

Progress of MRI-based radiomics and deep learning for predicting the prognosis of locally advanced rectal cancer (Review)

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Abstract. Rectal cancer (RC) ranks among the most common malignant tumors worldwide, with ~30% of patients presenting at a locally advanced stage at the time of diagnosis. The standard treatment for locally advanced RC (LARC) combines neoadjuvant chemoradiotherapy (nCRT) with total mesorectal excision. While this treatment paradigm has been effective in reducing the local recurrence rate, its efficacy in enhancing overall survival and disease-free survival is still limited. Consequently, the identification of adverse prognostic factors in patients with LARC is crucial for improving long-term survival outcomes. Traditional imaging methods offer limited predictive power for early diagnosis, treatment

efficacy assessment and prognosis in LARC. Recent advancements in MRI-based radiomics and deep learning (DL), leveraging high-dimensional feature extraction and nonlinear modeling, have markedly enhanced prognostic predictive performance. Single-sequence MRI radiomics models derived from pre-nCRT imaging demonstrate areas under the curve (AUC) of 0.79-0.87 for predicting local recurrence and distant metastasis. Multiparametric radiomic models further improve predictive accuracy, achieving AUCs of 0.81-0.83. Delta radiomics, which captures temporal-spatial heterogeneity evolution in tumors during therapy, elevates AUC performance to 0.77-0.89. Notably, DL-based models exhibit superior and more stable predictive capabilities, with concordance indices (C-indices) ranging from 0.82 to 0.94. This paper reviews recent progress in MRI-based radiomics and DL for predicting the prognosis of patients with LARC subjected to nCRT.

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Abbreviations: ADC, apparent diffusion coefficient; AUC, area under the curve; CEA, carcinoembryonic antigen; CE-TIWI, contrast-enhanced T1-weighted imaging; C-index, concordance index; CNNs, convolutional neural networks; CRC, colorectal cancer; CT, computed tomography; DFS, disease-free survival; DL, deep learning; DM, distant metastasis; DMFS, DM-free survival; DWI, diffusion-weighted imaging; EMVI, extramural vascular invasion; LARC, locally advanced rectal cancer; LASSO, least absolute shrinkage and selection operator; LR, local recurrence; LRFS, local recurrence-free survival; LRR, local recurrence rate; MRF, mesorectal fascia; MRI, magnetic resonance imaging; MS, manual segmentation; MSI, microsatellite instability; nCRT, neoadjuvant chemoradiotherapy; OS, overall survival; PET/CT, positron emission tomography/computed tomography; PFS, progression-free survival; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RC, rectal cancer; RF, random forests; ROI, regions of interest; SVM, support vector machines; TNM, tumor-node-metastasis; TRG, tumor regression grade; T2WI, T2-weighted imaging; ViT, vision transformer

Key words: locally advanced rectal cancer, neoadjuvant chemoradiotherapy, radiomics, deep learning, prognosis

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1. Introduction

Colorectal cancer (CRC) is the third most common malignant tumor worldwide and the second leading cause of cancer-related deaths (1). Epidemiological projections estimate that by 2040, the number of new CRC cases will reach 3.2 million, with deaths rising to 1.6 million, posing a major threat to global health (2). Rectal cancer (RC) accounts for approximately one-third of CRC cases, with 30-50% of patients diagnosed at a locally advanced stage (3). Locally advanced RC (LARC) is typically defined as RC with clinical or pathological stage T3-T4 and/or positive regional lymph nodes, without distant metastasis. It is typically treated with neoadjuvant chemoradiotherapy (nCRT) followed by total mesorectal excision (4,5). This approach

reduces tumor volume, stage and local recurrence rate (LRR), and improves surgical resection and anal sphincter preservation rates (6,7). However, it has not significantly improved overall survival (OS) (8). Distant metastasis (DM), which occurs in 25-40% of cases (9,10), remains the primary cause of treatment failure and death, with current chemotherapy and immunotherapy regimens yielding suboptimal OS.

In recent years, groundbreaking advancements have been made in two therapeutic domains. First, for the microsatellite instability-high (MSI-H)/mismatch repair-deficient (dMMR) subtype, which constitutes ~3% of patients with LARC (11), immune checkpoint inhibitors targeting programmed cell death 1 (PD-1)/PD-1 ligand 1 have demonstrated remarkable efficacy (12). A phase II prospective study by Cercek *et al* (13) enrolled 16 patients with dMMR LARC. Among them, 12 patients achieved clinical complete response (cCR) following 6-month neoadjuvant dostarlimab therapy, with comprehensive imaging and endoscopic biopsy confirming the absence of residual tumor. During a median follow-up of 12 months (range, 6-25 months), none of the patients required chemoradiotherapy or surgical intervention, and no recurrence or disease progression was observed. These findings were further validated by a multicenter retrospective study by Yang *et al* (14), which included 20 patients with dMMR/MSI-H LARC treated with PD-1 inhibitor monotherapy. The overall CR rate reached 90% (18/20), comprising 11 cases with pathological CR (pCR) and 7 cases managed with watch-and-wait strategies for cCR/near-cCR. After a median follow-up of 25 months, all patients remained free from LR or DM, with 2-year disease-free survival (DFS) and OS rates both maintained at 100%. These results suggest that for patients with dMMR RC achieving cCR/near-cCR after neoadjuvant PD-1 inhibitor therapy, adopting a watch-and-wait strategy could enable non-surgical management without compromising survival outcomes. Second, the total neoadjuvant therapy (TNT) paradigm, which consolidates chemotherapy and radiotherapy into the preoperative phase, has significantly improved treatment completion rates and enabled early control of micrometastases, offering a novel approach to enhance prognosis. Multiple phase III trials (15,16) have confirmed that TNT outperforms conventional regimens by elevating pCR rates and improving long-term outcomes. For instance, the RAPIDO trial reported a pCR rate of 28.4% in the TNT group (vs. 14.3% in controls) (17), while the PRODIGE23 trial demonstrated superior 7-year DFS and OS rates of 67.6 and 81.9%, respectively, in the TNT cohort (vs. 62.5 and 76.1% in controls), with distant metastasis risk reduced to 73.6% (vs. 65.4%) (18). However, 5-year follow-up data from the RAPIDO trial (19) revealed an elevated LRR in the TNT group (10 vs. 6%, $P < 0.027$), potentially attributable to dose limitations of short-course radiotherapy. These findings underscore the critical need for early prognostic prediction in patients with LARC to refine therapeutic decision-making.

The tumor-node-metastasis (TNM) staging system (20-22) is still one of the primary methods for predicting the prognosis of LARC. It has been shown that the pathological status of lymph nodes after nCRT is strongly linked to the risk of LR and DM (23). However, the predictive accuracy of the TNM system is limited by tumor heterogeneity and the subjectivity involved in manual assessments (24).

In addition to tumor staging, several clinicopathological factors, such as neurovascular invasion and tumor differentiation, play a role in prognostic evaluations. The tumor regression grade (TRG) is a key tool for assessing tumor response after nCRT (25) and can indirectly reflect prognosis. However, it is only applicable to postoperative pathological specimens, which limits its ability to assess prognosis before treatment in patients with LARC. KRAS and TP53 mutations are often considered markers of poor nCRT efficacy in LARC, correlating with a worse prognosis (26). However, determining the mutational status typically requires pathological examination of tumor tissue. Tumoral heterogeneity, both within the tumor and across different tumor sites, poses significant challenges to histological methods (27). The inability to monitor real-time genetic changes during treatment further limits the capacity of these methods to dynamically assess tumor biology. Additionally, commonly used tumor markers, such as carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9, have low sensitivity and specificity. These markers often result in high false-negative rates and have delays in reflecting patient prognosis (28). Many of the aforementioned methods rely on invasive procedures, which restrict their routine use in patient monitoring and surveillance.

Imaging plays a vital role in diagnosing and managing LARC, with computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography/computed tomography (PET/CT) being the primary modalities used. CT is essential for staging LARC due to its rapid acquisition, clear visualization of lesions and ability to assess peri-lesional involvement (29). Although there is insufficient evidence to confirm CT's ability to predict recurrent or metastatic lesions before the onset of other symptoms, it is invaluable for whole-body assessment in symptomatic patients or those with elevated CEA levels. However, its low soft-tissue resolution and associated radiation risk often necessitate combining it with other diagnostic tests to confirm a definitive diagnosis. PET/CT, which integrates functional and anatomical imaging, provides crucial information for accurately assessing treatment efficacy and predicting prognosis. This is achieved by revealing the metabolic activity and anatomical details of tumors. A meta-analysis comparing ultrasound, CT, MRI and PET/CT in the early detection of gastrointestinal tumor metastases found that PET/CT exhibited the highest sensitivity for diagnosing metastases (30). However, the high cost of PET/CT limits its widespread use in routine follow-up examinations.

MRI has emerged as the preferred modality for diagnosing, staging and prognosticating LARC, owing to its superior soft-tissue resolution and its ability to perform multi-sequence, multi-parameter imaging (31). MRI provides detailed and accurate assessments of lesion size, depth of infiltration, involvement of neighboring organs and distant metastasis. T2-weighted imaging (T2WI) is commonly used to evaluate tumor response to nCRT. It defines the TRG by observing the gradual homogenization of tumor signal intensity, changes in tumor volume and size, and the degree of fibrotic replacement (32). Diffusion-weighted imaging (DWI), a functional imaging sequence, assesses tumor response by measuring the diffusion of water molecules between tissues. This diffusion is positively correlated with tumor cell density. Sequences such as the apparent diffusion coefficient (ADC) and contrast-enhanced

T1-weighted imaging (CE-TIWI) provide non-invasive insights into tumor cell density, degree of differentiation, microcirculatory perfusion and blood supply (33). Furthermore, imaging features such as extramural vascular invasion (EMVI) and mesorectal fascia (MRF) involvement are critical prognostic factors (34,35). To standardize MRI reporting and improve clinical decision-making consistency, international consensus guidelines recommend structured reporting templates. As proposed by Smith *et al* (36,37), a comprehensive MRI reporting framework for RC should incorporate essential anatomical descriptors, including tumor distance from the anal verge, MRF status and EMVI. Mnemonic systems such as DISTANCE (Distance, Involvement of Sphincter, T stage, Anal canal, Nodes, Circumferential Resection Margin, Extramural Venous Invasion) and its extended variant DISTANCED-DIS (incorporating Depth of invasion, Signal intensity, Spread) (38,39) facilitate systematic acquisition of key imaging parameters, thereby enhancing surgical planning and prognostic stratification. Despite reducing interobserver variability through standardized terminology, conventional MRI interpretation remains heavily reliant on subjective radiologic expertise, potentially compromising diagnostic comprehensiveness and accuracy. Consequently, there is an urgent need for new methods to provide prognostic information before nCRT, guiding more personalized and precise clinical decision-making.

With the ongoing advancements in precision medicine, radiomics and deep learning (DL) are increasingly applied in the diagnosis and treatment of various diseases (40,41). Radiomics extracts high-throughput, quantitative image data that are often imperceptible to the naked eye, and uses these data to build predictive models that enhance accurate diagnosis, treatment assessment and prognostic prediction. DL automates the extraction and selection of high-dimensional features, enabling comprehensive analysis of image data to identify and predict disease characteristics.

Several studies have explored the use of radiomics from CT and PET/CT imaging to predict the prognosis of LARC treated with nCRT, yielding promising results. A retrospective study involving 411 patients with LARC demonstrated that CT-based radiomics features could independently predict OS in patients with LARC undergoing nCRT (42). The study further showed that combining radiomics features with clinical data significantly enhanced the predictive performance of the model. In a study by Bundschuh *et al* (43), which analyzed data from 27 patients with LARC treated with nCRT, baseline PET/CT-derived texture parameters demonstrated strong predictive value for progression-free survival (PFS), though they showed limited predictive ability for OS. Similarly, Bang *et al* (44) found that texture parameters extracted from PET/CT images could serve as an indicator of tumor heterogeneity, useful for predicting the response to nCRT and LR in LARC. Despite these advances, studies using CT and PET/CT to predict the prognosis of nCRT in LARC are limited. This is due, in part, to CT's limitations in soft tissue discrimination and the low prevalence of PET/CT imaging.

Conventional imaging modalities, such as MRI and CT, predominantly rely on morphological indicators (e.g., tumor size, enhancement patterns), which are insufficient to distinguish viable tumor residues from post-therapeutic fibrosis

during pretreatment or early treatment phases. Furthermore, existing prognostic biomarkers, such as TRG, require postoperative pathological confirmation and thus fail to dynamically guide therapeutic adjustments. Additional limitations include the lack of objective quantification methods for intratumoral heterogeneity, inadequate integration of multimodal data (imaging, genomic and clinical parameters), and challenges associated with the 'black-box' nature of DL models and their poor cross-center generalizability. These issues have substantially hindered the clinical translation of precision predictive frameworks. This review focuses on radiomics and DL technologies, delineating how they overcome the constraints of conventional approaches by addressing critical research gaps-specifically, the limited timeliness of early prediction, insufficient analysis of tumor heterogeneity and the absence of synergistic multidimensional data integration. By resolving these challenges, the present analysis provides innovative conceptual frameworks to advance precision oncology frameworks for LARC.

As a result, this paper will focus on recent research exploring MRI-based radiomics and DL for prognostic prediction in patients with LARC undergoing nCRT (Table I). The PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), Web of Science (<https://www.webofscience.com/>) and Google Scholar (<https://scholar.google.com/>) databases were searched for studies conducted before August 31, 2024. During the search, keywords such as 'locally advanced rectal cancer', 'neoadjuvant chemoradiotherapy', 'magnetic resonance imaging', 'survival', 'prognosis', 'metastasis', 'radiomics' and 'deep learning' were used. The inclusion criteria were as follows: i) The study population was clearly defined as patients with LARC and all patients received nCRT; ii) MRI was used as the imaging modality; iii) radiomics or DL was employed to predict the prognosis of LARC; iv) an English abstract and a complete methodology description (including the number of cases, dataset partitioning strategy, image segmentation method, feature extraction process, statistical modeling and quantitative analysis indicators) were provided. The following exclusion criteria were applied: i) Studies aimed only at predicting the response to nCRT; ii) article types such as review article, conference abstract, editorial letter, case reports and non-original studies; iii) studies with incomplete methodological information or lacking quantitative validation; and iv) non-English literature. Since this study is not a systematic review, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and tools for assessing methodological heterogeneity and selection bias were not applied (45).

2. Process of radiomics

Radiomics, first introduced by Lambin *et al* (46) in 2012, is a non-invasive technique that analyzes tumor heterogeneity by extracting and quantifying a range of shape, texture and other features from regions of interest (ROI) in medical images that are not visually detectable. The radiomics workflow generally includes several key stages: Image acquisition, ROI identification and segmentation, feature extraction and selection, and model building and validation (47). In the ROI segmentation step, either automated segmentation algorithms or manual techniques define the tumor region, from

Table I. Summary of radiomics and deep learning applications for predicting prognosis after nCRT.

Study	No. of patients	Design	MRI timing	Sequence	Feature type	Feature selection	Classification	Prediction target	AUC	C-index	Accuracy	Sensitivity	Specificity	Main finding	(Refs.)
Jalil <i>et al</i> , 2017	56	Retrospective single center	Pre-nCRT, post-nCRT	T2WI	Radiomics feature	Filtration histogram	Histogram	OS, DFS, RFS	/	/	/	/	/	Lower mean MPP in medium texture was independently associated with OS and DFS, kurtosis in medium texture predicted RFS	(60)
Meng <i>et al</i> , 2018	108	Retrospective single center	Pre-nCRT	CE-T1WI	Radiomics feature, clinical feature	LASSO, Cox regression	LASSO, Cox regression	DFS	Training=0.842, validation=0.837	Training=0.804 (95% CI: 0.736-0.873), P=0.001; validation=0.788 (95% CI: 0.718-0.857), P=0.005	/	/	/	/	(69)
Jeon <i>et al</i> , 2019	101	Retrospective single center	Pre-nCRT, post-nCRT	T2WI	Radiomics feature	LASSO	Cox proportional hazards	LR, DM, DFS	/	/	/	/	/	Both 2D and 3D Rad scores emerged as independent prognostic factors	(62)
Chiloire <i>et al</i> , 2020	213	Retrospective single center	Pre-nCRT, post-nCRT	T2WI	Radiomics feature	MWU, PCC	Logistic regression	DM	/	/	0.785	0.714	0.857	/	(63)
Park <i>et al</i> , 2020	78		Pre-nCRT	T2WI	Radiomics feature, clinical feature	Chi-square test or independent t-test	Logistic regression	LR	0.639	/	0.677	0.657	0.596	GLRLM_LRLGE was significantly able to predict LR	(65)
Liu <i>et al</i> , 2020	629		Pre-nCRT	T2WI, ADC	Radiomics feature, clinical feature	ICC, Cox regression, PCC	LASSO, Cox regression	DM	Primary=0.97, validation1=0.86, validation2=0.89,	Primary=0.855 (95% CI: 0.812-0.899), validation1=0.848	/	/	/	/	(57)

Table I. Continued.

Study	No. of patients	Design	MRI timing	Sequence	Feature type	Feature selection	Classification	Prediction target	AUC	C-index	Accuracy	Sensitivity	Specificity	Main finding	(Refs.)
Cui <i>et al.</i> , 2021	186	Retrospective single center	Pre-nCRT	T2WI, ADC, CE-T1WI	Radiomics feature, clinical feature	ICC, Boruta algorithm, RF	Boruta, Multivariate Cox regression	DFS	validation ³ = 0.85	(95% CI: 0.773-0.923), validation ² = 0.831 (95% CI: 0.742-0.920), validation ³ = 0.825 (95% CI: 0.728-0.921)	/	/	/	/	(55)
Tibermacine <i>et al.</i> , 2021	146	Retrospective multi-center	Pre-nCRT, post-nCRT	T2WI	Radiomics feature, clinical feature	Wilcoxon test	RF	DFS	Training= 0.77-0.89, validation= 0.67-0.76	/	/	/	/	/	(59)
Liu <i>et al.</i> , 2021	235	Retrospective multi-center	Pre-nCRT	T2WI, DWI	DL feature	/	CNN	DMFS	Primary= 0.938, validation= 0.892	Primary= 0.851 (95% CI: 0.795-0.906), validation= 0.747 (95% CI: 0.665-0.830)	/	/	/	/	(74)
Jayaprakasam <i>et al.</i> , 2022	236		Pre-nCRT	T2WI	Radiomics feature, clinical feature	MWU, LASSO	SVM	LR, DM	LR: 0.79, DM: 0.87	/	/	LR: 0.683, DM: 0.800	LR: 0.807, DM: 0.884	/	(54)
Chiloire <i>et al.</i> , 2022	48		Pre-nCRT, post-nCRT	T2WI	Radiomics feature, clinical feature	MWU, PCC	Logistic regression	DFS	0.92	/	/	1	0.775	/	(64)
Xie <i>et al.</i> , 2022	166		Pre-nCRT, post-nCRT	T2WI	Radiomics feature, clinical feature	ICC	LASSO, Cox regression	PFS	/	Training= 0.942 (95% CI: 0.922-0.962),	/	/	/	/	(51)

Table I. Continued.

Study	No. of patients	Design	MRI timing	Sequence	Feature type	Feature selection	Classification	Prediction target	AUC	C-index	Accuracy	Sensitivity	Specificity	Main finding	(Refs.)
Chiloiro <i>et al</i> , 2023	203	Retrospective single center	Pre-nCRT, post-nCRT	T2WI	Radiomics feature	MWU	Logistic regression	DFS	Training=0.79, validation=0.70	/	/	Training=0.62, validation=0.91	Training=0.88, validation=0.46	/	(52)
Wang <i>et al</i> , 2023	260	Retrospective single center	Pre-nCRT	T2WI	Radiomics feature, clinical feature	ICC, Cox regression, PCC, LASSO	LASSO, Cox regression	DM	Training=0.83, validation=0.74	Validation=0.788 (95% CI 0.751-0.825)	/	/	/	/	(68)
Zhang <i>et al</i> , 2023	800	Pre-nCRT	T2WI, DWI, ADC	DL feature	/	CNN	OS, DMFS, LRFS	/	/	OS=0.7234 (95% CI: 0.6674-0.7796), DMFS=0.7097 (95% CI: 0.6515-0.7679), LRFS=0.6794 (95% CI: 0.5605-0.7982)	/	/	/	/	(76)
Jiang <i>et al</i> , 2023	725	Pre-nCRT	T2WI	DL feature	/	XGBoost	OS, DFS	/	/	OS=0.82, DFS=0.69	/	/	/	/	(75)
Huang <i>et al</i> , 2024	454	Retrospective multi-center	Pre-nCRT	T2WI, DWI, CE-T1WI	Radiomics feature	LASSO	Logistic regression	LR or DM	Training=0.83, internal validation=0.81, external validation=0.82	/	/	0.58-0.87	0.58-0.87	/	(56)

ADC, apparent diffusion coefficient; AUC, area under the curve; CE-T1WI, contrast-enhanced T1-weighted imaging; C-index, concordance index; CNN, convolutional neural network; DFS, disease-free survival; DM, distant metastasis; DMFS, DM-free survival; DWI, diffusion-weighted imaging; ICC, intraclass correlation coefficient; LASSO, least absolute shrinkage and selection operator; LR, local recurrence; LRFS, local recurrence-free survival; MWU, Mann-Whitney U-test; nCRT, neoadjuvant chemoradiotherapy; OS, overall survival; PCC, Pearson correlation coefficient; PFS, progression-free survival; RF, random forest; SVM, support vector machine; T2WI, T2-weighted imaging; XGBoost, eXtreme gradient boosting.

which high-throughput features are extracted (48). These features include first-order features, texture features, shape features, model-based features, transform-based features and higher-order features. Techniques such as least absolute shrinkage and selection operator (LASSO), principal component analysis and minimum redundancy maximum relevance are commonly applied to select the most relevant features and prevent model overfitting (49). The predictive power of radiomics models can be enhanced by integrating selected radiomic features with clinical data, pathological findings and treatment details. Logistic regression is frequently used due to its simplicity and effectiveness as a supervised classifier, while other widely used classifiers include support vector machines (SVM), random forests (RF), k-nearest neighbors, decision trees, neural networks and Bayesian classifiers (50-52). Finally, validating model performance is essential and typically involves assessing metrics such as the receiver operating characteristic curve, calibration curve, specificity, sensitivity and decision curve analysis. For robust reproducibility, models should undergo internal validation, and, if feasible, external validation across multiple centers (53).

3. Applications of radiomics to predict prognosis

Baseline-based radiomics. Prior to nCRT in patients with LARC, baseline MRI can provide pivotal tumor characteristics, including tumor size, morphology, location, MRF invasion and lymph node metastasis. Such information is crucial for predicting tumor behavior, devising personalized treatment strategies and evaluating therapeutic outcomes. T2WI is often used for segmenting the tumor ROI due to its superior soft tissue contrast and multiplanar imaging capabilities. Accordingly, numerous studies extracted radiomics features based on pre-treatment T2WI to construct predictive models. For instance, in a retrospective study by Jayaprakasam *et al* (54), researchers explored the value of radiomics features extracted from mesorectum on pre-treatment T2WI in predicting outcomes for patients with LARC undergoing nCRT. They developed models to predict both LR and DM, achieving strong predictive performance. The area under the curve (AUC) for the LR and DM models was 0.79 and 0.87, respectively, with corresponding accuracies of 78.3 and 88.4%.

Several studies have enhanced predictive models by incorporating multiple MRI sequences, such as DWI, apparent ADC and CE-TIWI, alongside T2WI (55-57). Using multiparametric radiomics features derived from these sequences has shown promise in improving model accuracy. For instance, Cui *et al* (55) developed a model using pre-treatment T2WI, ADC and CE-TIWI to predict DFS in patients with LARC after nCRT. Their results demonstrated that the multiparametric model offered better DFS prediction accuracy than models using single sequence alone. In a larger multicenter retrospective study, Huang *et al* (56) extracted radiomics features from pre-treatment T2WI, DWI and CE-TIWI sequences to develop and validate a multiparametric MRI-based radiomics model for predicting LR or DM in patients with LARC treated with nCRT. The model achieved robust performance, with AUC values of 0.83 in the training set and 0.81 and 0.82 in the two validation sets, respectively.

These findings highlight the value of baseline MRI radiomics features, which provide extensive quantitative data to inform predictive models. The single-sequence models achieved AUC values ranging from 0.79 to 0.87 for predicting LR/DM (54), while multiparametric models exhibited improved predictive performance with AUC values of 0.81-0.83 (56). By capturing prognostic information prior to treatment, baseline MRI radiomics can help identify patients more likely to respond favorably to therapy, enabling the design of targeted treatment strategies. Furthermore, multiparametric imaging captures tumor characteristics more comprehensively than single-sequence methods, offering valuable insights for more accurate prognostic predictions (58).

Timing-based radiomics. Tumor heterogeneity in RC and its changes during treatment underscore the importance of post-treatment imaging analysis. Tibermacine *et al* (59) applied 2D manual segmentation (MS), 3D MS and bounding box methods to extract radiomics features from pre- and post-treatment T2WI following nCRT. Their model demonstrated strong predictive performance for both LR and DM, with AUC values ranging from 0.77 to 0.89 for predicting DFS. Further research by Jalil *et al* (60) explored the predictive value of textural features in pre- and post-treatment T2WI of patients with LARC treated with nCRT. The study found that both pre- and post-treatment texture features were significant predictors of recurrence-free survival ($P<0.01$), offering valuable insights for clinical prognostic assessments. These findings emphasize the predictive potential of both pre- and post-treatment imaging. They highlight the importance of comprehensive lesion analysis throughout the course of treatment to accurately assess prognosis and guide clinical decision-making.

Delta radiomics quantifies changes in tumor morphology and heterogeneity by analyzing differences between pre- and post-treatment images. It enables early prediction of tumor behavior, such as nCRT efficacy, LR and DM. As a result, it provides a foundation for personalized treatment strategies for patients (21,61). Jeon *et al* (62) extracted radiomics features from lesions in pre- and post-treatment T2WI of 101 patients with LARC. By performing phase subtraction, they derived Delta radiomics features and constructed nomograms to predict LR, DM and DFS after nCRT. These nomograms effectively risk-stratified the patients. Similarly, Chiloiro *et al* (63) developed a model to predict DM using an MRI-based Delta radiomics approach, achieving an accuracy of 80.9%, specificity of 85.7% and sensitivity of 71.4%. This demonstrated that Delta radiomics features are significantly associated with DM. In a subsequent study (64), they also confirmed that Delta radiomics features were valuable in predicting DFS in patients with LARC treated with nCRT using 0.35T MRI-guided radiotherapy. Current evidence demonstrates that delta radiomics captures the spatiotemporal heterogeneity of the tumor treatment response (predictive AUC range: 0.77-0.89), exhibiting unique advantages in clinical translation applications, including dynamic monitoring during nCRT, prognostic stratification and precision therapeutic interventions.

Based on multimodal radiomics. In the management of LARC, several factors beyond radiomic features influence patient

prognosis, including tumor indicators, pathological T-stage, N-stage, EMVI and MRF status (34,35). Park *et al* (65) found that integrating imaging signs with texture features from baseline MRI could effectively predict the efficacy of nCRT and the risk of LR. In particular, their model, which utilized the long-stroke low grey emphasis (GLRLM_LRLGE) texture feature, significantly predicted LR ($P=0.039$). Texture features are thought to correlate with histological characteristics that reflect tumor heterogeneity (66,67), and increased heterogeneity is often associated with higher malignancy. Therefore, texture features that capture the varying levels of tumor heterogeneity in LARC could enhance the ability to predict individual responses to nCRT and survival outcomes.

Certain studies suggest that combining radiomics features with clinical parameters in a joint model could enhance predictive accuracy. In a multicenter retrospective study involving 629 patients, Liu *et al* (57) developed a column chart based on MRI-derived radiomics features, which successfully predicted DM-free survival (DMFS). Furthermore, their combined model, which incorporated radiomics features alongside clinicopathological ypT and ypN staging, significantly improved the classification accuracy of DMFS outcomes. A subsequent study (68) confirmed that integrating radiomics features with ypT-stage and ypN-stage in a combined clinicopathology-imaging histology model outperformed the clinicopathology-only model in predicting DMFS. Meng *et al* (69) constructed a joint model combining pre-treatment enhanced MRI radiomics features with ypN staging and MRF status, achieving enhanced prediction accuracy for DFS, with P-values of 0.001 and 0.005 in the training and validation sets, respectively. Cui *et al* (55) developed a joint model that integrated multiparametric radiomics features with clinicopathological variables, which outperformed the clinicopathological model alone in predicting DFS, with a concordance index (C-index) of 0.803 and 0.780 in the training and validation sets, respectively. Collectively, these studies demonstrate that combining radiomics features with clinicopathological data can substantially improve the accuracy of prognosis prediction in patients with LARC.

Although radiomics-based imaging methods have shown improved predictive power for assessing nCRT outcomes in patients with LARC, manual lesion outlining for radiomics analysis remains time-consuming and labor-intensive. As a result, DL approaches may offer valuable potential for advancing research in this area.

4. Deep learning processes and applications

DL encompasses a broad range of machine learning algorithms based on multi-layer deep neural networks, rather than a specific model. Unlike radiomics, DL automatically learns to extract and select high-dimensional features through neural networks, enhancing the robustness of the model and enabling more comprehensive extraction of image information (70). Convolutional neural networks (CNNs), one of the most commonly used DL models in medical imaging, offer distinct advantages in tasks such as image segmentation and classification. A typical CNN consists of an input layer, a convolutional layer, a pooling layer, a fully connected layer and an output layer, with the convolutional layer serving as the core. CNN

directly takes the image as input, extracts features through multiple convolutional and pooling layers, processes the extracted features in the fully connected layer and produces the output based on the specific task at hand.

DL offers several advantages over radiomics: First, DL automatically learns and extracts features from images, eliminating the need for expert-driven manual feature extraction. This reduces bias and increases efficiency. Second, while radiomics features are generally applicable, they often lack specificity. In tumors that tend to undergo significant transformations, such as colorectal cancer, traditional radiomics can be less effective. By contrast, DL can extract more disease-specific features tailored to the particular type or stage of disease. Additionally, DL models exhibit strong adaptability and excellent generalization, allowing them to be adjusted and optimized for different tasks and data types. As a result, they can maintain high performance across diverse datasets and scenarios (71).

Studies using DL have primarily focused on evaluating the efficacy of nCRT in patients with LARC (72,73). Recently, however, researchers have begun exploring its potential for predicting prognosis. In a multicenter retrospective study, Liu *et al* (74) developed a multiparametric MRI-based DL model to predict DM in patients with LARC undergoing nCRT. The results demonstrated that features extracted from pre-treatment MRI scans performed well in predicting DM, with AUCs of 0.938 and 0.894 in the training and validation sets, respectively. Furthermore, incorporating clinicopathological factors into a joint model enhanced prognostic prediction, outperforming the DL model and clinical model alone ($P<0.001$).

In a multinational, multicenter study with a large cohort, Jiang *et al* (75) developed a vision transformer (ViT)-based DL model to predict the prognosis of patients with LARC using pre-treatment T2WI. The ViT model demonstrated strong predictive performance for OS, achieving a C-index of 0.82. This result highlights its potential as a preoperative risk stratification tool. Additionally, the study found that ViT outperformed conventional CNN in predicting OS, with a C-index of 0.82 for ViT compared to 0.67 for CNN. This suggests that ViT can serve as a viable alternative to CNN for imaging analysis in LARC prognosis prediction. In a multicenter retrospective study with a large sample size, Zhang *et al* (76) developed a 3D CNN model (MuST), an imaging radiomics model based on pre-treatment T2WI, DWI and ADC to predict OS, DMFS and local recurrence-free survival (LRFS), respectively. The comparison revealed that the MuST model significantly outperformed the radiomics model, as evidenced by a higher C-index. This finding suggests that DL offers a more accurate and stable approach for predicting the prognosis of patients with LARC. Current studies indicate that the predictive performance of DL models for key endpoints (OS, DM and LRFS) is consistently stable, with C-index values ranging from 0.82 to 0.94.

These studies highlight that DL models, compared to traditional machine learning models (e.g., RF, logistic regression) and manual radiological assessment, have evolved with deeper algorithmic development and model training, resulting in superior performance in prognostic prediction. This progress offers clinicians the potential for early, non-invasive risk assessment of patients and could eventually replace the labor-intensive

process of manual outlining. However, DL-based studies remain limited compared to traditional radiomics. Therefore, further research is necessary to validate model stability and explore their clinical potential.

Comparative analysis demonstrates distinct performance variations between radiomics and DL approaches in prognostic prediction. Radiomic models utilizing pre-T2WI imaging combined with clinical covariates exhibit moderate predictive capability for DM. For instance, the model developed by Wang *et al* (68) achieves AUCs of 0.83 (training) and 0.74 (validation), with the validation C-index of 0.788 (95% CI: 0.751-0.825). By contrast, the DL model integrating multiparametric MRI (T2WI + DWI) displays superior predictive performance. The DL-based DM prediction framework by Liu *et al* (74) significantly outperforms radiomic methods, attaining higher AUCs of 0.938 vs. 0.83 (training) and 0.892 vs. 0.74 (validation), alongside elevated C-index values of 0.851 (95% CI: 0.795-0.906) and 0.747 (95% CI: 0.665-0.830), respectively. This performance disparity underscores DL's inherent capacity to decode complex imaging patterns, particularly when synergizing multiparametric data with clinical features.

In predicting the prognosis of nCRT for LARC, radiomics and DL each show potential but differ in accuracy, usability and clinical feasibility. Radiomics demonstrates certain accuracy in predicting DFS, LR and DM. For instance, the radiomics model based on multiparametric MRI achieves an AUC of 0.83 for predicting LR or DM (56) and shows accuracies of 0.803 and 0.780 (55). However, its clinical application faces three major challenges: i) Variations in MRI scanning protocols across centers hinder data standardization and feature comparability; ii) manual ROI delineation is time-consuming and introduces observer-dependent bias, limiting usability; and iii) instability in feature extraction algorithms restricts model generalizability.

By contrast, DL exhibits superior predictive performance. A DL model based on pre-treatment MRI achieves AUC values of 0.938 and 0.894 in the training and validation sets, respectively, for predicting distant metastasis, and the MuST model shows a significantly higher C-index than radiomics models (74,76). The advantages of DL include automatic feature extraction to avoid human bias and adaptive learning to enhance model generalizability. However, its limitations are also evident: Complex network structures are prone to overfitting, reliance on large-scale annotated data and the 'black-box' nature that affects the interpretability of results.

Overall, both technologies face challenges related to data heterogeneity, insufficient generalizability and reproducibility. Current studies are mostly based on single-center, small-sample retrospective data and lack external validation. In radiomics workflows, subtle differences in image acquisition, ROI segmentation and feature extraction can lead to variability in results. DL models are significantly influenced by the quality of training data and the parameter optimization process is complex, making complete reproducibility across studies difficult. Future research should focus on constructing multi-center standardized databases, developing more robust feature extraction algorithms and addressing the 'black-box' issue of models through explainable technologies to enhance their clinical application value and feasibility.

5. Challenges and prospects

Radiomics, as an emerging technology, still faces several challenges in clinical application. One major issue is data standardization and quality control. Variations in equipment and inconsistencies in scanning parameters can impact the accuracy of image feature extraction and the generalization of models. Additionally, the stability and reproducibility of radiomics features limit the broader applicability of these models. Another challenge is the manual delineation of lesion ROIs, which is not only time-consuming but also prone to subjective bias, potentially compromising model accuracy. Future advancements in fully or semi-automated segmentation technologies are expected to address this limitation. Currently, most radiomics studies rely on small, single-center datasets. To improve the accuracy and reliability of these models, further validation through large-scale, multicenter, prospective studies is essential.

Likewise, the performance of DL models is heavily contingent upon the availability of extensive, high-quality labeled image datasets. Nonetheless, in the domain of medical imaging, the assembly of such datasets poses considerable challenges, especially when dealing with lesions that exhibit substantial variability. Despite the growing trend towards automated data annotation, the incorporation of manual review and verification processes remains essential to guarantee the precision and reliability of the data. Additionally, DL models, particularly complex neural networks, are often criticized as 'black boxes' because their decision-making processes are opaque, hindering their interpretability and trustworthiness in clinical settings (77). To enhance the clinical applicability of these models, it is essential to uncover the causal mechanisms underlying them and improve the transparency and interpretability of their decision-making processes. Optimizing DL algorithms is crucial for enhancing model accuracy, efficiency and interpretability. However, the significant computational resources required for DL models may limit their use in resource-limited settings. Future research should focus on developing more efficient algorithms and exploring methods to effectively integrate domain knowledge, thereby improving the utility and reliability of DL models in medical image analysis.

The clinical implementation of artificial intelligence (AI)-based prognostic models faces critical ethical and technical challenges. First, data bias compromises model fairness, as training datasets with insufficient racial, age or gender representation (e.g., overrepresentation of specific populations) reduce predictive accuracy in minority groups. Second, technical biases from cross-institutional variations in MRI field strengths and scanning protocols introduce systematic feature extraction errors. Finally, the opacity of 'black-box' decision mechanisms in DL models undermines clinical credibility, where nonlinear decision pathways lack transparency and conflict with medical traceability requirements.

Current studies demonstrate that multimodal radiomics models, which combine preoperative CT and MRI data, offer substantial advantages in predicting the response to nCRT in patients with LARC, outperforming any single imaging modality (78). However, the fusion of multiple imaging techniques, such as MRI, CT or PET/CT, has not been extensively studied for predicting the prognosis of patients with LARC (79).

Future research should explore this area further, aiming to enhance the accuracy and reliability of prognostic predictions by integrating data from various imaging modalities.

Future research should prioritize three key directions to address current limitations. First, a standardized multicenter validation framework should be established through international collaboration, including unified MRI protocols (e.g., field strength, sequence parameters, contrast agent use) and open-access LARC imaging databases. Additionally, prospective clinical trials are needed to evaluate model performance in real-world settings, providing evidence for translational practice. Second, an Explainable AI model should be developed by integrating Class Activation Mapping to visualize decision regions and Shapley Additive Explanations values to quantify imaging feature contributions (80). Third, multimodal omics integration should be pursued by merging radiomics with genomics and molecular biomarkers to comprehensively characterize tumor heterogeneity. For instance, Fathi Kazerooni *et al* (81) performed a radiogenomics analysis by integrating multiparametric MRI and whole-transcriptome sequencing in pediatric low-grade gliomas, enabling dual prediction of prognosis and therapy based on immune features.

Traditional medical imaging captures the morphological features of LARC from a macroscopic perspective, revealing overall structural and functional changes. By contrast, genetic and pathological analyses provide an in-depth view of the molecular mechanisms and histological alterations at the microscopic level, offering a more detailed understanding of tumor biology (82,83). Imaging genomics and multi-omics techniques bridge the gap between macroscopic imaging features and microscopic molecular events. These methods enable a comprehensive characterization of disease heterogeneity by extracting quantitative features from imaging data and integrating them with genomic, transcriptomic and pathological information. This integration enhances not only disease diagnosis and precise staging but also the prediction of treatment responses and patient prognosis, laying the foundation for personalized treatment strategies.

Looking ahead, improving data quality, fostering multicenter collaborations and applying advanced analytics will be crucial. The ongoing development of automated DL segmentation algorithms and end-to-end modeling approaches has the potential to overcome the limitations of current technologies. Additionally, the integration of multimodal models combining radiomics, pathomics and genomics will likely offer a more holistic view of prognosis, improving predictive accuracy and further advancing the field of precision medicine.

6. Conclusion

MRI-based radiomics and DL show promising predictive performance in assessing the prognosis of nCRT in LARC. These technologies hold substantial clinical potential as tools for early, non-invasive assessment, aiding clinicians in patient risk stratification and playing a pivotal role in the development of personalized treatment plans.

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Authors' contributions

JS and QH designed and conducted this review. JS critically revised the final version of the manuscript. YS, TD and JL conceived and drafted the manuscript. YS and TD prepared the table. JS provided funding for the research. Data authentication is not applicable. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

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Not applicable.

Competing interests

The authors declare that they have no competing interests.

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