Special Review



Application of Radiomics in the Efficacy Evaluation of Transarterial Chemoembolization for Hepatocellular Carcinoma: A Systematic Review and Meta-analysis

Yingxuan Wang, Min Li, Zhe Zhang, Mingzi Gao, Liqin Zhao

Rationale and Objectives: This meta-analysis was aimed at evaluating the predictive value of radiomics in the context of transarterial chemoembolization (TACE) therapeutic response (TR) for hepatocellular carcinoma (HCC) and patients' survival status (SS) and providing favorable evidence for clinical application.

Materials and Methods: We searched for literature in which radiomics was applied to assess the TR of TACE for HCC and the affected patients' survival status across PubMed, Embase, Cochrane Library and Web of Science until Jul 12, 2023. The quality of included literature was evaluated using a radiomics quality score (RQS) approach, and a meta-analysis was conducted using Stata15.0.

Results: Twenty-four studies were included in the analysis. The meta-analysis revealed that the overall concordance-index (C-index) based on radiomics for predicting the TR and SS with TACE was 0.85 and 0.78, respectively. The combined radiomics-clinical model provided the best performance in evaluating the TR and SS associated with TACE. The C-index was 0.93 and 0.88 for TR and 0.84 and 0.80 for SS, in the training and validation sets, respectively. These values were higher than the 0.87 and 0.79 for TR and 0.79 and 0.70 for SS, respectively with the radiomics model, and 0.71 and 0.66 for TR and 0.72 and 0.66 for SS, respectively with the clinical model.

Conclusion: The radiomics prediction model for the efficacy of TACE in HCC showed a satisfactory prediction performance. The combined radiomics-clinic prediction model had the best performance.

Keywords: Hepatocellular carcinoma; Chemoembolization; Therapeutic; Radiomics; Meta-analysis.

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Abbreviations: BCLC Barcelona Clinic Liver Classification, C-index Concordance-index, HCC Hepatocellular carcinoma, OS Overall survival, PLC Primary liver cancer, ROS Radiomics quality score, SS Survival status, TR Therapeutic response, TACE Transarterial chemoembolization

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INTRODUCTION

pproximately 906,000 new cases of primary liver cancer (PLC) were reported in 2020 (1). Hepatocellular carcinoma (HCC) accounts for approximately 90% of PLC (2), and the associated morbidity and mortality are increasing worldwide. Different treatment options are recommended for HCC patients at different Barcelona Clinic Liver Cancer (BCLC) stages. An early-stage option can be surgical resection, with the 3- and 5-year survival rates being 87.8% and 77.2%, respectively (3). However, early HCC presents no obvious symptoms. It is usually diagnosed in the intermediate or advanced stage and when the optimal timing for surgical resection is missed. Liver transplantation is an effective treatment for HCC (4), with a 5-year patient survival rate as high as 71% (5). Unfortunately, this option is limited by the scarcity of donated organs and the post-transplantation recurrence risk (4).

Transarterial chemoembolization (TACE) is a palliative therapy that can control tumor growth, prolong the survival of patients with unresectable HCC, and improve patients' quality of life. The 2022 BCLC guidelines first recommended TACE as the standard treatment for intermediate-stage (B) HCC (6), and it has been widely applied in clinical practice. A meta-analysis that included 101 literature pieces enrolled 10,108 HCC cases showed that the objective response rate of efficacy and survival status (SS) after TACE was 52.5%. The 1- and 5-year overall survival (OS) rates were 70.3% and 32.4%, respectively, and the median OS was 19.4 months (7). TACE can also be used as a neoadjuvant therapy before liver transplantation to achieve de-escalation or buffer therapy for liver transplantation patients. It is recommended for some advanced HCC patients with acceptable liver function accompanied by portal vein tumor thrombi (8,9). However, not all patients may benefit from TACE therapy (10), because of factors such as dual blood supply from both the hepatic artery and portal vein and collateral circulation, making complete tumor necrosis after TACE difficult, as well as a high recurrence rate. Early identification of patients with a good response to TACE may facilitate early repeat management to eliminate residual tumors or guide decision-making for subsequent treatment modalities, thereby minimizing therapy-related complications. Additionally, early identification of patients who do not respond to TACE aids in a timely transition to other therapies, such as radiofrequency ablation, surgical resection, or systemic therapy (molecular targeted therapy) (11,12). Therefore, using non-invasive means to accurately assess and predict the efficacy of TACE can guide individualized treatment and improve their OS effectively.

Radiomics is an emerging field and it can extract highthroughput image features from medical images and convert unquantifiable imaging information into precise data, allowing for quantitative analysis and data mining (13,14). It is extensively utilized in HCC management and yielded satisfactory results in the analysis of tumor genotype behavior, evaluation of therapeutic response (TR), and prediction of SS (15). In some recent studies, radiomics-based prediction models for efficacy in HCC patients were constructed, which is of great importance in assessing the TR to TACE and predicting patient SS. However, due to the lack of standard implementation guidelines, the overall effectiveness of the prediction models remains unclear, which hinders their full clinical application. The purpose of the current meta-analysis was to assess the TR to TACE and the effectiveness of the models for predicting SS in HCC patients. We also aimed to evaluate the quality of the radiomics-based methodology to provide a basis for personalized clinical management.

MATERIALS AND METHODS

This meta-analysis was reported in accordance with the criteria in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses published in the 2020 (PRISMA2020) statement. The study protocol has been registered with the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY) (INPLASY202260100; DOI number: 10.37766/inplasy2022.6.0100).

Literature Search

PubMed, Embase, Cochrane Library, and Web of Science were searched with the subject headings and free words such as "Carcinoma, Hepatocellular" (Mesh), "Radiomics" (Mesh), and "Chemoembolization, Therapeutic" (Mesh). The deadline for searching the databases was July 12, 2023. Detailed search strategies are described in Supplementary Materials.

Literature Inclusion and Exclusion Criteria

The following studies were included: (1) the language of the publication was English; (2) studies with patients clinically diagnosed as HCC and were treated with TACE; and (3) studies in which the outcome indicators of the predictive models value could be assessed directly or indirectly.

The exclusion criteria were as follows: (1) reviews, case report, conference abstracts, animal experiments, and repeated publications; (2) no predictive models to assess the TACE efficiency in HCC patients, though radiomic data were included in the study and (3) patient had received radiotherapy, chemotherapy, radio-frequency ablation, or other antitumor treatments.

Literature Screening, Information Extraction, and Quality Appraisal

Literature screening, information extraction, and quality appraisal were independently performed by two researchers (YW, ML) with over 3 years of experience in radiological diagnosis. A third researcher (LZ) assisted in reaching an agreement if there were any disagreements between the former two researchers. The data extracted included names of first authors, country, publication year, number of cases, equipment, treatment methods, prediction feature, radiomic software, feature selection, predictive model, and ROC curves.

The quality of the literature was assessed using the radiomics quality score (RQS) (16), which was used worldwide to evaluate the quality of radiomics literature. Its aim was to minimize bias and enhance the effectiveness of prediction models by establish standardized assessment criteria and reporting guidelines for radiomics research (16). It is made of a total of 16 criteria. Each criterion corresponds to a different score, depending on the degree to which the literature conforms to the criterion, and the total score ranged from -8 to 36 points. A higher score indicated a higher quality.

Statistical Methods

A meta-analysis was performed using Stata 15.0 (StataCorp LLC, College Station, TX) software. The predictive HCC efficacy model evaluated the TR to TACE and SS with TACE. Therefore, the outcome indicator used was the C-index. The inconsistency index (I^2) reflected the heterogeneity among the models. When $I^2 > 50\%$, a random-effects model was adopted to compute the combined effect index. Meanwhile, a subgroup analysis using the clinical, radiomics, and combined radiomics-clinical models were considered.

RESULTS

Overall, 1050 articles were initially retrieved. After further screening using Endnote, 488 duplicates were excluded. Then another 520 irrelevant articles were excluded by reviewing the titles, abstracts. Full texts of the remaining 42 studies were assessed for eligibility. Finally, 24 articles that satisfied the requirements were included (shown in Figure 1).

Basic Characteristics of the Included Literature

The 24 eligible articles (17–40) were published between 2019 and 2023, and all were retrospective analyses. Overall, 4191 patients were enrolled. Sixteen of the articles reported the application of CT scans. One article used both CT and MR scans (24). The remaining seven focused on MR scans. Regarding the research content, 13 (17,18,21,23,24,26, 27,30,33,34,36,37,40) of the 24 articles explored the TR to TACE for HCC, nine reported SS (22,25,28,29,31,32,35, 38,39), and two (19,20) focused on both TR and SS after the TACE session. Notably, five retrospective studies (20,27, 31,33,38) involved data collected from multicenter clinical trials. Six of the articles (19,21,23,36,37,39) applied deep learning. The screening method of modeling variables was

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only



Figure 1. Literature screening flowchart.

least absolute shrinkage and selection operator (LASSO) regression, and the prediction models for TR were logistic, random forest, support vector machine, deep learning, and other diversified learning methods. Logistic regression was predominantly applied while Cox regression was adopted for SS. The basic characteristics of each study are shown in Table 1.

Quality Appraisal of the Literature

The RQS results revealed that the total score of the 24 studies ranged from seven to 23 points, with an average score of 16.92 points. The relative average score in the RQS assessment was 47.0% (range: 19.44-63.89%). Most studies reported welldocumented image protocol quality and met the criteria for multiple segmentations. Feature reduction or adjustment for multiple testing and Multivariable analysis with non-radiomic features were applied to all studies. Only one study (37) did not conduct any validation, and the remaining studies performed internal validation, external validation and cross-validation. Four studies (18,26,32,40) included cost-effectiveness analyses. Fifteen studies (19,21-24,26-30,32,36,38-40) evaluated whether the model was applicable for clinical utility analysis by using decision curves. None of the studies was prospective study registered in a trial database. Two studies (23,39) were open science and data, one of which (23) applied elucidate the detect and discuss biological correlates. The scores of RQS quality assessment are shown in Table 2.

Meta-analysis Results

Prediction of Postoperative TR After TACE for HCC

The results showed that the overall C-indexes exhibited a moderate level of accuracy, with values of 0.85 and 0.78 for the training and validation sets, respectively. The combined radiomics-clinical model provided the best performance in evaluating the TR to TACE. The C-indexes of the training and validation sets were 0.93 and 0.88, respectively. The radiomics model ranked second in performance, with a C-indexes of 0.87 and 0.79 in training and validation sets, respectively. The clinical model has the poorest predictive efficiency, with a C-indexes of 0.71 and 0.66 in the training and validation sets being, respectively (Figs. 2 and 3).

Prediction of SS After TACE for HCC

The results showed that the overall C-indexes exhibited a moderate level of accuracy, with values of 0.78 and 0.72 for the training and validation sets, respectively. The combined radiomics-clinical model of HCC after TACE had the best performance, with the C-indexes of the training and validation sets being 0.84 and 0.80, respectively. Then followed by the radiomics model in the training and validation sets, with C-index of 0.79 and 0.70, respectively. The results for the SS were similar to those for the postoperative TR, with the combined radiomicsclinical model has the best prediction efficiency, and the clinical model has the poorest performance. The C-indexes of the training and validation sets were 0.72 and 0.66, respectively (Figs. 4 and 5).

DISCUSSION

Radiomics models have been used to evaluate the TR to TACE among HCC patients and their SS. Three models, the radiomics model, clinical model, and the combined radiomics-clinical model, were established in this meta-analysis.

The results showed that the combined radiomics-clinical model provided the best performance in evaluating the TR to TACE, better than that of the radiomics and clinical models. This finding was similar to the current research. Kim et al. used clinical data and radiomic features of CT images in the arterial phase to establish a prediction model for TACE efficacy among HCC patients. Studies have shown that the combined radiomics-clinical model in predicting the post-operative efficacy of TACE (41). Ali Morshid et al. (42) also constructed a predictive model to evaluate the postoperative response to TACE among HCC patients. Their results showed that the accuracy of prediction was 62.9% when using the BCLC staging model alone and 74.2% when combined a deep learning model of radiomics.

Integration of radiomics and deep learning were also used to predict the treatment response to TACE in HCC. The results showed the model had notable accuracy for predicting the initial response to TACE treatment (33,37). Although some researchers assume that the predictive performance of deep learning is better than that of common single machine learning methods, more attention should be given to the selection of effective predictors, especially during the radiomics application processes. Because limited studies have been performed on the application of deep learning to establish a radiomics model in the context of TACE among HCC patients. There is a lack of data to confirm the effectiveness of deep learning in this field.

In this meta-analysis, we also studied the SS of TACE-treated HCC patients. The results showed that the performance of the combined radiomics-clinical model was again better than that of the other two prediction models, with the radiomics model performing better than the clinical model. Jin et al. (43) predicted the possibility of extrahepatic spread or vascular invasion in patients with liver cancer after the initial TACE. Their findings indicated that the AUCs of the combined radiomics-clinical model and radiomics model were higher than those of the clinical model both in the training and validation sets. These results were similar to those of the present study. Zhang et al. (44) established an overall survival prediction model for TACE combined with sorafenib in the treatment of unresectable HCC patients based on deep learning. Their results showed that the combined clinical nomogram and deep learning signature model had a more satisfactory prediction performance compared to that of the clinical and deep learning signature model alone.

TABLE 1. Bas	sic Character	istics of Includ	ded Studies.						
First Author	Country	Publication Year	Equipment	Prediction Feature	Number of Cases	Radiomic Software	Feature Selection	Predictive Model	Reference Standard
An (17) Bai (18)	China China	2023 2022	ਰ	TT TT	289 111	Pyradiomics PyRadiomics	LASSO LASSO	Combined C Combined	mrecist mrecist
Bernatz (19)	Germany	2023	ст	SS+TR	61	PyRadiomics	LASSO	C B	mRECIST
Chen (20)	China	2021	ст	SS + TR	473	PyRadiomics	LASSO	Combined C Combined	mRECIST
Chen (21)	China	2023	MRI	Ħ	172	PyRadiomics	LASSO	Compilied C	mRECIST
Dai (22)	China	2022	ਹ	SS	102	PyRadiomics	LASSO Cox regression	Combined R C	
Dai (23)	China	2023	ट	Ħ	38	PyRadiomics	LASSO	Combined C Combined	mRECIST
Fan (24)	China	2023	CT + MR (1.5T or 3.0T)	Ħ	92	Deep-wise software	LASSO	Combined Combined	LR-TR
Guo (25)	China	2021	cī	SS	94	MATLAB 2014b Python 3.6	LASSO	R C Combined	
Kong (26)	China	2021	MR	Я	6	AIK	LASSO	Combined Combined	mRECIST
Kuang (27)	China	2021	MR (1.5T or 3.0T)	TR	153	AIK	LASSO	C R C	mRECIST
Li (28)	China	2021	ст	SS	60	AIK	LASSO logistic regression	R Combined	
Liu A (29)	China	2022	CT	SS I	20	3D Slicer software	LASSO Cox regression	жОц	FOIDT
	Cuina	7707	ЧZ	Ĩ	140	Pyradiomics	LASSO	н С Combined	шкесо
Meng (31) Niu (32)	China China	2020 2021	ਰਹ	SS SS	162 219	Pyradiomics Pyradiomics	LASSO LASSO	к к с	
Peng (33) Shi (34)	China China	2021 2023	cī cī	R R	130 164	Pyradiomics 3D Slicer	LASSO LASSO	сс	mRECIST1.1 mRECIST

First Author	Country	Publication Year	Equipment	Prediction Feature	Number of Cases	Radiomic Software	Feature Selection	Predictive Model	Reference Standard
Song (35)	China	2020	MR (1.5T or 3.0T)	SS	184	AIK	LASSO	Combined R C	
Sun (36)	China	2022	ст	Я	399	Deep-wise software	LASSO	Combined R C	mRECIST
Tian (37)	China	2022	MR (1.5T or 3.1T)	Т	71	Pyradiomics	DL	Combined R	mRECIST
Wang (38)	China	2022	CT	SS	243	PyRadiomics	LASSO logistic regression	R C Combined	
Wang (39)	China	2022	ст	SS	543	ITK-SNAP	LASSO	C C C C C C C C C C C C C C C C C C C	mRECIST 1.1
Zhao (40)	China	2021	MR (1.5T or 3.0T)	Η	122	AIK	LASSO	Combined Combined	mRECIST1.1
AIK, artificial ir TR, liver imaginę	ntelligence kit g reporting ar	software; C, cli id data system t	inical model; Combined, con treatment response; mRECIS	nbined radiomic ST, modified res	ss-clinical mod	el; DL, deep learning; LA on criteria in solid tumor	SSO, least absolute s s; R, radiomics model	hrinkage and sele I; SS, survival sta	ection operator; LR- tus; TR, therapeutic

TABLE 1 (Continued)

response.

TABLE 2. RQS Qui	ality Ass	essmen	it Resul	ts of Inc	luded S	tudies.												
Study ID	5	V2	V3	V4	V5	V6	۲۷	V8	67	V10	V11	V12	V13	V14	V15	V16	Total	Total
																	Score	Score (%)
An 2023 (17)	٦	-	0	٢	3	1	0	0	2	-	0	2	2	0	0	0	14	38.89
Bai 2022 (18)	-	-	0	0	e	-	0	-	÷	0	0	0	0	0	÷	0	13	36.11
Bernatz 2023 (19)	-	-	0	0	e	-	0	0	2	0	0	0	0	0	0	0	14	38.89
Chen 2021 (20)	-	-	0	÷	ო	-	0	-	2	2	0	5	2	0	0	0	19	52.78
Chen 2023 (21)	-	-	0	-	ო	-	0	0	-	-	0	0	2	0	0	0	15	41.67
Dai 2022 (<mark>22</mark>)	-	-	-	÷	e	-	0	-	÷	2	0	2	0	0	0	0	18	50.00
Dai 2023 <mark>(23)</mark>	-	-	-	÷	ო	-	-	0	2	2	0	e	2	0	0	-	21	58.33
Fan 2023 (24)	-	-	0	0	ę	-	0	0	2	2	0	0	2	0	0	0	16	44.44
Guo 2021 (<mark>25</mark>)	-	-	0	-	ო	-	0	-	2	0	0	0	0	0	0	0	14	38.89
kong 2021 (26)	-	-	-	-	e	-	0	-	-	2	0	2	2	2	-	0	19	52.78
Kuang 2021 (27)	-	-	0	0	ო	-	0	-	-	2	0	4	2	0	0	0	18	50.00
Li 2021 (28)	-	-	0	-	ო	-	-	0	2	2	0	0	0	0	0	0	18	50.00
Liu A 2022 (29)	-	-	-	-	e	-	0	0	2	2	0	2	2	2	0	0	18	50.00
Liu Q 2022 (30)	-	-	-	-	ო	-	0	-	2	2	0	4	2	0	0	0	21	58.33
Meng 2020 (31)	-	-	0	0	ი	-	0	-	0	0	0	5	0	0	0	0	18	50.00
Niu 2021 (32)	-	-	0	-	ი	-	0	-	-	2	0	ი	0	2	-	0	19	52.78
Peng 2021 (33)	-	-	0	0	ო	-	0	-	0	0	0	4	0	0	0	0	15	41.67
Shi 2023 (34)	-	-	0	-	ო	-	0	-	2	2	0	0	0	0	0	0	16	44.44
Song 2020 (35)	-	-	0	-	ო	-	0	0	0	2	0	2	2	0	0	0	15	41.67
Sun 2022 (36)	-	-	-	0	ი	-	0	-	0	0	0	0	0	0	0	0	18	50.00
Tian 2022 (<mark>37</mark>)	-	-	0	-	ი	-	0	-	2	0	0	-5	0	0	0	0	7	19.44
Wang 2022 (38)	-	-	-	-	ი	-	-	-	2	0	0	5	2	0	0	0	23	63.89
Wang 2022 (39)	-	-	0	-	ი	-	0	-	-	-	0	ი	0	0	0	-	18	50.00
Zhao 2021 (40)	-	-	-	-	e	-	0	0	2	N	0	2	2	2	-	0	19	52.78
RQS, radiomics que reduction or adjustmu statistics; V10, calibre fectiveness analysis; ¹	ality scor ent for n ttion sta /16, ope	e; V, vai Jultiple t tistics; V n scienc	riation; \ esting; \ '11, pros ie and d	/1, imag /6, multi spective ata.	le protoc ivariable study re	ol qualit; analysis igistered	y; V2, π with nc in a triɛ	nultiple s nn-radioi al databi	segment mic feat ase; V12	:ation; V; ures; V7 2, validat	3, phanto , detect ; tion; V13,	m study and discu compari	on all sc iss biolog son to gc	anners; V jical corri old stand:	/4, imagin elates; Vε ard; V14,	ig at mult s, cut off potential	tiple time pc analyses; V I clinical utili	ints, V5, feature 9, discrimination ty; V15, cost ef-

		%
Study ID	c-index (95% CI)	Weight
Clinical model	0.66 (0.54, 0.78)	1.71
Bai [18] (2022)	0.61 (0.42, 0.79)	1.24
Bernatz [19] (2023)	0.62 (0.43, 0.80)	1.25
Bernatz [19] (2023)	0.64 (0.55, 0.73)	1.92
Chen [21] (2023)	0.75 (0.68, 0.82)	2.04
Onen [21] (2023)	0.73 (0.83, 0.82)	1.04
Vana (28) (2023)		1.01
Kong [20] (2021)	0.78 (0.08, 0.87)	1.01
Kuang [27] (2021)	0.77 (0.67, 0.86)	1.88
Kuang [27] (2021)	0.79 (0.69, 0.87)	1.93
Liu Q [30] (2022)		2.27
Sun [36] (2022)	 0.74 (0.64, 0.85) 	1.83
Zhao [40] (2021)	0.71 (0.65, 0.77)	19.79
Subtotal (I-squared = 84.5%, p = 0.000)	\diamond	
Radiomics model	1.00 (1.00, 1.00)	0.00
Bernatz [19] (2023)	0.88 (0.76, 1.00)	1.72
Bernatz [19] (2023)		0.00
Bernatz [19] (2023)	0.77 (0.70, 0.85)	2.01
Chen [21] (2023)	0.87 (0.81, 0.93)	2.11
Chen [21] (2023)		2.19
Chen (211 (2023)	▲ 0.93 (0.88, 0.97)	2.18
Chen (21) (2023)		2.20
Chan [21] (2023)	• • 0.70 (0.70, 0.86)	2.207
Onen (21) (2023)	0.78 (0.72, 0.85)	2.07
Dai (20) (2023)	0.80 (0.81, 0.91)	2.10
Dai [23] (2023)	0.88 (0.80, 0.98)	1.90
Fan [24] (2023)	0.81 (0.71, 0.91)	1.83
Kong [26] (2021)	0.83 (0.75, 0.91)	1.98
Kuang [27] (2021)	0.84 (0.77, 0.91)	2.04
Kuang [27] (2021)		1.87
Liu Q [30] (2022)	0.80 (0.73, 0.87)	2.02
Peng [33] (2021)		2.06
Peng [33] (2021)	0.84 (0.77, 0.90)	2.07
Peng [33] (2021)	0.97 (0.94, 0.99)	2.25
Peng [33] (2021)	• 0.98 (0.96, 1.00)	2.26
Peng (33) (2021)	♠ 0.85 (0.81, 0.88)	2.21
Shi (24) (2021)	0.84 (0.80, 0.88)	2.10
Shi [34] (2023)	0.78 (0.50, 0.03)	1.20
Shi [34] (2023)	0.70 (0.38, 0.84)	0.08
Shi [34] (2023)	0.95 (0.93, 0.97)	2.20
Shi [34] (2023)	• 0.85 (0.84, 0.85)	2.27
Sun [30] (2022)	• 0.80 (0.80, 0.87)	2.21
Sun [36] (2022)	 0.85 (0.72, 0.98) 	1.64
Tian [37] (2022)	0.87 (0.75, 0.99)	1.69
Tian [37] (2022)		2.09
Tian [37] (2022)	0.84 (0.75, 0.92)	1.95
Zhao [40] (2021)		56.83
Subtotal (I-squared = 94.1%, p = 0.000)	0	
The combined radiomics-clinical model	1.00 (1.00, 1.00)	0.00
An [17] (2023)	♦0.94 (0.89, 1.00)	2.13
Bai [18] (2022)		2.11
Bernatz [19] (2023)		2.28
Chen (20) (2021)	▲ 0.07 (0.05, 1.00)	2.24
Chan (21) (2022)	◆ 0.87 (0.83, 1.00)	2.18
Dai (22) (2023)	↓ 0.07 (0.02, 0.91)	2.10
Dai [25] (2025)	0.91 (0.84, 0.98)	2.02
ran [24] (2023)	0.80 (0.77, 0.95)	1.93
Kong [20] (2021)	0.81 (0.72, 0.87)	2.02
Liu Q [30] (2022)		2.22
Shi [34] (2023)	• 0.94 (0.94, 0.95)	2.27
Sun [36] (2022)	0.88 (0.81, 0.95)	2.03
Zhao [40] (2021) Subtotal (leguared = 75.2%, p = 0.000)	0.93 (0.91, 0.95)	23.38
	0.85 (0.81, 0.88)	100.00
	6	
Overall (I-squared = 99.3%, p = 0.000)	Ť	

Figure 2. Forest map of radiomics to predict the therapeutic response to TACE among HCC patients in the training set. HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization.

Study ID	c-index (95% CI)	% Weight
Clinical model Bai [18] (2022) Bernatz [19] (2023) Bernatz [19] (2023) Chen [21] (2023) Dai [23] (2023) Dai [23] (2023) Kong [26] (2021) Kuang [27] (2021) Kuang [27] (2021) Liu Q [30] (2022) Sun [36] (2022) Zhao [40] (2021) Subtotal (I-squared = 63.8%, p = 0.001)	0.55 (0.44, 0.65) 0.69 (0.47, 0.91) 0.65 (0.42, 0.83) 0.69 (0.51, 0.86) 0.54 (0.45, 0.64) 0.77 (0.63, 0.90) 0.71 (0.59, 0.83) 0.67 (0.49, 0.84) 0.73 (0.51, 0.94) 0.73 (0.51, 0.94) 0.75 (0.61, 0.87) 0.75 (0.60, 0.92) 0.66 (0.61, 0.72)	1.88 1.13 1.09 1.40 1.98 1.69 1.79 1.42 1.16 1.54 1.54 1.54 1.70 2.32 1.49 20.58
Radiomics model Bernatz [19] (2023) Bernatz [19] (2023) Chen [21] (2023) Dai [23] (2023) Dai [23] (2023) Dai [23] (2023) Dai [23] (2023) Fan [24] (2023) Kong [26] (2021) Kuang [27] (2021) Liu Q [30] (2022) Peng [33] (2021) Peng [33] (2021) Peng [33] (2021) Peng [33] (2021) Peng [33] (2021) Peng [33] (2021) Sun [36] (2022) Sun [36] (2022) Zhao [40] (2022)	0.60 (0.36, 0.83) 0.67 (0.45, 0.90) 0.55 (0.31, 0.79) 0.67 (0.49, 0.85) 0.69 (0.51, 0.86) 0.75 (0.58, 0.91) 0.84 (0.70, 0.97) 0.82 (0.43, 0.83) 0.66 (0.48, 0.84) 0.80 (0.65, 0.94) 0.77 (0.64, 0.90) 0.75 (0.52, 0.88) 0.69 (0.60, 0.77) 0.77 (0.64, 0.90) 0.75 (0.62, 0.89) 0.66 (0.53, 0.80) 0.76 (0.64, 0.89) 0.88 (0.73, 1.00) 0.81 (0.45, 0.75) 0.78 (0.71, 0.84) 0.81 (0.75, 0.87) 0.90 (0.94, 0.99) 0.81 (0.75, 0.87) 0.90 (0.94, 0.99) 0.81 (0.75, 0.87) 0.90 (0.94, 0.99) 0.81 (0.86, 0.96) 0.81 (0.75, 0.87) 0.90 (0.94, 0.99) 0.87 (0.86, 0.98) 0.87 (0.86, 0	1.05 1.11 1.03 1.39 1.41 1.49 1.68 1.34 1.44 1.38 1.58 1.44 2.03 1.70 1.67 1.68 1.70 1.67 1.66 1.73 1.66 1.73 1.66 1.73 1.66 1.73 1.66 2.10 2.16 2.31 2.32 2.33 1.63 50.75
The combined radiomics-clinical model An [17] (2023) Bai [18] (2022) Bernatz [19] (2023) Chen [20] (2021) Chen [21] (2023) Chen [21] (2023) Dai [23] (2023) Dai [23] (2023) Fan [24] (2023) Kong [26] (2021) Liu Q [30] (2022) Shi [34] (2023) Sun [36] (2022) Zhao [40] (2022) Zhao [40] (2021) Subtotal (I-squared = 69.3%, p = 0.000) Overall (I-squared = 95.2%, p = 0.000) NOTE: Weights are from random effects analysis		2.20 2.20 1.15 2.27 2.22 1.67 2.06 1.74 1.75 1.73 1.80 1.73 1.80 1.73 2.22 2.34 1.60 28.67 100.00

Figure 3. Forest map of radiomics to predict the therapeutic response to TACE among HCC patients in the validation set. HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization.

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Study		%
ID	c-index (95% CI)	Weight
Clinical model	0.70 (0.00 0.04)	0.74
Chen [20] (2021)		3.71
Dai [22] (2022)		4.49
Guo [25] (2021)		2.24
Liu A [29] (2022)		2.70
Niu [32] (2021)		4.30
Song [35] (2020)		4.29
Wang D [38] (2022)		3.83
Wang H [39] (2022)		3.78
Subtotal (I-squared = 58.4% , p = 0.018)	0.72 (0.68, 0.76)	29.33
Padiamics model		
Dai [22] (2022)		2 62
Guo [25] (2022)		2.02
Li [28] (2021)	0.83 (0.79, 0.87)	4 49
Liu A [20] (2021)		2.80
Liu A [29] (2022)		2.03
Meng [31] (2020)		4.18
Niu [32] (2021)	0.72 (0.63, 0.73)	3.78
Niu [32] (2021)	0.84 (0.76, 0.90)	3.84
Song [35] (2020)	→ 0.73 (0.68, 0.79)	4.09
Wang D [38] (2022)	0.86 (0.79, 0.92)	4.04
Wang H [39] (2022)	↓ 0.82 (0.74, 0.90)	3.52
Wang H [39] (2022)	0.69 (0.55, 0.83)	2.31
Wang H [39] (2022)	— 0.77 (0.69, 0.85)	3.52
Subtotal (I-squared = 55.4%, p = 0.008)	0.79 (0.75, 0.82)	44.39
The combined radiomics-clinical model		
Chen [20] (2021)	↓ ◆ 0.85 (0.82, 0.89)	4.58
Dai [22] (2022)	0.81 (0.70, 0.95)	2.53
Guo [25] (2021)	0.84 (0.72, 0.96)	2.64
Li [28] (2021)	★ 0.83 (0.79, 0.87)	4.47
Song [35] (2020)	→ 0.74 (0.68, 0.79)	4.18
Wang D [38] (2022)		4.35
Wang H [39] (2022)	0.89 (0.81, 0.98)	3.54
Subtotal (I-squared = 74.9%, p = 0.001)	0.84 (0.79, 0.88)	26.29
Overall (I-squared = 81.3%, p = 0.000)	0.78 (0.75, 0.81)	100.00
NOTE: Weights are from random effects analysis		
The religned are non random enects analysis		
077	0.077	

Figure 4. Forest map of radiomics to predict the survival status of TACE-treated HCC patients in the training set. HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization.

RQS is a rigorous quality rating scale for evaluating the performance of a radiomics-based design. We evaluated the methodological quality by using the RQS method in our meta-analysis. Our results showed that the average RQS was 16.92 (47.0% of the total score). The average score on RQS was 4.9–10.83 in the previous systematic reviews on radiomics studies (45–49). Our results were slightly better than those of previous research, but did not reach a higher level.

Detect and discuss biological correlates, prospective study registered in a trial database, and open science and data are important components in the assessment of RQS. However, they were rarely applied in the literature included in our study. In addition, validation and cost effectiveness analysis are crucial for the assessment of RQS quality, which could effectively help acquire information (50). However, only five studies used multicenter validation (20,27,31,33,38) and four

Study	c-index (95% CI)	% Weight
		Weight
Clinical model		
Chen [20] (2021)		3.30
Dai [22] (2022)	0.65 (0.51, 0.80)	2.43
Guo [25] (2021)	0.75 (0.60, 0.90)	2.35
Niu [32] (2021)		4.21
Song [35] (2020)	0.69 (0.62, 0.77)	3.71
Wang D [38] (2022)	0.71 (0.51, 0.84)	2 14
Wang H [39] (2022)	0.59 (0.50, 0.68)	2.14
Wang H [30] (2022)	0.66 (0.57, 0.75)	3.30
Subtotal (Leguared = 10.2%, p = 0.277)		24.01
Subtotal (I-squared = 19.5%, p = 0.277)	0.00 (0.02, 0.09)	24.91
Radiomics model		
Dai [22] (2022)	0.77 (0.50, 1.00)	1.29
Guo [25] (2021)		2 45
Li [28] (2021)	0.75 (0.69, 0.80)	4.06
Meng [31] (2020)		3.21
Niu (22) (2020)		3.64
Niu [32] (2021)		3.04
Niu [32] (2021)		3.75
Song [35] (2020)		3.80
wang D [38] (2022)	0.84 (0.75, 0.93)	3.34
Wang H [39] (2022)	0.71 (0.63, 0.80)	3.44
Wang H [39] (2022)		3.35
Wang H [39] (2022)	0.58 (0.51, 0.64)	3.83
Wang H [39] (2022)		2.93
Wang H [39] (2022)	← 0.65 (0.60, 0.71)	4.02
Wang H [39] (2022)	 0.55 (0.50, 0.61) 	3.99
Subtotal (I-squared = 82.8%, p = 0.000)	O.70 (0.65, 0.75)	47.11
<u>.</u>		
The combined radiomics-clinical model		
Cnen [20] (2021)	→ 0.81 (0.75, 0.84)	4.13
Dai [22] (2022)	→ 0.77 (0.58, 0.81)	2.99
Guo [25] (2021)	0.81 (0.68, 0.95)	2.64
Li [28] (2021)	••• 0.79 (0.72, 0.87)	3.66
Song [35] (2020)	→ 0.80 (0.74, 0.86)	3.93
Wang D [38] (2022)		3.60
Wang H [39] (2022)	↔ 0.75 (0.70, 0.81)	4.01
Wang H [39] (2022)	0.73 (0.62, 0.84)	3.03
Subtotal (I-squared = 33.6%, p = 0.160)	0.80 (0.77, 0.83)	27.98
Overall (I-squared = 82.5%, p = 0.000)	0.72 (0.69, 0.76)	100.00
NOTE: Weights are from random effects analysis		
no re. molgina are nom random enecta analysis		

Figure 5. Forest map of radiomics to predict the survival status of TACE-treated HCC patients in the validation set. HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization.

studies underwent cost effectiveness analysis (18,26,32,40). The RQS tool should be continuously updated to be more widely used in radiomics-associated research (51,52).

New progress has been made in the field of radiomics with regard to the diagnosis, evaluation of growth pattern of tumor blood vessels and vascular micro invasion of HCC (53-56), prognosis after surgical treatment (57,58), and complications after

TACE treatment (59). However, there are relatively few studies on the response to TACE among HCC patients and their SS. Our study makes up for the lack of radiomics in HCC research to some extent.

Our study has several limitations. (1) The scanning parameters were not unified in the absence of standards for image acquisition and post-processing. Different software used for radiomics analysis also caused certain errors in the delineation of the region of interest. (2) Most of the studies were singlecenter, retrospective studies with relatively small sample sizes. (3) The TACE techniques, such as conventional TACE (cTACE) or drug-eluting beads TACE was not mentioned in most of the included studies. (4) Radiomics research requires multidisciplinary collaboration. Many algorithms were inconsistent during the process of data processing, and the verification methods were not completely unified.

Although there are major challenges to the application of radiomics in clinical settings, its prospect is worth looking forward to with the development of artificial intelligence. The combined radiomics-clinical model will yield greater value in evaluating the efficacy of TACE in HCC patients and guiding clinical decision-making. In the future, a large number of unified prospective studies are needed to confirm the efficacy of TACE among HCC patients and predicting patient survival based on radiomics prediction models.

DECLARATION OF COMPETING INTEREST

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Liqin Zhao reports was provided by National Natural Science Foundation of China (No. 82072003).

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AUTHOR CONTRIBUTIONS

LZ and YW contributed to the study design and the original protocol. YW, ML, ZZ, and MG collected and analyzed the data. YW, ML, MG, and LZ interpreted the data. YW wrote the manuscript. LZ, ML, MG, and ZZ revised the manuscript. All the authors have reviewed the final version of the manuscript and approved it for publication.

APPENDIX A. SUPPORTING MATERIAL

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.acra.2023.08.001.

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