Evidence Supporting Diagnostic Value of Liver Imaging Reporting and Data System for CT- and MR Imaging-based Diagnosis of Hepatocellular Carcinoma: A Systematic Review and Meta-analysis

Hayder Suhail Najm Alareer (PhD)[1], Arvin Arian (MD)[2]*, Maryam Fotouhi (MD)[3], Hayder Jasim Taher (PhD)[4], Ayoob Dinar Abdullah (PhD)[5]

[1]Department of Radiology, College of Health and Medical Technology, Al-Ayen University, Thi-Qar, 64001, Iraq
[2]Cancer Institute ADIR, Tehran University of Medical Sciences (TUMS), Tehran, Iran
[3]Quantitative MR Imaging and Spectroscopy Group (QMISG), Research Centre for Molecular and Cellular Imaging (RCMCI), Advanced Medical Technologies and Equipment Institute (AMTEI), Tehran University of Medical Sciences (TUMS), Tehran, Iran
[4]Department of Radiology, Hilla University College, Babylon, Iraq
[5]Department of Radiology Technology, Al-Manara College for Medical Sciences, Missan, Iraq

ABSTRACT

Background: Based on the Liver Imaging Data and Reporting System (LI-RADS) guidelines, Hepatocellular Carcinoma (HCC) can be diagnosed using imaging criteria in patients at risk of HCC.

Objective: This study aimed to assess the diagnostic value of LI-RADS in high-risk patients with HCC.

Material and Methods: This systematic review is conducted on international databases, including Google Scholar, Web of Science, PubMed, Embase, PROQUEST, and Cochrane Library, with appropriate keywords. Using the binomial distribution formula, the variance of each study was calculated, and all the data were analyzed using STATA version 16. The pooled sensitivity and specificity were determined using a random-effects meta-analysis approach. Also, we used the chi-squared test and I^2 index to calculate heterogeneity among studies, and Funnel plots and Egger tests were used for evaluating publication bias.

Results: The pooled sensitivity was estimated at 0.80 (95% CI: 0.76-0.84). According to different types of Liver Imaging Reporting and Data Systems (LI-RADS), the highest pooled sensitivity was in version 2018 (0.83 (95% CI: 0.79-0.87) (I^2: 80.6%, *P* of chi 2 test for heterogeneity: <0.001 and T^2: 0.001). The pooled specificity was estimated as 0.89 (95% CI: 0.87-0.92). According to different types of LI-RADS, the highest pooled specificity was in version 2014 (93.0 (95% CI: 89.0-96.0) (I^2: 81.7%, *P* of chi 2 test for heterogeneity: <0.001 and T^2: 0.001).

Conclusion: LI-RADS can assist radiologists in achieving the required sensitivity and specificity in high-risk patients suspected to have HCC. Therefore, this strategy can serve as an appropriate tool for identifying HCC.

Citation: Suhail Najm Alareer H, Arian A, Fotouhi M, Taher HJ, Dinar Abdullah A. Evidence Supporting Diagnostic Value of Liver Imaging Reporting and Data Sys-tem for CT- and MR Imaging-based Diagnosis of Hepatocellular Carcinoma: A Systematic Review and Meta-analysis. *J Biomed Phys Eng*. 2024;14(1):5-20. doi: 10.31661/jbpe.v0i0.2211-1562.

Keywords

Carcinoma; Hepatocellular; Magnetic Resonance Imaging; CT; LI-RADS

*Corresponding author:
Arvin Arian
Cancer Institute ADIR, Tehran University of Medical Sciences (TUMS), Tehran, Iran
E-mail:
fjmk7789@gmail.com

Received: 8 November 2022
Accepted: 12 March 2023

Introduction

Hepatocellular carcinoma (HCC) or hepatoma is a common type of cancer starting in the liver [1], and is also recognized as the fourth greatest cause of cancer-related fatalities and the sixth most prevalent cancer [2]. The sex incidence ratio of this cancer is 2 to 1,

i.e., males to females [3]. The most significant risk factor for this cancer type, particularly in Western countries, is cirrhosis, a late-stage liver disease. Notwithstanding various etiologies for cirrhosis, chronic hepatitis C, excessive alcohol consumption, and nonalcoholic steatohepatitis are the most frequent reasons for this disease across the globe. Infection with the hepatitis B virus (HBV) is the main cause of HCC and liver cirrhosis worldwide, and due to direct carcinogenic effects, this virus may predispose individuals to develop HCC before cirrhosis [4]. The five-year survival rate for HCC may reach more than 50% if detected at an initial stage and treated with surgery, percutaneous radiofrequency ablation, or orthotopic liver transplantation [5-7].

Imaging, particularly multiphase contrast-enhanced Computerized Tomography (CT) scan and Magnetic Resonance Imaging (MRI), is crucial for the diagnosis of HCC [8]. The Liver Imaging Reporting and Data System (LI-RADS) assigns a five-point scale, ranging from LR-1 (definitely benign) to LR-5 (definitely HCC), to a lesion based on its probability of HCC. LI-RADS classification includes both major and auxiliary features. Major features, including arterial hyperenhancement and capsule appearance, are used to classify hepatic lesions. Using auxiliary features, the classification of a lesion is upgraded (not beyond LR-4) or downgraded. The LI-RADS offers a diagnostic algorithm, an illustrated atlas, and a standard terminology to standardize the imaging diagnosis of HCC [9]. However, LI-RADS does not have the potential for the characterization of HCC from other hepatic cancers. Evaluating the diagnostic value of LI-RADS in high-risk patients suspected to have HCC was the goal of the present investigation.

Material and Methods

Search strategy

In this systematic review, three radiologists independently conducted a meta-analysis search based on Google Scholar, Web of Science, PubMed, Embase, PROQUEST, and Cochrane Library databases to find articles published before February 2021. The following keywords and their combinations, abbreviations, and Mesh-terms were used for the systematic search: “hepatocellular carcinoma (HCC)” OR “Hepatic Cirrhotic masses”, AND “Liver Reporting and Data System”, OR “LI-RADS versions 2014, 2016, 2017, and 2018”, AND “magnetic resonance imaging (MRI)”, AND LI-RADS MRI Sequence”.

Study selection

The following criteria were considered to include studies for this review: (1) English original articles and (2) articles with a minimum sample size of 20 patients and sufficient data for the calculation of false negative and positive, as well as true negative and positive values. Exclusion criteria for this study were: (1) case reports and series, review articles, or meta-analysis, (2) original articles written in other languages than English, (3) articles that did not evaluate sensitivity and specificity, (4) articles with insufficient data for building rows and columns 2×2 contingency, (5) studies with population overlap, and (6) studies discussed cancers other than HCC, e.g., metastatic cancer, epidermoid carcinoma, and cholangiocarcinoma.

Screening and extracting data

The identified articles were independently evaluated by two reviewers considering the inclusion and exclusion criteria. Figure 1 shows the process of selecting articles. The articles were screened out based on the title and abstract and then the full text, respectively. Finally, the extraction of data from studies was conducted by two independent reviewers. The information extracted from studies were first author name, authors’ country, year of publication, study design, gender, age, sample size, pathological complete response, specificity, sensitivity, and accuracy, as well as

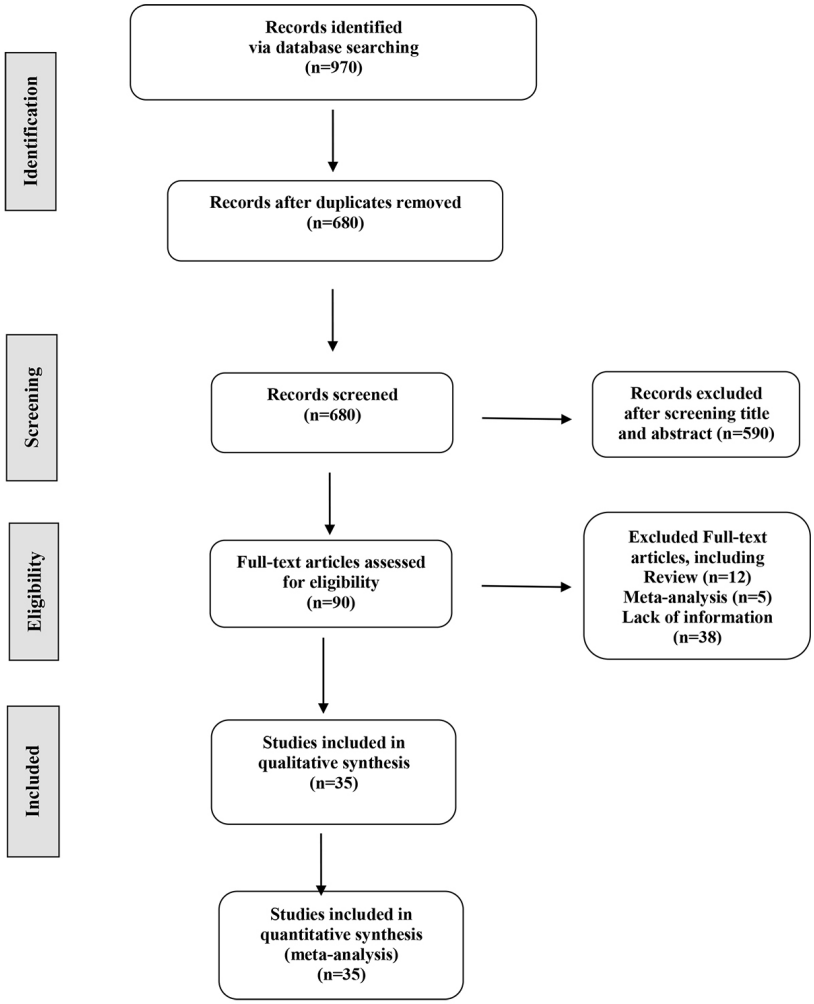


Figure 1: PRISMA flow diagram illustrating process of selecting articles

negative and positive predictive values. In case of any disagreement between two reviewers regarding the extracted data, a third reviewer assessed all discrepant cases.

Quality assessment for risk of bias

The quality of included studies was assessed by an author using QUADAS criteria, a tool used in systematic reviews for evaluating the risk of bias and assessing the quality of studies of diagnostic accuracy. This tool consists of four key domains, comprising (1) patient selection, (2) index test(s), (3) reference standard, and (4) patient flow and timing of tests [10].

Risk of bias across studies

To estimate the potential publication bias, we used Begg's and Egger's tests.

Statistical analysis

The effect size and the 95% CI were calculated using Stata version 17 (StataCorp, College Station, TX, USA). Also, the publication bias was assessed using Begg's test. The heterogeneity of each group was measured using the inconsistency index (I^2), and an I^2 greater than 50%, or a *P*-value lower than 0.05 is recognized as significant heterogeneity. If the heterogeneity was high, a random-effect model was used to calculate the pooling effect and 95% CI. Otherwise, the fixed effect

was used. The diagnostic value of LI-RADS in high-risk patients with HCC was determined by calculating pooled specificity, sensitivity, and accuracy with 95% confidence intervals (CI).

Results

After searching the above-mentioned databases, 35 relevant publications were found using PubMed/Medline and Science Direct databases during 2014-2019. The characteristics of included studies and their sensitivity and specificity estimation are represented in Tables 1 and 2. These investigations (LI-RADS 2014, LI-ADS 2017, and LI-RADS 2018 types of research) were divided into three groups, and seven methodological variables were taken from each group (Tables 1 and 2).

Estimation of pooled specificity

Based on the random-effects model, the pooled specificity was predicted to be 0.89 (95% CI: 0.87-0.92), indicating that this test could detect 0.89 real negative instances. There was substantial variability across studies in terms of pooled specificity (I^2: 90.7%; *P*-value<0.001 for heterogeneity; T^2: 0.001). The maximum pooled specificity (93%) was observed in LI-RADS version (v) 2014 (95% CI: 89.0-96.0; I^2: 81.7%, *P*-value<0.001 for heterogeneity; T^2: 0.001). Table 3 and Figure 2 provide further details on the pooled estimation of specificity that in lesion size ≤20 was 0.88 in the assessment of specificity for the various subgroups of lesion size (≤20 and >20; 95% CI: 0.85-0.92). There was also high inter-study heterogeneity (I^2: 88.3%; *P*-value=0.001 for heterogeneity; T^2: 0.001). Additionally, the combined estimate of specificity for lesions less than 20 was 0.90% (95% CI: 0.87-0.93). Moreover, significant differences were across studies (I^2=91.3%; *P*-value<0.001 for heterogeneity; T^2: 0.01; Figure 3).

Estimation of pooled sensitivity

The sensitivity of pooled data for 35 articles was 0.80% (95% CI: 0.76-0.84), suggesting that the test has an accuracy of 0.80% for genuine positive cases. Considerable variability was found across studies in terms of pooled sensitivity (I^2: 93.1%; *P*-value<0.001 for heterogeneity; T^2: 0.01). LI-RADS v2018 had the greatest pooled sensitivity (0.83%; 95%: 0.79-0.87; I^2: 80.6%; *P*-value<0.001 for heterogeneity; T^2: 0.001). Table 3 and Figure 2 provide further details on the pooled estimation of sensitivity details. The pooled sensitivity estimates in lesion size ≤20 were 0.81 in the calculation of sensitivity for the various subgroups of lesion size (>20; 95% CI: 0.73-0.90; I^2: 96.7%; *P*<0.001 for heterogeneity; T^2: 0.02). There was considerable heterogeneity among the studies. Furthermore, the pooled sensitivity estimated in lesions >20 was 0.79% (95% CI: 0.75-0.84). Significant differences were also detected across trials (I^2: 88.3%; *P*-value<0.001 for heterogeneity; T^2: 0.01; Figure 4).

Meta-regression

The impact of factors, such as sample size and publication year of various articles on the pooled specificity and sensitivity were evaluated to determine the reason for the heterogeneity across studies. The effect of sample size (*P*-value=0.49 and *P*-value=0.72) and study year (*P*-value=0.80 and *P*-value=0.17) on estimating the heterogeneity of pooled sensitivity and specificity across studies was statistically insignificant, respectively. The distribution of sensitivity and specificity for various sample sizes is displayed in Figure 5.

Publication bias

Both sensitivity and specificity showed a strong publication bias in the findings of Begg's and Egger's tests, with *P*-value=0.001 and *P*<0.001 (Figure 6).

Table 1: The characteristics of studies included in this study

#	Author (year)	LI-RADS version	Strength of magnetic field/ vendor (Tesla)	NO. of the lesion (no. of HCC)	Study type	Imaging interpretations
1	A-Hong Ren et al. (2019) [11]	LI-RADS v2018	1.5 T GE 3.0 T GE	146	Retrospective	3 Radiologists with 10, 9, and 5 years of experience in abdominal imaging
2	Dong Ik Cha et al. (2020) [12]	LI-RADS v2018	3.0 T Philips Healthcare	122	Prospective	Two Radiologists with experience in abdominal imaging
3	Daniel R. Ludwig et al. (2019) [13]	LI-RADS v2018	1.5 T GE	27	Retrospective	two fellowships trained abdominal radiologists with 7 and 3 years of post-fellowship experience
4	Mohammad Chaudhry et al. (2019) [14]	LI-RADS v2018	3.0-T GE	53	Retrospective	3 faculty abdominal radiologists (2, 7, and 8 years of post-fellowship experience in abdominal MRI)
5	Andrea S. Kierans et al. (2020) [15]	LI-RADS v2018 LI-RADS v2017	1.5- or 3-T Trio, Siemens Healthcare	40	Retrospective	abdominal imaging radiologist with 5 years of post-fellowship experience
6	A.M. DE GAETANO et al. (2019) [16]	LI-RADS v2018	1.5 (GE) Healthcare	17	Retrospective	2 board-certified radiologists with15 & 5 experienced in the interpretation of liver MR imaging.
7	Andrew Chan et al. (2019) [17]	LI-RADS v2018	3.0 T Philips Healthcare	87	Retrospective	two radiology residents (AC in 2nd year, MS in 3rd year)
8	Victoria Chernyak et al. (2018) [18]	LI-RADS v2018	1.5- or 3-T Siemens Healthcare	100	Retrospective	Radiologists of experience in abdominal imaging
9	Sunyoung Lee et al. (2020) [19]	LI-RADS v2018	3.0-T Siemens 3.0 -T GE	263	Retrospective	Two board-certified abdominal radiologists (Two radiologists with 27 and 8 years of experience in liver imaging, respectively)
10	Hanyu Jiang et al. (2019) [20]	LI-RADS v2018	3.0 T Siemens	173	Retrospective	two abdominal radiologists (with 10 years and 4 years of experience in liver imaging)
11	Gaurav Khatri et al. (2019) [21]	LI-RADS v2018	1.5T and 3T	93	Prospective	Five radiologists
12	Yeun-Yoon Kim et al. (2019) [22]	LI-RADS v2018	1.5-T Philips 3.0-T Siemens	165	Retrospective	Two board-certified radiologists with 25 years and 3 years of experience with liver MRI retrospectively and independently analyzed the images.
13	Federica Vernuccio et al. (2019) [23]	LI-RADS v2018	1.5-T GE 3-T Philips	109	Retrospective	Two radiologists with expertise in abdominal imaging
14	Jeong Hee Yoon et al. (2018) [24]	LI-RADS v2018	1.5T GE 3T Trio, Siemens	43	Prospective	Three fellowship-trained board-certified with 25, 11, 11 years of experience in liver MRI.
15	Paul Smereka et al. (2020) [25]	LI-RADS v2018	1.5-T Siemens 3-T GE	71	Prospective	Three fellowship-trained abdominal radiologists (10, 5, and 2 years of experience)
16	Grzegorz Rosiak et al. (2018) [26]	LI-RADS v2017	1.5T Siemens Magnetom Avanto.	70	Prospective	Radiologists of experience in abdominal imaging

#	Author (year)	LI-RADS version	Strength of magnetic field/ vendor (Tesla)	NO. of the lesion (no. of HCC)	Study type	Imaging interpretations
17	Mohammad Abd Alkhalik Basha et al. (2019) [27]	LI-RADS v2017	1.5-Tesla Philips	67	Prospective	two radiologists had more than 10 years of experience in hepatic MRI
18	Ying Ding et al. (2018) [28]	LI-RADS v2017	1.5-T Siemens	145	Prospective	Two radiologists with more than 10 years of experience in abdominal MRI
19	Youngwoo Kim et al. (2017) [29]	LI-RADS v2017	1.5T or 3T GE	41	Prospective	Two abdominal radiologists.
20	Weimin Liu et al. (2017) [30]	LI-RADS v2017	1.5-T Aera, Siemens	170	Retrospective	Two radiologists (with 8 years of experience in abdominal radiology)
21	Tong Zhang et al. (2019) [31]	LI-RADS v2017	3.0 T Siemens	245	Retrospective	Two radiologists (with ten years of experience in abdominal radiology)
22	Ji Soo Song et al. (2014) [32]	LI-RADS v2014	1.5-T Siemens	77	Prospective	Two abdominal radiologists.
23	Tyler J. Fraum et al. (2018) [33]	LI-RADS v2018	1.5-T Avanto Siemens 3-T Siemens	138	Retrospective	Three abdominal radiologists with 10-17 years of post-fellowship experience.
24	Jae Seok Bae et al. (2017) [34]	LI-RADS v2017	1.5-T GE 3-T Siemens	167	Retrospective	Two clinically experienced abdominal radiologists both with 10 years of experience in abdominal imaging).
25	Anton S. Becker et al. (2016) [35]	LI-RADS v2014	1.5-T SIEMENS	55	Retrospective	Four board-certified radiologists with different experiences in liver imaging.
26	Milena Cerny et al. (2018) [36]	LI-RADS v2017	1.5-T or 3.0-T	-	Retrospective	Two fellowship-trained abdominal radiologists with experience in liver imaging.
27	Ningxin Chen et al. (2016) [37]	LI-RADS v2014	1.5-T GE 3-T GE	111	Retrospective	Two fellowship-trained abdominal radiologists
28	Aless andro Furlan et al. (2018) [38]	LI-RADS v2017	3-T GE	71	Retrospective	3 board-certified and fellowship-trained abdominal radiologists
29	Robert M. Hicks et al. (2016) [39]	LI-RADS v2014	3.0T Siemens	68	Prospective	Two abdominal radiologists (with three- and ten-years' experience)
30	Natally Horvat et al. (2017) [40]	LI-RADS v2014	1.5-T 3-T	51	Retrospective	Two senior board-certificated abdominal radiologists
31	Ijin Joo et al. (2016) [41]	LI-RADS v2014	1.5-T GE 3.0-T GE	71	Retrospective	Three fellowship-trained radiologists
32	Weimin Liu et al. (2017) [30]	LI-RADS v2014	1.5-T GE	151	Retrospective	2 radiologists (with eight years of experience in abdominal radiology)
33	Maxime Ronot et al. (2017) [42]	LI-RADS v2014	1.5 or 3 T magnets in three centers.	341	Retrospective	senior abdominal radiologists
34	QI Tang et al. (2018) [43]	LI-RADS v2017	3.0-T Siemens	42	Prospective	Two radiologists with 20 and 12-years of liver imaging experience randomly.
35	Sunyoung Lee et al. (2020) [19]	LI-RADS v2018	3.0-T systems Trio Tim, Siemens Healthineers	263	Retrospective	-
36	A-Hong Ren et al. (2019) [11]	LI-RADS v2017	1.5 T GE 3.0 T GE	146	Retrospective	3 Radiologists 10, 9, and 5 years of experience in abdominal imaging

LI-RADS: Liver Imaging Reporting and Data System, HCC: Hepatocellular Carcinoma, MRI: Magnetic Resonance Imaging, GE: General Electric

Table 2: The estimated sensitivity and specificity in the studies included in the current meta-analysis

#	Author (year)	Lesion size (mm)	Reference standard	Sensitivity (95%CI)	Specificity (95%CI)
1	A-Hong Ren et al. (2019)) [11]	<20	Liver biopsy, follow-up	80.8	90.1
2	Dong Ik Cha et al. (2020) [12]	≤30	Histopathologic	90.3	96
3	Daniel R. Ludwig et al. (2019) [13]	≤30	Pathologic diagnosis, Biopsy	66.7	98.5
4	Mohammad Chaudhry et al. (2019) [14]	21 (11–54)	Histopathology	87	85
5	Andrea S. Kierans et al. (2020) [15]	20≥	Histopathology, Biopsy	77.4	91.6
6	A.M. DE GAETANO et al. (2019) [16]	≤20	Pathologic	94.1	55.7
7	Andrew Chan et al. (2019) [17]	≤20	Pathologic diagnosis, Biopsy	80.8	88
8	Victoria Chernyak et al. (2018) [18]	≤30	Pathologic diagnosis	86	75
9	Sunyoung Lee et al. (2020) [19]	≥10	MRI and pathological diagnosis	67.5	98.1
10	Hanyu Jiang et al. (2019) [20]	≤50	Histopathologic examination	86	82
11	Gaurav Khatri et al. (2019) [21]	≤60	Clinical follow-up criteriapathologic diagnosis	92.1	88.6
12	Yeun-Yoon Kim et al. (2019) [22]	12-115	Histopathological diagnosed	83	89
13	Federica Vernuccio et al. (2019) [23]	10–20	Pathological diagnosis	84	84
14	Jeong Hee Yoon et al. (2018) [24]	10–19	Pathologic, imaging follow-up	62.2	97.7
15	Paul Smereka et al. (2020) [25]	≥20	Pathologically	87.2	96.6
16	Grzegorz Rosiak et al. (2018) [26]	≥20	Biopsyfollow-up imaging	96	75
17	Alkhalik Basha et al. (2019) [27]	≥20	Histopathological diagnosed	97.01	88.43
18	Ying Ding et al. (2018) [28]	<10	Histopathological diagnosed	73.8	71
19	Youngwoo Kim et al. (2017) [29]	≤20	Histopathological diagnosed	82	79
20	Weimin Liu et al. (2017) [30]	≥20	Surgical pathology, needle biopsy, two years of follow-up	84.8	95.8
21	Tong Zhang et al. (2019) [31]	≥30	Histological diagnosis	61.2	92.5
22	Ji Soo Song et al. (2018) [32]	8–72	Histological findings	76.6	89.6
23	Tyler J. Fraum et al. (2018) [33]	≥20	Pathologic analysis	56.4	81.8
24	Jae Seok Bae et al. (2017) [34]	≥20	Pathologic analysis	91	90
25	Anton S. Becker et al. (2016) [35]	≥20	Pathologic analysis	34.5	98
26	Milena Cerny et al. (2018) [36]	≥20	Surgical resection, biopsy	87.9	87.5
27	Ningxin Chen et al. (2016) [37]	≥20	Pathologic analysis	84	96
28	Aless andro Furlan et al. (2018) [38]	≥20	Surgical resection, biopsy	80	87
29	Robert M. Hicks et al. (2016) [39]	≥20	Pathologic analysis	91	94
30	Natally Horvat et al. (2017) [40]	≥10	Pathologic analysis	93.3	84.2
31	Ijin Joo et al. (2016) [41]	≥10	Surgical resection, biopsy	65.2	93.3
32	Maxime Ronot et al. (2017) [42]	≥20	Pathologic analysis, follow-up	72.5	89.9
33	Ql Tang et al. (2018) [43]	≥10	Surgical resection, Biopsy, follow-up	71.1	55.6
34	Sunyoung Lee et al. (2020) [19]	≥20	Pathologic analysis	85.6	88.1
35	A-Hong Ren et al. (2019) [11]	≥50	Biopsy, follow-up	71.2	91.5

CI: Confidence Intervals, MRI: Magnetic Resonance Imaging

Table 3: Pooled estimation of sensitivity and specificity according to the types of Liver Imaging Reporting and Data System

Types of LI-RADS	Number of studies	Pooled estimation (95% CI)	$P_{heterogeneity}$	I^2 (%)	T^2
Sensitivity					
2014	8	74.0 (60.0- 87.0)	<001	95.7	0.04
2017	12	81.0 (75.0-88.0)	<001	94.0	0.01
2018	15	83.0 (79.0-87.0)	<001	80.6	0.001
Overall	35	80.0 (76.0-84.0)	<001	93.1	0.01
Specificity					
2014	8	93.0 (89.0-96.0)	<001	81.7	0.001
2017	12	85.0 (79.0-91.0)	<001	92.5	0.01
2018	15	91.0 (88.0-94.0)	<001	88.0	0.001
Overall	35	89.0 (87.0-92.0)	<001	90.7	0.001

LI-RADS: Liver Imaging Reporting and Data System, CI: Confidence Intervals

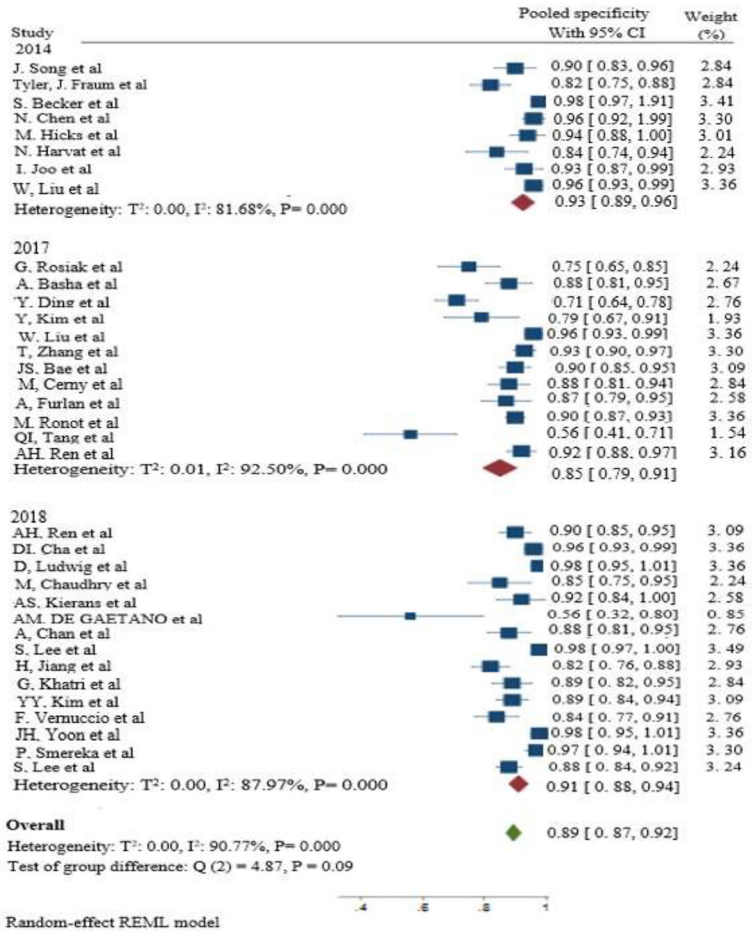


Figure 2: The pooled estimation of the sensitivity and specificity of liver imaging reporting and data system (LI-RADS) in the detection of hepatocellular carcinoma according to different versions of LI-RADS. (CI: Confidence Intervals)

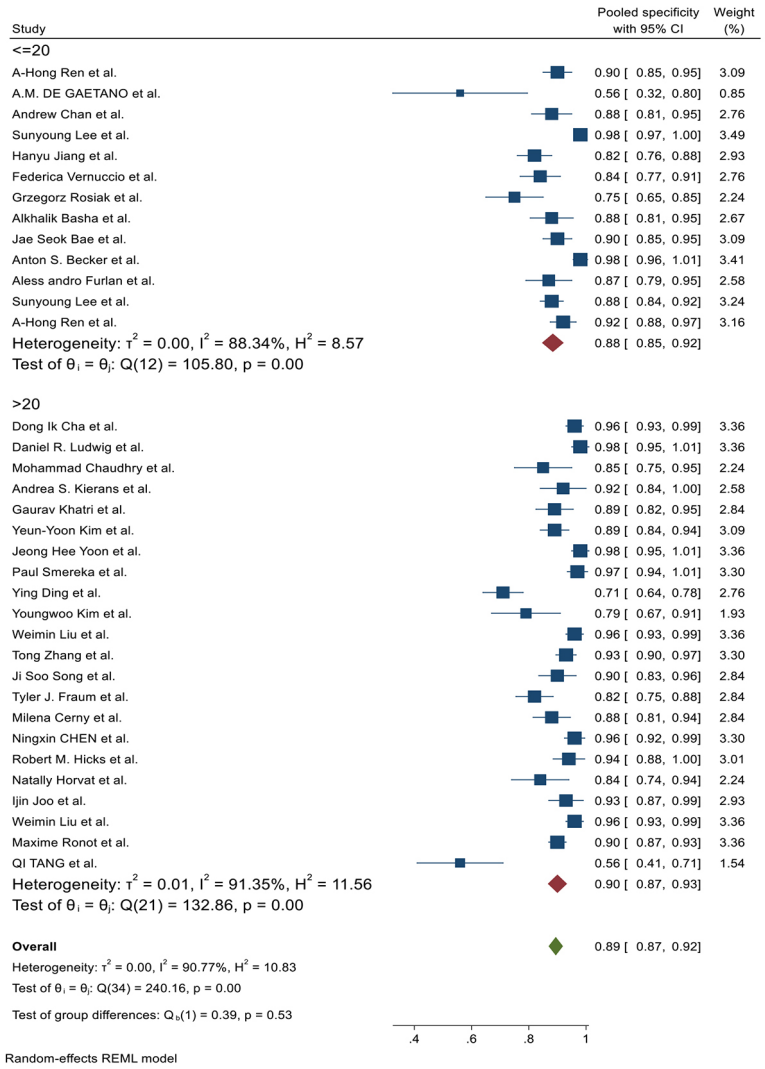


Figure 3: The pooled estimation of specificity of imaging reporting and data system in the detection of hepatocellular carcinoma according to the lesion size. (CI: Confidence Intervals)

Discussion

We investigated the value of the LI-RADS in the detection and characterization of HCC. Based on the results, the pooled sensitivity and specificity were estimated as 0.80 (95% CI: 0.76-0.84) and 0.89 (95% CI: 0.87-0.92), suggesting this test can detect 0.80 of true positive cases and 0.89 of true negative cases, respectively. According to different subgroups of lesion size (≤20 and >20), the sensitivity and specificity were 0.81 and 0.79 (95% CI: 0.73-0.90 and 0.75-0.84) and 0.88 and 0.90 (95% CI: 0.85-0.92 and 0.87-0.93), respectively. This finding signifies that the sensitivity of LI-RADS in the detection of low-grade lesions is higher than that of high-grade lesions. MRI-based radiomics analysis, in comparison to other imaging methods, demonstrated a sensitivity of 93.8% in the detection of HCC [44]. The discrepancy between the estimation rates of sensitivity and specificity in studies can be due to varied sample sizes and diagnostic techniques used on patients with different clinical stages.

Regarding different versions of LI-RADS, the highest pooled sensitivity was in LI-RADS

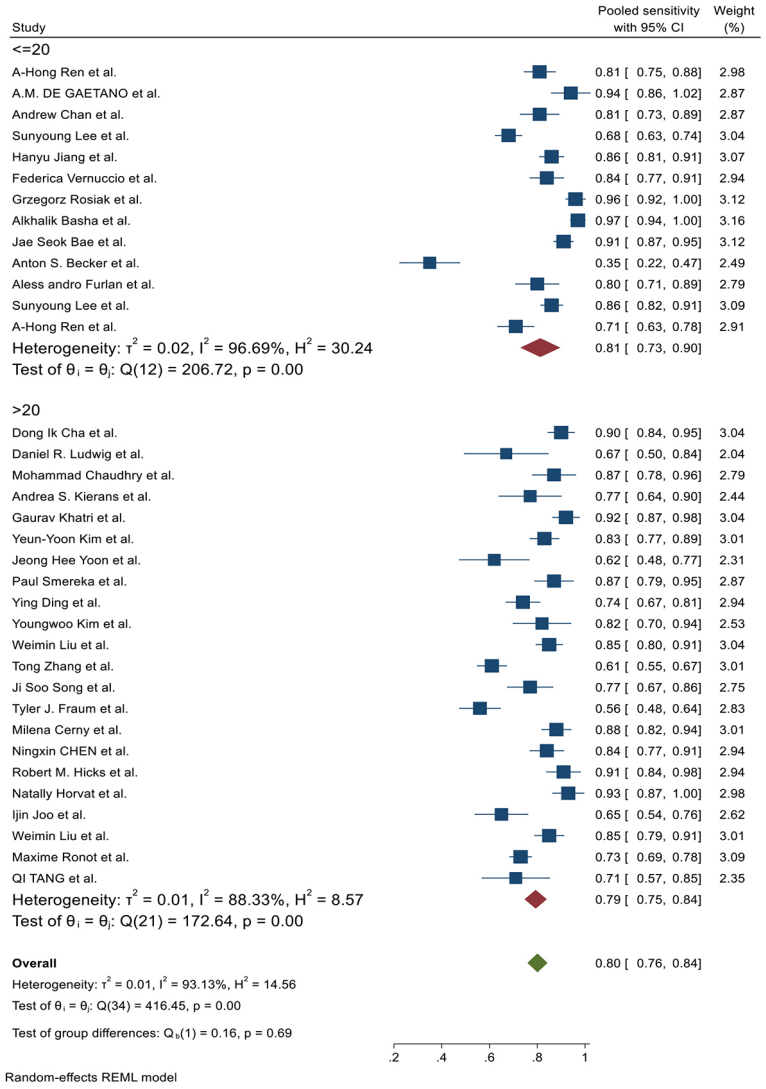
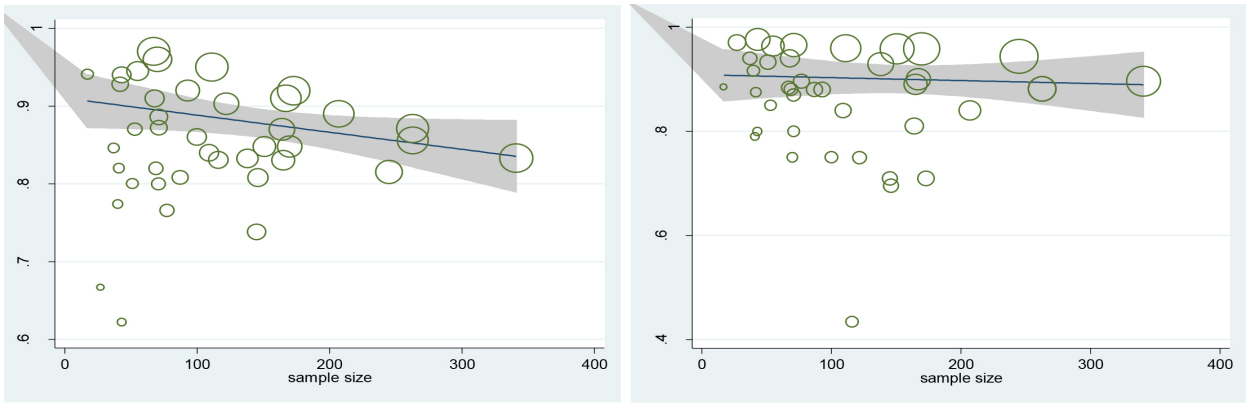


Figure 4: The pooled estimation of sensitivity of imaging reporting and data system in the detection of hepatocellular carcinoma according to the lesion size. (CI: Confidence Intervals, REML: Restricted Maximum Likelihood)

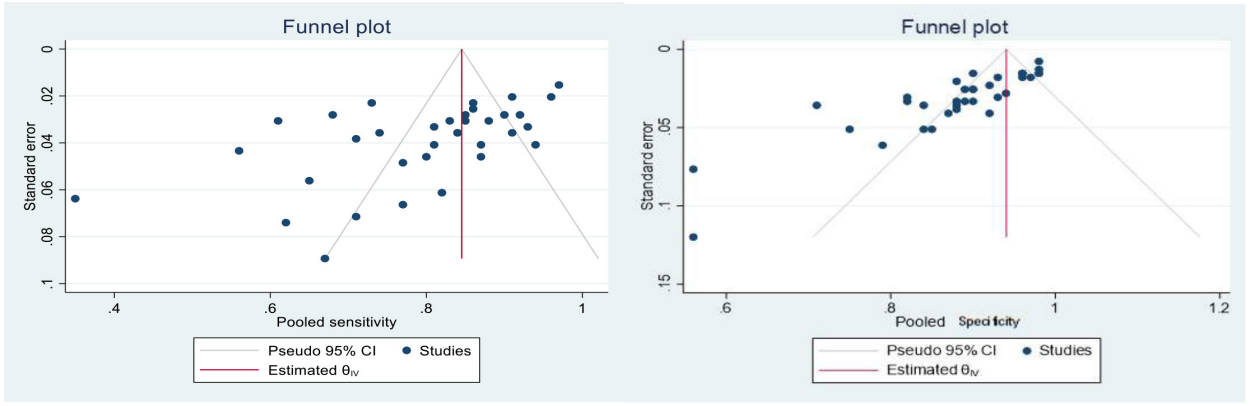
v2018 (0.83%; 95% CI: 0.79-0.87), while that of specificity was detected in LI-RADS v2014 (93.0%; 95% CI: 89.0-96.0). In another study, the LI-RADS version 2018 showed higher sensitivity than LI-RADS v2017 (81% vs. 68%). Also, in low-grade lesions, the sensitivity of LI-RADS v2018 was indicated to be higher than LI-RADS v2017 (76% vs. 11%), but the specificity of LI-RADS v2018 was lower than LI-RADS v2017 (94% vs. 99%) [45]. The higher sensitivity for LI-RADS v2018 has been reported in another original study.

The estimated sensitivity of LR-5 criteria of LR-TIV v2018 and v2017 was 63.9% and 55.2%, respectively, whereas the specificity for the two versions was the same (97.3%) [15]. The performance of varying versions of the LI-RADS (v2017 vs v2014) in the detection of HCC assessed in other studies showed a positive predictive value and high specificity for the mentioned versions [46-48]. The results of heterogeneity among included stud-



a) b)

Figure 5: The distribution of estimated sensitivity (a) and specificity (b) according to different sample sizes. (CI: Confidence Intervals)



a) b)

Figure 6: The funnel plot to assess publication bias in estimated sensitivity (a) and specificity (b). (CI: Confidence Intervals)

ies can be attributed to different factors, such as clinician skills and the situation of understudy patients. However, it should be regarded that the balance between sensitivity and specificity is very important, especially for diseases with high mortality [49].

The sensitivity of gadoxetate disodium-enhanced MR imaging in detecting HCC was estimated to be 0.85%, and this rate for multidetector CT was 0.69% [50]. In a meta-analysis, the pooled sensitivity results of contrast-enhanced CT and gadolinium-enhanced MRI in detecting HCC were 73.6% and 77.5%, respectively, while those of non-contrast-enhanced US were 59.3% [51]. The sensitivity estimated by the above-mentioned approaches is fewer than that estimated by the current study.

Various appearances of the lesion are based on the kind of lesion, as well as its size and echogenicity. Small, localized HCC, compared to normal liver, looks hypoechoic. Larger lesions are heterogeneous due to fatty change, fibrosis, calcification, and necrosis. Focal fatty sparing-diffuse HCC may have a peripheral halo of hypoechogenicity, and this

feature may be challenging to diagnose or separate from underlying cirrhosis.

The main goal of using MRI and CT scan in the medical care of HCC patients is the early diagnosis of the disease and initiation of early intervention. Both diagnostic techniques have high specificity; thus, treatment can begin without the use of additional invasive diagnostic methods, such as biopsy [52, 53]. However, due to low cost-effectiveness, MRI and CT scans are not recommended by national clinical practitioners [54]. Therefore, the LI-RADS, as an advanced and cost-effective method, can be used in the care of patients at risk of or with HCC. Based on previous studies, the sensitivity of LI-RADS US for detecting HCC has a wide range (20.5-94%) [51, 52, 55]. LI-RADS US generally has a lower sensitivity for detecting HCC in patients at high risk of HCC [51]. The obtained result of the current study has a much higher sensitivity than those of a recent meta-analysis, which reported a sensitivity of 47% for the early detection of HCC [51]. According to the results of the study by Son et al. (2019) in the surveillance of patients at high risk of HCC, US liver imaging report classification, and US-3 data system showed high specificity but low sensitivity for HCC diagnosis [56].

The present study had some limitations, as follows: 1) significant heterogeneity between included studies, leading to using the random effects model, 2) the lack of data, resulting in not performing some sub-group analyses regarding the etiology of the chronic liver disease and presence of cirrhosis, and 3) the presence of significant publication bias.

Conclusion

The results of sensitivity and specificity estimated in the current study were acceptable. Therefore, LI-RADS can assist radiologists in achieving the required sensitivity and specificity. The LI-RADS criteria were developed for diagnosing high-specificity progressed HCCs, namely HCCs, that have progressed along the hepatocarcinogenesis pathway to the point where they are malignant, with the potential for vascular invasion and metastasis.

Acknowledgment

Authors would like to thank the cooperation of the Tehran University of Medical Sciences, Tehran, Iran.

Authors' Contribution

A. Arian and H. Suhail Najm Alareer designed the conception of the study; HJ. Taher and A. Dinar Abdullah conducted a statical analysis; of A. Arian and H. Suhail Najm Alareer performed technical support and conceptual advice. All authors contributed to the drafted manuscript, revised it critically, and approved the final version.

Conflict of Interest

None

References

1. Kudo M. Surveillance, diagnosis, treatment, and outcome of liver cancer in Japan. *Liver Cancer*. 2015;**4**(1):39-50. doi: 10.1159/000367727. PubMed PMID: 26020028. PubMed PMCID: PMC4439792.
2. Bruix J, Reig M, Sherman M. Evidence-Based Diagnosis, Staging, and Treatment of Patients With Hepatocellular Carcinoma. *Gastroenterology*. 2016;**150**(4):835-53. doi: 10.1053/j.gastro.2015.12.041. PubMed PMID: 26795574.
3. Puoti C. New insights on hepatocellular carcinoma: epidemiology and clinical aspects. *Hepatoma Res*. 2018;**4**:57.
4. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin*. 2015;**65**(2):87-108. doi: 10.3322/caac.21262. PubMed PMID: 25651787.
5. Ayuso C, Rimola J, Vilana R, Burrel M, Darnell A, García-Criado Á, et al. Diagnosis and staging of hepatocellular carcinoma (HCC): current guidelines. *Eur J Radiol*. 2018;**101**:72-81. doi: 10.1016/j.ejrad.2018.01.025. PubMed PMID: 29571804.
6. Elsayes KM, Hooker JC, Agrons MM, Kielar AZ, Tang A, Fowler KJ, et al. 2017 Version of LI-RADS for CT and MR Imaging: An Update. *Radio-*

graphics. 2017;**37**(7):1994-2017. doi: 10.1148/rg.2017170098. PubMed PMID: 29131761.

7. Poulou LS, Botsa E, Thanou I, Ziakas PD, Thanos L. Percutaneous microwave ablation vs radiofrequency ablation in the treatment of hepatocellular carcinoma. *World J Hepatol.* 2015;**7**(8):1054-63. doi: 10.4254/wjh.v7.i8.1054. PubMed PMID: 26052394. PubMed PMCID: PMC4450182.
8. Choi JY, Lee JM, Sirlin CB. CT and MR imaging diagnosis and staging of hepatocellular carcinoma: part I. Development, growth, and spread: key pathologic and imaging aspects. *Radiology.* 2014;**272**(3):635-54. doi: 10.1148/radiol.14132361. PubMed PMID: 25153274. PubMed PMCID: PMC4263631.
9. Tang A, Valasek MA, Sirlin CB. Update on the Liver Imaging Reporting and Data System: What the Pathologist Needs to Know. *Adv Anat Pathol*. 2015;**22**(5):314-22. doi: 10.1097/PAP.0000000000000089. PubMed PMID: 26262514.
10. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med.* 2011;**155**(8):529-36. doi: 10.7326/0003-4819-155-8-201110180-00009. PubMed PMID: 22007046.
11. Ren AH, Zhao PF, Yang DW, Du JB, Wang ZC, Yang ZH. Diagnostic performance of MR for hepatocellular carcinoma based on LI-RADS v2018, compared with v2017. *J Magn Reson Imaging*. 2019;**50**(3):746-55. doi: 10.1002/jmri.26640. PubMed PMID: 30648327.
12. Cha DI, Choi GS, Kim YK, Kim JM, Kang TW, Song KD, Ahn SH. Extracellular contrast-enhanced MRI with diffusion-weighted imaging for HCC diagnosis: prospective comparison with gadoxetic acid using LI-RADS. *Eur Radiol.* 2020;**30**(7):3723-34. doi: 10.1007/s00330-020-06753-5. PubMed PMID: 32128620.
13. Ludwig DR, Fraum TJ, Cannella R, Tsai R, Naeem M, LeBlanc M, et al. Expanding the Liver Imaging Reporting and Data System (LI-RADS) v2018 diagnostic population: performance and reliability of LI-RADS for distinguishing hepatocellular carcinoma (HCC) from non-HCC primary liver carcinoma in patients who do not meet strict LI-RADS high-risk criteria. *HPB (Oxford)*. 2019;**21**(12):1697-706. doi: 10.1016/j.hpb.2019.04.007. PubMed PMID: 31262487.
14. Chaudhry M, McGinty KA, Mervak B, Lerebours R, Li C, Shropshire E, et al. The LI-RADS Version 2018 MRI Treatment Response Algorithm: Evaluation of Ablated Hepatocellular Carcinoma. *Radiology*. 2020;**294**(2):320-6. doi: 10.1148/radiol.2019191581. PubMed PMID: 31845843.
15. Kierans AS, Song C, Gavlin A, Roudenko A, Lu L, Askin G, Hecht EM. Diagnostic Performance of LI-RADS Version 2018, LI-RADS Version 2017, and OPTN Criteria for Hepatocellular Carcinoma. *Am J Roentgenol.* 2020;**215**(5):1085-92. doi: 10.2214/AJR.20.22772. PubMed PMID: 32877248.
16. De Gaetano AM, Catalano M, Pompili M, Marini MG, Rodríguez Carnero P, et al. Critical analysis of major and ancillary features of LI-RADS v2018 in the differentiation of small (≤ 2 cm) hepatocellular carcinoma from dysplastic nodules with gadobenate dimeglumine-enhanced magnetic resonance imaging. *Eur Rev Med Pharmacol Sci*. 2019;**23**(18):7786-801. doi: 10.26355/eurrev_201909_18988. PubMed PMID: 31599447.
17. Chan A, Sertic M, Sammon J, Kim TK, Jang HJ, Guimaraes L, et al. Diagnostic imaging of hepatocellular carcinoma at community hospitals and their tertiary referral center in the era of LI-RADS: a quality assessment study. *Abdom Radiol (NY).* 2019;**44**(12):4028-36. doi: 10.1007/s00261-019-02237-3. PubMed PMID: 31555846.
18. Chernyak V, Fowler KJ, Kamaya A, Kielar AZ, Elsayes KM, Bashir MR, et al. Liver Imaging Reporting and Data System (LI-RADS) Version 2018: Imaging of Hepatocellular Carcinoma in At-Risk Patients. *Radiology*. 2018;**289**(3):816-30. doi: 10.1148/radiol.2018181494. PubMed PMID: 30251931. PubMed PMCID: PMC6677371.
19. Lee S, Kim MJ, Kim SS, Shin H, Kim DY, Choi JY, Park MS, Mitchell DG. Retrospective comparison of EASL 2018 and LI-RADS 2018 for the noninvasive diagnosis of hepatocellular carcinoma using magnetic resonance imaging. *Hepatol Int.* 2020;**14**(1):70-9. doi: 10.1007/s12072-019-10002-3. PubMed PMID: 31802388.
20. Jiang H, Liu X, Chen J, Wei Y, Lee JM, Cao L, et al. Man or machine? Prospective comparison of the version 2018 EASL, LI-RADS criteria and a radiomics model to diagnose hepatocellular carcinoma. *Cancer Imaging.* 2019;**19**(1):1-13. doi: 10.1186/s40644-019-0266-9. PubMed PMID: 31806050. PubMed PMCID: PMC6896342.
21. Khatri G, Pedrosa I, Ananthakrishnan L, De Leon AD, Fetzer DT, Leyendecker J, et al. Abbreviated-protocol screening MRI vs. complete-protocol diagnostic MRI for detection of hepatocellular carcinoma in patients with cirrhosis: An equiva-

lence study using LI-RADS v2018. *J Magn Reson Imaging*. 2020;**51**(2):415-25. doi: 10.1002/jmri.26835. PubMed PMID: 31209978.

22. Kim YY, Kim MJ, Kim EH, Roh YH, An C. Hepatocellular Carcinoma versus Other Hepatic Malignancy in Cirrhosis: Performance of LI-RADS Version 2018. *Radiology.* 2019;**291**(1):72-80. doi: 10.1148/radiol.2019181995. PubMed PMID: 30694166.
23. Vernuccio F, Cannella R, Meyer M, Choudhoury KR, Gonzáles F, Schwartz FR, et al. LI-RADS: Diagnostic Performance of Hepatobiliary Phase Hypointensity and Major Imaging Features of LR-3 and LR-4 Lesions Measuring 10-19 mm With Arterial Phase Hyperenhancement. *Am J Roentgenol.* 2019;**213**(2):W57-65. doi: 10.2214/AJR.18.20979. PubMed PMID: 31039012.
24. Yoon JH, Lee JM, Lee YJ, Lee KB, Han JK. Added Value of sequentially performed gadoxetic acid-enhanced liver MRI for the diagnosis of small (10-19 mm) or atypical hepatic observations at contrast-enhanced CT: A prospective comparison. *J Magn Reson Imaging*. 2019;**49**(2):574-87. doi: 10.1002/jmri.26199. PubMed PMID: 30102433.
25. Smereka P, Doshi AM, Lavelle LP, Shanbhogue K. New Arterial Phase Enhancing Nodules on MRI of Cirrhotic Liver: Risk of Progression to Hepatocellular Carcinoma and Implications for LI-RADS Classification. *Am J Roentgenol.* 2020;**215**(2):382-9. doi: 10.2214/AJR.19.22033. PubMed PMID: 32432909.
26. Rosiak G, Podgorska J, Rosiak E, Cieszanowski A. Comparison of LI-RADS v.2017 and ESGAR Guidelines Imaging Criteria in HCC Diagnosis Using MRI with Hepatobiliary Contrast Agents. *Biomed Res Int*. 2018;**2018**:7465126. doi: 10.1155/2018/7465126. PubMed PMID: 30105242. PubMed PMCID: PMC6076943.
27. Basha MAA, Refaat R, Mohammad FF, Khamis MEM, El-Maghraby AM, El Sammak AA, et al. The utility of diffusion-weighted imaging in improving the sensitivity of LI-RADS classification of small hepatic observations suspected of malignancy. *Abdom Radiol (NY)*. 2019;**44**(5):1773-84. doi: 10.1007/s00261-018-01887-z. PubMed PMID: 30603882.
28. Ding Y, Rao SX, Wang WT, Chen CZ, Li RC, Zeng M. Comparison of gadoxetic acid versus gadopentetate dimeglumine for the detection of hepatocellular carcinoma at 1.5 T using the liver imaging reporting and data system (LI-RADS v.2017). *Cancer Imaging*. 2018;**18**(1):48. doi: 10.1186/s40644-018-0183-3. PubMed PMID: 30526674. PubMed PMCID: PMC6286579.
29. Kim Y, Furlan A, Borhani AA, Bae KT. Computer-aided diagnosis program for classifying the risk of hepatocellular carcinoma on MR images following liver imaging reporting and data system (LI-RADS). *J Magn Reson Imaging*. 2018;**47**(3):710-22. doi: 10.1002/jmri.25772. PubMed PMID: 28556283.
30. Liu W, Qin J, Guo R, Xie S, Jiang H, Wang X, Kang Z, Wang J, Shan H. Accuracy of the diagnostic evaluation of hepatocellular carcinoma with LI-RADS. *Acta Radiol.* 2018;**59**(2):140-6. doi: 10.1177/0284185117716700. PubMed PMID: 28648125.
31. Zhang T, Huang ZX, Wei Y, Jiang HY, Chen J, Liu XJ, et al. Hepatocellular carcinoma: Can LI-RADS v2017 with gadoxetic-acid enhancement magnetic resonance and diffusion-weighted imaging improve diagnostic accuracy? *World J Gastroenterol.* 2019;**25**(5):622-31. doi: 10.3748/wjg.v25.i5.622. PubMed PMID: 30774276. PubMed PMCID: PMC6371008.
32. Song JS, Choi EJ, Hwang SB, Hwang HP, Choi H. LI-RADS v2014 categorization of hepatocellular carcinoma: Intraindividual comparison between gadopentetate dimeglumine-enhanced MRI and gadoxetic acid-enhanced MRI. *Eur Radiol.* 2019;**29**(1):401-10. doi: 10.1007/s00330-018-5559-z. PubMed PMID: 29922928.
33. Fraum TJ, Tsai R, Rohe E, Ludwig DR, Salter A, Nalbantoglu I, Heiken JP, Fowler KJ. Differentiation of Hepatocellular Carcinoma from Other Hepatic Malignancies in Patients at Risk: Diagnostic Performance of the Liver Imaging Reporting and Data System Version 2014. *Radiology*. 2018;**286**(1):158-72. doi: 10.1148/radiol.2017170114. PubMed PMID: 28853673.
34. Bae JS, Kim JH, Yu MH, Lee DH, Kim HC, Chung JW, Han JK. Diagnostic accuracy of gadoxetic acid-enhanced MR for small hypervascular hepatocellular carcinoma and the concordance rate of Liver Imaging Reporting and Data System (LI-RADS). *PLoS One.* 2017;**12**(5):e0178495. doi: 10.1371/journal.pone.0178495. PubMed PMID: 28558068. PubMed PMCID: PMC5448778.
35. Becker AS, Barth BK, Marquez PH, Donati OF, Ulbrich EJ, Karlo C, et al. Increased interreader agreement in diagnosis of hepatocellular carcinoma using an adapted LI-RADS algorithm. *Eur J Radiol.* 2017;**86**:33-40. doi: 10.1016/j.ejrad.2016.11.004. PubMed PMID: 28027763.

36. Cerny M, Chernyak V, Olivié D, Billiard JS, Murphy-Lavallée J, et al. LI-RADS Version 2018 Ancillary Features at MRI. *Radiographics.* 2018;**38**(7):1973-2001. doi: 10.1148/rg.2018180052. PubMed PMID: 30289735.

37. Chen N, Motosugi U, Morisaka H, Ichikawa S, Sano K, Ichikawa T, et al. Added Value of a Gadoxetic Acid-enhanced Hepatocyte-phase Image to the LI-RADS System for Diagnosing Hepatocellular Carcinoma. *Magn Reson Med Sci.* 2016;**15**(1):49-59. doi: 10.2463/mrms.2014-0149. PubMed PMID: 26104079.

38. Furlan A, Almusa O, Yu RK, Sagreiya H, Borhani AA, Bae KT, Marsh JW. A radiogenomic analysis of hepatocellular carcinoma: association between fractional allelic imbalance rate index and the liver imaging reporting and data system (LI-RADS) categories and features. *Br J Radiol.* 2018;**91**(1086):20170962. doi: 10.1259/bjr.20170962. PubMed PMID: 29565672. PubMed PMCID: PMC6223296.

39. Hicks RM, Yee J, Ohliger MA, Weinstein S, Kao J, Ikram NS, Hope TA. Comparison of diffusion-weighted imaging and T2-weighted single shot fast spin-echo: Implications for LI-RADS characterization of hepatocellular carcinoma. *Magn Reson Imaging.* 2016;**34**(7):915-21. doi: 10.1016/j.mri.2016.04.007. PubMed PMID: 27108359. PMCID: PMC5325126.

40. Horvat N, Nikolovski I, Long N, Gerst S, Zheng J, Pak LM, et al. Imaging features of hepatocellular carcinoma compared to intrahepatic cholangiocarcinoma and combined tumor on MRI using liver imaging and data system (LI-RADS) version 2014. *Abdom Radiol (NY).* 2018;**43**(1):169-78. doi: 10.1007/s00261-017-1261-x. PubMed PMID: 28765978. PubMed PMCID: PMC6598685.

41. Joo I, Lee JM, Lee SM, Lee JS, Park JY, Han JK. Diagnostic accuracy of liver imaging reporting and data system (LI-RADS) v2014 for intrahepatic mass-forming cholangiocarcinomas in patients with chronic liver disease on gadoxetic acid-enhanced MRI. *J Magn Reson Imaging.* 2016;**44**(5):1330-8. doi: 10.1002/jmri.25287. PubMed PMID: 27087012.

42. Ronot M, Fouque O, Esvan M, Lebigot J, Aubé C, Vilgrain V. Comparison of the accuracy of AASLD and LI-RADS criteria for the non-invasive diagnosis of HCC smaller than 3 cm. *J Hepatol.* 2018;**68**(4):715-23. doi: 10.1016/j.jhep.2017.12.014. PubMed PMID: 29274407.

43. Tang Q, Ma C. Performance of Gd-EOB-DTPA-enhanced MRI for the diagnosis of LI-RADS 4 category hepatocellular carcinoma nodules with different diameters. *Oncol Lett.* 2018;**16**(2):2725-31. doi: 10.3892/ol.2018.8884. PubMed PMID: 30008946. PubMed PMCID: PMC6036548.

44. Mayerhoefer ME, Schima W, Trattnig S, Pinker K, Berger-Kulemann V, Ba-Ssalamah A. Texture-based classification of focal liver lesions on MRI at 3.0 Tesla: a feasibility study in cysts and hemangiomas. *J Magn Reson Imaging.* 2010;**32**(2):352-9. doi: 10.1002/jmri.22268. PubMed PMID: 20677262.

45. Lee SM, Lee JM, Ahn SJ, Kang HJ, Yang HK, Yoon JH. LI-RADS Version 2017 versus Version 2018: Diagnosis of Hepatocellular Carcinoma on Gadoxetate Disodium-enhanced MRI. *Radiology.* 2019;**292**(3):655-63. doi: 10.1148/radiol.2019182867. PubMed PMID: 31310175.

46. Lee S, Kim SS, Roh YH, Choi JY, Park MS, Kim MJ. Diagnostic Performance of CT/MRI Liver Imaging Reporting and Data System v2017 for Hepatocellular Carcinoma: A Systematic Review and Meta-Analysis. *Liver Int.* 2020;**40**(6):1488-97. doi: 10.1111/liv.14424. PubMed PMID: 32145134.

47. Van Der Pol CB, Lim CS, Sirlin CB, McGrath TA, Salameh JP, Bashir MR, et al. Accuracy of the Liver Imaging Reporting and Data System in Computed Tomography and Magnetic Resonance Image Analysis of Hepatocellular Carcinoma or Overall Malignancy-A Systematic Review. *Gastroenterology.* 2019;**156**(4):976-86. doi: 10.1053/j.gastro.2018.11.020. PubMed PMID: 30445016.

48. Kim DH, Choi SH, Park SH, Kim KW, Byun JH, Kim SY, et al. Meta-analysis of the accuracy of Liver Imaging Reporting and Data System category 4 or 5 for diagnosing hepatocellular carcinoma. *Gut.* 2019;**68**(9):1719-21. doi: 10.1136/gutjnl-2019-318555. PubMed PMID: 31300516.

49. Moura Cunha G, Chernyak V, Fowler KJ, Sirlin CB. Up-to-Date Role of CT/MRI LI-RADS in Hepatocellular Carcinoma. *J Hepatocell Carcinoma.* 2021;**8**:513-27. doi: 10.2147/JHC.S268288. PubMed PMID: 34104640. PubMed PMCID: PMC8180267.

50. Di Martino M, Marin D, Guerrisi A, Baski M, Galati F, Rossi M, et al. Intraindividual comparison of gadoxetate disodium-enhanced MR imaging and 64-section multidetector CT in the Detection of hepatocellular carcinoma in patients with cirrhosis. *Radiology.* 2010;**256**(3):806-16. doi: 10.1148/radiol.10091334. PubMed PMID: 20720069.

51. Hanna RF, Miloushev VZ, Tang A, Finklestone LA,

Brejt SZ, Sandhu RS, et al. Comparative 13-year meta-analysis of the sensitivity and positive predictive value of ultrasound, CT, and MRI for detecting hepatocellular carcinoma. *Abdom Radiol (NY).* 2016;**41**(1):71-90. doi: 10.1007/s00261-015-0592-8. PubMed PMID: 26830614.

52. Tzartzeva K, Obi J, Rich NE, Parikh ND, Marrero JA, Yopp A, et al. Surveillance Imaging and Alpha Fetoprotein for Early Detection of Hepatocellular Carcinoma in Patients With Cirrhosis: A Meta-analysis. *Gastroenterology.* 2018;**154**(6):1706-18. doi: 10.1053/j.gastro.2018.01.064. PubMed PMID: 29425931. PubMed PMCID: PMC5927818.
53. Kim SY, An J, Lim YS, Han S, Lee JY, Byun JH, et al. MRI With Liver-Specific Contrast for Surveillance of Patients With Cirrhosis at High Risk of Hepatocellular Carcinoma. *JAMA Oncol.* 2017;**3**(4):456-63. doi: 10.1001/jamaoncol.2016.3147. PubMed PMID: 27657493. PubMed PMCID: PMC5470420.
54. Marrero JA, Kulik LM, Sirlin CB, Zhu AX, Finn RS, Abecassis MM, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2018;**68**(2):723-50. doi: 10.1002/hep.29913. PubMed PMID: 29624699.
55. Chou R, Cuevas C, Fu R, Devine B, Wasson N, Ginsburg A, et al. Imaging Techniques for the Diagnosis of Hepatocellular Carcinoma: A Systematic Review and Meta-analysis. *Ann Intern Med.* 2015;**162**(10):697-711. doi: 10.7326/M14-2509. PubMed PMID: 25984845.
56. Son JH, Choi SH, Kim SY, Jang HY, Byun JH, Won HJ, et al. Validation of US Liver Imaging Reporting and Data System Version 2017 in Patients at High Risk for Hepatocellular Carcinoma. *Radiology.* 2019;**292**(2):390-7. doi: 10.1148/radiol.2019190035. PubMed PMID: 31210614.