

Research Progress of MRI Radiomics in Diagnosis, Treatment and Prognosis of Cervical Cancer

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Abstract: cervical cancer (CC) is one of the most common gynecological malignancies. Early diagnosis can improve the prognosis of patients. Magnetic resonance imaging (MRI) can clearly show the size and location of tumor lesions and the relationship with adjacent tissues, and has high sensitivity and specificity. It is an important evaluation method for the diagnosis, staging and prognosis of CC. Relative to traditional MRI images, radiomics is analyzed by extracting a large number of features from the image images, which can be used to analyze the image, it has been gradually used in CC lymph node metastasis, parauterine invasion, vascular invasion, tumor staging and prognosis. Therefore, this article reviews the research progress of MRI-based radiomics in the diagnosis, treatment and prognosis of CC.

Keywords: Cervical Cancer; Magnetic Resonance imaging; Radiomics.

1. Introduction

Cervical cancer (CC) is the fourth most common cancer in women worldwide after breast, colorectal, and lung cancer, with squamous-cell carcinoma (SCC) being the most common histologic type[1], the leading cause of cancer death in individual women, is the only disease with a clear etiology among currently known neoplasms and is thus largely preventable [2]. The clinical symptoms of early CC are not obvious, and the diagnosis is mostly in the middle and late stages. Therefore, early diagnosis and treatment are of great significance to improve the prognosis of patients. MRI has excellent contrast resolution for pelvic tissues and organs, and can clearly show the anatomy of the cervix, uterus and vagina. It is now widely used in the diagnosis and evaluation of cervical cancer [3]. However, the interpretation of MRI images depends on the experience of radiologists and lacks objectivity to some extent. In recent years, radiomics technology has emerged to extract and analyze high-dimensional quantitative features from multimodal medical images, and then analyze and guide the diagnosis, treatment and prognosis of tumors. At present, radiomics has shown significant advantages in clinical staging, lymph node metastasis, vascular invasion, Parauterine invasion and prognosis evaluation of neoadjuvant chemoradiotherapy, its clinical value is increasingly valued and recognized [4,5].

2. Diagnosis and Figo Staging of CC by MRI Radiomics

The concept of radiomics was first proposed by Dutch scholar Lambin in 2012[6]. The research mainly includes six steps: image acquisition, image preprocessing, image segmentation, feature extraction, feature selection and model construction and evaluation [7]. Early identification and diagnosis of CC is very important for the treatment and prognosis of patients, but the diagnosis of CC depends on pathological biopsy, so providing a noninvasive and diagnostic method will benefit CC patients. As a non-invasive evaluation technique, MRI radiomics has been widely used in the field of oncology medicine in recent years. Some

scholars[8] extracted radiomic features from sagittal T2WI and T1CE images, and constructed individual and combined models based on the above features to predict early CC, the results show that the combined prediction performance of T1CE and T2WI is the best, and the AUC value of its joint model reaches 0.85, which is higher than that of the separate models of T1CE and T2WI. This study shows that early CC invisible in MRI can be detected based on radiomics analysis, which can provide reference value for the early detection of CC, the development of treatment strategies and the improvement of prognosis.

Traditionally, tumor stage information is obtained by performing imaging studies and pathological biopsies, and many studies have shown that imaging omics techniques for preoperative tumor staging also have some predictive value [9-11]. Wu[12] retrospectively analyzed the imaging data of 100 CC patients on preoperative MRI, and extracted radiomic features from T2-weighted images (T2WI) and apparent diffusion coefficient (ADC); Subsequently, the model is constructed by resampling, the least absolute shrinkage and selection operator algorithm, and the minimum redundancy maximum correlation algorithm, and the performance of the model is analyzed and evaluated to predict the I-IIA and IIB-IV phases of CC, which provides a basis for the future development of CC, the results show that the AUC of the combined model is 0.902 and 0.856 in the training set and the test set, respectively, which is higher than that of the individual models of T₂WI and ADC. The National Comprehensive Cancer Network (NCCN), based on the Figo staging system, has developed detailed treatment recommendations for patients with CC of different stages, in which stage IB is a carcinoma confined to the cervix without involvement of the vagina, and stage IB is a carcinoma confined to the cervix without involvement of the vagina, for stage IB CC patients with fertility requirements, hysterectomy can be performed to preserve fertility[13]. Xu[14] extracted the 6 mm peritumoral radiomics features of 120 CC patients in stages IB and IIA, and constructed different peritumoral radiomics models and combined models, respectively, in the training group and external validation group, the AUC was 0.952 and 0.939, respectively, and the

radiomics nomogram constructed based on the intratumoral and peritumoral 3 mm omics features of T2WI could better predict the stage IB and stage IIA of CC, indicating that the radiomics nomogram constructed based on the intratumoral and peritumoral omics features of T2WI could better predict the stage IB and stage IIA of CC, to evaluate the vaginal invasion of patients with early stage CC, help to improve the clinical diagnosis rate of stage IB and Stage IIA CC, and select the appropriate treatment for patients. Therefore, MRI-based radiomics has great potential in the diagnosis and staging of CC. However, most of the studies at home and abroad predict the lymph node metastasis and para-uterine invasion of cervical cancer by studying the intratumoral characteristics alone, and there are not many reports on predicting the FIGO stage of cervical cancer by combining intratumoral and peritumoral features, the mining of peritumoral information for the evaluation of cervical cancer vaginal invasion and the accurate staging of cervical cancer may be the key point to promote the auxiliary diagnostic value of radiomics to clinical diagnosis and treatment.

3. LNM and LVSI Status of CC were Evaluated by MRI Radiomics

The presence of Lymph node metastasis (LNM) and the number of metastatic LNS are positively correlated with the poor prognosis of CC patients, the updated FIGO staging system of the International Federation of Obstetrics and Gynecology, published in 2018, recommends that patients with CC with LNM should be diagnosed with stage IIIc or above, suggesting that LNM status plays a key role in the prognosis of patients with CC[15]. Evaluation of lymph node involvement in CC patients is important for treatment planning and prognosis[16].

A scholar[17] extracted the radiomic features of 247 CC patients based on T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI) peritumoral and peritumoral regions for predicting LNM, the results showed that combined with the radiomic features of tumors in T2WI, the peritumoral 3 mm in DWI and T2WI achieved the best performance in the training and test sets, with AUCs of 0.868 and 0.846, respectively. Nomograms combining age and maximum tumor diameter with radiomic features had a c-index of 0.884 in predicting LNM. Wang[18] retrospectively analyzed the data of 124 patients with CC, and extracted radiomic features and risk factors for LNM from T2WI, T2WI fat suppression sequence (T2WI-spair), and apparent diffusion coefficient (ADC) sequences, the T2WI, T2WI-spair, ADC and joint sequence RADIOMICS scores and joint prediction models were constructed respectively, and then the radiomics scores were performed, the results showed that the joint prediction model reached the highest AUC value of 0.923, indicating that the MRI radiomics-based model showed good accuracy when used to predict LNM in CC patients.

Lymph-vascular space infiltration (LVSI) refers to the presence of tumor embolization within the dilated endothelial lining space, such as lymphatic vessels or small capillaries in the anterior part of the tumor invasion. As a critical initial step in the invasion-metastasis cascade, LVSI is an early sign of lymph node and other distant metastases and poor prognosis, especially in those cases showing negative lymph node status[19]. Cui[20] in their LVSI and prognosis study based on pre-treatment multi-parametric Magnetic Resonance Imaging

(MPMRI) radiomics features combined with clinical variables to build a model to predict CC; By extracting and analyzing MPMRI imaging omics features of 125 patients with CC. The radiomics score (Rad-score) and clinical indicators were combined to construct a stepwise logistic regression model. The results showed that the AUC of the training set was 0.823, the corresponding progression-free survival (PFS) was significantly different between the LVSI groups predicted by the model, indicating that MPMRI radiomics features combined with clinical variables can predict LVSI and prognostic outcomes in CC patients. Ma[21] extracted the radiomics features of 124 CC patients based on apparent diffusion coefficient (ADC), T2WI-SPAIR, and T2WI to predict the LVSI status of CC, which may be useful for clinical practice, the results showed that the model of establishing nomograms by combining MRI-based radiomics scores and related clinical characteristics exhibited higher AUC values of 0.897 and 0.833 in the training and test cohorts, respectively, indicating that nomograms can be used to evaluate the clinical outcomes of the patients, it is shown that the MRI radiomics-based model can be effectively predicted as lymphovascular space invasion (LVSI) in cervical cancer patients, effectively guiding healthcare decision-making and treatment planning for CC patients. Whereas in a previous study, some scholars[22] investigated the effects of small field of view (SFOV), T2-weighted MRI (T2WI), apparent diffusion coefficient (ADC), T2WI fat suppression (FS-T2WI), and fat suppression (T2WI) on the development of hyperlipidemia, as well as axial and sagittal contrast-enhanced T1-weighted MRI (T1CE) to extract imaging information from 125 CC patients to detect LVSI in CC patients based on a radiomics model of multiparametric magnetic resonance imaging (MPMRI), the results showed that the mPMRI-based combined radiomics model achieved the highest performance with an AUC of 0.940. The above studies show that radiomics has certain value for the identification of LNM and LVSI status, and provides ideas for the prognosis and treatment of patients.

4. CC Pathological Typing and Gene Phenotype were Evaluated by MRI Radiomics

The treatment and prognosis of patients with different pathological types and genetic phenotypes vary greatly. The pathological type of CC is mainly squamous-cell carcinoma, followed by adenocarcinoma, and patients with adenocarcinoma have low sensitivity to chemoradiotherapy and poor prognosis, so the pathological type and genetic phenotype are crucial for the prognosis of CC patients[23,24]. Meng[25] extracted regions of interest from MRI images of 79 CC patients using diffusion-weighted imaging (DWI), intravoxel incoherent motion imaging (IVIM), and diffusion kurtosis imaging (DKI) techniques, the results showed that the higher the degree of differentiation of CC, the higher the ADC (apparent diffusion coefficient) value, d value (true diffusion coefficient), and MD (average diffusion rate) value, the smaller the D^* (pseudo-diffusion coefficient) value, f (perfusion fraction) value, M_k (mean kurtosis), the parameter values of DWI, IVIM, and DKI can be used to distinguish CC from normal cervical tissue, and the higher the D^* (pseudo-diffusion coefficient) value, f (perfusion fraction) value, M_k (mean kurtosis) value, and DKI value can be used to distinguish CC from normal cervical

tissue, therefore, it has an important diagnostic value in differentiating the pathological types of CC, and may be of great significance in the differential diagnosis of different degrees of CC. In another study, investigators analyzed the T₂WI, DWI, and T₁CE radiomics features of patients with locally advanced CC to diagnose the pathologic classification of keratosis versus nonkeratosis in patients with locally advanced CC, the results show that in the training set and the test set, the AUC of the multi-sequence joint model reaches 0.88 and 0.79 respectively, which shows the highest prediction power compared with the single sequence model [26]. It can be seen that radiomics has high application value in image information extraction, and the radiomics model combined with high-throughput image features of multimodal sequences can be complementary, providing more data dimensions to make up for the lack of a single sequence feature.

Cancer cell metabolic gene expression is often associated with patient prognosis, drug resistance, and vulnerability to specific therapies[27].Deng[28]retrospectively analyzed the clinical and imaging data of 163 CC patients, of whom 118 were vascular endothelial growth factor (VEGF-RRB-expression, screening 9 radiomic features to construct VEGF prediction model, the AUC of Training Group and Test Group reached 0.82 and 0.70, respectively. In recent years, with the continuous progress of technology and the wide promotion of application, the genetic characteristics and molecular mechanisms of tumors have been deeply understood in the monitoring of tumor progression by gene sequencing expression, thus providing more precise treatment guidance, to promote the development of personalized therapy.

5. Evaluation of Curative Effect and Prognosis of CC by MRI

The combination of neoadjuvant chemoimmunotherapy with radical surgery, as a potential modality of novel treatment for locally advanced CC, is valuable in reducing recurrence and improving survival in patients with early CC[29].Yao[30]divided 212 CC patients who underwent surgery and adjuvant therapy into training, internal validation, and external validation cohorts, finally, eight radiomic features were screened out, and the results showed that the extreme gradient boosting (XGboost) model based on MRI image omics features performed best in recurrence prediction, the AUC in the internal and external validation cohorts was 0.833 and 0.822, respectively, whereas the nomogram integrating radiomic features and clinical factors was 0.806 and 0.718, respectively, in the internal and external validation cohorts, this study demonstrates that nomograms based on T2WI radiomics features and clinical factors are valuable for predicting recurrence risk, allowing timely planning of effective treatment for CC with high recurrence risk.

A scholar [31] collected multimodal MRI parameters, clinical features, postoperative pathological characteristics, and postoperative disease-free survival of 186 CC patients with stage IB-IIA, the clinicopathologic model, radiomics model and combined model were constructed to compare the predictive power of disease-free survival of early cervical cancer patients. The results showed that the combined model had the highest diagnostic power, the c-index of the training set and the validation set reached 0.848 and 0.784, respectively, indicating that the radiomics score based on T₁CE combined with clinicopathological features has a high

predictive power for disease-free survival of early cervical cancer.

6. Application of MRI Radiomics and Artificial Intelligence in CC

Over the past decade, dramatic increases in computing power and memory usage have enabled the development and implementation of state-of-the-art Artificial Intelligence (AI-RRB- technologies for processing radiological images, the use of AI in cancer imaging has driven the application of AI-based analysis of cancer tumors, the development of AI can now leverage radiomics and artificial intelligence in radiology to predict tumor outcome, response to various treatment modalities, and tumor mutations and molecular pathological features, among others[32].

Zhang[33]explored the predictive value of machine learning-based radiomics, intravoxel incoherent motion (IVIM) , diffusion-weighted imaging (DWI) , and their combined models for Parauterine invasion (PI) , lymph node metastasis (LNM) , deep muscle invasion (DMI) , lymphovascular space invasion (LVSI) , pathological type (PT) , degree of differentiation (DD) , and ki-67 expression levels in patients with cervical cancer, the optimal radiomics score (Rad-score) was calculated using seven machine learning methods by retrospectively analyzing the data of 180 patients with cervical cancer, combining IVIM-DWI and clinical parameters to construct nomogram pairs for the prediction of CC risk factors, the results showed that the diagnostic efficacy of nomograms based on clinical and imaging parameters was significantly better than that of MRI assessment alone. The AUC values of nomogram and MRI assessment for PI, LNM, and DMI were 0.981,0.848, and 0.896, respectively. Nomograms also performed well in assessing the expression levels of LVSI, PT, DD, and Ki-67, with aucs of 0.796,0.854,0.806,0.839, and 0.840, 0.856, 0.810, 0.832 for the training and validation groups, respectively, and nomograms of 0.840, 0.856, 0.810, 0.832, it is shown that nomograms based on machine learning can be used as a useful tool to evaluate the risk factors of cervical cancer patients after surgery.

Wang[34]in a study exploring the utility of machine learning-based radiomics in predicting disease-free survival (DFS) and overall survival (OS) in patients with locally advanced CC treated with concurrent chemoradiotherapy (CCRT) ; Six machine learning methods were used to construct the best radiomics model by collecting the data of 700 patients with IB2-IVA CC who underwent CCRT and continued follow-up for radiomics features of T₂WI and peritumoral 5 mm, the results show that in the prediction of DFS, the Random Survival Forest Model (RSF) model combining tumor and peritumoral radiomics shows the best prediction power, and the prediction accuracy is better than that of other models, the AUCS for predicting 1-, 3-, and 5-year DFS in the training, validation, and test sets were 0.986,0.989,0.990, and 0.884,0.838,0.823, and 0.829, 0.809, 0.841, respectively. Among the predictions of Os, the gradient boosting machine (GBM) model performed best, with aucs of 0.999,0.995, 0.978 and 0.981,0.975,0.837and 0.904, 0.860, 0.905. respectively, it is shown that the machine learning-based radiomics model is helpful to predict the DFS and OS after CCRT in LACC patients, while suggesting that the combination of tumor and peritumoral information has higher predictive power, which can be used to predict the prognosis

of LACC patients, it can provide a reliable basis for the treatment decision of patients with CC. As a powerful machine learning method, deep learning has made significant progress in medical image analysis in the current medical research field. Through deep learning algorithms, more accurate image features can be extracted to perform individualized analysis of patients and provide clinicians with more comprehensive information to develop more accurate personalized treatment plans. However, due to the various factors affecting the acquisition of imaging data, including equipment parameters, scanning technology, operator experience, etc., it is necessary to take measures to ensure the reliability and stability of the data, therefore, the application of artificial intelligence still has a lot of space for development.

7. Summary

Radiomics uses high-throughput computing to extract a large number of quantitative feature metrics from a specific medical imaging modality, which can be used to identify specific imaging modalities, mining the correlation between pathological indicators or multi-omics analysis to provide auxiliary value for oncological diagnosis, prognosis and outcome monitoring. MRI radiomics has a broad development prospect in the application of CC, and it can be used in the diagnosis and prognosis of cancer, a wide range of imaging techniques and methods have evaluated the role of radiomics in identifying prognostic factors of CC, assessing response to therapy, and predicting CC recurrence and lymph node metastasis, vascular invasion, etc. In recent years, artificial intelligence has been used in combination with radiomics features, and artificial intelligence-based methods have made important progress in the field of cervical cancer imaging. While radiomics can aid clinical classification and prediction, most studies are retrospective and still face challenges in clinical practice such as generalizability, interpretability, and convenience, etc., in addition, the parameters and quantity of radiomics are determined by the subjectivity of the operator. At present, there are no optimal standard guidelines, and there are certain bias estimates, therefore, this requires continuous efforts and exploration of scientific researchers in future research.

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