLD adopted LI-RADS because of the growing evidence that LI-RADS categories effectively classify the probability of HCC and overall malignancy [9].

When analyzing imaging data from high-risk people, the LI-RADS system sorts the information according to the level of suspicion for HCC and the total malignancy. Based on the CT findings, the categories range from very benign (LR-1) to highly cancerous (LR-5), malignant (LR-M), or tumor in vain (LR-TIV). However, for each LI-RADS group, the exact percentage of HCC and total malignancy is yet uncertain. Finding out what percentage of CT scans in HCCs and other cancers fall into each LI-RADS group is the primary goal of this study [10].

The objective of this study was to assess the function of LI-RADs in establishing a uniform system for reporting and gathering CT data from patients who are at risk of HCC.

Patients and Methods

This research was conducted on a sample of 40 adult patients, including both males and females, who presented with hepatic focal lesions thought to be HCC. These patients exhibited elevated alpha fetoprotein levels and had sonographically identified focal lesions that suggested malignancy. The research was conducted between July 2021 and July 2022, after the authorization of the Ethical Committee of Tanta University Hospitals in Tanta, Egypt. The patients provided informed written consent.

Exclusion criteria were patients with previously treated HCC, patients with multiple hepatic focal lesions known to be metastatic or with known primary malignancy, hypersensitivity to contrast media, patients with renal impairment and pregnant females.

All patients were subjected to history taking, laboratory investigations and triphasic CT of liver with contrast.

Triphasic CT of liver with contrast

It was performed using 320 multidetector CT Scanner. Fasting for 4 to 6 hours before scan. The procedure was explained for the patients for reassurance. The weight of patients was measured to calculate the dose of contrast media. To guarantee the effective cannulation of the right antecubital vein, a cannula was inserted. To do this, a manual saline injection was administered at a high flow rate, while the patient's arms were in the scanning position. A preliminary assessment was conducted on the scouts from an antero-posterior perspective, focusing on the area from the bifurcation of the trachea to the symphysis pubis. This examination was performed in both before and after contrast series. For the pre-contrast series, a nominal section thickness of 10mm, a slice pitch of 1.5, a gantry rotation time of 0.6 second, and a table speed of 15 mm per rotation were used. The voltage applied to the X-ray tube was 120 kilovolts, while the current ranged from 240 to 280 milliamperes. The patients received injections of non-ionic contrast material ranging from 100 to 120 ml, with an infusion rate of 4-5 ml/sec, administered by a power injector. The liver underwent three separate periods of contrast enhancement: the Hepatic arterial phase, the portal venous phase, and the equilibrium phase. A volumetric acquisition was conducted using a collimation of 0.6 mm, a pitch value of 1.2, and a voltage range of 120kV and a current range of 160-440 mAs. A thickness of 1 mm and a reconstruction index of 0.8 were used to recreate the images.

Tumour diameter: Measuring the maximum dimension, from the outside edge to the outer edge, without considering any changes in the surrounding perfusion.

Arterial phase hyper-enhancement

It was stated when the entire or only portion of the observation enhances more than the liver. The optimal evaluation of hepatic arterial phase hyper-enhancement often occurs during the late arterial phase.

Washout appearance

It was only mentioned when there was a decrease in enhancement over time, moving from one phase to another.

Capsule: The presence of a smooth hyper-enhancement at the perimeter of an observation in the portal venous or delayed phase was indicative of a "capsule" lesion.

The tumor growth rate if possible

The required growth rate entails a minimum rise of 5 mm in the size of the lesion, followed by either a 50% or higher increase in size before or at the 6-month mark, or a 100% or higher increase in size after the 6-month period. Then a final LIRADS score was assigned in 1–5 range by following these steps: [Definitely and probably benign lesions were assigned LR-1 and LR-2 respectively and LR-3, LR-4 and LR- 5 categories were assigned according to LIRADS] as following: Each observation was characterized using the LIRADS Table, and the corresponding cell was selected based on the degree of arterial phase enhancement, diameter (<20 mm vs.≥20 mm if arterial phase hypo- or iso-enhancing and <10 mm vs. 10–19 mm vs. ≥20 mm if arterial phase hyper-enhancing) and the number of features such as "washout," "capsule," and threshold growth.

The assignments of LR-3, LR-4, and LR-5 were determined by selecting the relevant columns and rows in the LIRADS database. The selection of the column was based on the enhancement pattern, namely the arterial phase hypo-enhancement or iso-enhancement against hyper-enhancement, as well as the diameter characteristics. The row was chosen based on the quantity of prominent characteristics observed, including washout look, capsule, and threshold expansion. The suitable category was thereafter identified at the point where the specified column and row intersected. It is important to observe that each liver observation in the dataset was distinct. For example, if a patient had several observations, each lesion was given a different LIRADS score.

The diagnosis of the LR-3, LR-4 and LR-5 lesions was either established

Histologic results from biopsy or surgery, or in individuals without these procedures, were used to make a diagnosis of HCCs using an integrative-evaluation criteria (IEC). Chronic viral hepatitis and/or cirrhosis in the past, high blood a-fetoprotein levels (>11 ng/mL), and recurrent detection of HCC on computed tomography scans were also part of the criteria. Afterwards, these lesions were classified as HCC.

LR-1 and LR-2 lesions were diagnosed by

The non-HCC group consisted of patients who had cross-sectional imaging modality (Such as US and CT) follow-up, histopathology if available, and patients with pathologically proved benign lesion. This group also included patients without histological confirmation and who did not meet the IEC criteria for HCC.

Statistical analysis

The statistical study was conducted using SPSS v26, developed by IBM Inc. in Chicago, IL, USA. The quantitative data were presented using the mean and standard deviation (SD), and then compared between the two groups using an unpaired Student's t-test. The Chi-square test or Fisher's exact test was used to report and analyze the frequency and percentage (%) of qualitative variables, as considered appropriate. The diagnostic performance was evaluated using the Roc curve, which measured sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). A result was considered statistically significant if the two-tailed P value was less than 0.05.

Results

The mean of ages was 56.375±4.775 years. 25(62.5%) patients were males, and 15(37.5%) patients were females. Most of them were found at the age group from 50 to 60 years. Regarding to number of focal lesions, 40(64.52%) focal lesions were HCC, and 22 (35.48%) of them were non-HCC including 2 atypical hemangiomas, 2 simple cysts, 1 fatty sparing, 2 focal fatty infiltration, 3 typical hemangiomas, 8 metastasis, 3 calcified hydatid cyst, 1 siderotic nodule. Table 1.

Table 1: Age, sex and number of focal lesions distribution of the studied patients

		N=40
Age (years)		56.375±4.775
>40-50 Years		4(10.0%)
>50-60 Years		30(75.0%)
>60-70 Years		6(15.0%)
Sex	Male	25(62.50%)
	Female	15(37.50%)
		N=62
HCC		40(64.52%)
Non-HCC	Metastasis	8(36.36%)
	Hemangioma	3(13.64%)
	Calcified hydrated cyst	3(13.64%)
	Hemangioma (Atypical)	2(9.09%)
	Focal fatty infiltration	2(9.09%)
	Simple cyst	2(9.09%)
	Fatty sparing	1(4.55%)
	Siderotic nodule	1(4.55%)

No statistically significant distinction existed in the diameter of the lesions when comparing the two groups. Significant differences were observed between the two groups with regard to arterial phase hyper-enhancement, washout, and capsule morphology (p<0.05). Table 2.

Table 2: Comparison between HCC lesions and non-HCC lesions according to major LI-RADS imaging features

	HCC		P
	Yes	No	
Arterial Enhancement	37(92.5%)	6(27.27%)	<0.001*
Venous Washout	34(85%)	0(0.0%)	<0.001*
Capsule	25(62.5%)	0(0.0%)	<0.001*
Diameter (mm)	56.90± 35.897	54.909± 36.594	0.836

Regarding the ROC analysis that was conducted for the purpose of detecting the sensitivity, specificity, and accuracy of the major imaging features of LI-RADS, the following values were recorded: 92.5% for arterial enhancement, 72.73% for specificity, and 85.48% for accuracy; 85% for venous washout, 100% for accuracy, and 75.81% for capsule appearance; and 97.5% for lesion diameter, 13.64% for specificity, and 51.5% for accuracy. Table 3.

Table 3: ROC analysis of the diagnostic accuracy of major LI-RADS features

	Cutoff	Sens.	Spec.	PPV	NPV	Accuracy
Arterial enhancement	-	92.5%	72.73%	86.05%	84.21%	85.48%
Venous Washout	-	85%	100%	100%	78.57%	90.32%
Capsule	-	62.5%	100%	100%	59.46%	75.81%
Diameter (mm)	>21	97.50%	13.64%	67.2%	75%	51.5%

Based on the primary imaging characteristics of LI-RADS, the focal lesions that were included were classified into the following categories: Out of the total number of focal lesions, 9 (14.52%) were classified as LI-RADS 1, 5 (8.06%) as LI-RADS 2, 3 (4.84%) as LI-RADS 3, 3 (4.84%) as LI-RADS 4, 34 (54.84%) as LI-RADS 5, and 8 (12.90%) as LI-RADS M. These findings indicate a substantial variation in the distribution of focal lesions. Table 4.

Table 4: LI-RADS categorization of all included focal lesions according to the major imaging features

	HCC		P
	Yes	No	
LIRAD 1	0(0.0%)	9(40.91%)	<0.001*
LIRAD 2	0(0.0%)	5(22.73%)	
LIRAD 3	3(7.5%)	0(0.0%)	
LIRAD 4	3(7.5%)	0(0.0%)	
LIRAD 5	34(85%)	0(0.0%)	
LIRAD M	0(0.0%)	8(36.36%)	

The receiver operating characteristic (ROC) curve for LI-RADS classification based on the primary imaging characteristics yields a sensitivity of 100%, specificity of 84.6%, and accuracy of 93.5%. Table 5.

Table 5: Diagnostic accuracy of LI-RADS categorization according to major imaging features

Diagnostic accuracy of LI-RADS categorization				
Sens.	**Spec.**	**PPV**	**NPV**	**Accuracy**
100%	84.6%	90%	100%	93.5%

Ancillary features impact on LI-RADS categories: The classification of the examined lesions before to and after the implementation of supplementary characteristics was the same in 96.77% of the lesions (60 out of 62). Based on the criteria established by LI-RADS v2018, it was observed that ancillary features influenced the classification in 3.22% of the total lesions, which corresponds to 2 out of 62 lesions. One lesion was classified as LR-3 based on its primary characteristics and then elevated to LR-4 owing to the presence of intra-lesional fat, which is considered accessory. The second lesion was classified as LR-3 based on its primary characteristics and reclassified as LR-2 based on additional findings. It was found to be a hemangioma with enhancement that matched the blood pool. One of the lesions classified as LR-4 based on prominent imaging characteristics exhibited fat sparing in the solid mass. However, even after including ancillary data, the lesion continued to be classified as LR-4, as per the LI-RADS criterion, which states that an LR-4 lesion cannot be elevated to LR-5.

Case 1

A 59-year-old male patient with history of chronic viral hepatitis, presented with elevated liver enzymes. Hepatic focal lesion was detected by US. Using LIRAD system***:*** the lesion is categorized LR-5: HCC. Final diagnosis: This lesion was biopsied, and the histopathological results confirmed HCC (HCC group). Figure 1.

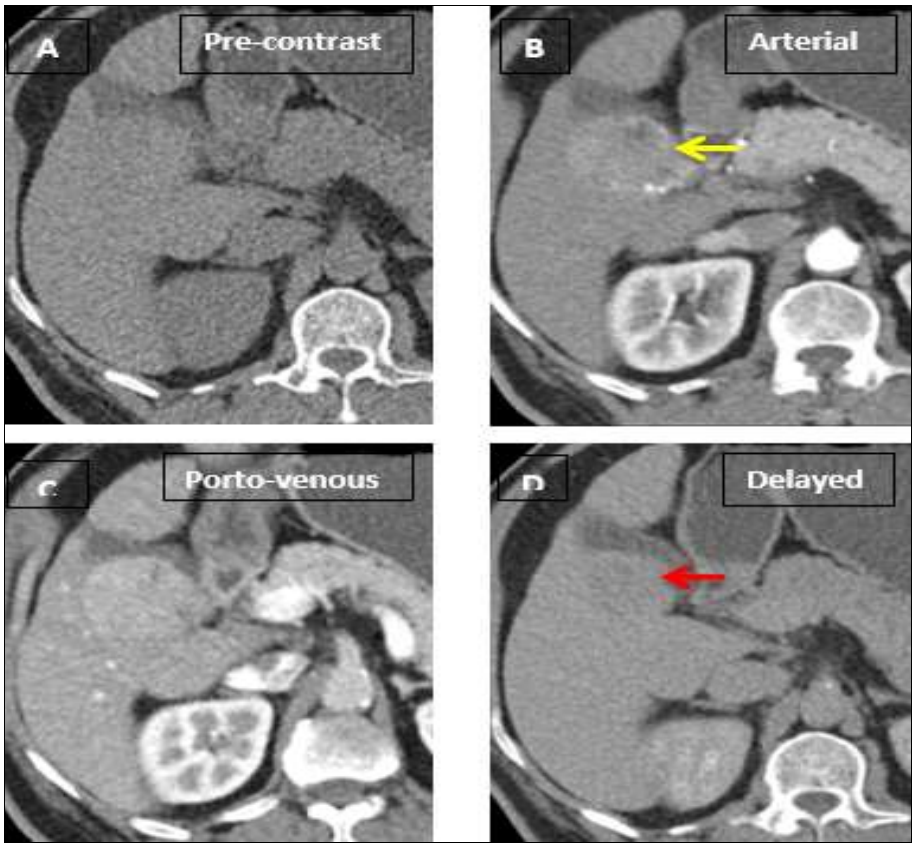

Fig 1: Axial CT images obtained before contrast administration (A) and after contrast administration at arterial phase (B), porto-venous phase (C) and delayed phase (D) revealed shrunken cirrhotic liver showing a 45-mm right hepatic lobe focal lesion at segment V showing hyper-enhancement at arterial phase (Yellow arrow) with enhancing capsule and washout at delayed phase (Red arrow)

Case 2

A 62-year-old male patient with history of liver cirrhosis presented with elevated AFP level. Using LIRAD system: the lesion is categorized LR-5: HCC. Final diagnosis: this case, diagnosis of HCC was based on IEC: History of cirrhosis, high levels of serum a-fetoprotein (>11ng/mL), consistent findings (concerning HCC) at CT images (HCC group). Figure 2.

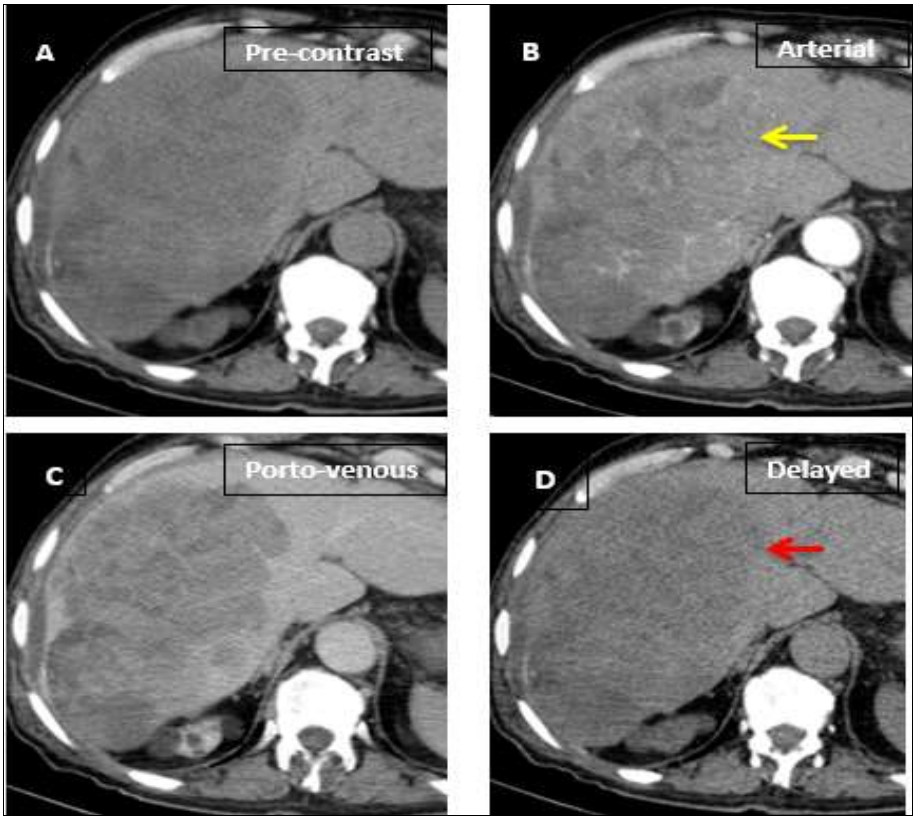

Fig 2: Axial CT images obtained before contrast administration (A) and after contrast administration at arterial phase (B), porto-venous phase (C) and delayed phase (D) revealed enlarged cirrhotic liver with a 136-mm right hepatic focal lesion showing enhancement at arterial phase (yellow arrow) with capsule and washout at delayed phase (Red arrow)

Case 3

A 62-year-old male patient with history of liver cirrhosis presented with elevated liver enzymes. Hepatic focal lesion was detected by US. Using LIRAD system: The CT findings are consistent with focal fatty infiltration. According to LIRADS, it is categorized as LR-1 (Definitely benign). So, no need for LIRADS table. Final diagnosis: Triphasic CT findings and correlation with US confirmed that the lesion is focal fatty infiltration. Figure 3.

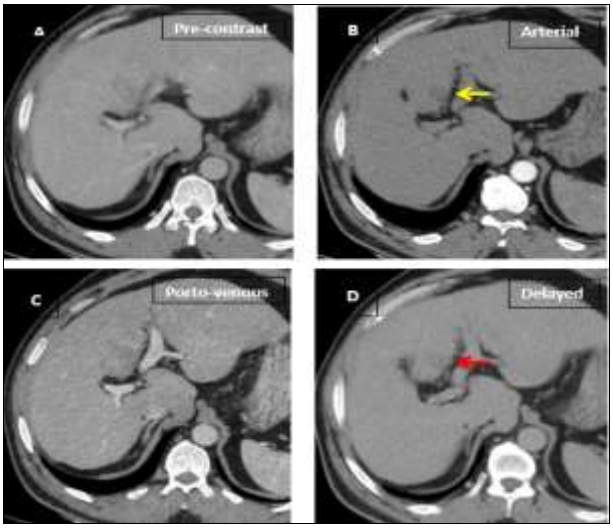

Fig 3: Axial CT images obtained before contrast administration (A) and after contrast administration at arterial phase (B), porto-venous phase (C) and delayed phase (D) revealed average sized cirrhotic liver showing ill-defined hypodense non enhancing area seen at the right hepatic lobe at segment IV (yellow arrow), with vascular branches seen traversing it

Discussion

The LI-RADS was designed to meet this need. LI-RADS offers a uniform vocabulary, rigorous diagnostic standards, a straightforward diagnostic algorithm, and reporting instructions to enhance the uniformity and precision of radiologist interpretation and reporting [11].

Twenty-nine patients in the current study had solitary hepatic focal lesions and 11 patients had multiple hepatic focal lesions. So, 40 patients were examined for assessment of 62 hepatic focal lesions. Regarding to the final outcome of the studied 40 patients depending on accepted standard reference, 40(64.52%) focal lesions were HCC, and 22(35.48%) of them were non-HCC including 2 atypical hemangiomas, 2 simple cysts, 1 fatty sparing, 2 focal fatty infiltrations, 3 typical hemangiomas, 8 metastases, 3 calcified hydatid cyst, 1 siderotic nodule.

The primary objective of the LI-RADS framework is to provide a uniform system for reporting and collecting imaging data on HCC [12].

Our findings compare the primary characteristics of LI-RADS between the HCC group and the non-HCC group. The primary elements of LI-RADS were used to evaluate each of the 62 lesions. In relation to the diameter of the lesions, the observed values varied between 8 and 150 mm. The mean diameter for HCC lesions was 56.9±35.897, while for non-HCC lesions it was 54.909±36.594. However, when comparing the two groups, no statistically significant difference was found. Similar findings were observed in the study by Park *et al*. [13]. Median sizes of 29.3 mm for HCC and 36.2 mm for non-HCC cancers were determined based on their study. But there was no discernible change between the two sets of data.

The key to accurately assessing HCC is to recognize the

enhancement pattern. Typically, the mass becomes more noticeable during the latter stage of arterial development (About 35 seconds) and then quickly disappears, becoming less distinct or weaker in the portal venous phase, in comparison to the rest of the liver [14]. Arterial phase hyper-enhancement was the most observed major criterion as seen in our study (69.35% of lesions) and was seen more frequently in HCC lesions than non-HCC lesions (92.5% vs 27.27%) with statistically significant difference between two groups. Washout appearance was the second most frequently seen major criterion, seen in our study (54.84% of lesions), and was seen only in HCC lesions with statistically significant difference between 2 groups. These results match with the results of Ludwig *et al*. [15] found that APHE were seen more frequently in HCC lesions (87%) than non-HCC lesions (26%). Also, washout was seen more in HCC lesions (72%) than non-HCC lesions (16%) so both APHE and washout show statistically significant difference between two groups.

Capsule appearance was seen only in 25/62 (40.32% of lesions) and was observed only in HCC lesions with statistically significant difference between two groups. These findings are similar to findings of Ludwig DR *et al*. [15] found that capsule was seen in 56% of HCC lesions and 21% of non-HCC lesions so there was significant difference between two groups.

According to the ROC analysis for detection of sensitivity, specificity and accuracy of major imaging features of LI-RADS, the arterial enhancement had sensitivity, specificity and accuracy of 92.5%, 72.73% and 85.48% respectively, the venous washout had sensitivity, specificity and accuracy of 85%, 100% and 90.32% respectively and capsule appearance had sensitivity, specificity and accuracy of 62%, 100% and 75.81% respectively, while the lesion diameter had sensitivity, specificity and accuracy of 97.5%, 13.64% and 51.5% respectively.

Cerny *et al*. [16] reported in their investigation found that the sensitivity of the key characteristics (arterial phase hyperenhancement, washout, and capsule) for HCC was 88.5%, 60.6%, and 32.9%, respectively. The specificity of these features was 18.6%, 84.8%, and 98.8%.

The ROC curve for LI-RADS classification based on the primary imaging characteristics yielded a sensitivity of 100%, specificity of 84.6%, and accuracy of 93.5%.

The LI-RADS categories 4 and 5 had sensitivity, specificity, and positive and negative predictive values of 93.8%, 88.2%, 92.3%, and 90.5%, respectively. The present results correlate with the research conducted by Liu *et al*. [17], whereby they observed that among a cohort of 249 patients, 191 were identified as malignant nodules, whereas 106 were classified as benign nodules. There were no high-grade carcinomas among the 44 LI-RADS category 1 lesions. Among the LR-2 lesions, 2/25 were HL-2 lesions, 3/35 were LR-3 lesions, 16/25 were LR-4 lesions, 151/156 were LR-5 lesions, and 3/12 were LR-M lesions. The Kappa coefficient was determined to be 0.44 (95% CI = 0.39–0.49) when comparing the performance of two observers in LI-RADS grading. This indicates that the LI-RADS classification method achieved a sensitivity of 100% in detecting HCC and an accuracy over 90%.

In relation to our findings, the influence of ancillary variables on LI-RADS categories is evident. The classification of the examined lesions before to and after the implementation of supplementary characteristics was the same in 96.77% of the lesions (60 out of 62). Based on the criteria established by LI-RADS v2018, it was observed that ancillary factors influenced the classification in 3.22% of the total lesions, which corresponds to 2 out of 62 lesions. One lesion was classified as LR-3 based on its primary characteristics and then elevated to LR-4 owing to the presence of intra-lesional fat, which is considered accessory. The second lesion was classified as LR-3 based on its primary characteristics and reclassified as LR-2 based on additional findings. It was found to be a hemangioma with enhancement that matched the blood pool. One of the lesions classified as LR-4 based on prominent imaging characteristics exhibited fat sparing in the solid mass. However, even after including ancillary data, the lesion continued to be classified as LR-4, as per the LI-RADS criterion, which states that an LR-4 lesion cannot be elevated to LR-5. According to the findings of Cerny *et al*. (2016), the incorporation of ancillary variables with primary features enhances the sensitivity of HCC diagnosis while maintaining a high level of specificity.

One of the limitations of this research was the very small sample size. The research was conducted at a singular facility. Furthermore, it is essential to extend the findings to other locations to validate their repeatability. In all situations, the ultimate diagnosis of HCC is not only reliant on histological diagnosis, but rather on a composite standard-reference.

Conclusion

The primary characteristics of LI-RADS play a crucial role in the classification of hepatic focal lesions for the purpose of diagnosing HCC. The use of supplementary characteristics on CT altered the ultimate classification of a limited number of instances.

Financial support and sponsorship: Nil.

Conflict of Interest: Nil.

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How to Cite This Article
Eldin FMK, El-Samea Al Arabawy RA, Elsawy AA, Nagy HA. Liver imaging reporting and data system (LI-RADs) of computed tomography in suspected hepatocellular carcinoma. International Journal of Radiology and Diagnostic Imaging. 2024;7(2):60-66.