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LETTER TO THE EDITOR

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SYSTEMATIC REVIEWS

Current status of magnetic resonance imaging radiomics in hepatocellular carcinoma: A quantitative review with Radiomics Quality Score

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Abstract

BACKGROUND

Radiomics is a promising tool that may increase the value of magnetic resonance imaging (MRI) for different tasks related to the management of patients with hepatocellular carcinoma (HCC). However, its implementation in clinical practice is still far, with many issues related to the methodological quality of radiomic studies.

AIM

To systematically review the current status of MRI radiomic studies concerning HCC using the Radiomics Quality Score (RQS).

METHODS

A systematic literature search of PubMed, Google Scholar, and Web of Science databases was performed to identify original articles focusing on the use of MRI radiomics for HCC management published between 2017 and 2023. The methodological quality of radiomic studies was assessed using the RQS tool. Spearman's correlation (ρ) analysis was performed to explore if RQS was correlated with journal metrics and characteristics of the studies. The level of statistical significance was set at $P < 0.05$.

RESULTS

One hundred and twenty-seven articles were included, of which 43 focused on HCC prognosis, 39 on prediction of pathological findings, 16 on prediction of the expression of molecular markers outcomes, 18 had a diagnostic purpose, and 11 had multiple purposes. The mean RQS was 8 ± 6.22, and the corresponding percentage was 24.15% ± 15.25% (ranging from 0.0% to 58.33%). RQS was positively correlated with journal impact factor (IF; ρ = 0.36, $P = 2.98 \times 10^{-5}$), 5-

years IF ($\rho = 0.33$, $P = 1.56 \times 10^{-4}$), number of patients included in the study ($\rho = 0.51$, $P < 9.37 \times 10^{-10}$) and number of radiomics features extracted in the study ($\rho = 0.59$, $P < 4.59 \times 10^{-13}$), and time of publication ($\rho = -0.23$, $P < 0.0072$).

CONCLUSION

Although MRI radiomics in HCC represents a promising tool to develop adequate personalized treatment as a noninvasive approach in HCC patients, our study revealed that studies in this field still lack the quality required to allow its introduction into clinical practice.

Key Words: Hepatocellular carcinoma; Systematic review; Magnetic resonance imaging; Radiomics; Radiomics quality score

Core Tip: This systematic review aimed at evaluating the status of magnetic resonance imaging (MRI) radiomic studies related to hepatocellular carcinoma (HCC) using the Radiomics Quality Score (RQS) to assess methodological quality. A systematic literature search identified 127 articles covering various steps of HCC management. The mean RQS was 8 ± 6.22, with significant variation. RQS was significantly correlated with journal impact factor (IF), 5-year IF, the number of patients involved, the number of radiomic features extracted, and the publication year. Despite the potential of MRI radiomics in HCC, its clinical implementation is hindered by a lack of quality in studies in this field.

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INTRODUCTION

Medical imaging has progressed over the last few decades from a simple diagnostic tool for diseases to a massive supply of quantitative data free of the normal subjective interpretation that characterizes conventional clinical practice. The introduction of technological advances and the quest for precision medicine have given rise to a new potential branch of research known as "radiomics". Radiomics is a quantitative technique that turns digitized medical pictures into high-dimensional mineable features that may be correlated with clinical endpoints such as pathological findings, treatment response, and survival. Radiomics can also be integrated with other quantitative data, such as genomics and pathomics data, to provide a comprehensive approach to disease[1-4]. As a quantitative analysis of digital images, radiomics has the potential to reveal specific disease characteristics that are otherwise inaccessible to the naked eye using conventional imaging modalities. This method may increase the quantity of clinically relevant data that may be extracted from medical images, offering the possibility of discovering innovative imaging biomarkers for the diagnosis, characterization, and prediction of outcomes in a wide range of diseases, including oncologic diseases[5]. In the field of oncology, the rationale behind radiomics is that biological tumor characteristics might be mirrored by quantifying medical image heterogeneity using extracted radiomic features, encompassing aspects of tumor progression, response to therapeutic interventions, and clinical outcomes. Quantitative imaging has garnered significant interest in the non-invasive detection of tumor heterogeneity, and recent radiomics studies across various oncological fields have shown a strong association between imaging heterogeneity and the characteristics of solid tumors[6].

Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related deaths worldwide and poses serious challenges for screening, early diagnosis and treatment firstly because most HCC is diagnosed at an advanced stage when curative treatment options are limited, and also because of its complex heterogeneity at multiple levels: heterogeneity between tumor nodules from the same patient (intertumor heterogeneity), within the same tumor nodule (intratumor heterogeneity) and between patients (interpatient heterogeneity)[7,8]. Furthermore, current clinical practice based on single bioptic or tumor tissue section fails to discover useful biomarkers, and many existing staging systems for HCC are based on postoperative pathological examinations, which cannot aid in preoperative decision-making[9]. In contrast to numerous other solid tumors, HCC can be diagnosed by using distinctive enhancement patterns on dynamic multiphasic CT or magnetic resonance imaging (MRI), without additional histopathologic confirmation[10,11]. Although imaging plays an important role in the screening, early identification, and management of HCC patients, the imaging evaluation of HCC is still based on subjective interpretation of qualitative imaging descriptors and tumor size estimate, both of which are prone to variability[10,12,13]. Of note, although CT is more generally available, faster, and needs less experience to administer and interpret pictures than MRI, its downsides include radiation exposure and low soft tissue contrast, which demands the use of iodinated contrast agents. The increased soft tissue contrast of MRI, on the other hand, enables for the examination of a range of tissue features that may be relevant in HCC therapy[14,15]. In this context, recent advantages in MRI radiomics can potentially address the urgent need for noninvasive, radiation-free strategies that can aid in the early detection of HCC and preoperative prediction of tumor behavior, as well as address the inherent variability of qualitative imaging descriptors and provide previously unavailable information to obtain a better

stratification of HCC patients for a more precise treatment decision making.

Over the last decade, there has been a significant increase in radiomics studies in the field of HCC. Many of these studies have demonstrated the effectiveness of radiomic features for differential diagnosis, grading, predicting microvascular invasion, overall survival, recurrence, and treatment response[16-19]. Nevertheless, radiomics is presently limited to academic literature in the context of HCC, as physicians question its utility due to the absence of a translation from research studies to clinical application. This is attributed, at least in part, to the overall deficiency of streamlined and productive methods for integrating imaging biomarkers into clinical practice[20-22]. Lambin *et al*[2] developed the Radiomics Quality Score (RQS) to provide a standardized evaluation of the radiomics performance, reproducibility, and clinical. The RQS metric system determines the validity and comprehensiveness of radiomics investigations. This tool is modality-independent tool and was designed to assess the methodological quality of radiomics studies. The methodology and analyses of a radiomics study are evaluated based on 16 criteria that reward or penalize, promoting the best scientific practice[2]. Recent research tried to examine the current state of the art in HCC radiomics, stressing the major concepts, clinical applications, and limitations[23-25]. However, it is clear from these research that the bulk of radiomic investigations on HCC have been conducted on CT, with only a few looking into MRI. Furthermore, the quality of science and reporting in HCC MRI radiomics research investigations is mainly unknown.

Hence, the objective of this study was to provide a comprehensive overview of the existing state of MRI radiomic investigations related to HCC. Simultaneously, we aimed to evaluate the methodological quality of each study using the RQS to assess the radiomics analyses conducted in prior publications. The study's goal is to promote the quality of MRI radiomics research studies in HCC as a diagnostic, prognostic, and/or predictive tool, to allow radiomics to become an appropriate medical decision-making tool by facilitating the combined analysis of clinical data and high-throughput imaging features, while taking advantage of the benefits arising from the MRI technique.

MATERIALS AND METHODS

Search strategy and selection criteria

A systematic search was conducted for all published studies exploring the role of MRI radiomics in the field of HCC. PubMed, Web of Science and Google Scholar electronic databases were comprehensively explored and used to build the search. Only studies published in the last six years were selected. The last search was performed on June 1, 2023. The search terms consisted in: ("radiomics" OR "texture" OR "histogram") AND ("MRI" OR "Magnetic Resonance Imaging") AND ("Hepatocellular Carcinoma" OR "HCC"). The literature search was limited to English language publications and studies of human subjects. Two reviewers, after having independently screened the identified titles and abstracts, assessed the full text of articles aiming at exploring MRI radiomics in the field of HCC and that were not review articles. For articles meeting these criteria with full text available, the following further selection criteria had to be fulfilled: Involvement of adult patients (age > 18 years); involvement of patients with HCC confirmed by pathology and/or surgery and/or overall analysis combined with medical history, clinical symptoms, and imaging data; presence of information about MRI protocol. Moreover, studies were excluded if they performed analyses on mixed patients (*e.g.*, groups of patients with multiple hepatic malignant diseases) that did not allow conclusions to be drawn only about HCC patients; if they did not evaluate an outcome measure; if they were focused only on semantic imaging features (radiologist-dependent). After selecting the studies that met the inclusion and exclusion criteria, reference lists of these studies were also searched in order to recruit any potential eligible studies. In addition, pre-existing reviews/systematic reviews/meta-analyses were also searched in order to recruit any other potentially eligible studies from their reference lists.

Planning and conducting the review

After the above-mentioned selection procedure, selected articles were analysed by two reviewers, and data useful for conducting the systematic review were collected in a predesigned sheet. Extracted data will include the following: first author name, publication year, Journal name, scientometric indexes [impact factor (IF), 5-years IF, CiteScore, H-index, first author IF with and without self-citations], study design, in particular prospective/retrospective, clinical purpose, specific output measured in the study, number and type of patients, imaging modalities used for radiomic feature extraction, information on region of interest (ROI)/volume of interest (VOI) placement (segmentation technique and ROI/VOI type), software used for radiomic feature extraction, number and features type, feature selection methods (if used), classification methods, information on if models were applied to a separate dataset, highest accuracy/most important results and main findings.

This systematic review was conducted according to the PRISMA statement[26].

Quality assessment with RQS

The methodological quality of each radiomics study was assessed by two reviewers using the RQS tool[2]. The assessment was performed independently, and any disagreement was resolved by consensus. RQS tool is composed of 16 items structured to assess various crucial steps in the workflow of radiomics analyses (see Supplementary Table 1). In particular, a maximum of 36 points can be assigned to each study: up to 2 points for the first RQS checkpoint (a single item, namely "Image protocol quality"), up to 3 points for the second RQS checkpoint (3 items, specifically on multiple segmentation strategies, the use of phantoms and multiple imaging time points) and up to 31 points for the third RQS checkpoint (12 items, encompassing feature extraction, exploratory analysis design as well as model building and validation). The total score ranges between −8 and 36 and can be translated into a final 0–100 RQS percentage, with −8 to

0 defined as 0%, indicating the lowest quality, and 36 as 100%, indicating the highest quality in terms of the methodology and reporting standards of the radiomics study[2].

Correlation analysis between RQS and journal metrics

Spearman's correlation (ρ) analysis was performed to explore if there was a correlation between RQS and journal metrics, comprising IF of the journal at the year of publication, 5-year IF, CiteScore, and H-index at the year of publication. Additionally, Spearman's correlation was used to explore the correlation between RQS and H-index of the first author at the year of publication of the study (both with and without self-citations), time of publication (calculated as time between the publication date and the date of last literature research, in months), as well as the association with the number of patients involved and the number of radiomic features extracted in the study. Finally, to explore if there was a difference in RQS according to clinical purpose of the study, a subgroup analysis using Kruskal-Wallis H test was performed. In case of significance, Wilcoxon rank-sum post hoc tests with Bonferroni correction were carried out on each pair of groups. The significance level was set at 0.05. All statistical analysis was performed using SPSS (version 27).

RESULTS

Study selection

A total of 537 articles were identified from scientific electronic scientific databases. Only 211 articles were retained after the removal of duplicates.

We reviewed the titles and abstracts of these records, excluding 59 due to non-compliance with inclusion criteria (29 unrelated to the topic, 16 were reviews, 5 conducted analyses on mixed patients, and 9 did not assess an outcome measure). The full text of 149 articles was assessed, leading to the exclusion of 16 off-topic articles. Additionally, four studies were excluded for not evaluating an outcome measure, and two for analyzing mixed patients. Thirteen more articles were found through references in selected articles or existing reviews/systematic reviews/meta-analyses, and seven of these were incorporated into the review. A total of 127 data sets were included in the review. Figure 1 shows the PRISMA flow diagram of the included studies based on the inclusion and exclusion criteria.

Characteristics of included studies

The details regarding the characteristics of the 127 studies chosen for this review are presented in Table 1. Approximately half of these studies (51 out of 127) were published in the last two years, and only 9 studies deviated from a retrospective design. Most of the selected studies (43 out of 127) explored radiomic approaches for HCC prognosis after surgical, radiofrequency ablation and/or trans-arterial chemo embolization treatment. Forty studies investigated the ability of radiomics in predicting pathological findings [*e.g.*, microvascular invasion (MVI), vessels encapsulating tumor clusters, histologic grade], of which 27 aimed at investigating the performance of radiomics analysis for MVI prediction. Sixteen studies aimed at exploring if MRI radiomics could infer the expression of molecular markers (*e.g.*, CK19, Ki67, GPC3) outcomes. Among the remaining studies, 24/127 aimed to evaluate the power of radiomics for distinguishing HCC from other solid hepatic lesions, while 11 had multiple aims.

The number of total included patients was 18.949, with a sample size varying from 17 to 602 patients (median: 309.5). Most studies (96 out of 127) explored more than one phase/sequence to perform radiomic analysis. Most studies (106 out of 127) performed 3D segmentation. In 114 of them, segmentation was manually performed, while in the remaining studies was used a semiautomatic (12 studies) or automatic (2 study) segmentation approach. Concerning software used for feature extraction, PyRadiomics was the most popular (used in 42 out of 127 studies), followed by AK software (used in 23 out of 127 studies) and Matlab (used in 19 out of 127studies). The number of radiomics features extracted from each phase/sequence ranged from 3 to 3144 (mean: 68 ± 206). Shape features were extracted in 55 out of 127 studies, first-order features in all but three studies, textural features in 82/127 studies, and features from filtered images (*e.g.*, wavelet, Laplacian of gaussian) in 34 out of 127 studies. Concerning feature selection algorithms, the Least Absolute Shrinkage and Selection Operator regression was the most widely used (used in 55 out of 127 studies). Other frequently used algorithms for feature selection were intra-class correlation coefficient (used in 25 studies), correlation (used in 12 studies) and minimum redundancy maximum relevancy (used in 9 studies). The performance metrics of the studies, when present, corresponded to accuracy in 9 out of 127 studies, area under the receiver operating characteristic curve (AUC) in 99 out of 127 studies and to C-index in 12 out of 127 studies. Most studies involved machine learning techniques for radiomic analysis, of which 51 splitted the subjects into training and test cohort to test the prediction models performance. Further details on these characteristics can be found in Table 1 and Supplementary Table 2.

Quality assessment with RQS

Supplementary Table 3 provides the RQS details of all included studies. The average total RQS score was 8 ± 6.22, corresponding to a percentage of 24.15% ± 15.25%, with a range from 0.0% to 58.33% (Figure 2). Concerning the first RQS checkpoint, nearly all studies, excluding ten, provided thorough documentation of the imaging protocol, yet none achieved the maximum points for utilizing a public protocol. In relation to the second RQS checkpoint (items 2 to 4), a majority of studies (84.25%, 107 out of 127) employed multiple segmentation, mainly by different radiologists, but none of the articles met the requirement for 'imaging at multiple time points' and only one article met the requirement for a 'phantom study'. With respect to the third RQS checkpoint (items 5 to 16), feature reduction techniques were applied in all but 15 studies (88.28%). Multivariable analysis with non-radiomics features was performed in 85 studies (66.92%) of

Table 1 Characteristics of included studies

Ref.	ST	CP	Specific outcome	NP (type)	Modalities used for feature extraction	Seg	Software used for feature extraction	Features number (type)	FS	CM	Model applied to a separate dataset?	Most important result	Main findings
Liu *et al* [42], 2023	R	PPF	MVI	104 (HCC)	T2WI	M, 3D	AK SOFTWARE	851 (first order, shape, GLCM, GLSZM, GLRLM, NGTDM, and GLDM)	LASSO, LR	LR	Yes	AUC = 0.867 in the TS, 0.820 in the VS	A prediction model using radiomic features from single T2WI can predict MVI in HCC
Wang *et al* [43], 2023	R	PR	LRT	100 (HCC)	AP, PVP, T2WI	M, 3D	3D SLICER	851 (first-order, shape, GLCM, GLDM, GLSZM, GLRLM, NGTDM and wavelet)	*t*-test/Mann Whitney, LASSO	ROC	Yes	AUC = 0.867	MRI-based radiomics analysis may serve as a promising and noninvasive tool to predict outcome of locoregional treatment in HCC patients
Gong *et al* [44], 2023	R	MC	PD-1/PD-L1	108 (HCC)	T2WI FS, AP, PVP	M, 3D	NS	352 (GLCM, GLRLM, intensity histogram, and shape)	ICC, *t*-test/ MANN WHYTNEY, LASSO	LR	Yes	AUC = 0.946 in the TS and 0.815 in the VS	A radiomics model based on multisequence MRI has the potential to predict the preoperative expression of PD-1 and PD-L1 in HCC
Zhang *et al* [45], 2023	R	MC	CK 19+/-HCC	311 (HCC)	T1WI, T2WI, DWI, AP, VP, and DP	M, 3D	uRP	2286 (first order, wavelet)	ICC, LASSO	LR	Yes	in the TS (C-index, 0.914), internal (C-index, 0.855), and external VS (C-index, 0.795)	The combined model based on clinic-radiological radiomics features can be used for predicting CK19+ HCC preoperatively
Zhang *et al* [46], 2023	R	PPF	MTM HCC	232 (HCC)	DCE-MRI	M, 3D	Pyradiomics	1037 (first order, shape GLRLM, GLSZM, NGTDM, GLCM, GLDM LoG and wavelet)	ICC, GBDT	LR, KNN, Naive-Bayes, Decision Tree, SVM	Yes	AUCs of 0.896 and 0.805 in the TS e VS	The nomogram containing radiomics, age, alpha-fetoprotein, tumour size, and tumour-to-liver ADC ratio revealed excellent predictive ability in preoperatively identifying the MTM-HCC Subtype
Dong *et al* [47], 2024	R	D, PR	VETC	221 (HCC)	DCE-MRI	M, 3D	Pyradiomics	1218 (FIRST ORDER)	ICC	LR, decision tree, RF, SVM, KNN, and Bayes	Yes	AUC = 0.844	The DLR model provides a noninvasive method

												to discriminate VETC status and prognosis of HCC patients preoperatively
Tabari *et al* [48], 2023	R	PPF	Pre-ablation tumor radiomics	97 (HCC)	AP, DCE-MRI	M, 3D	NS	112 first-order, (GLCM, GLDM, GLRLM, GLSZM, NGTDM)	mRMR	RF	Yes	AUC = 0.83	Pre-ablation MRI radiomics could act as a valuable imaging biomarker for the prediction of tumor pathologic response in patients with HCC
Cao *et al* [49], 2023	R	PR	RFS	249 (HCC)	T2WI FS, T1WI FS, DCE-MRI	M, 3D	Pyradiomics	NS (first-order, shape, and texture, wavelet, Laplacian)	LASSO	Cox regression	Yes	C-index = 0.893 TS, 0.851 (test set), 0.797 (external)	The combined radiomic model provides superior ability to discern the possibility of recurrence-free survival in HCC over the total radiomic and the clinical–radiological models
İnce *et al* [50], 2023	R	PPF	TARE	82 (HCC)	DCE-MRI	S, 3D	Pyradiomics	1128 (first-order, GLCM, GLDM, GLRLM, GLSZM, and NGTDM)	ICC, PCA, SFS	SVM, LR, RM, LightGBM	No	AUC = 0.94	Machine learning–based clinicoradiomic models demonstrated potential to predict response to TARE
Chen *et al* [51], 2023	R	PR	TACE	144 (HCC)	T2WI, AP, PVP, DP	M, 3D	Pyradiomics	110 (NS)	mRMR, LASSO, DNN	SVM, LR	Yes	AUC = 0.974	DNN model performs better than other classifiers in predicting TACE response. Integrating with clinically significant factors, the CD model may be valuable in pre-treatment counseling of HCC patients who may benefit the most from TACE intervention
Jiang *et al* [52], 2023	R	PPF	MVI	102 (HCC)	T1_in, T1_A, T2W, DWI	M, 3D	Pyradiomics	1967 (first-order, shapes, textures, GLCM, GLSZM, GLDM, GLRLM, and filter-transformed)	LASSO	ULR	Yes	AUC = 0.901, 0.923 for TS and VS	The multiparametric MRI-based radiomics nomogram is a promising tool for the preoperative diagnosis of peritumoral MVI in

												HCCs
Hu *et al* [53], 2023	R	D, MC	CK19+	110 (HCC)	AP, VP, HBP	M, 3D	PyRadiomics	1130 (shape, first order, GLCOM, GLRLM, GLSZ, GLDM)	ICC	RFE	No	AUC = 0.92	The established radiomics signature based on preoperative gadoxetic acid-enhanced MRI could be an accurate and potential imaging biomarker for HCC CK19 (+) prediction
Chong *et al* [54], 2023	R	MC, PR	Glypican 3-Positive HCC	259 (HCC)	T2WI, DWI, PRE, AP, PVP, TP and HBP	M, 3D	PyRadiomics	749 (first order statistics, shape and size) and textural property types (GLSZM, GLCM, GLDM, GLRLM, and NGTDM)	Test-retest procedure, ICC, LASSO, RF, SVM	LR, RF, SVM	Yes	AUC = 0.943 *vs* 0.931 TS and VS respectively	Preoperative EOB-MRI radiomics-based nomogram satisfactorily distinguished GPC3 status and outcomes of solitary HCC 5 cm
Hu *et al* [55], 2023	R	D, PPF	Functional liver reserve	403 (HCC)	DCE MRI	M, 3D	Pyradiomics	851 (shape, first-order GLCM, GLRLM, GLSZ, GLDM, NGTDM, wavelet)	ICC, Spearman's correlation	LR, SVM	No	AUC = 0.71	A radiomics model based on gadoxetic acid-enhanced MRI was constructed in this study to discriminate HCC with different histopathologic grades
Tao Y *et al* [56], 2023	R	MC	PD-L2	108 (HCC)	T2WI, AP, PV	M, 3D	R	1130	ICC, LASSO	ROC	No	AUC = 0.871	Prediction based on the radiomic characteristics of MRI could noninvasively predict the expression of PD-L2 in HCC
Yang *et al* [57], 2022	R	PR	ER	181 (HCC)	T1WI, T2WI	M, 3D	LIFEx	34 (Histogram, Shape)	LASSO	ROC	Yes	AUC = 0.79	The model for early recurrence of HCC after ablation based on the clinical, imaging, and radiomics features presented good predictive performance
Liu *et al* [58], 2023	R	PPF	MVI	161 (HCC)	AP, PVP, DP	M, 3D	3D Slicer, Pyradiomics	321 (shape, first-order histogram, GLCM, GLDM, GLRLM, GLSZM, NGTDM)	LASSO, ICC	LR	Yes	AUC = 0.87	The nomogram model can effectively predict MVI in patients with HCC
Zhang *et al* [59], 2022	R	PPF	MVI	189 (HCC)	HBP	M, 3D	IBEX SOFTWARE	1768	LASSO, ICC	nomogram	Yes	AUC = 0.884	Depending on the clinicoradiological factors and

												radiological features, nomograms can effectively predict MVI status in HCC patients
Sim *et al* [60], 2022	R	PPF	MVI	50 (HCC)	T1 AP, T1PVP	M, 2D	MaZda	290 (area, histogram, gradient, GLCM, GLRLM, autoregressive, and wavelet)	Mutual Information, recursive pruning	SVM	No	Accuracy = 0.878	Texture analysis of tumours on pre-operative MRI can predict presence of MVI in HCC
Zhang *et al* [61], 2022	R	PR	RFA, ER	90 (HCC)	T1WI, T2WI, CE-MRI	M, 2D	AK Software	1316 (first-order histogram, shape, texture, GLCM, GLRLM, GLSZM, NGTDM, GLDM, and local binary pattern, high-order, and wavelet)	ANOVA	RF, LASSO	Yes	AUC of 0.822 in the TS and 0.812 in the VS	The multi-parametric MRI-based radiomics nomogram has a high predictive value for ER of small HCC after RFA
Zhao *et al* [62], 2023	R	PR	HAIC	112 (HCC)	T2WI	M, 3D	AK software	396 (histogram, form factor, texture, GLZSM, GLCM, GLRLM, and Haralick)	LASSO	ROC	Yes	Accuracy = 0.81	The nomogram based on the combined model consisting of MRI radiomics and ALBI score could be used as a biomarker to predict the therapeutic response of unresectable HCC after HAIC
Lu *et al* [63], 2022	R	PPF	MVI	165 (HCC)	T2WI, DWI (b = 800 s/mm^2), T1WI, AP, PP, TP, and HBP	M, 3D	Pyradiomics	1227 (shape, first-order, texture, GLSZM, GLRLM, GLCM, NGTDM, and GLDM)	LASSO	multivariate LR	Yes	AUC = 0.826	The combined model based on radiomics features of Gd-EOB-DTPA enhanced MRI, tumour margin, and peritumoural hypointensity was valuable for predicting HCC MVI
Yang *et al* [64], 2022	R	PPF	MVI	110 (HCC)	DCE-MRI	M, 3D	A.K. Software	11 (Grey Histogram, GLCM)	NO	ROC	No	AUC = 0.797	The combination of MR image features and texture analysis may improve the efficiency in prediction of MVI
Ameli *et al* [65], 2022	R	D	Degree of tumor differentiation	129 (HCC)	ADC, VE MAPS	S, 3D	MATLAB R2017B	95 (global, histogram, GLCM, GLRLM, GLSZM, NGTDM)	multi-class classification algorithm	RF	Yes	AUC = 0.832	The addition of radiomics-based texture analysis improved HCC grading over that of

												ADC or venous enhancement values alone
Li *et al*[66], 2022	R	PR	ER	302 (HCC)	T2WI, DWI (800 s/mm^2), AP, and PVP	M, 3D	Pyradiomics	853 (shape, first order, texture, and wavelet)	SPSS, LASSO, ICC	ROC	Yes	AUCs of 0.91 and 0.87 in the TS and VS	The proposed predictive model incorporating clinico-radiological factors and the fusion radiomics signature derived from multiparametric MR images may be an effective tool for the individualized prediction of postoperative ER in patients with HCC
Zeng *et al* [67], 2022	R	PPF	BETA-CATENIN MUTATION	98 (HCC)	AP, PVP, DP, HBP	M, 3D	Pyradiomics	1674 (first order, GLCOM, GLSZM, GLRLM, GLDM)	T-test, fisher's exact test	LSVC	Yes	AUC = 0.86	The RHBP radiomics model may be used as an effective model indicative of HCCs with b-catenin mutation preoper-atively
Aujay *et al* [68], 2022	R	PR	TARE	22 (HCC)	AP, PVP	M, 3D	Pyradiomics	107 (Shape, first- and second- order)	Mann-Whitney U test	LR	No	AUC = 0.92	Radiomics could aid in the prediction of early treatment response following TARE in patients with HCC
Chen *et al* [69], 2022	R	PPF	MVI	415 (HCC)	T1WI, T2WI, DWI, AP, PVP, HBP	M, 3D	R	1409 (First order, shape, two order texture, Laplacian, wavelet, logarithmic, and exponential filters)	LASSO	SVM, XGBoost, RF, LR	Yes	AUC = 0.979	Machine learning with an LR classifier yielded the best radiomics score for HBP and DWI. The radiomics nomogram developed as a noninvasive preoperative prediction method showed favorable predictive accuracy for evaluating MVI in sHCC
Wu *et al* [70], 2023	R	D	DP-HCC	179 (DPHCC, non DPHCC)	DCE-MRI	M, 3D	PyRadiomics	1781 (first-order statistics, shape, and texture)	PCC, RFE	SVM, LR, LR-LASSO	Yes	AUC = 0.908	MRI radiomics models may be useful for discriminating DPHCC from non-DPHCC before

												surgery
Li *et al*[71], 2022	R	PPF	MVI	113 (HCC)	T2WI, T1WI, DCE MRI	M, 2D	MaZda	101 (histogram, GLCOM, GLRLM)	*t*-test, Mann-whitney *U* test	ROC	No	AUC = 0.939	Noninvasive MRI radiomic model based on MDF values and imaging biomarkers may be useful to make preoperative prediction of MVI in patients with primary HCC
Wang *et al* [72], 2022	R	PR	ER	190 (HCC)	T2WI, T2WI FS, DCE MRI	M, 3D	PyRadiomics	1316 (first-order histogram, texture, shape, GLZSM, GLRLM, GLCM, GLDM, and NGTDM, wavelet, local binary pattern, and Laplacian of Gaussian)	ICC, LASSO	LASSO, ICC, LR	Yes	AUC = 0.90	The predictive model incorporated the clinical–radiological risk factors and radiomics features that could adequately predict the individualized ER risk in patients with solitary HCC ≤ 5 cm
Zhang *et al* [73], 2023	P	PPF	MVI	602 (HCC)	T1WI, T2WI, AP, VP, HBP and ADC	M, 3D	Radcloud platform	1409 (First order, second order, shape, texture)	LASSO	LR, RF, SVM	Yes	AUC = 0.824 E 0.821 in the TS and VS	The combination of clinicoradiological factors and fusion radiomics signature of AP and VP images based on Gd-EOB-DTPA-enhanced MRI can effectively predict MVI
Brancato *et al*[74], 2022	R	PPF	IABR	38 (HCC)	T2WI, DCE-MRI	M, 3D	Pyradiomics	386 (shape, first-order, and texture)	correlation filter, Wilcoxon-rank sum test, MI	LR	No	AUC = 0.96	Radiomics MRI based on T2 and DCE-MRI revealed promising results concerning both HCC detection and grading
Fan *et al* [75], 2022	R	PR	VEGF	202 (HCC)	AP, PV, HBP, BP, DP	M, 3D	PyRadiomics	1906 (first order, shape)	ICC, ANOVA	LR	Yes	AUC = 0.892 in the TS, 0.800 in the VS	The combined model acquired from Gd-EOB-DTPA enhanced MRI could be considered as a credible prognostic marker for the level of VEGF in HCC
Gao *et al* [76], 2022	R	PPF	MVI	115 (HCC)	T2WI, T1WI, AP, PVP, DP, and HBP	M, 3D	Pyradiomics	107 (shape, first-order, and textural)	LR, SVC, RFC, and AdaBoost	LR	Yes	AUCs of 0.866 in the TS and 0.855 in the VS	The fusion model of multi-region radiomics achieves an enhanced prediction of the individualized

												risk estimation of MVI in HCC patients
Hu *et al* [77], 2022	R	PPF	MVI	501 (HCC)	T1WI, AP, PVP, HBP	M, 3D	Pyradiomics	2600 (first order, shape, GLCM, GLRLM, GLSZM, GLDM and NGTDM)	LASSO	ROC	Yes	AUC = 0.962	The radiomics signatures of the dual regions for tumor and peritumor on AP and PVP images are of significance to predict MVI
He *et al* [78], 2022	R	PR	DFS, OS	103 (HCC)	DCE MRI	M, 2D	AK software	1217 (First order, Morphological, GLCM, GLRLM, GLSZM, GLDM, LOG)	ICC, Lasso, cox regression	LASSO	Yes	AUC = 0.884	Multimodal radiomics models can serve as effective visual tools for predicting prognosis in patients with liver cancer
Ren *et al* [79], 2023	R	PR	HCC grade	270 (HCC)	T2WI	M, 3D	Pyradiomics	1197 (first-order and shape, GLCM, GLRLM, GLRM, and spatial gray scale corre-lation matrix)	MIC, Spearman's correlation, LR	LR	Yes	AUC = 0.864	The clinical–radiomics model integrating radiomics features and clinical factors can improve recurrence predictions beyond predictions made using clinical factors or radiomics features alone
Luo *et al* [80], 2022	R	PR	TACE	61 (HCC)	T1WI, T1WI AP, T1WI PP, T2WI, DWI (b = 800), ADC	M, 3D	Pyradiomics	1782 (shape, GLCM, GLRLM, GLSZM, NGTDM)	RF, single cox regression	ROC	No	AUC = 0.71	Radiomic signatures derived from pretreatment MRIs could predict response to combined Lenvatinib and TACE therapy. Furthermore, it can increase the accuracy of a combined model for predicting disease progression
Wang *et al* [81], 2022	R	PPF	MVI	113 (HCC)	AP	M, 3D	MATLAB	12 (first order)	NO	Mann-Whitney *U* test, LR	No	AUC = 0.741	Peritumoral AP enhanced degree on MRI showed an encouraging predictive performance for preoperative prediction of MVI
Mao *et al* [82], 2022	R	PPF	HCC GRADE	122 (HCC)	T2WI (AP, HBP phases)	M, 3D	Image Analyzer	121 (histogram, shape, texture, GLRLM and GLCM)	ICC	ANN, LR	Yes	AUC = 0.889	Prediction models consisting of clinical parameters and Gd-

												EOB-DTPA-enhanced MRI radiomic features could distinguish between high-grade HCCs and low-grade HCCs
Anderson *et al*[83], 2023	P	PR	IVIM	17 (HCC)	DWI-MRI	M, 2D	Matlab	3 (10^{th}, 50^{th}, and 90^{th} percentiles)	NO	Wilcoxon signed-rank test	No	NS	DW-MRI with IVIM and histogram analysis revealed significant reductions of D* early after treatment as well as an association between D at baseline and smaller tumor growth at three months
Li *et al*[84], 2022	R	PPF	SEV, MVI	43 (HCC)	DWI, DCE-MRI	M, 2D	Matlab, SPSS, Medcalc	8 (Histogram)	NO	ROC	No	AUC = 0.863	Histogram parameters DDC and ADC, but not the α value, are useful predictors of MVI. The fifth percentile of DDC was the most useful value to predict MVI of HCC
Li *et al*[85], 2022	R	PPF	MVI	301 (HCC)	T1WI, T2WI	M, 3D	MITK SOFTWARE	328 (first-order, GLCM, GLRLM, form factor)	LASSO, ANOVA, MANN-WHITNEY TEST	LASSO	Yes	AUC = 0.914	The preoperative MRI-based radiomic-clinical model predicted the MVI of HCC effectively and was more efficient compared with the radiomic model or clinical model alone
Wang *et al* [86], 2022	R	D	DD (cCC-HCC, HCC, CC)	196 (33 cHCC-CC, 88 HCC and 75 CC)	DCE (ART, PVP, DP)	M; 3D	Pyradiomics	1316 (shape, first-order, texture - GLCM, GLSZM, GLRLM, GLDM, NGTDM- from original, LoG and wavelet filtered images)	MI, F-test, Chi2-test, LASSO	SVM	No	AUC = 0.91	The classification ability of cHCC-CC, HCC and CC can be further improved by extracting MRI high-order features and using a two-level feature selection method
Yang *et al* [87], 2021	R	PPF	MVI	201 (HCC)	DCE (Pre-T1WI, AP, PVP, DP and HBP)	S; 3D	AK software	851 (shape, first-order, texture-GLCM, GLSZM, GLRLM, GLDM, NGTDM-, wavelet-	mRMR, LASSO	ROC; LR	Yes	Radiomics: AUC = 0.896 (TS), 0.788 (VS); Radiomics + clinical: AUC = 0.932 (TS), 0.917	The preoperative nomogram integrating clinicoradiological risk factors and the MR radiomics signature

								transformed)				(VS)	showed favourable predictive efficiency for predicting MVI
Lv *et al*[88], 2021	R	PR	AIR of RFA-treated HCC	58 (HCC)	DCE	S; 3D	AK software	396 (histogram, GLCM, GRLM, GLSZM, formfactor)	LASSO	LASSO, ROC	Yes	AUC = 0.941 and 0.818 in the TS and VS	The predictive nomogram integrated with clinical factors and CE-T1WI -based radiomics signature could accurately predict the occurrence of AIR after RFA
Yu *et al* [89], 2022	R	PPF, PR	VECT, PFS in VETC + and VETC-patients	182 (HCC)	HBP	M; 3D	Pyradiomics	1316 (shape, first-order, texture-GLCM, GLRLM, GLSZM, GLDM, NGTDM-)	LASSO	Multivariate LR; forest, SVM; DT	Yes	AUC = 0.972 (peritumoral radiomics model), AUC = 0.91 (intratumoral model)	The intratumoral or peritumoral radiomics model may be useful in predicting VETC and patient prognosis preoperatively. The peritumoral radiomics model may yield an incremental value over intratumoral model
Fang *et al* [90], 2021	R	PR	PFS of TACE + RFA treated HCC	113 (HCC)	DCE (HAP, PVP, SPP, and DP)	S; 3D	AK software	396 (histogram, GLCM, GLSZM GRLM)	LASSO	Cox regression; ROC	Yes	C-index radiomics: 0.646 and 0.669 in TS and VS; C-index combined model: 0.772 and 0.821 in TS and VS	A nomogram combining radiomics and clinical factors predicted the PFS of intermediate and advanced HCC treated with TACE plus RFA
Yang *et al* [91], 2021	R	MC	CK19+ HCC	257 (HCC)	T2WI; DWI	M; 3D	MATLAB	968 (shape, first-order, texture-GLCM, GLRLM, GLSZM, NGTDM-, wavelet)	Univariate analysis, mRMR	Multiple LR; SVM; RF; ANN	Yes	ANN-model: AUROCs = 0.857, 0.726, and 0.790 in the TS and VS A and B	The combined model based on mpMRI-radiomics accurately classify CK19+ HCC
Chen *et al* [92], 2021	R	MC	CK19+ HCC	141 (HCC)	HBP	S; 3D	Python (U-Net)	1024 (Deep semantic)	grid search	GBDT	Yes	AUC = 0.820 and 0.781 in TS and VS	DCE-MRI-based radiomics DLR model can preoperatively predict CK19-positive HCCs
Horvat *et al* [93], 2021	R	PR	Sustained complete response in RFA-treated HCC	34 (HCC)	DCE (AP and EP)	M; 3D	Pyradiomics	107 (shape, first-order, texture-GLDM, NGTDM, GLSZM, GLCM-)	NO	ROC	No	AUC > 0.7	Second-order features extracted from equilibrium phase obtained highest discriminatory performance
Alksas *et al*	R	D	DD (types and	95 (38 benign	DCE (Pre-	M; 3D	NS	249 (morphological,	Wrapper approach,	RF; SVM; NB,	No	Accuracy = 0.88	The identified

[94], 2021			grades of liver tumors)	tumors, 19 intermediate tumors, 38 HCC)	T1WI, LAP, PVP, and DP)			functional, first-order, texture-GLCM, GLRLM-)	and Gini impurity-based selection	KNN; LDA			imaging markers and CAD system can early and accurately detect and grade liver cancer
Chong *et al* [95], 2021	R	PR	2 yr RFS after hepatectomy	23 (HCC)	DCE (AP, PVP, TP, HBP)	M; 3D	Pyradiomics	2950 (shape, first-order, texture-GLCM, GLRLM, GLSZM, GLDM, NGTDM- from original and filtered images -Wavelets, Gaussian, Laplacian Sharpening-)	Inter-correlation, LASSO	LR, RF, SVM	Yes	AUC = 0.93 and 0.84 in TS and VS	DCE-MRI-based peritumoral dilation radiomics is a potential preoperative biomarker for early recurrence of HCC patients without MVI
Ding *et al* [96], 2021	R	D	DD (HCC *vs* FNH)	224 (149 HCC, 75 FNH)	AP and PVP	M; 3D	Pyradiomics	2260 (shape, first-order, texture - GLDM, GLCM, GLRLM, GLSZM, NGTDM-, from original LoG and wavelet filtered images)	mRMR, RF, correlation, LASSO	LR	Yes	AUC combined model = 0.984 and 0.972 in TS and VS	The combined model can differentiate HCC from FNH in non-cirrhotic liver with higher accuracy than the clinical model
Fan *et al* [97], 2021	R	MC	Ki67+ HCC	51 (HCC)	DCE (AP, PVP, HPB); T2WI	M; 3D	Pyradiomics	1300 (shape, first-order, texture - GLCM, GLSZM, GLRLM, GLDM, NGTDM- from original, LoG and wavelet filtered images)	LASSO	LR	Yes	Combined model: AUC = 0.922 (TS) and 0.863 (VS)	Combined AP-Rad-score-serum AFP model can preoperatively predict Ki-67 expression in HCC and outperforms AP-based radiomics model
Gao *et al* [98], 2021	R	PPF	MVI	225 (HCC)	T2WI	M; 3D	Matlab, SE-DenseNet	180 low level (intensity, shape, GLCM, GLRLM) + high-level semantic with CNN	LASSO	LR, KNN, RF, SVM, CNNs	Yes	AUC = 0.826	The proposed ensemble learning algorithm is proved to be an effective method for MVI prediction
Li *et al*[99], 2022	R	MC	GOLM1, SETD7, and RND1 expression levels	92 (HCC)	T2WI	M; 2D	MATLAB	307 (first-order statistics, GLCM, GLRLM, GLSZM, NGTDM), with five, LBP, fractal analysis, shape metrics, FOS, variance, power)	Correlation, RELIEFF	SVM	Yes	$r = 0.67$	MRI radiomics features could help quantify GOLM1, SETD7, and RND1 expression levels and predict the recurrence risk for early-stage HCC patients
Shi *et al* [100], 2022	R	PR	Functional liver reserve	60 (HCC)	HBP	M; 3D	QTIELAB	165 (shape, histogram, texture-GLCM, GLRLM, GLZSM-)	Boruta algorithm	RF	No	AUC = 0.90, 0.95, 0.99 for ICG R15 < 10%, < 15%, and < 20%	Radiomics analysis of Gd-EOB-DTPA enhanced hepatic MRI can be used for assessment of functional liver

												reserve in HCC patients
Dai *et al* [101], 2021	R	PPF	MVI	69 (HCC)	DCE (Pre-T1WI, AP, PVP or HBP)	M; 3D	Matlab	106 (texture -GLCM, GLRLM, GLSZM, SGLDM, NGTDM, and NGLDS-)	LASSO, SVM-RFE, mRMR, LASSO-RFE	GBDT; SVM; LR; RF	No	AUC = 0.792 for HBP model	The radiomics model based on the HBP had better predictive performance than those based on the AP, PVP, and pre-enhanced T1W
Fan *et al* [102], 2021	R	PPF	VECT+ HCC	81 (HCC)	DCE (AP and HBP)	M; 3D	Pyradiomics	1316 (first-order, texture -GLCM, GLSZM, GLRLM, GLDM, NGTDM- from original, wavelet and LoG filtered images)	ICC, LASSO	ROC; LR	No	AUC = 0.84	Texture analysis based on Gd-EOB-DTPA-enhanced MRI can help identify VETC-positive HCC
Yang *et al* [103], 2021	R	PPF	Poorly differentiated HCC	188 (HCC)	T1WI, T2WI, DCE (AP, PP and DP)	M; 3D	LIFEx	200 (shape, histogram, texture -GLCM, NGLDM, GLRLM, GLZLM-)	LASSO	LASSO	Yes	Model1: AUC = 0.623 and 0.576 in TS and VS, while it is 0.576 in the validation cohort. Model2: AUC = 0.721, and 0.681 in TS and VS	The MRI-based radiomics signature and clinical model can distinguish HCC patients that belong in a low differentiation group fromother patients
Chen *et al* [104], 2021	R	PPF	MVI	269 (HCC)	T2WI; DWI, DCE (AP, PVP, and HBP)	M; 3D	Pyradiomics	1395 (first-order, GLRLM, GLCM from original, Laplacian, logarithmic, exponential, and wavelet filtered images)	Variance threshold, LASSO	KNN SVM, XGBoost, RF, LR, DT	Yes	For HBP model: AUC = 0.942 (SVM), 0.938 (XGBoost), and 0.936 (LR)	Radiomics signatures with machine learning can further improve the ability to predict MVI and are best modeled during HBP
Kong *et al* [16], 2021	R	PR	Response to TACE	99 (HCC)	T2WI	M; 3D	AK software	396 (histogram, texture-GLSZM, GLCM, GLRLM-)	LASSO, correlation	ROC	Yes	AUC = 0.861 and 0.884 in TS and VS	The radiomics and clinical-based nomogram can well predict TR in intermediate-advanced HCC
Zhao *et al* [105], 2021	R	MC	GPC3	143 (HCC)	DCE-MRI, DWI	M; 3D	MedCalc, R	6 (Histogram)	NO	Mann-Whitney *U* test	No	C-INDEX = 0.804	Elevated serum AFP levels and lower 75th percentile ADC values were helpful in differentiating GPC3-positive and GPC3-negative HCCs. The combined nomogram achieved satisfactory preoperative risk

													prediction of GPC3 expression in HCC patients
Song *et al* [106], 2021	R	PPF	MVI	601 (HCC)	T2WI FS; DWI; ADC; DCE (AP, PVP, and DP)	M; 3D	PyRadiomics	110 (shape, first-order, texture)	PCA, ANOVA	SVM, AE, LDA, RF, LR, LASSO, AdaBoost, DT, Gaussian process, NB, DL	Yes	DLC model: AUC = 0.931 for MVI prediction; AUC = 0.793 for MVI-grade stratification	DLC model predicts and grades MVI better than DL model
Zhong *et al* [107], 2021	R	D	DD (small HCC 3 cm *vs* benign nodules)	150 (112 HCC, 44 benign nodules)	in phase sequence; T2WI FS; ADC	M; 2D	MaZda	837 (histogram, GLCM, RLM, wavelet, absolute gradient, autoregressive model)	ICC, Mann-Whitney, LASSO	LR; ROC	No	AUC = 0.917	MRI-based radiomics analysis showed additive value to the LI-RADS v 2018 algorithm for differentiating small HCCs from benign nodules in the cirrhotic liver
Zhao *et al* [105], 2021	R	MC	GPC3 expression	143 (HCC)	ADC	M;3D	MR Multiparametric Analysis software	6 (histogram)	Univariate analysis (*t*-test, Mann-Whitney, Pearson, χ^2, Fisher)	LR	No	C-index = 0.804	The combined nomogram achieved satisfactory preoperative risk prediction of GPC3 expression in HCC patients
Chen *et al* [108], 2021	R	PR	Post hepatectomy liver failure	144 (HCC)	HBP	M; 2D	AK software	1,044 (shape, first-order, texture-GLSZM, GLCM, GLRLM-)	Correlation, RFE	LR; ROC; liver failure model	Yes	AUC = 0.956 and 0.844 in TS and VS	The LF model is able to predict PHLF in HCC patients
Liang *et al* [109], 2021	R	PPF	MVD	30 (HCC)	DCE	M; 2D	AK software	376 (histogram, texture-GLSZM, GLCM, GLRLM-)	Mann-Whitney	LR	No	AUC = 0.83 and 0.94	DITET model provides a better indication of the microcirculation of HCC than SITET
Zhang *et al* [110], 2021	R	PR	RFS of HCC patients treated with surgical resection	153 (HCC)	T2WI FS; DCE (AP, PVP, and HBP)	M; 3D	Pyradiomics	107 (shape, first-order, texture - GLCM, GLSZM, GLRLM, GLDM, NGTDM-)	LASSO	LASSO Cox regression	Yes	C-index 0.725	The prediction model combining MRI radiomics signatures with clinical factors predicts the prognosis of surgically resected HCC patients
Zhang *et al* [111], 2021	R	PR	RFS after curative ablation	132 (HCC)	T2WI FS; T1WI FS; DCE (AP, PVP, and HBP)	M; 3D	Pyradiomics	1316 (shape, first-order, texture - GLCM, GLSZM, GLRLM, GLDM, NGTDM-, LoG, wavelet)	RandomForestSRC	Cox regression; random survival forest; ROC	Yes	C-index = 0.706	The radiomics model combining DCE-MRI with clinical characteristics could predict HCC recurrence after curative ablation
Zhang *et al*	R	PPF	MVI	195 (HCC)	T2WI FS;	M; 3D	AK software	396 (histogram,	ANOVA, Mann-	Multivariate LR	Yes	AUC = 0.901 and	The combined

[112], 2021					DWI; ADC; DCE (AP, PP, DP)			GLCM, GLSZM, RLM, formfactor, haralick)	Whitney U-test, correlation, LASSO			0.840 in the TS and VS	radiomics-clinical model can preoperatively and noninvasively predict MVI in HCC
Zhao *et al* [113], 2021	R	PR	Response to TACE	122 (HCC)	DCE (AP, PVP, and DP)	M; 3D	AK software	789 (histogram,GLCM, GLRLM, GLZSM, Haralick,Gaussian transform)	ICC, Spearman's correlation, univariate LR, LASSO	LR; ROC	Yes	AUC = 0.838 and 0.833 in TS and VS	The combined model (radiomics score + clinical-radiological risk factors) showed better performance than the clinical-radiological model in predicting TACE efficacy in HCC patients
Kuang *et al* [114], 2021	R	PR	Predict short-term response after TACE in HCC	153 (HCC)	T2WI; DCE (AP)	A; 3D	AK software	396 (shape, histogram, GLSZM, GLCM, RLM)	mRMR, LASSO	LR	Yes	AUC = 0.83 and 0.81 in TS and VS	MRI-based nomogram has greater predictive efficacy to predict the response after TACE than radiomics and clinics models alone
Meng *et al* [115], 2021	R	PPF	MVI	402 (HCC)	T1WI, T2WI, DWI, CE-CT	M, 3D	Pyradiomics	1288	ICC, MANN-WHITNEY, LASSO	LR	Yes	AUC = 0.804	CT and MRI had a comparable predictive performance for MVI in solitary HCC. The RS of MRI only hadsignificant added value for predicting MVI in HCC of 2–5 cm
Zhu *et al* [116], 2021	R	D	DD (MTM-HCC *vs* HCC)	88 (32 MTM-HCCs, 56 Non-MTM-HCC)	T2WI FS; in-phase and out-of-phase sequences; DCE (AP, PVP, and DP)	M; 2D	MaZda	101 (histogram, the absolute gradient, GLRLM, GLCM, autoregressive model and wavelet transform)	Fisher, MI, POE + ACC, LASSO	LR; ROC	No	AUC = 0.785	A DCE-MRI-based radiomics nomogram can predict MTM-HCC
Liu *et al* [117], 2021	R	PR	TACE, MWA	102 (HCC)	T1WI, T2WI, PVP	M, 2D	MaZda	20 (First order, GLCM)	NS	ROC	No	AUC = 0.876	MR imaging texture features may be used to predict the prognosis of HCC treated with TACE combined with MWA
Chong *et al* [118], 2021	R	PR	MVI, RFS after curative surgery (HCC≤ 5 cm)	356 (HCC)	DWI, DCE (Pre-T1WI, AP, PVP, TP, HBP)	M; 3D	Pyradiomics	854 (shape, first-order, texture - GLCM, GLDM, GLRLM, NGTDM, GLSZLM- from original and wavelet	LASSO	RF; LR	Yes	AUC = 0.920 with RF, 0.879 with LR in validation cohort	Preoperative radiomics-based nomogram using random forest is a potential biomarker of MVI and RFS

								filtered images)					prediction for solitary HCC ≤ 5 cm
Gu *et al* [119], 2020	R	MC	GPC3+ HCC	293 (HCC)	DCE (DP)	M; 3D	Pyradiomics	853 (shape, histogram, texture - GLCM, GLSZM, GLRLM, GLDM, NGTDM-, wavelet)	ICC, Mann-Whitney, Fisher	LR; SVM	Yes	AUC = 0.926 and 0.914 in TS and VS	The combined AFP + radiomics nomogram may provide an effective tool for noninvasive and individualized prediction of GPC3-positive in HCC patients
Zhao *et al* [120], 2021	R	PR	ER after partial hepatectomy	113 (HCC)	T2WI; in-phase and out-of-phase sequences; DWI; DCE (AP, PVP, and DP)	M; 3D	AK software	1146 (shape, histogram, texture - GLCM, GLRLM, GLSZM-)	Spearman's correlation, LASSO, stepwise LR	Multivariate LR	Yes	Radiomics: AUC = 0.771 in the VS. Combined nomogram: AUC = 0.873	A combined nomogram incorporating the mpMRI radiomics score and clinicopathologic-radiologic characteristics can predict ER (≤ 2 yr) in HCC
Ai *et al* [121], 2020	R	D	DD (HCC, HH, HC)	89 (33 HH, 22 HC, 34 HCC)	IVIM	M; 3D	MITK-DI	13 (histogram)	Kruskal-Wallis	ROC	No	AUC = 0.883	A multiparametric histogram from IVIM is an effective means of identifying HH, HC, and HCC
Shaghaghi *et al*[122], 2021	R	PR	Post-TACE OS and TFS	104 (HCC)	ADC	S; 3D	NS	3 (mean, skewness, and kurtosis)	NO	NO	No	Significant results for changes in ADC mean and Kurtosis	Changes in mean ADC and ADC kurtosis can be used to predict post-TACE OS and TFS in well-circumscribed HCC
Li *et al* [123], 2020	R	D	DD (HCC *vs* HMRC)	75 (41 HCC, 34 HMRC)	DCE	M; 2D	OmniKinetic	67 (First order, histogram, GLCM, Haralick, RLM)	*t*-test, ROC	FDA	No	AUC = 0.86 (radiomics + pharmacokinetic) and 0.89 (DA based on radiomics)	A model based on DCEMRI radiomics and pharmacokinetic parameters was useful for differentiating HCC from HMRC
Geng *et al* [124], 2021	R	PPF, MC	MVI; GRADE; CK-7, CK-19, GPC3 expression status	53 (HCC)	SWI	M;3D	PyRadiomics	107 (first-order, shape, GLCM, GLRLM, GLSZM, NGTDM)	ICC	LR	No	AUC = 0.905 (CK-19+), 0.837 (CK-7+), 0.800 (high histopathologic grade) and 0.760 (GPC-3+)	Extracting the radiomics features from SWI images was feasible to evaluate multiple histo-pathologic indexes of HCC
Zhang *et al* [125], 2020	R	PR	OS after surgical resection	136 (44 MCC, 59 HCC, 33 CHCC)	DCE (EP); DWI	M; 3D	AK software	384 (histogram, GLCM, GLSZM, RLM, formfactor,	mRMR method and the elastic network algorithm	Multivariable cox regression	No	Parameters independently associated with OS	Clinicopathological and radiomics features are

							haralick)				($P < 0.05$)	independently associated with the OS of patients with primary liver cancer
Zhang *et al* [126], 2020	P	PR	OS after surgical resection	120 (HCC)	T2WI FS; DCE (AP, PVP, TP, and HBP)	S; 2D	AK software	350 (histogram, form factor, GLCM, GLRLM)	ICC, LASSO	LASSO Cox regression	Yes	C-index = 0.92	Radiomics + clinic-radiological predictors can efficiently aid in preoperative HCC prognosis prediction after surgical resection with respect to clinic-radiological model
Hectors *et al*[127], 2020	P	PR	6- and 12- week response to 90 yr	24 (HCC)	DCE-MRI, IVIM-DWI	M; 3D	Matlab	40 DCE MRI histogram parameters and 20 IVIM DWI histo-gram parameters	Stepwise feature selection	LR	No	AUC = 0.92	Diffusion and perfusion MRI can be combied to evaluate the response of HCC to radioembolization
Shi *et al* [128], 2020	P	PPF, MC	HCC GRADE, KI67+ HCC, CAPSULE FORMATION+	52 (HCC)	IVIM	M; 3D	ImageJ, Mazda	15 (histogram)	*t*-test	LR	No	AUC = 0.92 (grading), 0.86 (Ki67+) and 0.84 (capsule formation)	Multiple prognostic factors can be accurately predicted with assistance of histogram metrics sourced from a single IVIM scan
Feng *et al* [129], 2020	R	D, MC	DD	104 (HCC)	Gd-EOB-DTPA-enhanced MRI and T2WI	M, 3D	Mazda	262 (Histogram, GLCOM, GLRLM, WAVELET TRANSFORM)	PCA, LDA, NDA, RDA	ROC	No	AUC = 0.879	Texture analysis of Gd-EOB-DTPA-enhanced MRI and T2WI was valuable and might be a promising method in identifying the HCC grade
Nebbia *et al* [130], 2020	R	PPF	MVI	99 (HCC)	T2WI; DCE (AP and PP); DWI	M; 3D	Pyradiomics	100 (shape, first-order, texture - GLCM, GLDM, GLSZM-)	LASSO	SVM; DT; KNN, NB	No	AUC = 0.867	Information from mpMRI sequences is complementary in identifying MVI
Schobert *et al*[131], 2020	R	PR	Response to DEB-TACE, PFS	46 (HCC)	DCE (HAP, PVP, and DP)	M; 3D	Pyradiomics	14 (shape, first-order)	Univariate analysis, stepwise forward selection	LinearRegression; Cox regression; Kaplan–Meier analysis	No	High NLR and PLR correlated with non-spherical tumor growth ($P = 0.001$ and $P < 0.001$)	This study establishes the prognostic value of quantitative inflam-matory biomarkers associated with aggressive nonspherical tumor growth and predictive of poorer tumor response and shorter PFS after DEB-TACE

Sun *et al* [132], 2020	R	PR	Early progression of unresectable HCC after TACE	84 (HCC)	T2WI; DWI; ADC	M; 3D	Pyradiomics	1597 (first-order, shape, texture - GLCM, GLRLM, GLSZM, NGTDM, GLDM-)	Variance threshold, Pearson's correlation, LASSO	LR	Yes	AUC = 0.800	mpMRI-based radiomic model predicts the outcome of TACE therapy for unresectable HCC outperforms monomodality radiomic models
Wilson *et al* [133], 2020	R	PPF, PR	MVI, OS, DFS after surgery	38 (HCC)	T2WI; in-phase and out-of-phase sequences; DCE (HAP, and PVP)	M; 2D	TexRAD	7 (histogram)	NO	LR	No	AUC = 0.83	Tumor entropy and mean are both associated with MVI. Texture analysis on preoperative imaging correlates with microscopic features of HCC
Hectors *et al*[134], 2020	R	MC, PR	Immuno-oncological markers (CD3, CD68, CD31), recurrence at 12 m	48 (HCC)	DCE (Pre-T1WI, AP, PVP, LVP, and HBP); ADC	M; 2D	MATLAB	36 (Haralick, qualitative and quantitative)	NO	LR	No	AUC = 0.76–0.80	MRI radiomics features may serve as noninvasive predictors of HCC immuno-oncological characteristics and tumour recurrence
Wang *et al* [135], 2020	R	MC	CK19+ HCC	227 (HCC)	DWI; ADC; T2WI; DCE (Pre-T1WI, AP, PVP, DP, and HBP)	M; 3D	Pyradiomics	647 (shape, histogram, texture, wavelet)	ICC, LASSO	Logistic model; ROC	Yes	AUC = 0.95	The combined model based on a fusion radiomics signature derived from AP and HBP can be a reliable biomarker for CK19 status of HCC
Wang *et al* [136], 2020	R	PR	5 yr survival after curative hepatectomy	201 (HCC)	T1WI; T2WI; DWI; ADC; DCE (AP, PVP, and EP)	S; 3D	Precision Medicine Open Platform	3144 (histogram, texture, wavelet, statistical)	Gini index	Random Forest	Yes	AUC = 0.9804 and 0.7578 in the TS and VS	This radiomics model is a valid method to predict 5-year survival in HCC patients
Song *et al* [137], 2020	R	PR	RFS after c-TACE	184 (HCC)	DCE (AP, and PVP)	S; 3D	AK software	396 (histogram, GLCM, GRLM, GLSZM)	ICC, LASSO	LASSO Cox regression	Yes	C-index = 0.802	The combined model is more valuable than the clinical-radiological model or radiomics model alone for evaluating the RFS of HCC patients after c-TACE
Zhang *et al* [138], 2019	R	PR	ER (1 yr after hepatectomy)	100 (HCC)	DCE (AP, PVP, and DP)	S; 3D	Omni Kinetic	6 (skewness, kurtosis, uniformity, energy, entropy, and correlation)	NO	LR	No	AUC = 0.867	Texture analysis based on preoperative MRI are potential quantitative predictors of ER in HCC patients after

													hepatectomy
Huang *al* [139], 2019	R	D, PR	DD (HCC *vs* DPHCC), DFS, OS after surgery	100 (HCC)	DCE (AP, PVP, DP, and HBP)	M; 3D	Huiying Medical Technology	1029 (First-order, shape, texture - GLCM, GLRLM, GLSZM-)	LASSO	Multi-layer perceptron; SVM; LR; K-nearest-neighbor; ROC	No	Accuracy of LR in PVP (0.77), DP (0.798), HBP (0.756) and of multi-layer perceptron in PVP (0.798)	The radiomics features extracted from DCE-MRI can be used to diagnose preoperative DPHCC
Ye *et al* [140], 2019	P	MC	Ki67 expression	89 (HCC)	T2WI FS; DCE (Pre-T1WI, AP, PVP, TP, and HBP)	M; 3D	AK software	396 (histogram, texture, GLCM, GLRLM)	LASSO	LR	No	C-index = 0.936	The combination of DCE-MRI texture signature and clinical factors demonstrated the potential to preoperatively predict Ki-67 status of HCC after curative resection
Zhang *et al* [141] 2019	R	PPF	MVI	267 (HCC)	T2WI FS; in-phase and out-of-phase sequences; T1WI; DWI; DCE (AP, PVP, and EP)	M; 3D	MATLAB	484 (intensity, texture, wavelet)	mRMR	LR	Yes	AUC = 0.784 and 0.820 in TS and VS	The radiomics nomogram can serve as a visual predictive tool for MVI in HCC and outperformed clinico-radiological model
Chen *et al* [142], 2020	R	MC	CK19+, EpCAM	115 (HCC)	T2WI, pre-T1WI, DCE (AP, PVP, HBP), ADC	M; 3D	AK software	23 (histogram)	Univariate analysis	LR	No	Accuracy = 0.86, C-index = 0.94	Noninvasive prediction of HCCs with progenitor phenotype can be achieved with high accuracy by integrated interpretation of biochemical and radiological information
Xu *et al* [143], 2019	R	PPF	HCC GRADE	51 (HCC)	ADC	M; 3D	SPSS	27 (histogram)	NO	NO	No	$\rho = -0.397$ for ADC 25^{th} percentile; AUC = 0.76 for ADC min	The 25^{th} percentile ADC showed a stronger correlation with the histological grade of HCC than other ADC parameters, and the minimum ADC value might be an optimal metric for determining poor and fair diferentiations of HCC in DWI
Li *et al* [144], 2019	R	MC	Ki67 expression	83 (HCC)	DCE (HAP, PVP, EP, and	M; 3D	MaZda	30 (histogram, GLCM, GLRLM,	Fisher coefficient, MI, POE + ACC,	ROC (accuracy)	No	Lowest misclassification rates: PCA-	Texture analysis of HBP, arterial phase,

					HBP); T2WI FS			absolute gradient, the autoregressive model, wavelet transform)	correlation			PVP = 40.96%; LDA-PVP = 9.64%; NDA-AP = 6.02%.	and portal venous phase are helpful for predicting Ki67 expression
Oyama *et al* [145], 2019	R	D	DD (HCC, MT, HH)	93 (50 HCCs, 50 MTs, 50 HHs)	T1WI	M; 3D	MATLAB	43 (GLCM, GLRLM, GLSZM, NGTDM)	correlation	LDA	No	Accuracy = 92% (texture analysis) and 85% (persistence imges analyses)	Texture analysis or topological data analysis support the classifcation of HCC, MT, and HH with considerable accuracy, solely based on non-contrast-enhanced T1WI 3D
Wang *et al* [146], 2019	R	MC	CK19+ HCC	48 (HCC)	T2WI FS; in-phase and out-of-phase sequences; DCE (AP, PVP, DP); DWI (b values 0 and 500 s/mm^2); ADC	M; 2D	In-house software	2415 (intensity, gradient, Gabor wavelet, local binary pattern histogram Fourier, GLCM, GLGCM)	LDA (AUC)	LR	No	AUC = 0.765	The StdSeparation 3D texture character may be a reliable imaging biomarker which can improve the diagnostic performance.
Zhu *et al* [147], 2019	R	PPF	MVI	142 (HCC)	DCE (AP, PVP)	M; 3D	Omni-kinetics software	58 (histogram, GLCM, Haralick, GRLM)	Kruskal-Wallis, univariate LR, Pearson's correlation	LR	Yes	AUC = 0.81	The combined model of arterial phase radiomic features with clinical-radiological features could improve MVI prediction ability
Zhang *et al* [148], 2019	P	PR	ER (1 yr after surgical resection)	155 (HCC)	T2WI FS, DCE (AP, PVP, TP, and HBP)	M; 3D	AK software	385 (histogram, texture, GLCM, GLRLM)	LASSO	LR; ROC	Yes	AUC = 0.844	The radiomics nomogram integrating the radiomics score with clinical-radiological risk factors showed better discriminative performance than the clinical-radiological nomogram
Gordic *et al* [149], 2019	R	PR	CR, PR, SD	22 (HCC)	volumetric ADC	M; 3D	MATLAB	7 (histogram)	Wald test	LR	No	AUC = 0.91	Diffusion histogram parameters obtained at 6w and early changes in ADC from baseline are predictive of subsequent response of HCCs treated with RE

Jansen *et al* [150], 2019	R	D	DD (adenomas, cysts, hemangiomas, HCC, metastases)	211 (40 adenomas, 29 cysts, 56 hemangiomas, 30 HCC, 56 metastases)	DCE-MRI, T2WI	M; 2D	NS	164 (contrast curve, histogram, and GLCM texture)	ANOVA F-SCORE	Randomized tree classifier	No	Accuracy = 0.77	The proposed classification system using features derived from clinical DCE-MR and T2WI, with additional risk factors is able to differentiate five common types of lesions and is a step forward to a clinically useful aid for focal liver lesion diagnosis
Ma *et al* [151], 2019	R	PR	Post RFA progression	64 (HCC)	ADC	M; 3D	Volume View	8 (histogram)	NO	Cox-regression	No	C-index = 0.62	Pre-RFA ADC histogram analysis might serve as a useful biomarker for predicting tumor progression and survival in patients with HCC treated with RFA
Wu *et al* [152], 2019	R	D	DD (HCC, HH)	369 (222 HCCs, 224 HHs)	In-phase and out-of-phase sequences; T2WI; DWI	M; 3D	PyRadiomics	1029 (shape, first-order, texture - GLCM, GLRLM, GLSZM-, exponential, square, square root, logarithm, and wavelet)	Variance threshold, select k best, LASSO	Decision tree; random forest; K nearest neighbours; LR; ROC	Yes	AUC = 0.86 and 0.89 in TS and VS	mpMRI radiomics signature is an adjunct tool to distinguish HCC and HH, outperformed a less experienced radiologist, and is nearly equal to an experienced radiologist
Kim *et al* [153], 2019	R	PR	ER (< = 2 yr), LR (> 2 yr) after curative resection	167 (HCC)	DCE (AP, PP, HBP, AP-PP, AP-HBP, PP-HBP, and AP-PP-HBP)	S; 3D	PyRadiomics	1301 (first-order, shape, texture - GLCM, GLRLM, GLSZM, NGTDM, GLDM-, LoG, wavelet)	RF minimal depth algorithm	random survival forest	Yes	C-index = 0.716	The clinicopathologic-radiomic model showed best performances, suggesting the importance of including clinicopathologic information in the radiomic analysis of HCC
Lewis *et al* [154], 2019	R	D	DD (HCC, ICC, HCC-ICC)	63 (36 HCC; 17 ICC; 12 HCC-ICC)	ADC	M; 3D	MATLAB	11 (histogram)	Wald criteria	Binary LR and AUROC	No	AUC = 0.9	The combination of quantitative ADC histogram parameters and LI-RADS categorization yielded the best prediction accuracy for distinction of HCC vs ICC and combined

													HCC-ICC
Chen *et al* [155], 2019	R	MC	Immunoscore (CD3+ and CD8+)	207 (HCC)	HBP	M; 3D	AK software	1044 (histogram, texture, factor parameters, GLCM, GLRLM, GLSZM)	Recursive elimination	LR	Yes	AUC = 0.92	The combined MRI-radiomics-based clinical nomogram is effective in predicting immunoscore in HCC
Feng *et al* [156], 2019	R	PPF	MVI	160 (HCC)	HBP	M; 3D	AK software	1044 (histogram, texture, wavelet transformed, filter transformed texture)	LASSO	LR	Yes	AUC = 0.85 and 0.83 in TS and VS	A combined intrat-umoural and peritu-moural radiomics model based on DCE-MRI is able to pre-operatively predict MVI in primary HCC patients
Wu *et al* [157], 2019	R	PPF	HCC grade	170 (HCC)	T1WI; T2WI FS	M; 3D	MATLAB	656 (histogram, shape, GLCM, wavelet)	LASSO	LR	Yes	AUC = 0.8	The combination of the radiomics signatures with clinical factors may be helpful for the preoperative prediction of HCC grade
Yang *et al* [158], 2019	R	PPF	MVI	208 (HCC)	T2WI FS; DWI; DCE (AP, PVP, DP, and HBP)	M; 3D	MATLAB	647 (shape, intensity, textur-GLCM, GLRLM, GLZLM, NGLDS-)	LASSO, AIC	LR	Yes	AUC = 0.94 and 0.86	The nomogram incorporating clinicoradiological risk factors and radiomic features derived from HBP images achieved satisfactory preoperative prediction of the individualized risk of MVI in HCC patients
Stocker *et al* [159], 2018	R	D	DD (HCC *vs* FNH *vs* HA)	108 (55 HCC, 24 HA, 29 FNH)	T1WI FS; T2WI; DCE (AP, PVP, and HBP)	M; 2D	MATLAB	19 (histogram, GLCM, GLRLM)	LR	LR; ROC	No	AUC = 0.92	2D-TA of MR images may help to distinguish HCC from benign hepatocellular tumors in the non-cirrhotic liver, with most promising results were found in TA features in the AP images
Ahn *et al* [160], 2019	R	PR	ER (1y after surgical resection)	179 (HCC)	HBP	M; 3D	In-house software program	13 (histogram, GLCM)	Univariate analysis	LR	No	AUC = 0.83	When added texture variables to MRI findings, the diagnostic performance for

													predicting early recurrence is improved
Hui *et al* [161], 2018	R	PR	ER (1yr), LNR (late or no recurrence) after surgery	50 (HCC)	T2WI; DCE (AP, PVP and EP)	M; 2D	MaZda	290 (histogram, texture, autoregressive model, GRLM, GLCM, wavelet)	PRTools	ROC	No	Accuracy 78%-84%	Texture analysis of preoperative MRI has the potential to predict ER of HCC with up to 84% accuracy using an appropriate, single texture analysis parameter
Zou *et al* [162], 2019	R	D	DD (IMCC and HCC)	33 IMCC, 98 HCC	volumetric ADC, DCE-MRI	M; 3D	SPSS	9 (histogram)	NO	ROC	No	AUC = 0.79	Volumetric ADC histogram analysis provides additional value to dynamic enhanced MRI in differentiating IMCC from HCC
Li *et al* [163], 2018	P	PPF	MVI	41 (HCC)	IVIM-DWI	M; 3D	MATLAB	10 (histogram)	Univariate analysis	ROC	No	AUC = 0.87	Histogram analysis of IVIM based on whole tumor volume can be useful for predicting MVI. The 5th percentile of D was most useful value to predict MVI of HCC
Wu *et al* [164], 2019	P	PR	TTP after TACE	55 (HCC)	IVIM-DWI	S; 3D	MR OncoTreat	8 histogram parameters	NO	Cox-regression	No	AUC = 0.82	Pre-TACE kurtosis of ADCtotal is the best independent predictor for TTP
Li *et al* [165], 2017	R	D	DD (HH *vs* HM *vs* HCC)	162 (55 HH, 67 HM, 40 HCC)	SPAIR T2WI	M; 2D	MATLAB	233 (histogram, GLCM, GLGCM, GLRLM, GWTF, ISZM)	CCC, DR, R2	ROC, KNN, BP-ANN, SVM, LR	Yes	Misclassification rates: 11.7% (HH *vs* HM), 9.6% (HM *vs* HCC) and 9.7% (HH *vs* HCC)	Texture features of T2WI SPAIR can classify HH, HM and HCC
Moriya *et al* [166], 2017	R	D	HCC grade	53 (HCC)	DWI, ADC	A; 3D	SPSS	11 (First Level)	ANOVA	ROC	No	sensitivity: 100%, specificity: 54%	Minimum ADC was most useful to differentiate poorly differentiated HCC in 3D analysis of ADC histograms

ST: Study type; R: Retrospective; P: Prospective; CP: Clinical purpose; D: Diagnosis; PPF: Prediction of pathological findings; PR: Prognosis; MC: Molecular characterization; NP: Number of patients; Seg: Segmentation; FS: Feature selection; CM: Classification method; DD: Differential diagnosis; cCC-HCC: Combined hepatocellular cholangiocarcinoma; HCC: Hepatocellular carcinoma; CC: Cholangiocarcinoma; MVI: Microvascular invasion; AIR: Aggressive intrasegmental recurrence; RFA: Radiofrequency ablation; VECT: Vessels encapsulating tumor clusters; PFS: Progression-free survival; TACE: Transcatheter arterial chemoembolization; CK19: Cytokeratin19; RFS: Recurrence-free survival; FNH: Focal nodular hyperplasia; GOLM1: Golgi membrane protein 1; SETD7: SET domain containing 7; RND1: Rho family GTPase 1; GPC3: Glypican-3; MVD: Microvessel density; MTM-HCC: Macrotrabecular-massive

hepatocellular carcinoma; ER: Early recurrence; HH: Hepatic hemangioma; HC: Hepatic cysts; OS: Overall survival; TFS: Transplant-free survival; HMRC: Hepatic metastasis of rectal cancer; CK7: Cytokeratin7; DEB-TACE: Drug-eluting bead-transcatheter arterial chemoembolization; DFS: Disease-free survival; DPHCC: Dual-phenotype HCC; EpCAM: Epithelial Cell Adhesion Molecule; MT: Metastatic tumor; CR: Complete response; PR: Partial response; SD: Stable disease; LR: Logistic regression; LRec: Late Recurrence; ICC: Intrahepatic cholangiocarcinoma; HA: Hepatic adenoma; LNR: Late regional recurrence; IMCC: Mass-forming cholangiocarcinoma; TTP: Time to progression; HM: Hepatic metastases; DCE: Dynamic contrast-enhanced; ART: Arterial phase; PVP: Portal venous phase; DP: Delayed phase; T1WI: T1-weighted imaging; AP: Arterial phase; HBP: Hepatobiliary phase; HAP: Hepatic arterial phase; SPP: Substantial period phase; T2WI: T2-weighted imaging; DWI: Diffusion-weighted imaging; EP: Equilibrium phase; LAP: Late arterial phase; TP: Transitional phase; PP: Portal phase; FS: Fat saturation; ADC: Apparent diffusion coefficient; DCE-MRI: DCE-Magnetic Resonance Imaging; IVIM: Intravoxel incoherent motion; SWI: Susceptibility weighted imaging; LVP: Late venous phase; SPAIR T2WI: Spectral attenuated inversion-recovery T2WI; M: Manually; S: Semi-automatic; A: Automatic; GLCM: Gray-level co-occurrence matrix; GLSZM: Grey Level Size Zone Matrix; GLRLM: Gray-level run-length; GLDM: Gray level dependence matrix; NGTDM: Neighboring gray tone difference matrix; CNN: Convolutional neural network; LBP: Local binary patterns; FOS: First-order statistics; NGLDS: Neighborhood gray-level difference statistics; RLM: Run-length matrix; GWTF: Gabor wavelet transform; ISZM: Intensity-size-zone matrix; MI: Mutual information; LASSO: Least absolute shrinkage and selection operator; mRMR: Minimum redundancy maximum relevance; RF: random forests; SVM-RFE: Support vector machine-recursive feature elimination; ICC: Intra-class correlation coefficient; PCA: Principal component analysis; RandomForestSRC: Random Forests for Survival, Regression, and Classification; LR: Logistic regression; POE + ACC: Classification error probability combined with average correlation coefficients; ROC: Receiver operating characteristic; LDA: Linesar discriminant analysis; AUC: Area under the curve; AIC: Akaike information criteria; CCC: Concordance correlation coefficient; DR: Dynamic range; ANN: Artificial neural network; GBDT: Gradient Boosting Tree; KNN: K-nearest Neighbours; XGBoost: Extreme gradient boosting; DT: Decision trees; DL: Deep learning; FDA: Fisher discriminant analysis; AUROC: Area under the receiver operating characteristic; BP-ANN: Back propagation artificial neural network; TS: Training sets; VS: Validation sets; ICG: Indocyanine green retention rate; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; CAD: Computer-aided diagnostic; TR: Transcatheter arterial chemoembolization response; SITET: Single-input two-compartment extended Tofts; DITET: Dual-input two-compartment extended Tofts; c-TACE: Conventional-transcatheter arterial chemoembolization; TA: Texture analysis; RE: Radioembolization.

the 128 included articles. However, only 40 (31.25%) identified and discussed biological correlates and only 50 (39.06%) provided cut-off analysis.

Of the 127 studies included, almost all (123) reported discrimination statistics and their statistical significance. About a quarter of these studies used resampling techniques. However, only 58 studies reported calibration statistics, and none of them applied resampling techniques.

A significant proportion (39.37%) of the studies (50 out of 127) did not provide any validation of their results. Only three studies validated their results using one external validation cohort and five studies used two external validation cohorts. Furthermore, only 47 out of 127 research examined the clinical utility of the produced model using decision curve analysis, while 42 out of 127 studies compared radiomics models with the particular gold standard (based on the study purpose).

Lastly, no study disclosed code and data to the public or performed a cost-effectiveness analysis.

Correlation analysis between RQS and journal metrics

A significant positive correlation was found between RQS and journal IF ($\rho = 0.36$, $P = 2.98 \times 10^{-5}$), 5-years IF ($\rho = 0.33$, $P = 1.56 \times 10^{-4}$), number of patients involved ($\rho = 0.51$, $P < 9.37 \times 10^{-10}$) and number of radiomics features ($\rho = 0.59$, $P < 4.59 \times 10^{-13}$) extracted in the study. On the other hand, there was a significant negative correlation between RQS and time between the publication and the performed literature research ($\rho = -0.23$, $P = 0.0072$) and there were no statistically significant differences identified in the RQS among studies with different objectives. Scatterplots with regression lines showing significant correlations between RQS and journal metrics are shown in Figure 3.

DISCUSSION

In this systematic review, we aimed at summarizing the current status of the fast-growing research on MRI radiomics for the management of HCC. We explored whether it could offer diagnostic, prognostic, and predictive information about pathological outcomes and molecular expression. Additionally, we assessed the quality of the science and reporting

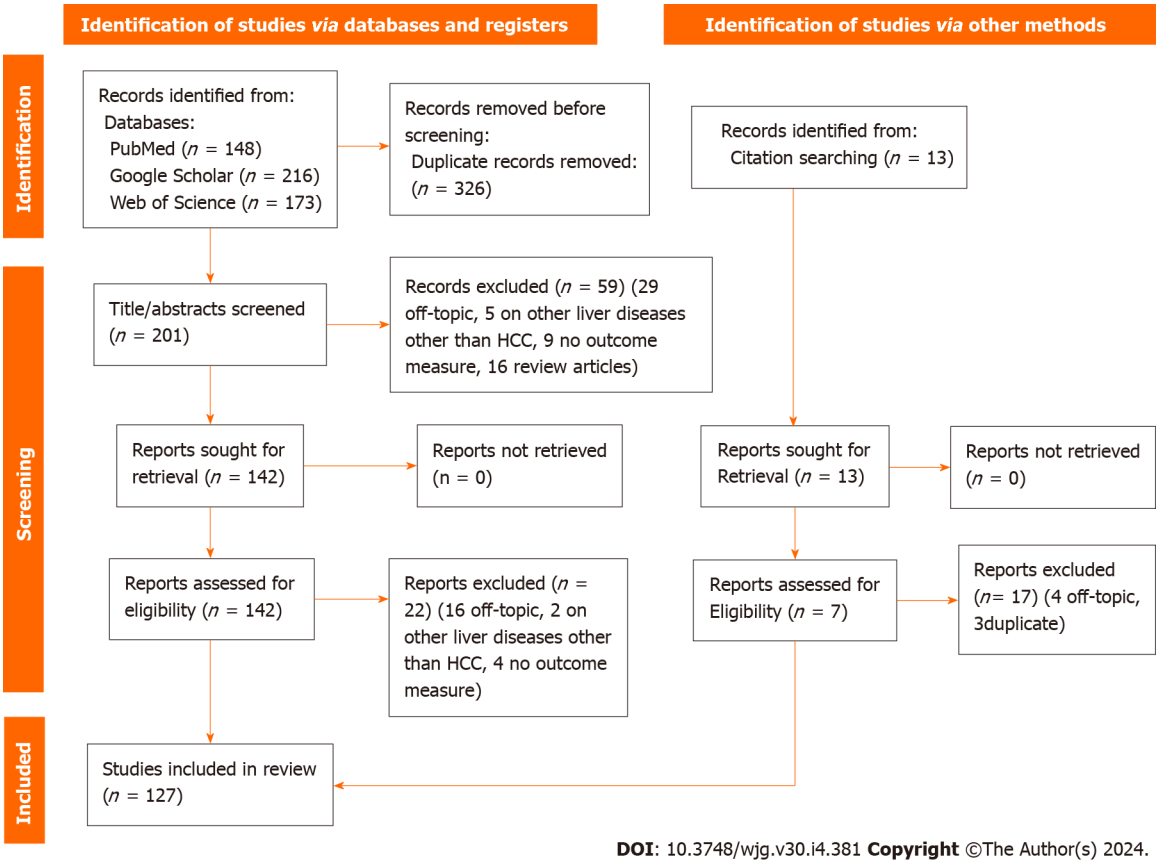

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Figure 1 PRISMA flow diagram of included studies. HCC: Hepatocellular carcinoma.

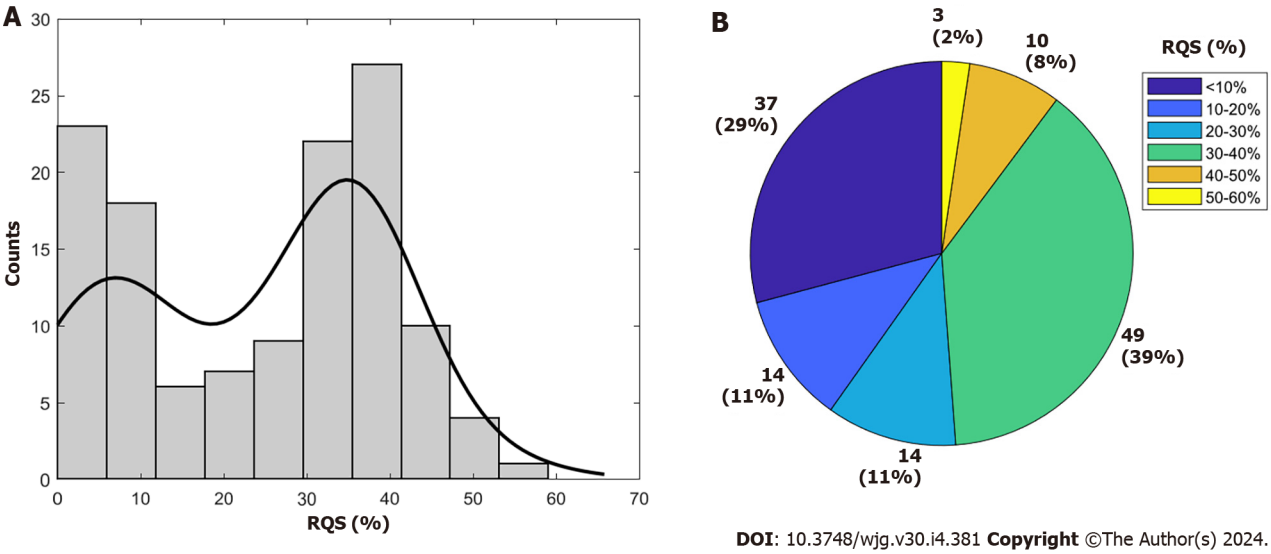

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Figure 2 Results of Radiomics Quality Score assessment. A: Histogram plot of row counts of included studies according to Results of Radiomics Quality Score (RQS) percentage; B: Pie chart of the mean RQS of included studies. RQS: Radiomics Quality Score.

across the studies using the RQS tools. 127 studies from November 2017 onwards were examined in our study. Despite promising results obtained from each of them (with best AUC and C-indexes reaching 0.98 and 0.94, respectively), our study revealed that the methodological variability of the research is considerable, and the reporting quality is insufficient.

Mean RQS was 8 out of 36, with a mean percentage RQS of 24.15%. These results are consistent with previously published data on a variety of tumors, including prostate, breast, lung, renal, and brain cancer[27-31]. Recent studies evaluating research quality in HCC radiomics also align with our findings[25,32]. However, direct comparison with our study is not possible due to differences in purpose and inclusion criteria.

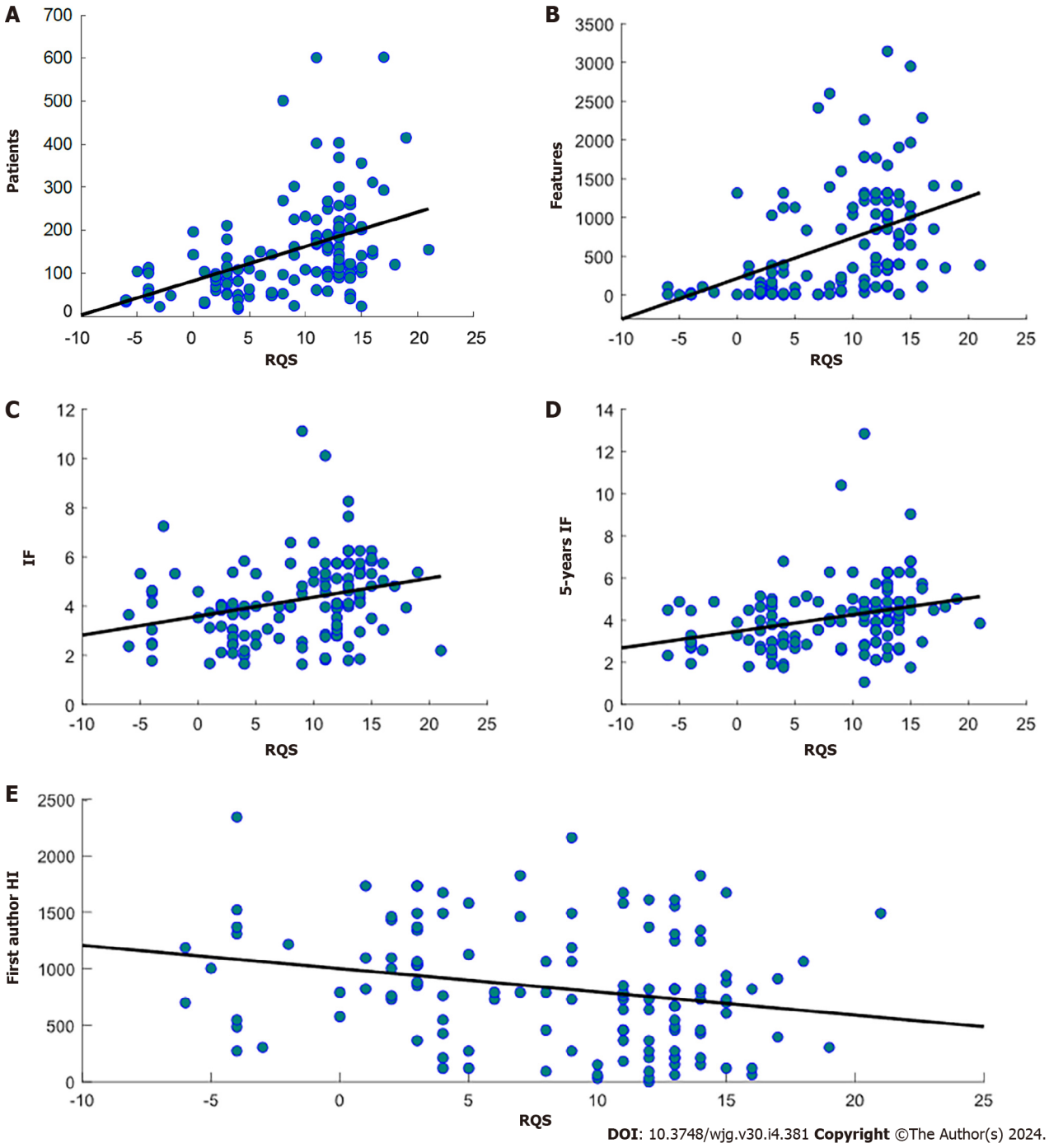

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Figure 3 Scatterplots with regression lines showing correlations between Radiomics Quality Score and journal metrics. A: Correlation between Radiomics Quality Score (RQS) and number of included patients; B: Correlation between RQS and number of radiomic features extracted; C: Correlation between RQS and impact factor (IF); D: Correlation between RQS and 5-years IF; E: Correlation between RQS and first author. Each point corresponds to a study. RQS: Radiomics Quality Score; IF: Impact factor; HI: H-Index.

The results of our analysis showed that the poor RQS scores of the included studies were mostly caused by the absence of rigorous procedures pertaining to radiomics workflow.

Regarding RQS checkpoint 1, practically all investigations have a thorough documentation of the imaging methodology. Nevertheless, the lack of public image methods in the investigations negatively impacts the radiomic studies' repeatability and reproducibility. Notably, the CE-T1WI MRI sequence emerged as the most extensively explored, given its primary role in preoperative HCC assessment. Nevertheless, there exists variability in MRI acquisition due to differences in manufacturers, scanning protocols, contrast media, and phases employed. A significant diversity across the included studies was also noted in terms of RQS checkpoint 2. Specifically, 108 out of 127 studies adopted multiple segmentations to mitigate bias arising from segmentation variability. It's crucial to highlight, however, the lack of consistency among studies regarding the type of ROI (2D/3D) and the segmentation method used (manual, semi-automatic, automatic). It is worth mentioning that the majority of studies used manual or semi-automated image segmentation with manual correction, which restricts the studies included. Both manual and semi-automatic

segmentation can introduce significant observation bias, which may affect studies on intra- and interobserver variation in ROI/VOI delineation[1].

None of the studies determined scanner/manufacturer variability or collected images at multiple time points, making it difficult to detect potential feature variability between scanners and manufacturers, as well as temporal variability. Positively, all but twelve studies performed feature reduction, which is consistent with the third RQS checkpoint. In fact, excessive dimensionality of features can negatively affect model performance and lead to overfitting[33]. The RQS showed high variability in items 6, 7 and 8. However, it is important to note that these items are highly dependent on the aim of the study.

Another notable finding from our review was that only nine of the studies in the review were prospective studies, which is the highest weighting in the RQS tool. This constitutes a significant drawback in radiological studies since a meticulously planned prospective trial serves to diminish and control potential confounding factors, thereby offering a superior level of evidence regarding the trial's quality. This elucidates the rationale behind assigning the highest weight (7 points) to studies with a prospective design in the RQS tool, representing approximately 20% of the total score. Thus, this limitation highlights the importance of conducting well-designed prospective studies.

It is noteworthy that nearly half of the examined papers lacked outcome validation which increases the risk of false-positive results and hinders the implementation of radiomics in clinical practice. However, approximately half of the studies that did not validate their results with an independent cohort chose to perform cross-validation.

The majority of the studies did not provide open access to their data sets, segmentations or codes, which limits the ability to verify and reproduce their results[34,35].

Cost-effectiveness analyses that evaluate radiomic prediction models from a health economic perspective when applied in clinical practice have the same limitation. The assumption is that a new predictor should be no more costly than existing predictors, given comparable accuracy. In addition, the health impact of a radiomics predictor is compared to a condition in which no radiomic predictor[2,32]. However, this criterion of RQS is not as important as the need to standardize and validate the models.

As far as we are aware, this is the first systematic review that looks into the possibility of employing MRI radiomics to gather information regarding the management of HCC and to assess studies using the RQS tool.

Previous studies evaluated the quality of radiomic analysis in different studies for different oncologic applications[27-31,36]. Similar to our study, Wakabayashi *et al*[25] assessed whether radiomics is a valuable and reproducible method for clinical management of HCC using RQS. However, their work included studies up to 2018 and was not focused on MRI modality. In addition, Wang *et al*[32] also aimed to assess the methodological quality of radiomics studies for HCC management. However, although similar findings with respect to our study were found (mean RQS of 10), their study was focused on the prediction of MVI in HCC patients and also included studies involving other imaging modalities than MRI.

I contrast to most studies that focus on assessing the quality of radiomic studies by means of RQS, our approach involved exploring the potential correlation between RQS and scientometric indixes. Our findings revealed that publications that have higher RQS were published in journals with higher IF and 5-years IF. However, studies with high/low RQS and low/high IF and 5-years IF were also found. Moreover, although no significant correlation was found, it was observed that RQS tended to increase with time (decreasing number of months passed from literature research). Interestingly, we discovered that the quality of included studies increased as the number of included patients and extracted attributes grew.

It is crucial to underscore that only 45 out of 127 studies referenced the Image Biomarker Standardization Initiative (IBSI) guidelines or utilized software for radiomic feature extraction compliant with IBSI standards (*e.g.*, PyRadiomics). Emphasizing the importance of adhering to standardized radiomic features nomenclature and calculation according to IBSI, our study highlights the need for future research to align with these standards, thus enhancing the reproducibility of scientific researches[37].

Despite the insights gained, our study is not without limitations. The RQS scoring system, as acknowledged in prior research, is not a definitive standard for evaluating radiomics studies and requires ongoing refinement for widespread acceptance in radiology. The existing research is limited by issues including conducting phantom studies across all scanners, applying imaging at multiple time points, and lacking definition for a particular study purpose[38,39]. Additionally, the predominantly retrospective nature of the included studies introduces bias, compounded by the absence of external validation cohorts and comparisons with reference standards, hindering conclusive remarks on the efficacy of MRI radiomics in HCC[40,41]. Variability in sample size, inclusion criteria, and methodological settings across studies precluded a meta-analysis aligned with study objectives. Furthermore, the study did not explore specific shared radiomic features among different studies, considering the wide-ranging variability in imaging protocols and software for feature extraction.

CONCLUSION

In summary, despite the potential of recent developments in MRI radiomics to fulfill the urgent requirement for noninvasive, radiation-free, and quantitative approaches to support decision-making in HCC treatment, the current studies in this domain lack the requisite quality for integration into clinical practice. Emphasizing the significance of external validation, addressing concerns related to feature reproducibility, conducting clinical utility analyses, and fostering scientific openness are crucial steps that need to be addressed. This endeavor aims to provide fresh perspectives and contribute to the establishment of a consensus regarding the application of the radiomic method in assessing HCC.

ARTICLE HIGHLIGHTS

Research background

Radiomics is a promising tool that may increase the value of Magnetic Resonance Imaging (MRI) for different tasks linked to the management of patients with hepatocellular carcinoma (HCC).

Research motivation

Over the last decade, there has been a substantial increase in radiomics studies in the field of HCC. Many of these studies have demonstrated the power of radiomic features for differential diagnosis, grading, predicting microvascular invasion, overall survival, recurrence, and treatment response. However, the use of radiomics in HCC is currently limited to academic literature, and no studies have yet been translated into clinical applications. This has led to doubts among clinicians about the radiomics validity. This is in part due to many issues related to the methodological quality of radiomic studies.

Research objectives

To summarize the status of MRI radiomic studies concerning HCC, using the radiomics quality score (RQS) to assess the quality of the methodology used in each study.

Research methods

We systematically reviewed PubMed, Google Scholar, and Web of Science databases to identify original articles focused on using MRI radiomics for HCC management published between 2017 and 2023. The RQS tool was employed to evaluate the methodological quality of radiomic studies. Spearman's correlation (ρ) analysis was conducted to investigate the association between RQS and journal metrics, as well as the characteristics of the studies. The threshold for statistical significance was established at $P < 0.05$.

Research results

127 articles were included, of which 43 focused on HCC prognosis, 39 on prediction of pathological findings, 16 on prediction of the expression of molecular markers outcomes, 18 had a diagnostic purpose, and 11 had multiple aims. Mean RQS was 8 ± 6.22, with the corresponding percentage of 24.15% ± 15.25% (ranging from 0.0 to 58.33%). RQS was positively correlated with journal impact factor (IF; $\rho = 0.36$, $P = 2.98 \times 10^{-5}$), 5-years IF ($\rho = 0.33$, $P = 1.56 \times 10^{-4}$), number of patients involved ($\rho = 0.51$, $P < 9.37 \times 10^{-10}$) and number of radiomics features ($\rho = 0.59$, $P < 4.59 \times 10^{-13}$) extracted in the study, and time of publication ($\rho = -0.23$, $P = 0.0072$).

Research conclusions

Although the MRI radiomics in HCC represents an auspicious tool for developing adequate personalized treatment as a noninvasive approach in HCC patients, our study revealed that studies in this field still lack the quality required to allow its introduction in clinical practice.

Research perspectives

Although recent advantages in MRI radiomics can potentially satisfy the urgent need for noninvasive, radiation-free and quantitative strategies that can aid in HCC treatment decision making, studies in this field still lack the quality required to allow its introduction in clinical practice. Future studies including external validation and adhering to the standardization of radiomics features are necessary. Moreover, limitations and challenges related to feature reproducibility, analysis of the clinical utility, and openness of science need to be addressed. This work may provide new insights and contribute to a common understanding of the use of radiomics in the assessment of HCC.

FOOTNOTES

Author contributions: Brancato V, Cerrone M and Cavaliere C conceptualized the problem determined the review scope and strategies; Cerrone M, Garbino N, and Cavaliere C conducted the searching and screening of the literature and reviewed the selected articles; Brancato V performed statistical analyses and drafted statistical sections; Cerrone M and Brancato V wrote the manuscript; Brancato V, Cerrone M, Salvatore M and Cavaliere C reviewed and edited the manuscript draft; all authors contributed to the article and approved the submitted version.

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