Original Research Paper

Volume - 11 | Issue - 01 | January - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Radiology

AGREEMENT BETWEEN CRITERIA FREE PSYCHOMETRIC SCALE (LIKERT) AND LIVER IMAGING REPORTING AND DATA SYSTEM (LI-RADS) IN DIAGNOSING HCC IN PATIENTS WITH CHRONIC LIVER DISEASE.

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ABSTRACT **Aim:** LI-RADS was introduced to improve the accuracy and consistency of liver lesion reporting while imaging a cirrhotic patient. The aim of our study is to determine the agreement between conventional criteria free LIKERT scale and LI-RADS criteria in diagnosing HCC and also to study the interobserver agreement between three radiologists in diagnosing HCC using LIKERT and LI-RADS criteria.

Methods: Data set consists of CECT observations of liver cirrhosis patients who underwent triple phase CT in HCC protocol from the department of Radiodiagnosis of Amrita Institute of Medical Sciences, Kochi during the period 2015 to 2020. Interpretation of data sets were done by 3 radiologists trained in abdominal imaging with a minimum 4 -week gap between LIKERT and LI-RADS scoring. The agreement between LIKERT and LI-RADS for categorizing liver nodules by the senior radiologist is studied by using Cohens Kappa. Interobserver agreement between 3 radiologists for LI-RADS and for LIKERT is also studied separately using Fleiss Kappa statistics.

Results: There is moderate agreement between LIKERT and LI-RADS [κ- 0.6 (0.516-0.751)] for characterizing liver lesions in CLD patients. The Fleiss Kappa coefficient shows almost perfect interreader agreement between three observers in characterizing liver lesions into HCC and non -HCC using LIKERT approach [κ- 0.81 (0.807-0.813)] and using LIRADS criteria [κ- 0.93 (0.921-0.927)] with more interreader agreement while reporting using LI-RADS criteria, especially in characterizing liver observations less than 3 cm .

Conclusion: Characterizing liver observations in CLD patients using LIKERT and LI-RADS approaches had significant uniformity and consistency in characterizing liver observations. However, LI-RADS showed a higher interreader agreement compared to non-standardized reporting especially for nodules less than 3 cm.

KEYWORDS : Cirrhosis, Hepatocellular carcinoma, Computed Tomography

INTRODUCTION

Hepatocellular carcinoma is the most common primary malignant hepatic tumor and the fifth most common tumor affecting the humans (1). Mostly HCC develops in patients having an underlying hepatic cirrhosis or chronic viral hepatitis. Various imaging modalities like ultrasound (US), contrast enhanced CT (CECT), and contrast enhanced multiparametric MRI are useful in diagnosis, surveillance, prognosis and also in the treatment of HCC. Triple phase CT in HCC protocol is used for improved lesion detection and lesion characterization (2). In patients with hepatic cirrhosis, lesions showing classic imaging features like arterial phase hyperenhancement, portal or delayed phase washout and presence of enhancing capsule on cross-sectional imaging confirms the diagnosis of HCC (3,4). Imaging-based diagnosis of HCC is widely accepted as a surrogate for histopathological confirmation in CLD patients. Still there were many controversies regarding incorporation of all imaging findings into a single algorithm for improving the diagnostic accuracy (5). Several studies have pointed out the constraints of a subjective criteria-free reporting approach (6,7). Depending up on the radiologist's knowledge, experience, and institutional protocols, significant differences were observed in liver lesion interpretation (3,5). Tissue confirmation is often waived due to the risk of tumor seeding and pivotal management decisions are made on the imaging-based diagnosis of HCC. Hence there is a strong necessity to provide reliable and accurate reports. A structured reporting system called Liver Imaging Reporting and Data System (LI-RADS) was introduced by the ACR for categorizing each observation to one of the five categories (LR 1–5) (8). The aim of LI-RADS is to improve the accuracy and consistency of liver lesion interpretation and reporting while imaging a cirrhotic patient who is at risk of developing HCC. Clarity regarding the concordance between conventional criteria-free reporting models and LI-RADS criteria is yet to be made. It still remains ambiguous whether this standardized reporting system is superior to the conventional reporting approach in terms of diagnostic accuracy. Therefore, the goal of our study is to determine the agreement between the criteria free approach (LIKERT) and standardized reporting (LI-RADS) in a cohort of CLD patients with liver lesions (3,5).

MATERIALS AND METHODS:

Institutional Review Board approval was taken for this prospective study. Informed consent was taken from all the patients before CT scan. Data set consists of CECT observations of CLD patients with liver lesions who underwent triple phase CT in HCC protocol from the department of Radiodiagnosis of Amrita Institute of Medical Sciences and research centre, Kochi during the period 2015 to 2020. We included 143 observations in this study.

Study population includes CLD patients with liver nodules of size more than 1 cm and less than 5cm. Patients with infiltrative HCC, treated nodules and technically inadequate scan were excluded. Imaging was performed using 256 slice MDCT (Brilliance-iCT;Philips Healthcare, Cleveland, OH) after intravenous injection of non-ionic iodinated contrast agent, Iohexol (Omnipaque™ 350, GE Healthcare, Princeton, NJ). A 1.5mL/kg body weight of the contrast was administered to the patients. The contrast was injected using power injector (OptiVantage, Guerbet, OH). Bolus triggering was used to obtain the contrast enhanced phases. The region of interest was placed over descending thoracic aorta, 2cm proximal to the diaphragm

and scanning was initiated after the threshold of 100 HU was reached. Arterial phase images were acquired at 25 seconds, portal phase images were acquired at 70 seconds and delayed hepatic venous phase images were acquired at 120 seconds after the injection. The data was reconstructed, analysed, and interpreted in Philips workstations (Intellspace portal, Cleveland, OH). The data set was initially screened by a senior radiologist of 20 years' experience applying the inclusion and exclusion criteria. Interpretation of data sets were done by 3 radiologists trained in abdominal imaging with a minimum 4-week gap between LIKERT and LI-RADS scoring to avoid the issue of recall bias. Initially the radiologists categorized all observations into HCC and non-HCC based on conventional criteria free approach (LIKERT), assigning a psychometric score (LK 1 to 5). After four weeks, the same data set was analysed using LI-RADS criteria. For statistical evaluation, we consider LK1, LK 2, LK3 and LR1, LR2 and LR3 as non-HCC and LK4, LK5 and LR4, LR5 as HCC. The agreement between LIKERT and LI-RADS for characterizing liver lesions by the senior radiologist was studied by using Cohens Kappa. Interobserver agreement between 3 radiologists for LI-RADS and LIKERT was also studied separately using Fleiss Kappa statistics.

Statistical analysis was done using IBM SPSS version 20.0 Windows (IBM SPSS, USA). For all the continuous variables, the results are given as mean +/- SD. All the categorical variables are expressed using frequency and percentage. To test the statistical significance of the agreement of results between LIKERT and LI-RADS, McNemar's Chi Square test was applied. If the p-value is found to be less than 0.05 the disagreement between the two methods was found to be a statistically significant difference. To assess the agreement between LIKERT and LI-RADS, Cohen's kappa analysis was performed. To assess the agreement of LIKERT and LI-RADS between 3 observers, Fleiss kappa analysis was performed.

RESULTS:

The mean age of the study population is 65.96 ± 9.3 years (range, 37-83 years). Out of 113 CLD patients, 95 (84.1 %) were males and 18 (15.9%) were females. There is moderate agreement between LIKERT and LI-RADS [κ- 0.6 (0.516-0.751)] for characterizing liver lesions into HCC and non-HCC by senior radiologist. The Fleiss Kappa coefficient shows almost perfect interreader agreement between three observers in characterizing liver lesions into HCC and non -HCC using LIKERT approach [κ- 0.81 (0.807-0.813)] and LIRADS criteria [κ- 0.93 (0.921-0.927)] with more interreader agreement while reporting using LI-RADS criteria (Table 1). The interreader agreement in characterizing liver observations less than 3 cm into HCC and non -HCC is also more while using LI-RADS criteria [κ- 0.941 (0.937-0.944)] than LIKERT [κ- 0.790 (0.787-0.794)] approach (Table 2). The Fleiss Kappa coefficient showing the interreader agreement between three observers in interpreting APHE is 0.662 (0.659-0.665), non-peripheral washout is 0.933 (0.930-0.936) and enhancing capsule is 0.384 (0.381-0.387), with maximum interreader agreement in interpreting non-peripheral washout(Table 3).

Table 1 - Comparison of interreader agreement between three observers in categorizing observations in CLD patients using LIKERT and LI-RADS criteria.

Variable	Kappa value	Confidence interval
LIKERT	0.81	0.807-0.813
LI-RADS	0.93	0.921-0.927

Table 2-Comparison of interreader agreement between three observers in categorizing observations less than 3 cm into HCC and non-HCC using LIKERT and LI-RADS criteria.

Variable	Kappa value	Confidence interval
LIKERT	0.790	0.787-0.794
LI-RADS	0.941	0.937-0.944

Table 3 -Comparison of interreader agreement between three observers in interpreting APHE, non-peripheral washout and enhancing capsule.

Variable	Kappa value	Confidence interval
APHE	0.662	0.659-0.665
Non-Peripheral Washout	0.933	0.930-0.936
Enhancing capsule	0.384	0.381-0.387

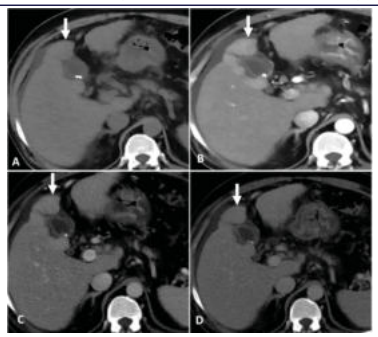

Figure 1. A 63 year-old male patient with cirrhosis having liver nodules. A- Axial plain CT showing cirrhotic liver with multiple isodense lesions in segment V adjacent to GB fossa (arrow). These lesions show arterial phase hyperenhancement (B, arrow) without any additional feature like portal or delayed phase washout (C, D arrows), capsule or threshold growth. These lesions will be characterized as dysplastic nodules while reporting using conventional criteria free approach. However, these lesions falls directly under probable HCC (LI-RADS 4) category as this arterial phase hyperenhancing lesion measures more than 20 mm (largest lesion size -23 mm).

DISCUSSION:

All patients with cirrhosis are at increased risk of developing HCC. Conventionally, HCC is diagnosed based on classic imaging features like APHE (arterial hyperenhancement), portal / delayed phase washout and presence of an enhancing capsule. However, significant differences in liver lesion interpretation was reported based on several factors like radiologist's knowledge, experience, personal preferences, and fixed hospital protocols (3). Hence, a structured reporting system (Liver Imaging Reporting and Data System or LI-RADS) was introduced by the ACR. In our study, the Cohens kappa value shows moderate intraclass agreement (κ -0.6) between LIKERT scale and LI-RADS in diagnosis of HCC by a senior radiologist of more than 20 years' experience. The study conducted by Zhang et al. also showed moderate intraclass agreement (κ-0.44) between LIKERTS and LI-RADS approach for stratifying 281 hepatic lesions (3).

In our study, the Fleiss Kappa coefficient showing the interreader agreement between three observers in diagnosing HCC using criteria free conventional LIKERT scale was 0.81 and using LI-RADS criteria was 0.924, both suggestive of almost perfect agreement between three observers. In a similar study by Barth et al., LIKERT and LI-RADS approach showed similar interreader agreement (κ value of 0.3 and 0.4 respectively) with higher interreader agreement for LI-RADS (14). Our study results also demonstrated similar overall interreader agreement in reporting liver observations using both approaches. There is a tendency towards increased interreader agreement when a systematic and highly standardized reporting scheme (LI-RADS criteria) is used when compared to a reporting approach based on observers' subjective impression. (3). Although the interreader agreement between LIKERT scale and LI-RADS criteria are almost similar in both the studies, interreader agreement for both LIKERTS and LI-RADS is more in our study. For observations less than 3 cm, there is substantial agreement (κ-0.79) between three observers in diagnosing HCC using LIKERT scale. Similarly, while using LI-RADS criteria for diagnosing HCC in liver observations having size less than 3 cm, there is almost perfect agreement (κ-0.94) between three observers. This implies that the structured reporting and data collection methodology used in LI-RADS helps the readers in stratification of small lesions into HCC and non-HCC more accurately, thereby increasing the interreader agreement when compared to LIKERT. Our results are contrary to the study by Barth et al. which showed only fair agreement between observers while using LIKERT and LI-RADS for smaller lesions (κ value - 0.31 and κ value - 0.37 respectively) (14). One reason for higher interreader agreement obtained in our study is lesser number of observers in our study (n=3) compared to the other study (n=10). In our study, the Fleiss Kappa coefficient shows substantial agreement (κ value- 0.662) between three observers in interpreting APHE. This is almost in concordance to study by Zhang et al. showing moderate agreement (κ value- 0.56) between observers in interpreting APHE (3). There is almost perfect agreement interreader agreement (κ value- 0.933) between three observers in interpreting non-peripheral washout .This is in contrast to the study by Zhang et al. which showed only substantial agreement

between observers (κ value- 0.63) (3). Interreader agreement between observers in interpreting washout is more in our study compared to other similar studies. There interreader agreement between three observers in interpreting presence of enhancing capsule is 0.384, suggestive of fair agreement between three observers. Study by Barth et al. also showed fair interreader agreement (κ value- 0.37) between observers for capsule appearance (147). However, study by Zhang et al. shows moderate agreement between observers (κ value- 0.58) in interpreting capsule appearance (3). In the study conducted by Davenport et al. comparing LI-RADS and OPTN criteria, moderate to substantial interreader agreement (κ, 0.59 – 0.69) was obtained for imaging features like "washout, enhancing capsule, and threshold growth" (5).

Some amount of innate subjectiveness cannot be eliminated while interpreting certain radiological findings. This may have led to inconsistency in interpreting 'enhancing capsule'. Similarly, limited interreader agreement was reported when BI-RADS was introduced (15). Moderate interreader agreement was reported by Berg et al. and Kerlikowske et al. for categorization of mammograms using BI-RADS (16,17). Berg et al. later showed that dedicated training in using BI-RADS have resulted in better agreement between the observers (18).

Our study demonstrates that there is moderate agreement between LIKERT and LI-RADS criteria in characterizing lesions in CLD patients. The interobserver agreement is more with LI-RADS criteria than with LIKERTS approach, which suggests that systematic and structured reporting helps in attaining more uniformity in interpretation of observations and hence the reporting.

CONCLUSION

We demonstrate that there is moderate agreement in liver observation reporting by conventional criteria free LIKERT and LI-RADS scoring system. Although both approaches had almost uniform consistency in determination of HCC and non-HCC lesions, LI-RADS showed a higher interreader agreement compared to non-standardized reporting especially for nodules less than 3 cm. LI-RADS holds the potential to become a widely established diagnostic algorithm for systematic and standardized reporting of liver observations in CLD patients.

Abbreviations:

ACR: American College of Radiology.
APHE: Arterial phase hyperenhancement.
BI-RADS: Breast Imaging Reporting and Data System.
CECT: Contrast-enhanced computed tomography.
CLD: Chronic Liver Disease.
HCC: Hepatocellular carcinoma.
LI-RADS: Liver Imaging Reporting and Data System.
LK: LIKERT.
LR: LI -RADS.
MDCT: Multidetector computed tomography.
MRI: Magnetic Resonance Imaging.
OPTN: Organ procurement and transplantation network.
US: Ultrasound.

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