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ORIGINAL RESEARCH

Development and Validation of Radiomics-Based Models for Predicting the Parametrial Invasion in Stage IB1 to IIA2 Cervical Cancer

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Objective: To develop an early warning system that enables accurate parametrial invasion (PMI) risk prediction in cervical cancer patients with early-stage.

Methods: We retrospectively collected 218 early-stage cervical cancer patients who were treated in Jingzhou Central Hospital from January 31, 2015, to January 31, 2023, and diagnosed with early stage cervical cancer by pathology. The prediction model training is achieved by randomly dividing 70% of the training queue population, with the remaining 30% used as the testing queue. Then, a prediction model based on machine learning algorithms (including random forest, generalized linear regression, decision tree, support vector machine, and artificial neural network) is constructed to predict the risk of PMI occurrence. Ultimately, the analysis of receiver operating characteristic curve (ROC) and decision curve analysis (DCA) is used to evaluate the predictive ability of various prediction models.

Results: We finally included radiomics-based candidate variables that can be used for PMI model. Multivariate logistic regression analysis showed that energy, correlation, sum entropy (SUE), entropy, mean sum (MES), variance of differences (DIV), and inverse difference (IND) were independent risk factors for PMI occurrence. The predictive performance AUC of five types of machine learning ranges from 0.747 to 0.895 in the training set and can also reach a high accuracy of 0.905 in the testing set, indicating that the predictive model has ideal robustness.

Conclusion: Our ML-based model incorporating GLCM parameters can predict PMI in cervical cancer patients with stage IB1 to IIA2, particularly the RFM, which could contribute to distinguishing PMI before surgery, especially in assisting decision-making on surgical scope.

Keywords: cervical cancer, machine learning, parametrial invasion, gray level co-occurrence matrix, prediction model

Introduction

Cervical cancer, as the fourth most common cancer among women worldwide, accounts for nearly 8% of female cancer deaths each year, making it an important component of the global cancer burden for women, especially in low- and middle-income countries.[1,2] In addition, in underdeveloped countries, the population with lagging health services may have a more worrying incidence rate of cervical cancer and a poor prognosis.[3] So far, over 90% of early cervical cancer patients who undergo radical hysterectomy can achieve survival benefits of at least 5 years.[4,5] However, a large number of research results of parahysterectomy cannot be ignored. The uterus is rich in vascular systems and autonomic nerve fibers. These vascular and neurological injuries can lead to many complications associated with parahysterectomy. Meanwhile, complications such as intraoperative bleeding, fistula formation, ureteral injury, and bladder dysfunction must be considered.[6] Therefore, timely and accurate preoperative staging is extremely important for improving the prognosis of early cervical cancer patients.

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Recently, more attention has been focused on identifying low risk populations for parametrial invasion (PMI) of early-stage cervical cancer to avoid radical hysterectomy. Previous studies have shown that depth of interstitial infiltration, absence of lymphatic infiltration, and lymph node metastasis are all high-risk factors for PMI.[7,8] However, the candidate variables of these models are all derived from postoperative data, resulting in a certain lag in the predictive models. In fact, if PMI is not included in whether to resect, the beneficial value of such extensive surgery may be questioned. Therefore, it is urgent to construct a preoperative PMI prediction and recognition model to better guide the surgical resection range, which is crucial for the prognosis of patients.

Encouragingly, in the recent study, radiomics is a rapidly developing research field that involves the extraction of quantitative indicators, known as radiomic features in medical images.[9,10] The advantage of radiological features is that they can non invasively capture image features and quantify parameters, which can be used for predicting high-risk characteristics of diseases, especially for early invasion and metastasis of tumors, and have unparalleled advantages.[11] Given this situation, radiomics is considered the most potential predictive tool for excluding the presence of PMI. So far, although a small number of studies have attempted to use radiomics parameters in the construction of prognosis models for gynecological malignant tumors, there has not been any research and clinical application of PMI combined with radiomics in early warning.

Given this situation, we use radiomics to identify image feature parameters and advanced supervised learning algorithms to construct a PMI warning model. The aim is to use non-invasive radiomics feature parameters as a representation of early tumor infiltration, assist surgeons in preoperative risk assessment, and provide reasonable guidance for surgical decision-making.

Materials and Methods

Inclusion of Population

We retrospectively collected 218 patients who were treated in Jingzhou Central Hospital from January 31, 2015, to January 31, 2023, and diagnosed with early-stage cervical cancer by pathology. The inclusion criteria of patients were as follows: (i) Patients diagnosed with IB1 to IIA2 cervical cancer according to the International Federation of Gynecology and Obstetrics (FIGO) stage; (ii) Patients with no previous history of radiation therapy or surgery (except for cervical cone resection); (iii) Patients suspected of cervical cancer undergoing multi-parametric diffusion-weighted imaging (mp-DWI) scan before surgery. Exclusion criteria: (i) Patients with unsatisfied image quality, such as motion artifacts and chemical shift artifacts; (ii) Postoperative pathological reports were unavailable; (iii) Patients with pelvic benign diseases affecting texture feature extraction or analysis. As a retrospective study, the Ethics Committee of Jingzhou Central Hospital has approved the implementation of the study and ensured the encryption of personal information of all patients included in the study, while strictly adhering to the Helsinki Declaration and exempting patients from informed consent. The patient inclusion process and prediction model construction strategy are summarized in Figure 1.

Radiomics Feature Recognition and Acquisition

We used an MR scanner (Signa LLC) to obtain radiomics parameters. Among them, the scanner's setting parameters include cross-sectional, coronal, and sagittal planes. All patients were operated by senior radiologists during the MR scanning process, and the objectivity and potential bias of the parameters were evaluated by two individuals after scanning the patients. The cross-sectional parameters were set to TR: 400–620ms, TE: 10–16ms; the coronal and sagittal parameters were set to TR: 1800–3400ms, TE: 24–34ms. At the same time, to ensure that the boundary of the tumor lesion was delineated with reference standards to normal tissue, we also performed ROI calibration to ensure parameter consistency.

Development and Validation of Predictive Models

We obtain candidate parameters for the prediction model based on ROI histogram and gray level co-occurrence matrix (GLCM), including energy, contrast, correlation, sum of squares (SOS), deficit (IND), mean sum (MES), sum variance (SUV), sum entropy (SUE), entropy, difference variance (DIV), and difference entropy (DIE). Then, artificial neural

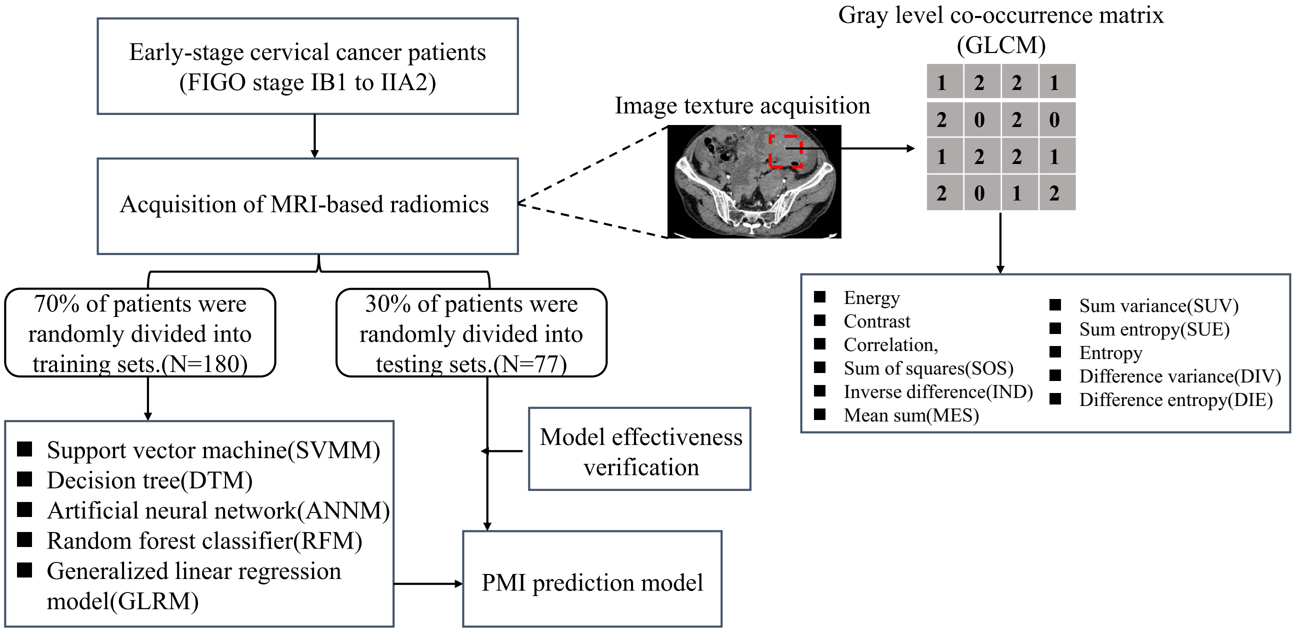

Figure 1 The flow chart of patient selection and data process.

network model (ANNM), decision tree model (DTM), support vector machine model (SVMM), random forest model (RFM), and generalized linear regression model (GLRM) were used to construct PMI prediction models. The optimal combination parameters for evaluating the minimum absolute shrinkage rate are used to screen the optimal combination variables for PMI.[12] Decision curve analysis (DCA) was used to evaluate the robustness of predictive models,[13] and the Area Under Receiver Operating Characteristic (AUROC) curve and Clinical Impact Curve (CIC) are used to evaluate the accuracy of the predictive model.[14]

Statistical Analysis

Categorical variable and continuous variables are presented using percentages and mean ± standard deviation, respectively, while inter group comparisons are compared using chi square test or *t*-test. The correlation comparison is presented using the Pearson correlation coefficient.[15] All data statistical analysis and visualization were carried out using R software, and a P-value less than 0.05 was considered statistically significant.

Results

Baseline Data and Feature Variable Selection

In this study, we randomly divided 218 early-stage cervical cancer patients into a predictive model training set and an internal testing set, with the training and testing sets accounting for 70% (N = 150) and 30% (N = 68), respectively. Among them, there were a total of 50 (33.33%) patients with PMI in the training set, and 18 (26.47%) patients with PMI in the testing set. The comparison of baseline population data and radiomics related extraction data between two groups showed significant statistical differences in some indicators of radiomics, such as energy, entropy, SUV, and DIV, whether in the training set or the internal test set ($P < 0.05$). To further screen candidate variables for PMI prediction models, significant correlations were found between energy, entropy, SUV, DIV, MES, entropy and energy with PMI through Pearson correlation analysis and optimal subset (ie minimum penalty coefficient) filtering. This indicated that the GLCM-based index extracted based on radiomics can serve as a potential candidate variable for PMI prediction models. The baseline data and radiomics related extracted variables of two groups of early-stage cervical patients were summarized in Table 1 and Supplementary Table 1.

Table 1 Clinicopathological Characteristics of Patients with Early-Stage Cervical Cancer

Variables	Overall (N=218)
Age (median [IQR]), year	53.00 [38.00, 65.00]
BMI (%), kg/m^2	
≤18.5	52 (24.0)
18.6–23.9	109 (50.2)
≥24	56 (25.8)
Menopause (%)	
Yes	107 (49.3)
No	110 (50.7)
Gestation (median [IQR])	3.00 [2.00, 6.00]
Production (median [IQR])	2.00 [1.00, 3.00]
Smoking (%)	
Yes	70 (32.3)
No	147 (67.7)
HPV (%)	
Positive	143 (65.9)
Negative	74 (34.1)
SCC (median [IQR]), μg/L	5.70 [4.10, 7.20]
Histology (%)	
SCC	149 (68.7)
Non-SCC	68 (31.3)
FIGO (%)	
IB	135 (62.2)
IIA	82 (37.8)
Grade (%)	
G1	81 (37.3)
G2	69 (31.8)
G3	67 (30.9)
Tumor diameter (median [IQR]), cm	5.20 [3.00, 8.30]
LNM (%)	
Yes	58 (26.7)
No	159 (73.3)
Treatment (%)	
Surgery	79 (36.4)
Surgery+CT	88 (40.6)
Surgery+CT+RT	50 (23.0)
Ki67 (median [IQR])	0.50 [0.40, 0.60]
Energy (median [IQR])	6.45 [3.85, 9.12]
Contrast (median [IQR])	316.40 [267.80, 354.40]
Correlation (median [IQR])	2.47 [2.06, 58.05]
SOS (median [IQR])	1.48 [1.12, 1.91]
IND (median [IQR])	1.62 [1.02, 2.33]
MES (median [IQR])	−0.68 [−0.88, −0.47]
SUV (median [IQR])	18.70 [15.50, 21.90]
SUE (median [IQR])	0.48 [0.37, 0.74]
Entropy (median [IQR])	0.56 [0.43, 0.85]
DIV (median [IQR])	309.50 [193.00, 402.50]
DIE (median [IQR])	190.00 [165.00, 208.00]

Abbreviations: IQR, inter-quartile range; BMI, body mass index; HPV, human papillomavirus; SCC, squamous cell carcinoma antigen; FIGO, The International Federation of Gynecology and Obstetrics; LNM, lymph node metastasis; CT, chemotherapy; RT, radiotherapy; SOS, sum of squares; IND, inverse difference; MES, mean sum; SUV, sum variance; SUE, sum entropy; DIV, difference variance; DIE, difference entropy.

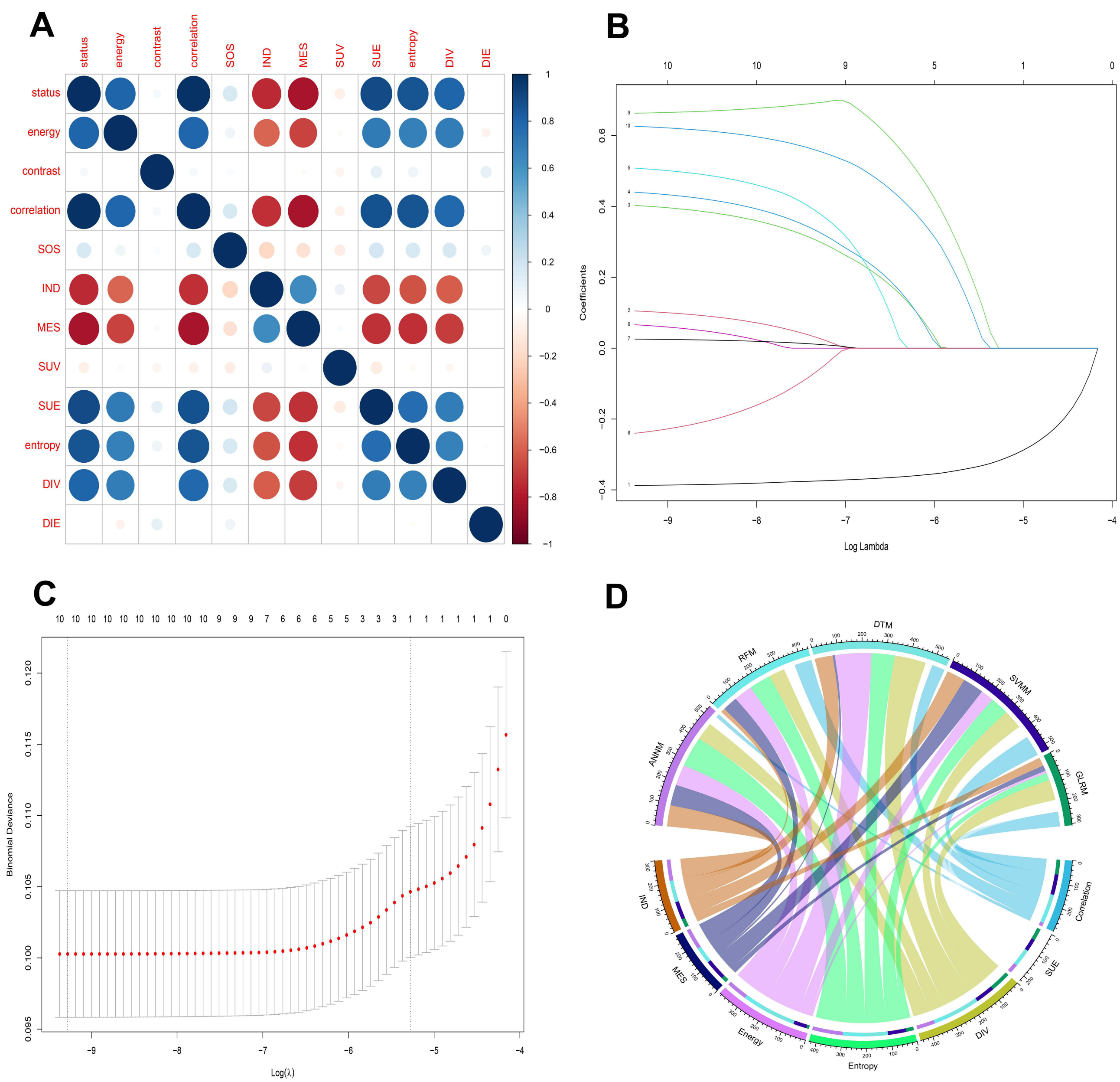

Figure 2 Variable screening and weight allocation. (**A**) Correlation matrix analysis of candidate features. (**B** and **C**) Feature selection by LASSO regression; (**D**) The weight distribution of the candidate variables of each ML-based model.

Construction of the ML-Based PMI Prediction Model

Five commonly used machine learning algorithms, namely RFM, DTM, ANNM, and SVM, have been widely used in the construction of prediction models.[16] As shown in Supplementary Table 2, in the RFM prediction model, entropy, variance, and energy obtained top ranking weight values, indicating that these variables can serve as potential candidate variables for RFM prediction of PMI (Figure 2). At the same time, in SVMM, ANNM, and DTM, the energy, entropy, SUV, DIV, MES, entropy and energy also served as candidate variables that can be used to predict PMI, and their allocation in the four different algorithm prediction models is equally important. For example, entropy was used as a predictive variable in both RFM and DTM (Figures 3, 4 and Supplementary Table 2), but it was evident that entropy contributes more to RFM, while energy played an equally important role in both types of models.

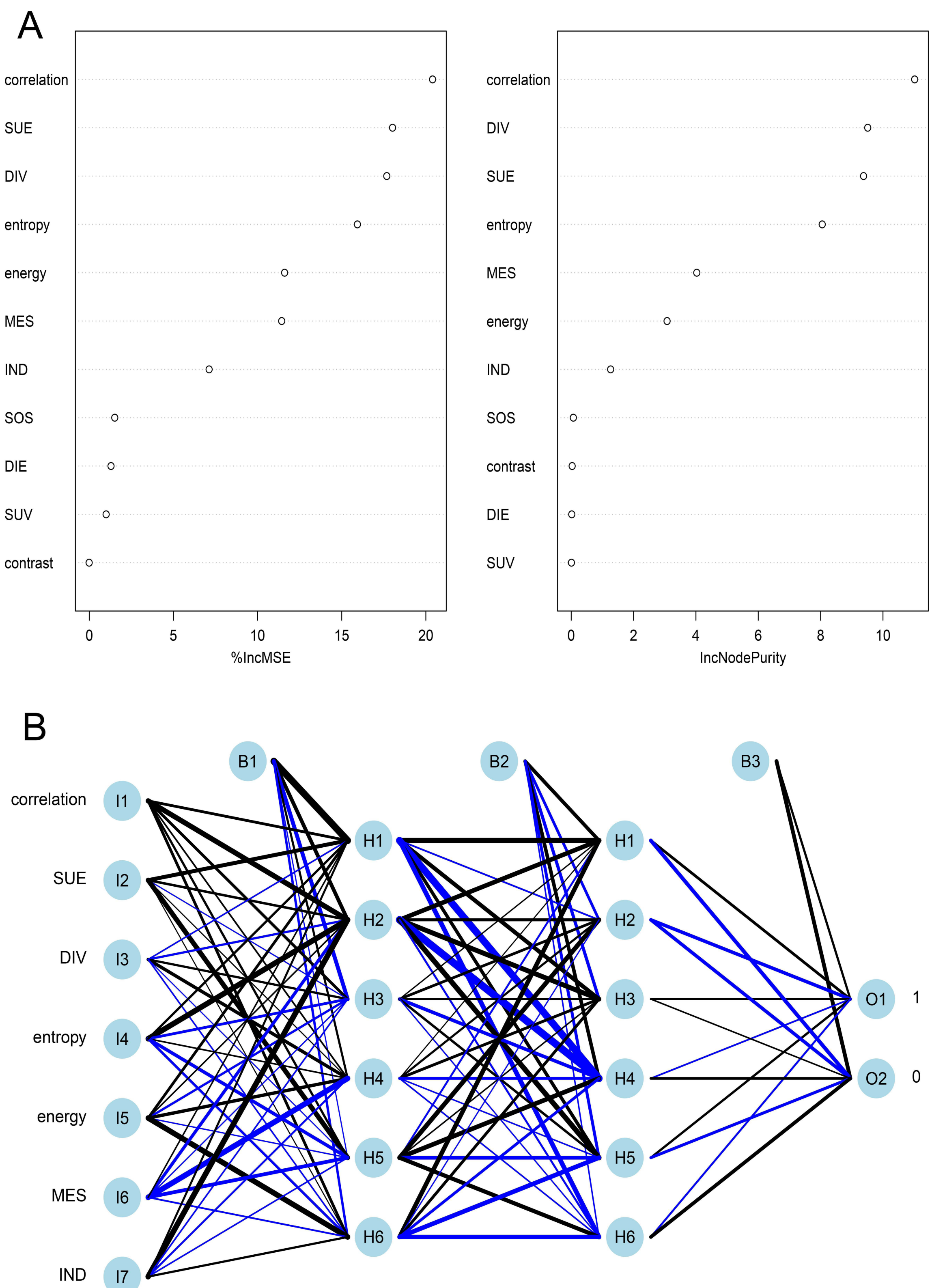

Figure 3 Predictive model visualization based on ML-based algorithm. (**A**) RFM. (**B**) ANNM.
Notes: The candidate factors associated with fracture risk were ordered via RF algorithm (**A**) and (**B**) prediction node and weight were allocated via ANN algorithm.

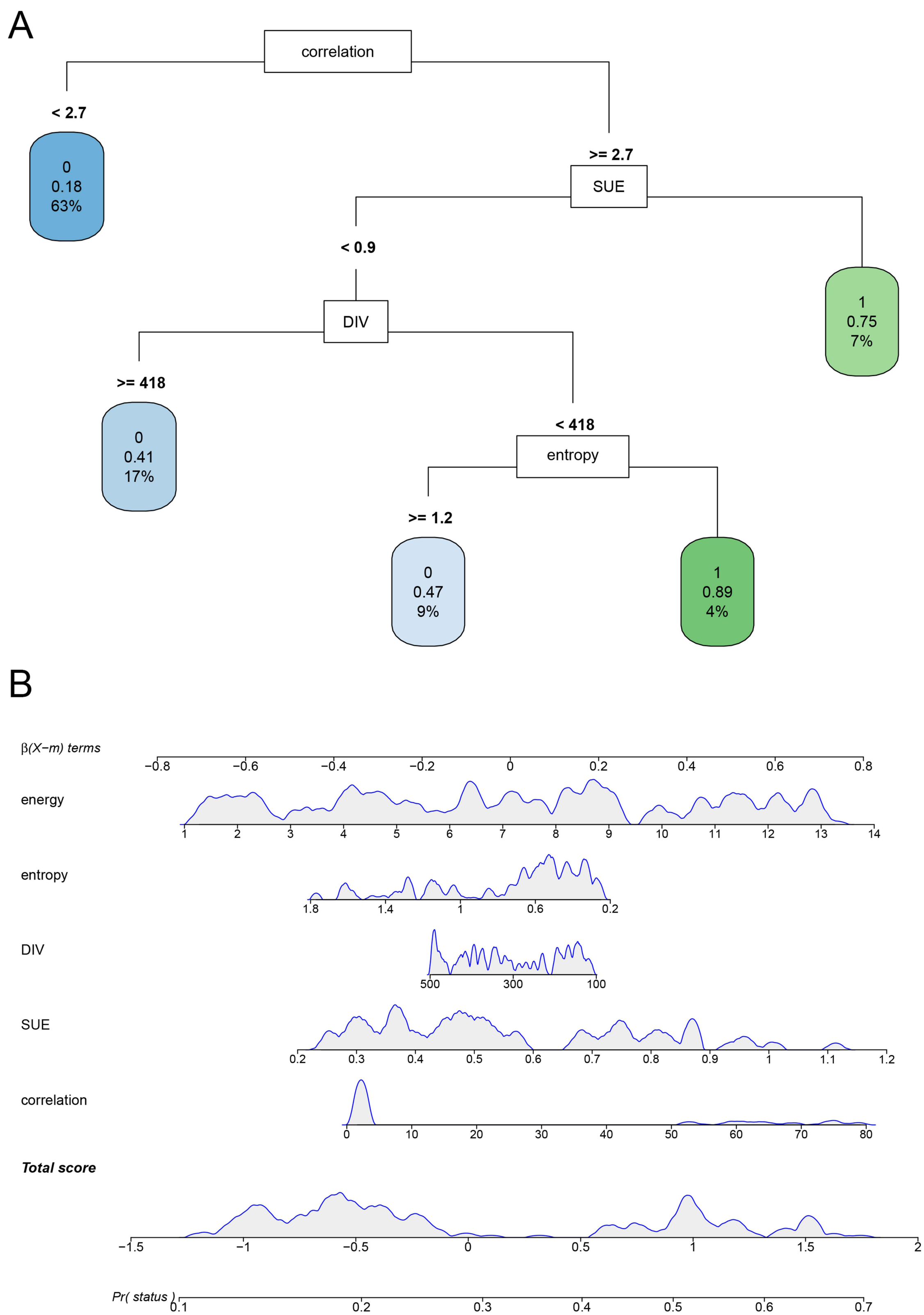

Figure 4 Predictive model visualization based on ML-based algorithm. (**A**) DTM. (**B**) GRLM.

Notes: The candidate factors associated with fracture risk were ordered via DT algorithm (**A**) and (**B**) prediction node and weight were allocated via GRL algorithm.

Construction of the GLRM-Based PMI Prediction Model

Generalized linear models are often widely used in the construction of predictive models. This study used the GLRM-based algorithm to filter and construct PMI predictive models. In the univariate and multivariate logistic regression analysis, energy, entropy, SUV, DIV, MES, entropy and energy were independent risk factors for PMI occurrence. Next, we constructed a visual nomogram based on independent risk factor candidate variables to evaluate the risk of PMI occurrence (Figure 4). The results showed that the predicted C-index values of the nomogram constructed based on radiomics indicators in the training set and internal validation set were 0.78 and 0.81, respectively. These results demonstrated that PMI candidate variables extracted based on the GLCM can obtain ideal accuracy and robustness in predicting PMI. The above research results indicated that whether in traditional algorithm based prediction models (GLRM) or ML-based PMI prediction models, GLCM-based radiomics variables can play an important predictive role, and radiomics candidate variables had a certain degree of universality.

Efficacy Evaluation of PMI Prediction Models

We used DCA's "net benefit" to fully evaluate the predictive robustness of five prediction models, and it can be seen that RFM has the best prediction file size, while ANNM, DTM, and SVM also demonstrate satisfactory predictive performance. In contrast, the predictive performance of GLRM is significantly weaker than the other four types of supervised learning prediction models (Figure 5). Similarly, the area under the curve of RFM is 0.895 and 0.905 in the training and validation sets, respectively, while the AUC values of ANNM in the training and validation sets are 0.863 and 0.871, respectively. The predictive performance evaluation of various prediction models is summarized in Table 2, indicating that the PMI prediction model constructed based on machine learning algorithms has robust predictive performance.

Predictive Value of ML-Based PMI Prediction Model

As illustrated in Supplementary Figure 1, in order to further evaluate the predictive performance of RFM, we evaluated the discriminative power of RFM in distinguishing between PMI and non PMI based on CIC interpretability. It can be seen that the CIC curve exhibits very clear discriminative power, indicating that RFM can accurately distinguish high-risk PMI populations, at least benefiting early cervical cancer patients with high PMI risk.

Discussion

In clinical practice, the preoperative clinical staging of cervical cancer is mainly used to guide the surgical resection range, and therefore has a significant impact on the prognosis of patients. Compared with surgical staging, clinical staging is often difficult to achieve accuracy, which causes great confusion for surgeons in determining the surgical resection range.[17,18] Previous studies have shown that about a quarter of patients with early-stage cervical cancer have inconsistent preoperative and postoperative FIGO staging.[4,19] In such a situation, it is urgent to optimize the FIGO classification system, especially for precise assessment of the size of the primary tumor and whether there is suspicious infiltration in adjacent tissues before surgery. Fortunately, computed tomography and MRI are considered the best imaging modes for evaluating tumor expansion status.[19–21] In contrast, MRI has an advantage in accuracy of PMI compared to clinical staging and computed tomography.[22,23] In view of this, this study uses MRI-based image capture to screen predictive variables for PMI, in order to better guide preoperative staging, surgical resection range, and improve patient prognosis in early-stage cervical cancer patients.

In this study, MRI has good soft tissue resolution and can perform multi plane and multi sequence imaging. Its biggest advantage is that it truly achieves high spatial resolution and large field scanning, which can display the stromal ring, muscular layer, and peripheral serous layer of the cervix very clearly. This type of feature based on special imaging parameters is mainly obtained from MRI images, and similar to this study, the T2W1 imaging sequence was used, which is crucial for fully displaying the cross-sectional area of the tumor. At the same time, the natural contrast of pelvic fat was utilized to clearly display the depth and extent of invasion of cervical cancer with its higher spatial resolution. However, it cannot be denied that T2W1 may have uneven signal intensity capture for the possible infiltration of parametrial cancer

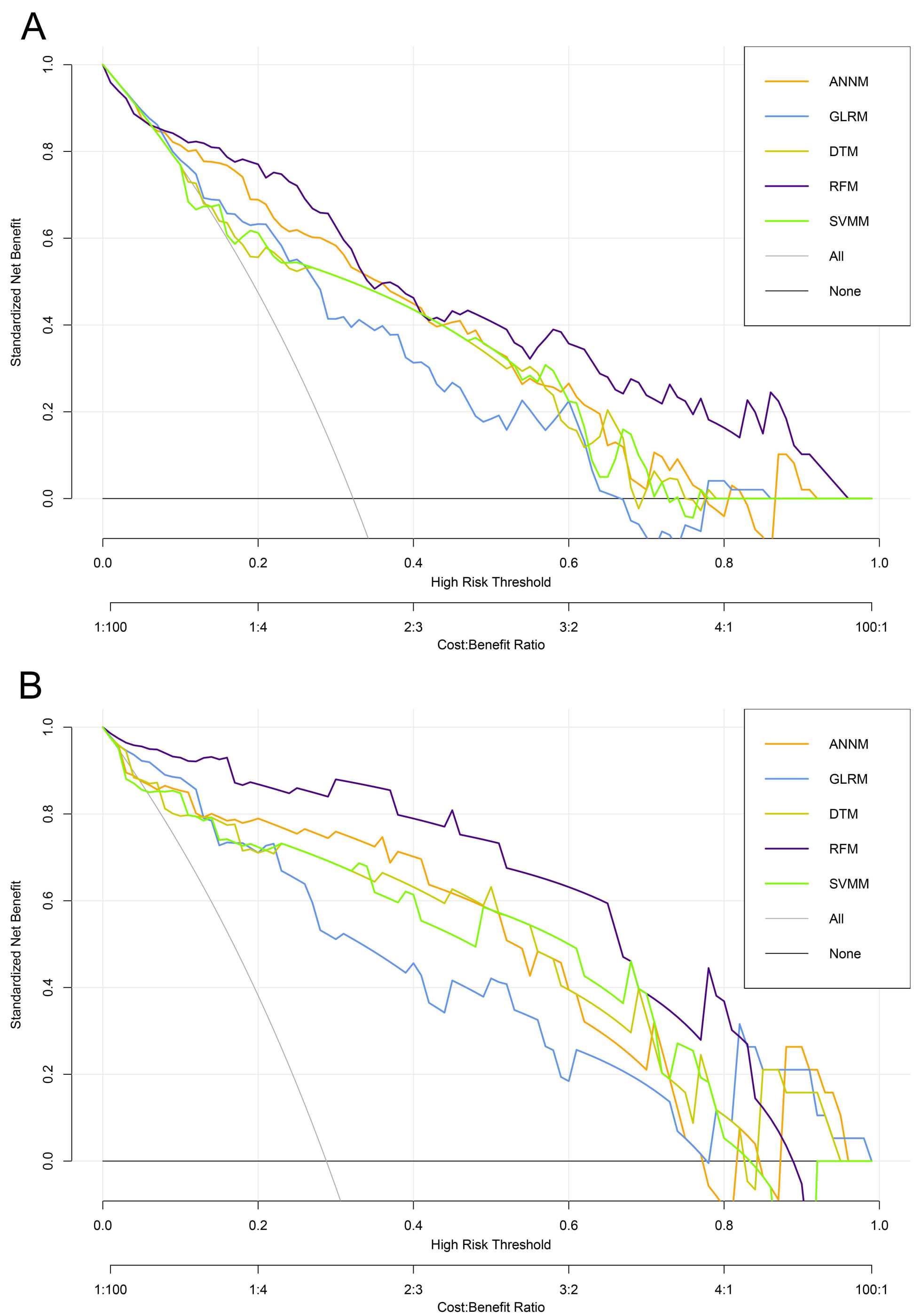

Figure 5 Prediction performance of candidate models based on ML-based algorithm. (**A**) DCA for five ML-based models in the training set. (**B**) DCA for five ML-based models in the testing set.

cells in the uterus, which can easily lead to confusion between some inflammatory lesions and tumor lesions. Previous studies have shown that the abundant venous plexus around the uterus creates atypical enhancement of high signal intensity on MRI, leading to false positives in staging.[24–26] In addition, it cannot be denied that lesion volume, inflammatory edema, and dilation of the uterine venous plexus may all be high-risk or confounding factors for PMI.

Nowadays, fully utilizing image textures to obtain quantitative parameters for the diagnosis and treatment of various diseases has become a trend, and its advantages are increasingly prominent in medical applications.[27,28] Our research indicates that there are clearly some texture features in the imaging data of PMI patients that are different from non PMI, which may be reflected in

Table 2 Comparison of Predictive Efficacy of PMI Prediction Models via ROC Curves

Model	Training Set			Internal Validation Set		
	AUC Mean	AUC 95% CI	Variables[&]	AUC Mean	AUC 95% CI	Variables[&]
RFM	0.895	0.838–0.952	7	0.905	0.845–0.965	7
SVMM	0.842	0.785–0.899	7	0.845	0.785–0.905	7
DTM	0.838	0.781–0.895	6	0.839	0.779–0.899	6
ANNM	0.863	0.806–0.920	7	0.871	0.811–0.931	7
GLRM	0.747	0.690–0.804	7	0.739	0.679–0.799	7

Notes: & – variables included in the model.

tumor blood vessels, tumor necrosis lesions, and tumor heterogeneity. Due to these potential differences, they can become predictive factors for PMI.[29] It has been proven that the image texture features we analyzed can indeed reflect the spatial distribution information of tumor lesions, and the radiomics parameters obtained based on GLCM have significant statistical differences. These candidate variables have also been shown to have a significant weight in PMI prediction. For example, we found a positive correlation between entropy difference and PMI, which is consistent with the reported results, proving that entropy difference, as a feature parameter for measuring image grayscale values, is particularly suitable for distinguishing malignant tumors.[30,31] This study also showed that entropy value was higher in patients with PMI. In this study, with the help of radiomics candidate parameters, clinicians can input meaningful candidate variables into the predictive model equation we constructed before surgery. After sufficient calculation, corresponding AUC values can be obtained. If the AUC value is greater than 0.7, it can fully indicate that the patient has high-risk PMI, and vice versa. In addition, we also incorporate predictive variables with contribution value into the machine learning algorithm prediction model, and the results demonstrated that without distinguishing the predictive variables, the prediction efficiency based on GLCM reached the highest of 0.972. This suggested that MRI examination before early-stage cervical cancer surgery and texture analysis using sequence images have considerable application prospects for predicting the risk stratification of PMI.

Of course, this study inevitably has the following limitations. First, this study had unified requirements for MRI scanning parameters and equipment of the included patients, so the sample size included in this study was relatively small and came from a single center. In the future, we still need to further expand the sample size study, and collect a prospective cohort study of multiple centers and large samples; Second, as a retrospective study, there was inevitably selection bias in study population inclusion, which cannot effectively eliminate bias errors caused by the researcher's personal experience or subjective judgment; Third, this study obtained GLCM related parameters based on MRI, but features such as higher-order textures were not included in the analysis. Therefore, it is necessary to continue to dig deeper into imaging pathological parameters in the future, discover predictive factors for PMI from a wider range of texture features, and further optimize PMI prediction models to make them more effective.

Conclusion

In summary, precise risk stratification of early cervical patients' PMI before surgery can be achieved by combining machine learning algorithms and radiomics features. Especially, the PMI prediction model constructed by integrating candidate parameters from radiomics using the random forest algorithm can have high accuracy and satisfactory robustness to assist in preoperative decision-making for PMI patients.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Bedell SL, Goldstein LS, Goldstein AR, Goldstein AT. Cervical Cancer Screening: past, Present, and Future. *Sexual Med Rev*. 2020;8(1):28–37. doi:10.1016/j.sxmr.2019.09.005
2. He WQ, Li C. Recent global burden of cervical cancer incidence and mortality, predictors, and temporal trends. *Gynecologic Oncol*. 2021;163 (3):583–592. doi:10.1016/j.ygyno.2021.10.075

3. Pimple SA, Mishra GA. Global strategies for cervical cancer prevention and screening. *Minerva Ginecol*. 2019;71(4):313–320. doi:10.23736/S0026-4784.19.04397-1
4. Poddar P, Maheshwari A. Surgery for cervical cancer: consensus & controversies. *Indian J Med Res*. 2021;154(2):284–292. doi:10.4103/ijmr.IJMR_4240_20
5. Rodriguez J, Viveros-Carreño D, Pareja R. Adjuvant treatment after radical surgery for cervical cancer with intermediate risk factors: is it time for an update? *Int J Gynecol Cancer*. 2022;32(10):1219–1226. doi:10.1136/ijgc-2022-003735
6. Touhami O, Plante M. Minimally Invasive Surgery for Cervical Cancer in Light of the LACC Trial: what Have We Learned? *Curr Oncol*. 2022;29(2):1093–1106. doi:10.3390/curroncol29020093
7. Ma C, Zhang Y, Li R, Mao H, Liu P. Risk of parametrial invasion in women with early stage cervical cancer: a meta-analysis. *Arch Gynecol Obstetrics*. 2018;297(3):573–580. doi:10.1007/s00404-017-4597-0
8. Matsuo K, Shimada M, Nakamura K, et al. Predictors for pathological parametrial invasion in clinical stage IIB cervical cancer. *Eur J Surg Oncol*. 2019;45(8):1417–1424. doi:10.1016/j.ejso.2019.02.019
9. Guiot J, Vaidyanathan A, Deprez L, et al. A review in radiomics: making personalized medicine a reality via routine imaging. *Med Res Rev*. 2022;42(1):426–440. doi:10.1002/med.21846
10. Lambin P, Leijenaar RTH, Deist TM, et al. Radiomics: the bridge between medical imaging and personalized medicine. *Nat Rev Clin Oncol*. 2017;14(12):749–762. doi:10.1038/nrclinonc.2017.141
11. Mayerhoefer ME, Materka A, Langs G, et al. Introduction to Radiomics. *J Nucl Med*. 2020;61(4):488–495. doi:10.2967/jnumed.118.222893
12. Alhamzawi R, Ali HTM. The Bayesian adaptive lasso regression. *Math Biosci*. 2018;303:75–82. doi:10.1016/j.mbs.2018.06.004
13. Van Calster B, Wynants L, Verbeek JFM, et al. Reporting and Interpreting Decision Curve Analysis: a Guide for Investigators. *Europ Urol*. 2018;74(6):796–804. doi:10.1016/j.eururo.2018.08.038
14. Hou N, Li M, He L, et al. Predicting 30-days mortality for MIMIC-III patients with sepsis-3: a machine learning approach using XGboost. *J Transl Med*. 2020;18(1):462. doi:10.1186/s12967-020-02620-5
15. Fay MP, Malinovsky Y. Confidence intervals of the Mann-Whitney parameter that are compatible with the Wilcoxon-Mann-Whitney test. *Stat Med*. 2018;37(27):3991–4006. doi:10.1002/sim.7890
16. Uddin S, Khan A, Hossain ME, Moni MA. Comparing different supervised machine learning algorithms for disease prediction. *BMC Med Inf Decis Making*. 2019;19(1):281. doi:10.1186/s12911-019-1004-8
17. Nitecki R, Ramirez PT, Frumovitz M, et al. Survival After Minimally Invasive vs Open Radical Hysterectomy for Early-Stage Cervical Cancer: a Systematic Review and Meta-analysis. *JAMA Oncol*. 2020;6(7):1019–1027. doi:10.1001/jamaoncol.2020.1694
18. Pennington KP, Urban RR, Gray HJ. Revisiting Minimally Invasive Surgery in the Management of Early-Stage Cervical Cancer. *J Nat Comprehens Cancer Netw*. 2019;17(1):86–90. doi:10.6004/jnccn.2018.7263
19. Thomakos N, Trachana SP, Davidovic-Grigoraki M, Rodolakis A. Less radical surgery for early-stage cervical cancer: to what extent do we justify it?-Our belief. *Taiwan J Obs Gynecol*. 2016;55(4):495–498. doi:10.1016/j.tjog.2016.01.004
20. Devine C, Viswanathan C, Faria S, Marcal L, Sagebiel TL. Imaging and Staging of Cervical Cancer. *Semin Ultrasound CT MR*. 2019;40(4):280–286. doi:10.1053/j.sult.2019.03.001
21. Manganaro L, Lakhman Y, Bharwani N, et al. Staging, recurrence and follow-up of uterine cervical cancer using MRI: updated Guidelines of the European Society of Urogenital Radiology after revised FIGO staging 2018. *Eur Radiol*. 2021;31(10):7802–7816. doi:10.1007/s00330-020-07632-9
22. Merz J, Bossart M, Bamberg F, Eisenblaetter M. Revised FIGO Staging for Cervical Cancer - A New Role for MRI. *RoFo*. 2020;192(10):937–944. doi:10.1055/a-1198-5729
23. Balcacer P, Shergill A, Litkouhi B. MRI of cervical cancer with a surgical perspective: staging, prognostic implications and pitfalls. *Abdomin Radiol*. 2019;44(7):2557–2571. doi:10.1007/s00261-019-01984-7
24. Haldorsen IS, Lura N, Blaakær J, Fischerova D, Werner HMJ. What Is the Role of Imaging at Primary Diagnostic Work-Up in Uterine Cervical Cancer? *Curr Oncol Rep*. 2019;21(9):77. doi:10.1007/s11912-019-0824-0
25. Zhao X, Wang X, Zhang B, et al. Classifying early stages of cervical cancer with MRI-based radiomics. *Magn Reson Imag*. 2022;89:70–76. doi:10.1016/j.mri.2022.03.002
26. Fournier LS, Bats AS, Durdux C. Diffusion MRI: technical principles and application to uterine cervical cancer. *Cancer Radiother*. 2020;24(5):368–373. doi:10.1016/j.canrad.2020.02.008
27. Shamsil A, Naish MD, Patel RV Texture-based Intraoperative Image Guidance for Tumor Localization in Minimally Invasive Surgery. *Annual International Conference of the IEEE Engineering in Medicine and Biology Society IEEE Engineering in Medicine and Biology Society Annual International Conference*. 2021;2021:3526–3530.
28. Litvin AA, Burkin DA, Kropinov AA, Paramzin FN. Radiomics and Digital Image Texture Analysis in Oncology (Review). *Sovrem Tehnol Med*. 2021;13(2):97–104. doi:10.17691/stm2021.13.2.11
29. Marusyk A, Polyak K. Tumor heterogeneity: causes and consequences. *BBA*. 2010;1805(1):105–117. doi:10.1016/j.bbcan.2009.11.002
30. de Oliveira ME, Neto LM. Directional entropy based model for diffusivity-driven tumor growth. *Math Biosci Eng*. 2016;13(2):333–341. doi:10.3934/mbe.2015005
31. Dercle L, Ammari S, Bateson M, et al. Limits of radiomic-based entropy as a surrogate of tumor heterogeneity: ROI-area, acquisition protocol and tissue site exert substantial influence. *Sci Rep*. 2017;7(1):7952. doi:10.1038/s41598-017-08310-5