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ORIGINAL RESEARCH

Magnetic Resonance Imaging Radiomics-Based Model for Prediction of Lymph Node Metastasis in Cervical Cancer

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Background: Cervical cancer remains a major cause of mortality among women globally, with lymph node metastasis (LNM) being a critical determinant of patient prognosis.

Methods: In this study, MRI scans from 153 cervical cancer patients between January 2018 and January 2024 were analyzed. The patients were assigned to two groups: 103 in the training cohort; 49 in the validation cohort. Radiomic features were extracted from T2-weighted imaging (T2WI) and apparent diffusion coefficient (ADC) maps. The ITK-SNAP software enabled three-dimensional manual segmentation of the tumor regions in cervical cancer to identify regions of interest (ROIs). The collected data was divided for the training and validation of the Support Vector Machine (SVM) model.

Results: The combined T2WI and ADC-based radiomics model exhibited robust diagnostic capabilities, achieving an area under the curve (AUC) of 0.804 (95% CI [0.712–0.890]) in the training cohort and an AUC of 0.811 (95% CI [0.721–0.902]) in the validation cohort. The nomogram that includes radiomic features, International Federation of Gynecology and Obstetrics (FIGO) stage, and LNM has a C-index of 0.895 (95% CI [0.821–0.962]) in the training cohort and a C-index of 0.916 (95% CI [0.825–0.987]) in the validation cohort. The C-statistics are all above 0.80, and the predicted variables are nearly aligned with the 45-degree line, consistent with the results shown in the calibration plot. This indicates that our model demonstrates good discrimination ability and satisfactory calibration.

Conclusion: The MRI radiomics model, leveraging T2WI combined with ADC maps, offers an effective method for predicting LNM in cervical cancer patients.

Keywords: MRI, radiomics, lymph node, metastasis, cervical cancer

Introduction

Cervical cancer ranks as the fourth most prevalent cancer among women globally, contributing substantially to both morbidity and mortality.[1] According to the World Health Organization, there were over 660,000 new cases and 350,000 deaths attributed to cervical cancer worldwide in 2022.[2] This high incidence underscores the need for effective diagnostic and treatment approaches, particularly in areas with limited healthcare resources. The presence of lymph node metastasis (LNM) is a pivotal factor in the prognosis of cervical cancer, as it markedly reduces survival rates.[3] Researches indicated that patients with LNM have a significantly lower 5-year survival rate of 50–55%, compared to 85–90% for those without LNM.[4,5] This stark contrast highlights the critical need for precise diagnostic methods to identify LNM at early stages.

Many attempts for detecting LNM in cervical cancer using imaging technologies like magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography combined with CT (PET/CT) have shown mixed results in terms of sensitivity and specificity. MRI and CT scans generally achieve sensitivity rates of 56–87% and specificity rates of 70–93%, whereas PET/CT scans tend to have higher specificity (up to 98%) but variable sensitivity ranging from 53–94%.[6–8] Recently, a radiomics-based model employing MRI has shown promise in enhancing the

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detection of clinically significant features that traditional imaging methods might miss, potentially raising both sensitivity and specificity above conventional levels.[9,10] Studies utilizing MRI-based radiomics models has reported area under the curve (AUC) values ranging from 0.76 to 0.89, demonstrating excellent predictive accuracy.[10] These models excel at identifying subtle imaging patterns associated with metastases, even in instances where lymph nodes are not visibly enlarged. Radiomics represents a substantial advancement over traditional imaging techniques, providing a deeper analysis of tumor biology and lymph node status. This methodology not only improves the accuracy of predicting LNM but also aids in more precise staging and treatment planning, which could lead to enhanced outcomes for patients with cervical cancer.

Despite representing a significant advancement over traditional imaging techniques in the in-depth analysis of tumor biology and lymph node status, radiomics faces several challenges in practical applications. Among these, variability in imaging protocols and feature reproducibility are major issues. Different imaging devices and environmental conditions can lead to significant differences in imaging features, potentially affecting the accuracy and applicability of the models. Therefore, ensuring consistency and reproducibility of features will be crucial when developing and implementing MRI-based radiomics models.

However, many previous studies focused on feature extraction, and relatively few studies comprehensively analyzed the repeatability and clinical relevance of features. This study aimed to develop and validate an imaging radiomics model based on MRI T2-weighted imaging (T2WI) combined with apparent diffusion coefficient (ADC) maps to predict LNM in cervical cancer patients. By leveraging Least Absolute Shrinkage and Selection Operator (LASSO) algorithm to analyze diverse radiomic features, we seek to enhance the precision of LNM detection, thereby improving the clinical management and prognosis of cervical cancer. The ultimate goal is to provide a non-invasive, reliable, and cost-effective predictive tool that could be seamlessly integrated into routine clinical workflows, offering substantial benefits for the staging and treatment planning of cervical cancer.

Materials and Methods

Study Design and Patients

This retrospective analysis included 153 cervical cancer patients admitted to our hospital from January 2018 to January 2024. Prior to any therapeutic intervention, all patients underwent MRI scans. The inclusion criteria were a diagnosis of cervical cancer, staging according to the International Federation of Gynecology and Obstetrics (FIGO) standards, and no prior treatment that could impact lymph node status. Exclusion criteria included previous pelvic surgeries or therapies that might alter lymphatic architecture. Patients were randomly divided into training and validation cohorts using random numbers. The cohort was segmented into a training set of 103 patients for model development and a validation set of 50 patients for performance evaluation.

Ethical Approval

Ethical approval for the study was secured from the institutional review board, and informed consent was obtained from all participants. This study is conducted in accordance with the Declaration of Helsinki.

MRI Acquisition and Segmentation

MRI data were collected using a 3.0 T GE MRI scanner equipped with a 16-channel phased-array coil. For T2WI, the parameters set were: Repetition time/Echo time (TR/TE) of 4000/90 ms, Field of View (FOV) of 320×290 mm, a matrix of 300 × 280, slice thickness of 4 mm, and a slice gap of 0.8 mm. Diffusion-weighted imaging (DWI) utilized parameters of TR/TE = 2800/70 ms, FOV = 320×300 mm, matrix = 95 × 90, thickness = 4 mm, and a gap of 0.8 mm, with b values of 0 and 1000 s/mm^2. ADC maps were then generated from these b values. Regions of interest (ROIs) were manually delineated by two experienced radiologists using ITK-SNAP software on axial slices from both T2WI and ADC maps (Figure 1). They are unaware of the LNM results. Profiles were then reviewed by dual-certified radiology and nuclear medicine physicians with >15 years of experience in MRI interpretation in oncology. Any discrepancies were agreed

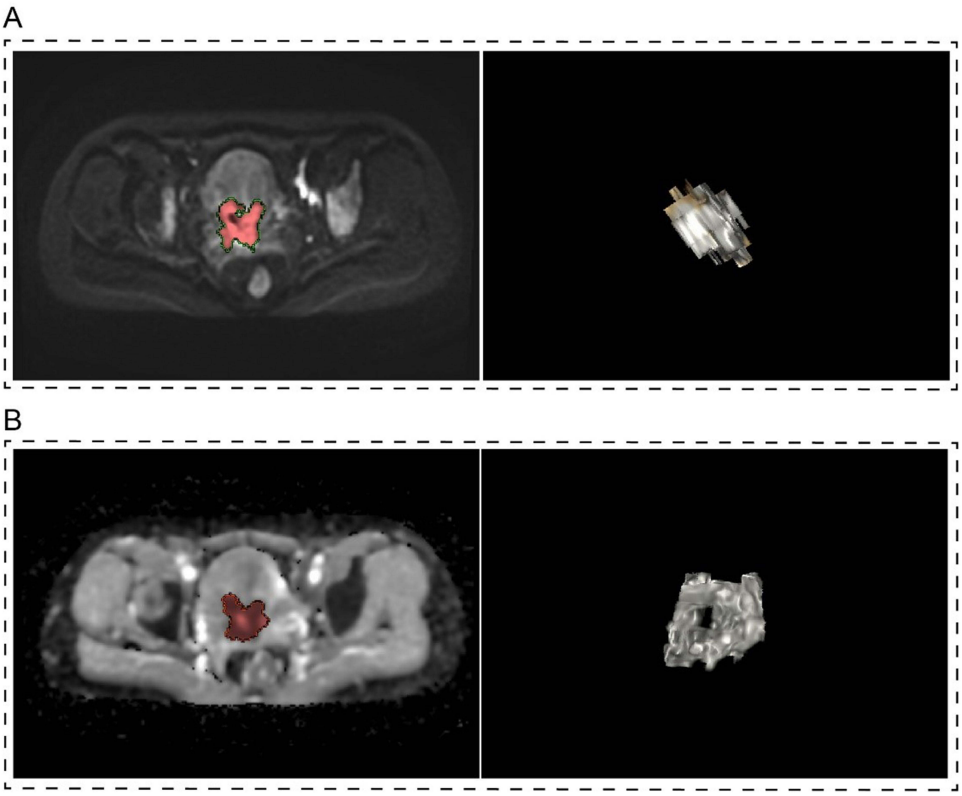

Figure 1 ROIs of MRI segmentation in this study (**A**). ROIs on T2WI; (**B**). ROIs on ADC.
Abbreviations: ROIs, regions of interest; MRI, magnetic resonance imaging; ADC, apparent diffusion coefficient.

upon by consensus. In subsequent analyses, only radiomics features with good interobserver reproducibility (intraclass correlation coefficient [ICC] >0.8) were included.

Radiomic Feature Extraction and Selection

From the segmented MRI images, a total of 1,264 radiomic features were extracted, encompassing shape-based, first-order statistics, textural features, and higher-order features derived through filter-based methods such as wavelet transforms. To select the most predictive features, we employed the LASSO method, which is particularly effective in managing multicollinearity and improving the interpretability of the model. Radiomics features were selected using the LASSO regression method with 10-fold cross-validation, resulting in 15 nonzero coefficients at the optimal lambda (λ).

Radiomics Model Construction and Validation

Feature extraction and selection were performed using in-house software (PyRadiomics package version 3.7.2). The feature extraction parameters were set as follows: resampledPixelSpacing: [1, 1, 1], normalize: true, normalizeScale: 500, padDistance: 10, with Original: () and Wavelet: (), while the remaining parameters were left at default settings. After feature selection, we employed a support vector machine (SVM) model with a radial basis kernel and a regularization parameter C to predict LNM using the selected features. We determined the optimal C value through 10-fold cross-validation in the training cohort, selecting the value that maximized the AUC as the optimal regularization parameter. After training the SVM model with this optimal C value, it predicts a radiomics signature reflecting the LNM probability for each patient. A 95% confidence interval (CI) was also determined to quantify the discriminative ability of the SVM model. For the imaging features of the predictive model, please refer to the Table S1 (Table S1, showing the selected features and associated coefficients).

Radiomics Nomograms Development and Performance

A multivariable logistic regression analysis was employed to construct a radiomics nomogram. The discrimination performance of the nomogram was evaluated using the C-index. Additionally, to assess the calibration performance, which determines how closely the model's predictions align with the observed outcomes, calibration curves were plotted. The Hosmer-Lemeshow (H-L) test was conducted alongside this, where a significant test statistic indicates a discrepancy between the model's prediction of lymph node metastasis and the observed metastasis outcomes. Radiomics features with both intraobserver and interobserver ICCs values greater than 0.80 were selected. Apply the LASSO Cox regression algorithm suitable for high-dimensional data in the training dataset to select the most predictive non-zero coefficient features from the selected texture features with good reproducibility. The linear combination of the selected features, weighted by their respective coefficients, derives a radiomic score for each patient, reflecting the risk of LNM.

Fifteen radiomics features with non-zero coefficients were selected from the LASSO logistic regression model. Radiomics features were constructed based on regression analysis and radiomics scores were calculated for each patient. The formula for calculating Radiomics feature scores was Score = Intercept + Coefficient × Radiomics feature. Details of the radiomics features are described in the Table S1 (Table S1, showing the selected features and associated coefficients).

Statistical Analysis

Statistical analyses were conducted using the R software. The LASSO logistic regression model was implemented utilizing the "glmnet" package. For constructing the nomogram and generating calibration plots, the "rms" package was employed. The H-L test was conducted using the "Resource Selection" package. Continuous variables were described using means and standard deviations, while categorical variables were summarized by counts and percentages. The equality of variances between the groups with positive and negative LNM for continuous clinical variables was tested using the two-sample *t*-test. For categorical variables, differences between groups were assessed using the Chi-square test and Fisher's exact test when appropriate. A p-value of less than 0.05 was considered statistically significant for all tests. The Supplementary Materials introduce the packages available in R software.

Results

Clinical Characteristics of Patients

The study comprised 153 cervical cancer patients, with 103 in the training cohort and 50 in the validation cohort. The participants had an average age of 48 years, with a range of 28 to 72 years. Approximately 98% of the patients were diagnosed at early stages (FIGO I–II), and the remaining 2% at advanced stages (FIGO III). In the training cohort, the proportion of LNM that was histopathologically confirmed was 25%, while in the validation cohort, this proportion was 28%. Additional clinical characteristics, such as histological type and lymphovascular space invasion (LVSI) status, were detailed in Table 1.

Feature Extraction and Selection

A total of 1,264 features were extracted from the ROIs of T2WI and ADC images. These features were methodically selected from the combined datasets of the two scan sequences to construct a comprehensive radiomics signatures. Subsequently, the LASSO regression was applied to hone in on the most significant predictors, refining the feature set down to 15 critical radiomic features. These features were selected based on their coefficients obtained from the LASSO logistic regression model, as depicted in Figure 2.

Radiomics Signature Construction and Validation

Based on the 15 significant features identified, radiomics scores for the patients in both the training and validation cohorts were calculated based on the SVM model, respectively. The distributions of these radiomic scores are presented in Figure 3. For the combined use of T2WI and ADC, the radiomics signature yielded an AUC of 0.804 (95% CI [0.712–0.890]) in the training cohort, and 0.811 (95% CI [0.721–902]) in the validation cohort, as shown in Figure 4.

Table 1 Characteristics of Patients in the Training and Validation Cohorts

Characteristics	Training Cohort (n=103)			Validation Cohort (n=50)		
	LNM+ (26)	LNM- (77)	*p*	LNM+ (14)	LNM- (36)	*p*
Age (years)						
Mean	49.34	45.18	0.089	50.49	46.79	0.085
SD	10.21	9.32		11.32	9.31	
BMI, kg/m2						
Mean	22.8	22.9	0.705	23.2	22.8	0.892
SD	2.1	2.2		2.3	2.1	
FIGO stage (n,%)						
IB	13 (50.00%)	24 (31.17%)	0.081	3 (21.43%)	16 (44.44%)	0.079
IIA	10 (38.46%)	31 (40.26%)		6 (42.86%)	13 (36.11%)	
IIB	3 (11.54%)	20 (25.97%)		5 (35.71%)	6 (16.67%)	
IIIA	0	2 (2.60)		0	1 (2.78)	
Histology (n,%)						
SCC	23 (88.46%)	62 (80.51%)	0.823	12 (85.71%)	31 (86.11%)	0.782
AC	3 (11.54%)	10 (12.99%)		2 (14.29%)	4 (11.11%)	
ASC	0	5 (6.49%)		0	1 (2.78%)	
LVSI (n,%)						
Negative	15 (57.69%)	35 (45.45%)	0.008	5 (35.71%)	15 (41.67%)	0.041
Positive	11 (42.31%)	42 (54.54%)		9 (64.29%)	21 (58.33%)	

Abbreviations: LNM, lymph node metastasis; FIGO, International Federation of Gynecology and Obstetrics; SCC, squamous cell carcinoma; AC, adenocarcinoma; ASC, adeno squamous carcinoma; LVSI, lymphovascular invasion; BMI, body mass index.

Radiomics Nomogram Development and Performance

The radiomics nomogram (shown in Figure 5), which integrated the optimal radiomics signature from the combined T2WI and ADC scans, achieved a C-index of 0.895 (95% CI [0.821–0.962]) in the training cohort and 0.916 (95% CI [0.825–0.987]) in the validation cohort. The calibration curve for the nomogram, indicating the probability of LNM, showed good agreement between the predicted and observed outcomes in both the primary and validation cohorts, as depicted in Figure 6. The H-L test resulted in insignificant values (p=0.437 and p=0.281 in the training and validation cohorts, respectively), suggesting that the model predictions closely align with the actual data, with no evidence of poor fit.

Discussion

The development and validation of an MRI radiomics-based model to predict LNM in cervical cancer represent a significant advancement in oncological imaging. By leveraging machine learning algorithms to analyze radiomic signatures, this model provided a high diagnostic accuracy, potentially leading to improved patient stratification and more tailored treatment strategies.[11,12] This approach aligns with the shift towards precision medicine, where therapeutic decisions are increasingly based on detailed individual patient data.[13]

Knowledge of lymph node status is crucial for deciding between options such as radical hysterectomy and adjuvant treatments in cervical cancer management.[14] Currently, the gold standard for assessing lymph node status in early-stage cervical cancer is through histopathologic examination, which, despite its accuracy, is invasive, costly, and associated with a significant risk of complications. In early-stage cervical cancer, the incidence of LNM is approximately 15–20%, indicating that up to 80–85% of patients may not have lymph node involvement.[15] For these patients, lymph node dissection might not offer direct benefits and could lead to unnecessary complications, thereby impacting their quality of

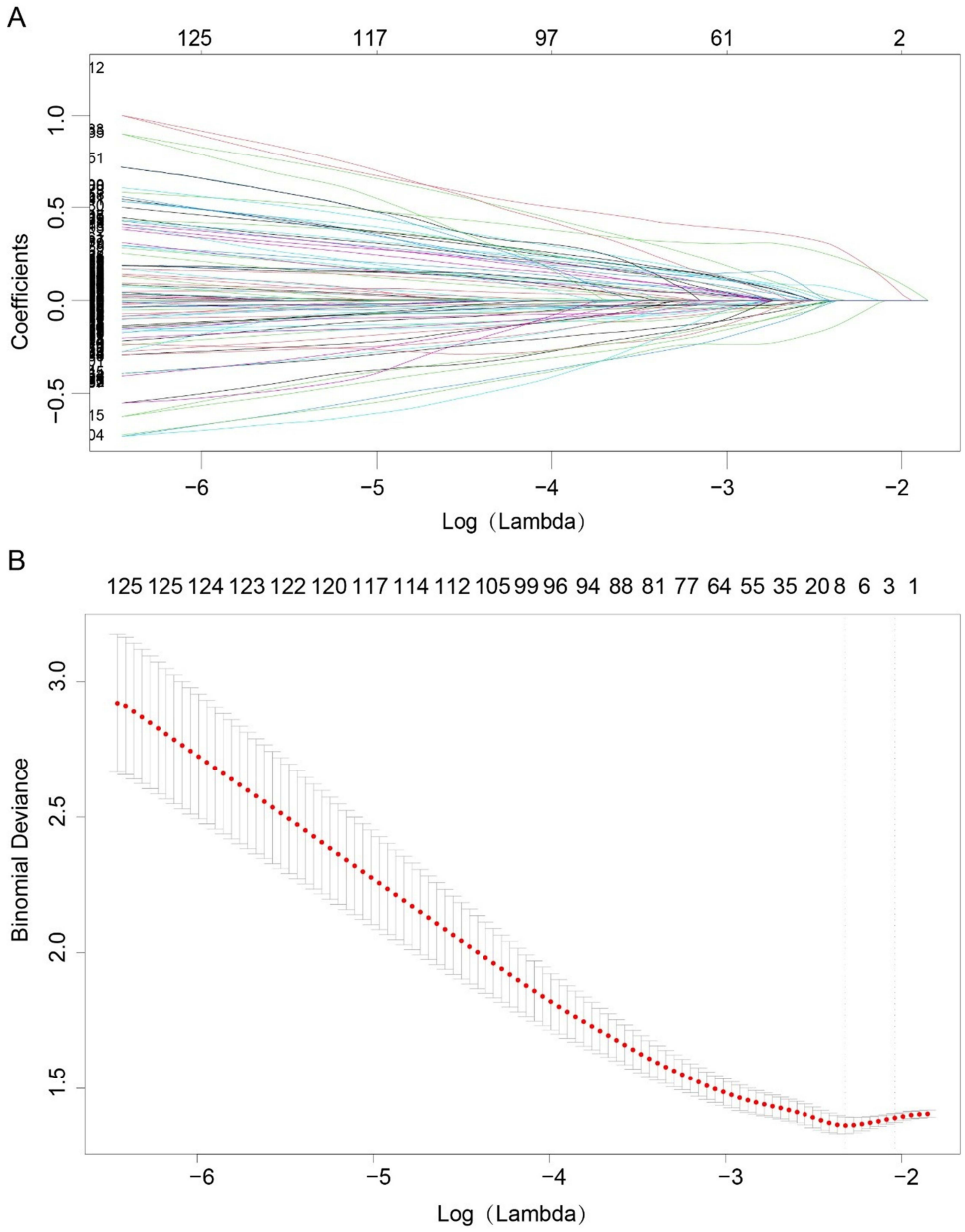

Figure 2 Feature selection process based on LASSO logistic regression model. (**A**). Radiomics features were selected using the LASSO regression method with 10-fold cross-validation, resulting in 15 nonzero coefficients at the optimal lambda (λ); (**B**). The tuning parameter λ in the LASSO model was determined using 10-fold cross-validation and minimum criteria.

Abbreviation: LASSO, Least Absolute Shrinkage and Selection Operator.

life.[15] A promising alternative is the development of radiomic models that use signatures derived from medical imaging to preoperatively assess the likelihood of lymph node involvement. These models provide a noninvasive and repeatable method to predict lymph node status, potentially allowing patients without LNM to avoid the risks and complications of unnecessary lymphadenectomy.[16–18] The present study contributes a valuable radiomic prediction tool that supports noninvasive identification of lymph node status in patients with cervical cancer, aligning with modern healthcare goals of minimizing intervention risks while maintaining effective cancer care.

The performance metrics reported in this study align with the burgeoning body of literatures that demonstrated the potential of radiomics in enhancing tumor detection and characterizing metastatic patterns across various cancers, including breast, colorectal, and prostate cancers. Specifically in cervical cancer.[16,18,19] Specifically in cervical cancer, recent research has shown that MRI radiomics models utilizing T2WI, T2WI-SPAIR, and ADC sequences hold

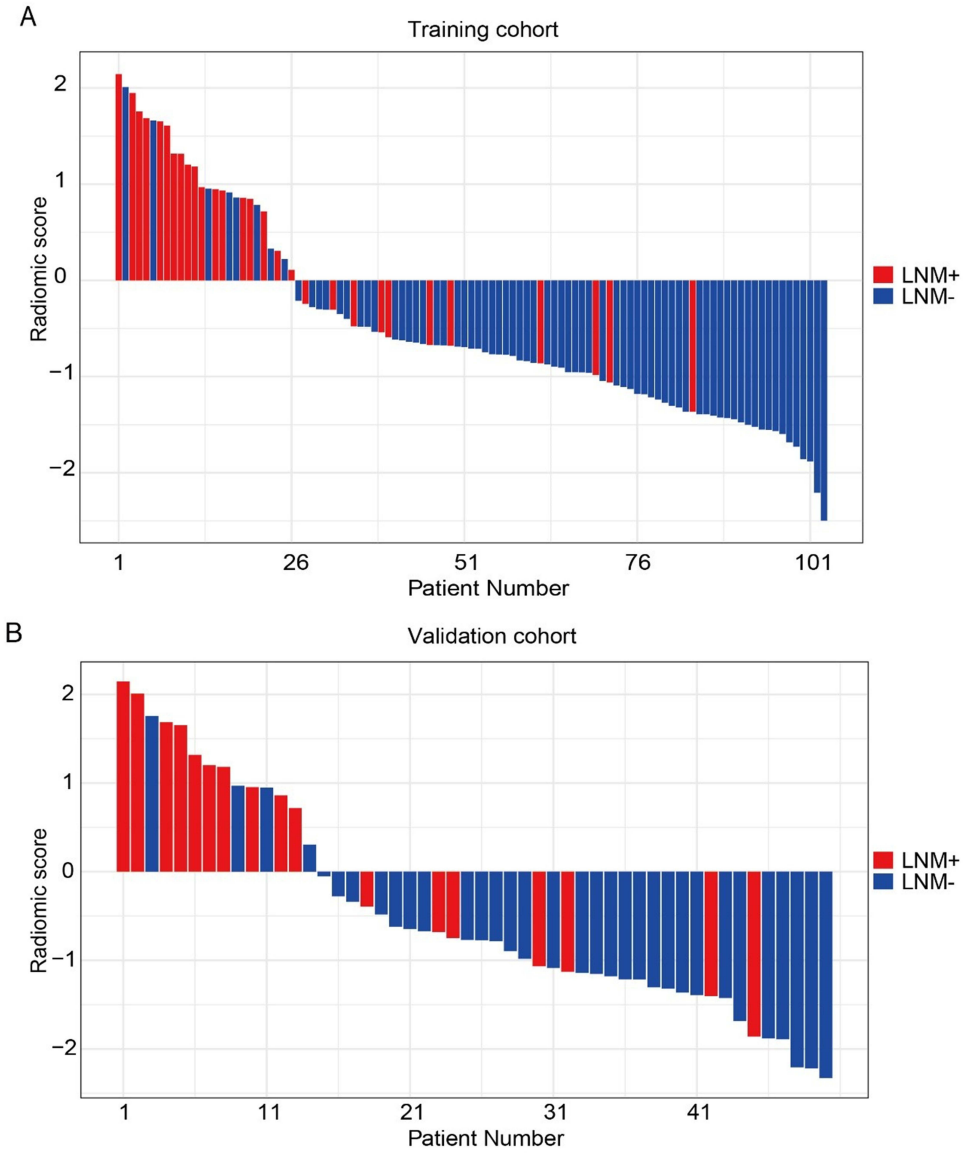

Figure 3 Distributions of the radiomic score and LNM status in the training and validation cohorts. (**A**). Radiomic score in training cohort; (**B**) Radiomic score in validation cohort. Radiomic score = Intercept + Coefficient × Radiomics feature. Details of the radiomics features are described in the Supplementary Material.
Abbreviation: LNM, lymph node metastasis.

substantial promise for accurately predicting LNM status.[20] In addition, Wang T et al[21] found that a radiomics signature combining T2WI and DWI achieves higher AUC values than those derived from T2WI or DWI alone in early-stage cervical cancer. Teo PT et al[22] used ensemble feature selection techniques to select features related to lymphedema in head and neck cancer, which reduced the data dimension of radiotherapy for head and neck cancer and improved the reliability and performance of feature selection. However, ensemble feature selection usually combines a variety of feature selection methods (such as LASSO, random forest, decision tree, etc). The results of each method are integrated through strategies such as voting and weighting. However, despite the promising findings from different studies,[23–26] there are some discrepancies in the results of these different studies that may stem from several factors.[10] One primary reason could be the heterogeneity in selected radiomic features and the algorithms employed, as each study may prioritize different feature sets based on varying imaging protocols, software, and statistical methods. Additionally, variations in the demographic and clinical characteristics of patient populations can affect the generalizability and applicability of findings. Differences in study design also play a role, with variations stemming from whether studies are

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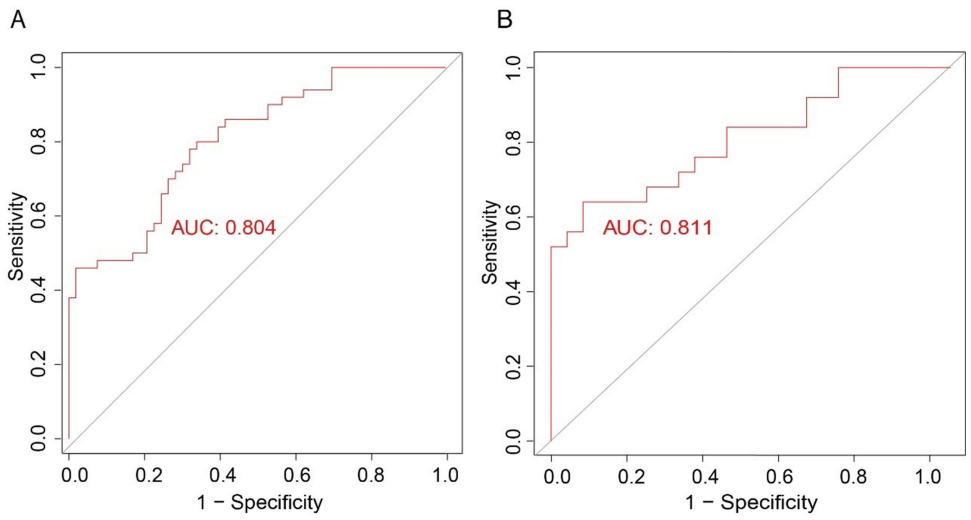

Figure 4 ROC curves of SVM models for radiomics signatures. (**A**) ROC curve in the training cohort; (**B**) ROC curve in the validation cohort.
Abbreviations: ROC, receiver operator characteristic; SVM, support vector machine.

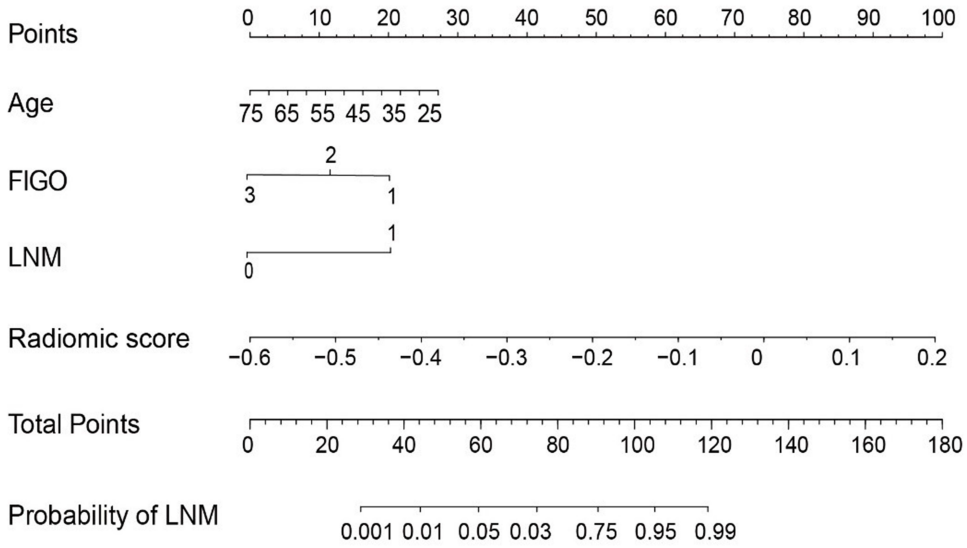

Figure 5 The nomogram of predictive model in the training cohort. Based on the training cohort, a nomogram was constructed using age, FIGO stage, LNM, and Radiomic score indicators. This chart allows for the quick calculation of the probability of LNM.
Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; LNM, lymph node metastasis.

retrospective or prospective, multicentric or single-center, and their specific inclusion and exclusion criteria. These discrepancies underscore the necessity for standardized protocols in radiomic studies. Establishing consensus on feature extraction techniques and machine learning models is crucial to ensure that findings are reproducible and can be reliably applied in clinical settings across diverse geographical and clinical contexts.

In addition, there are more and more researches on deep learning methods in recent years. Deep learning methods use neural networks, especially convolutional neural networks (CNN), to automatically learn features directly from image data. These models are trained on large datasets to identify complex patterns and hierarchical features without manual feature extraction. Deep learning has the potential to improve prediction performance by revealing relationships in the data that may not be readily apparent. However, the resulting features are generally more difficult to interpret because they arise from multiple levels of complex calculations rather than explicit measurements. The main difference between hand-designed image-based radiomics features and deep learning image features lies in feature extraction methods and

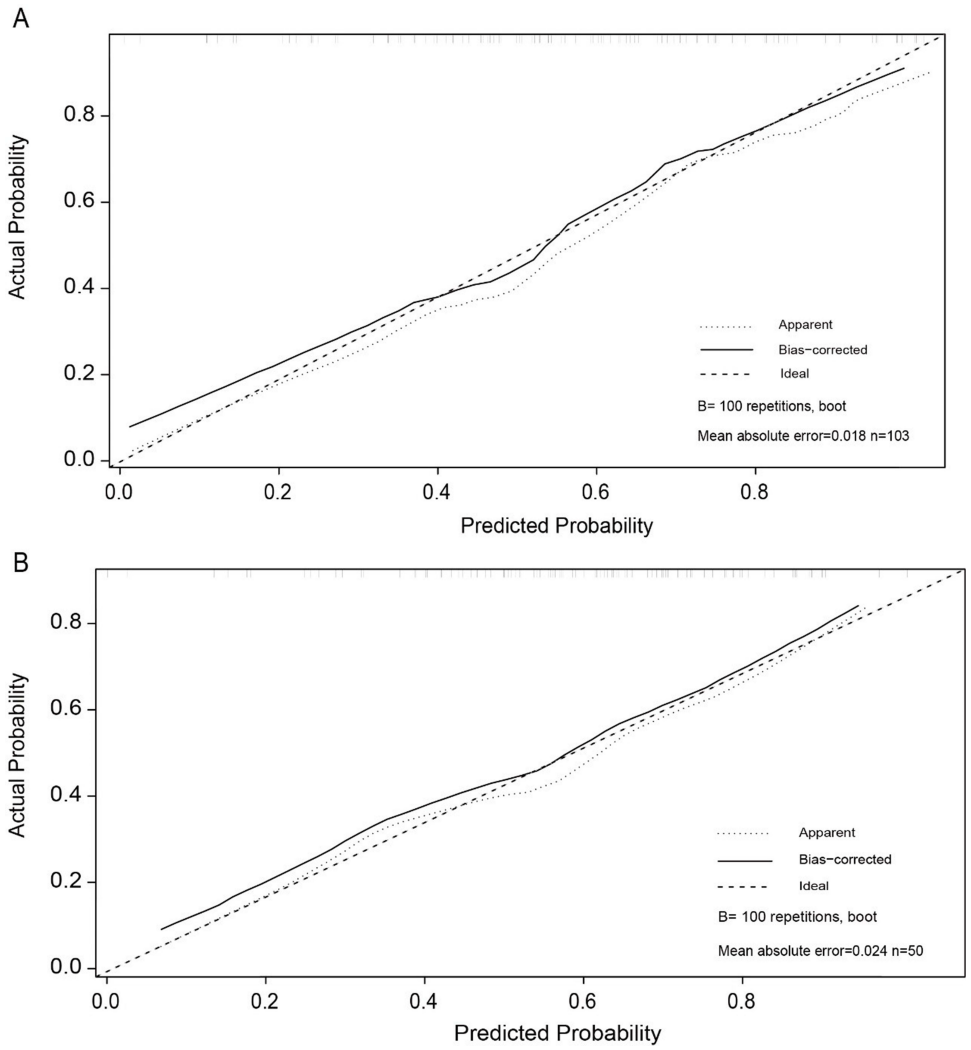

Figure 6 Calibration curves of the radiomics nomogram for predicting LNM. (**A**) Calibration curve in training cohort (p = 0.437); (**B**) Calibration curve in validation cohort (p = 0.281). The "Apparent" line represents the calibration accuracy of the original model, while the "Bias-corrected" line illustrates the relationship between actual and predicted probabilities of the bootstrap model. The "Ideal" line serves as the reference. The plot shows a strong agreement between the Apparent and Bias-corrected calibrations.

interpretability. Manual features provide a more transparent link between image features and clinical outcomes, while deep learning models provide higher prediction accuracy through automated, complex feature learning.

Although this study has shown promising results, there are indeed several limitations that warrant attention. Firstly, the retrospective design may introduce potential selection bias, as the data may not comprehensively represent the broader population of cervical cancer patients. This bias could affect the study's outcomes and conclusions. Secondly, reliance on a single type of MRI scanner may limit the applicability of the findings across different clinical settings. This specificity may hinder the generalization of the radiomics model to other environments.

Secondly, the quality of the MRI dataset, where image quality may vary due to factors such as differences in patient positioning, changes in scanner calibration, and inherent limitations of the imaging technique used. This may have an impact on the reliability of radiomics analysis and predictive modeling. For future studies, we would like to incorporate advanced image quality control techniques and utilize machine learning methods to better handle the variations in image quality, as these developments may further enhance the effectiveness of radiomics-based prediction.

Regarding performance metrics, we did not focus on the F1-score and Brier score in this study. Considering these aspects, future research may benefit from adopting a more diverse range of model evaluation methods. By combining traditional and appropriate scoring approaches, researchers can more comprehensively assess model performance,

particularly in terms of calibration and predictive confidence. Additionally, the small size of the study cohort, particularly in the validation group, could further compromise statistical robustness, making it difficult to detect smaller yet clinically significant differences.

To address these limitations, future research should aim to conduct larger, multi-center studies to robustly validate the findings and refine the radiomics model across a more diverse patient population. Moreover, the use of a single model (LASSO) in this study may introduce model bias. Future studies will integrate ensemble feature selection methods to enhance our findings and ensure the robustness and reliability of the selected features.

Finally, incorporating a wider array of clinical variables (such as tumor size and invasion size) could significantly enhance the predictive accuracy and clinical relevance of the model, further supporting its utility in personalized medicine for cervical cancer. We recognize the limitations of focusing solely on image-based radiomics features, and future research should consider integrating patient demographics, clinical characteristics, treatment details, and radiation dose parameters to enhance the model's comprehensiveness and clinical applicability.

Conclusion

In conclusion, this study successfully developed and validated an effective and accessible radiomics model that utilizes T2WI and ADC data for the preoperative prediction of LNM metastasis in patients with cervical cancer. This integration of MRI radiomics holds the potential to significantly enhance individualized treatment planning for patients with cervical cancer, thereby improving prognostic accuracy and optimizing therapeutic strategies tailored to individual patient profiles. Future research should aim to conduct larger-scale multicenter studies to more robustly validate the research findings and refine radiomics models in a more diverse patient population.

Data Sharing Statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethic Statement

This research project has been approved by Xi'an People's Hospital and operated in strict accordance with ethical standards. In this study, we respect and protect the rights and privacy of participants and ensure the confidentiality of their personal information.

Participants' Informed Consent

We explained the purpose, process, risks and benefits of the study to all individuals involved in the study orally or in writing, and obtained their informed consent. Participants have the right to know that their participation is voluntary and can withdraw from the study at any time.

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Disclosure

The authors declare that there is no competing interest associated with the manuscript.

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