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Application value of MRI radiomics in differential diagnosis of osteoporotic and malignant neoplastic vertebral compression fractures

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► ***Original article***

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ABSTRACT

Background: To explore the radiomics features of osteoporotic and malignant neoplastic vertebral compression fractures (VCFs), and to analyze the application value of radiomics in differential diagnosis of osteoporotic and malignant neoplastic VCFs. ***Materials and Methods:*** Fifty-one patients with VCFs caused by malignant tumors and forty-nine patients with osteoporosis-induced VCFs treated in the Xiaoshan Hospital Affiliated to Hangzhou Normal University from January 2020 to June 2023 were retrospectively collected into a training set (70 cases) and a verification set (30 cases) according to a stratified random sampling design and a 7:3 ratio. The radiomics parameters of T2WI images of the diseased vertebral bodies were extracted, and the parameters with statistical differences were screened out by dimensionality reduction, so as to build a prediction model. Receiver operating characteristic (ROC) curves were drawn to evaluate the differential diagnosis performance of radiomics for the etiology of vertebral fractures. ***Results:*** Eight radiomics features were obtained after dimensionality reduction using the LASSO algorithm. The constructed model was effective in differentiating osteoporotic and malignant neoplastic VCFs, with an area under the ROC curve (AUC) of 0.95; while the AUC for the validation set was 0.84. ***Conclusions:*** The radiomics features of T2WI images of vertebral fractures have high efficiency in the differential diagnosis of fracture etiology.

INTRODUCTION

Vertebral compression fractures (VCFs) are a common disease, mainly due to osteoporosis in elderly patients. However, the spine is also a common site for malignancies, especially metastatic tumors [1]. About one-third of cancer patients will develop pathological fractures of the spine at the terminal stage [2], which leads to up to 20% misdiagnosis of spinal fractures [2], resulting in the wrong choice of follow-up treatment schemes, delayed illness, and reduced quality of life of patients. Therefore, a correct diagnosis of the etiology of vertebral fractures is critical, which is related to the correct selection of follow-up treatment plans for patients with malignancies and the avoidance of unnecessary vertebral biopsies in patients with osteoporosis.

Imageological examinations, especially magnetic resonance imaging (MRI), play an irreplaceable role in detecting VCFs. However, in differentiating neoplastic VCFs from osteopeotic VCFs, the specificity (SPE) of routine T1 (T1WI) and T2-weighted imaging (T2WI) and short tau inversion recovery (STIR) sequences is low, especially for patients with unclear imaging characteristics, which makes the correct diagnosis challenging [3]. Radiomics is a rapidly developing discipline in recent years, and has achieved good results in various fields [4-9]. However, there is still a lack of reliable studies demonstrating its effectiveness in the identification of VCFs. In recent years, the incidence of VCFs is showing an increasing trend year by year, and how to effectively identify the types of VCFs is still a key research finding that deserves clinical attention.

The purpose of this study is to combine T2WI sequence with radiomics features to construct a vertebral fracture radiomics prediction model based on routine MRI examination sequences, so as to provide a more noninvasive and accurate biological marker for the correct diagnosis and treatment of VCFs in clinical practice. This is also the first study related to the diagnosis of osteoporotic VCFs and malignant VCFs in the clinic for MRI imaging histology parameters, which is an important reference.

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MATERIALS AND METHODS

General information

From January 2020 to June 2023, patients with malignant neoplastic VCFs admitted to the Xiaoshan Hospital Affiliated to Hangzhou Normal University were collected as malignant group and those with osteoporotic VCFs as benign group.

Inclusion criteria for the malignant group: (1) Patients with surgical pathological findings or a history of malignant tumors, with confirmed primary malignant neoplastic vertebral tumors or metastatic vertebral tumors. (2) Those who had not undergone vertebral surgery before MRI examination. (3) Good MRI image quality and complete T2WI sequence with no artifact interference. Exclusion criteria: (1) Spinal inflammation, tuberculosis and other diseases. (2) Poor MRI image quality that resulted in the ability to extract valid data. (3) Those who had underwent vertebral surgery prior to MRI examination.

Inclusion criteria for the benign group: (1) Those with no clear history of malignancies or no tumors found after 6 months of follow-up. (2) Presence of VCFs shown by plain film X-ray or computerized tomography (CT). (3) Patients with significant alleviation in symptoms after percutaneous vertebroplasty or conservative treatment. (4) Those who had not undergone any treatment before MRI examination. (5) Good MRI image quality, complete T2WI sequence and no artifact interference. Exclusion criteria: (1) Confirmed malignancies, spinal inflammation, tuberculosis and other diseases. (2) Inability to obtain valid data due to poor MRI image quality. (3) Patients who had been treated before MRI examination.

According to the above exclusion and inclusion criteria, 51 patients in the malignant group and 49 patients in the benign group were selected. The subjects in both groups received medical history collection, laboratory inspection, health checkups and MRI examination. This study was approved by the Ethics Committee of Xiaoshan Hospital Affiliated to Hangzhou Normal University (2023-099), the date is April 21, 2023.

Methods

MRI examination

HDxt 1.5T superconducting MRI instrument (GE Medical Systems, LLC, USA), spine integrated 16-channel coil and fast spin-echo T2WI sequence were used. scanning parameters: cervical vertebra repetition time (TR): 2321 ms, echo time (TE): 105 ms, field of view (FOV): 24.0 × 24.0 cm, slice thickness: 3 mm, interspace gap: 0.3 mm, thoracic vertebra TR: 2778 ms, TE: 104 ms, FOV: 30.0 × 30.0 cm, slice thickness: 3 mm, interslice gap: 0.3 mm, lumbar TR: 2500 ms, TE: 121 ms, FOV: 28.0 × 28.0 cm, slice thickness: 4 mm, interspace gap: 0.4 mm.

Image segmentation and feature extraction

The 3D-Slicer software (Brainlab, Germany) was used to sketch the regions of interest (ROIs) in the spine sagittal T2WI images and extract features, with the ROIs covering each level of the vertebral body in the sagittal view of the VCF (figure 1). These procedures were performed independently by one resident (4 years of experience) and one senior physician (15 years of experience) using a blind method. The consistency of the feature extraction results of the two physicians was determined by intraclass correlation coefficients (ICCs) and features with an ICC > 0.75 were selected for further study.

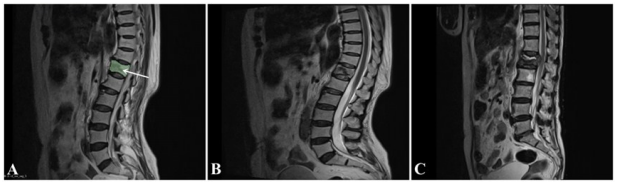

Figure 1. ROI of spinal T2WI sagittal images. **A:** ROI delineation of vertebral compression fractures. **B:** Osteoporotic fracture of the T12 vertebral body. **C:** Pathological fracture caused by L1 vertebral body metastasis.

Extraction, screening and modeling of radiomics parameters

A total of 100 cases (51 cases in malignant group and 49 cases in benign group) were included in this study. Through stratified random sampling, 70 cases were included in training dataset and 30 cases in the testing dataset according to a ratio of 7:3. In order to eliminate the imbalance of the training dataset, we increased the samples by repeating random cases to make the sample balanced. The eigenmatrix was normalized. In addition, the mean and standard deviation of each eigenvector were calculated, with each eigenvector minus the mean and divided by the standard deviation. After normalization, the center of each eigenvector was zero and the unit standard deviation was zero. Due to the high-dimensional feature space, we compared the similarity of each feature pair and removed one of them if the PCC value of the feature pair was greater than 0.990. After this process, least absolute shrinkage and selection operator (LASSO) was used for feature dimensionality reduction, with each feature independent of each other. Before building the model, we used the recursive feature elimination (RFE) approach to select features. The goal of RFE is to select classifier-based features by recursively considering smaller feature sets. Support vector machine (SVM), an effective and robust classifier, was used as the classifier. Kernel functions have the ability to map features to higher dimensions, which are suitable for searching hyperplanes to separate cases with different labels. Herein, we used the linear Kernel function because it is easier to interpret the eigencoefficients of the final model. In order to determine the model's hyperparameters (such as the

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number of features), we applied 5-fold cross-validation on the training dataset. The hyperparameters were set based on the model's performance in the validation dataset.

The model's performance was evaluated by receiver operating characteristic (ROC) curve analysis. The area under the ROC curve (AUC) was calculated for quantification. Sensitivity (SEN), SPE, positive predictive value (PPV) and negative predictive value (NPV) were also calculated at the critical value to maximize the value of Youden index. We also estimated the 95% confidence interval (CI) by bootstrapping 1000 samples. All the above processes were implemented by R software (Version 3.4.1, https://www.r-project.org/).

Statistical methods

SPSS26.0 software (IBM, USA) and R software (version 3.4.1, AT&T, USA) were used for statistical analyses. Measurement data were first tested by the Kolmogorov–Smirnov test for normality, the normally distributed measurement data were described as the mean ± standard deviation ($\bar{x} \pm s$). ROC curves were plotted for statistically significant parameters and the AUCs were calculated. $P < 0.05$ was the statistical significance threshold for all analyses.

RESULTS

Clinical data

Among the 51 patients in the malignant group, the male-to-female ratio was 31:2 and the age range was 46-90 years (mean: 69.4); there were 4 cases of lymphoma, 4 cases of myeloma and 43 cases of bone metastases, with the tumor found in cervical vertebra in 3 cases, thoracic vertebra in 20 cases and lumbar vertebra in 28 cases. In the benign group, there were 49 patients, including 19 males and 30 females aged 58-86 years (mean: 70.9), the tumors occurred in the cervical spine in 0 cases, the thoracic spine in 23 cases and the lumbar spine in 26 cases (table 1).

Table 1. Clinical baseline information of the study population.

	Malignant group (n=51)	Benign group (n=49)
Age	69.4 [46-90]	70.9 [58-89]
Male	31 (60.78)	19 (38.78)
Female	20 (39.22)	30 (61.22)
Types of tumors		
Lymphoma	4 (7.84)	-
Myeloma	4 (7.84)	-
Bone metastases	43 (84.31)	-
Site of fracture		
Cervical vertebrae	3 (5.88)	0 (0.0)
Thoracic spine	20 (39.22)	23 (46.94)
Lumbar spine	28 (54.90)	26 (53.06)

Radiomics results

The consistency of data extracted by the two physicians was high, with an ICC ranging from 0.761 to 0.882. After dimensionality reduction using the LASSO algorithm (figure 2), our model finally incorporates eight radiomics features (figures 3 and 4). This radiomics model obtained the highest AUC in the training dataset, with the AUC reaching 0.953 (≈ 0.95, P < 0.001) and the accuracy (ACC) reaching 0.914 (≈ 0.91, P < 0.001), for the testing dataset, the AUC and ACC of the model reached 0.836 (≈ 0.84, P < 0.001) and 0.833 (≈ 0.83, P < 0.001), respectively. ROC curves are shown in figure 5. Clinical statistics and selected characteristics at the time of diagnosis can be found in tables 2 and 3.

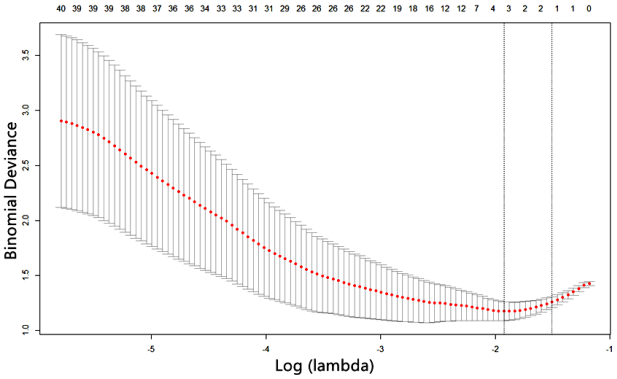

Figure 2. Diagram of dimensionality reduction using the LASSO algorithm. The abscissa is the log (Lambda) value, and the value at the top of the picture is the feature number. The LASSO method is used to reduce the dimensionality of radiomics parameters. In order to prevent over-fitting, eight radiomics parameters are selected for modeling.

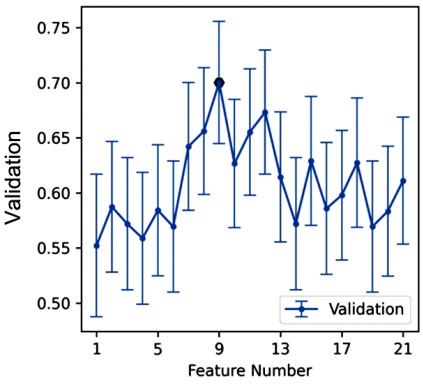

Figure 3. Diagram of changes in AUC with feature number. The figure shows that the model reaches the highest AUC when the number of features is 8.

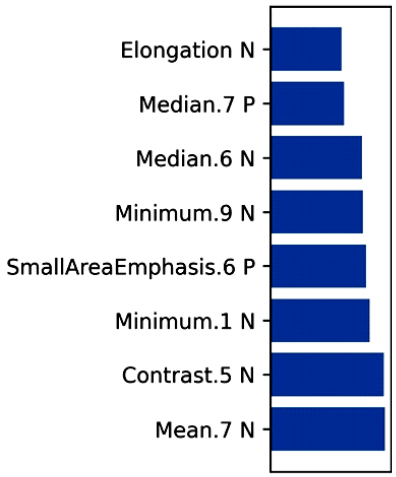

Figure 4. Weighted contribution of included features. The figure shows that the feature "Mean.7N" has the highest weight in the model.

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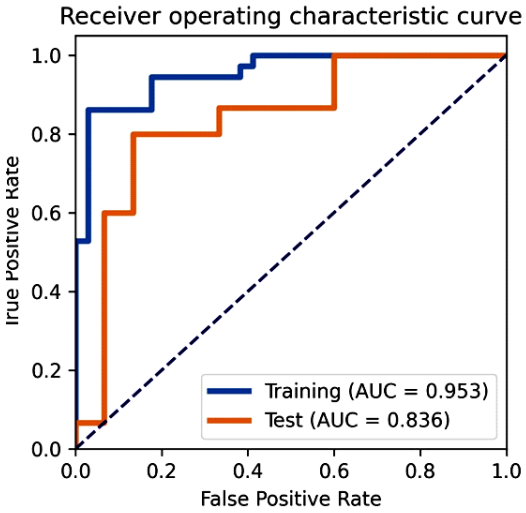

Figure 5. Logistic regression analysis of ROC curves. The AUCs for the training set and testing set were 0.953 and 0.836, respectively.

Table 2. Clinical statistics at the time of diagnosis in the training set and testing set.

Statistics	Training set	Testing set
Accuracy	0.9143	0.8333
AUC	0.9534	0.8356
AUC 95% CIs	0.9092-0.9977	0.6795-0.9916
NPV	0.8684	0.8125
PPV	0.9688	0.8571
Sensitivity	0.8611	0.8000
Specificity	0.9706	0.8667
P	<0.001	<0.001

Table 3. Correlation coefficients of model construction.

Features	Coef in model
Intercept	-0.307
Elongation	-0.485
Minimum.1	-0.674
Contrast.5	-0.770
Mean.7	-0.779
Median.6	-0.623
SmallAreaEmphasis.6	0.648
Median.7	0.500
Minimum.9	-0.629

DISCUSSION

Osteoporotic and malignant neoplastic VCFs, which are common spinal disorders, have great similarities in clinical manifestations and imaging features. In addition, both of them tend to occur in the elderly, which may explain the varying degrees of osteoporosis and spinal degeneration at the onset of the disease in most cases. In conventional MRI, hyperintensities on T1WI and hyperintensities on T2WI and STIR are commonly observed, making it impossible to completely distinguish them from the signal characteristics alone. Experienced radiologists can make a correct diagnosis based on the history of the primary tumor, multiple vertebral metastases, soft tissue masses, *etc*. However, it is difficult to distinguish neoplastic vertebral fractures from osteoporotic ones for young physicians or in case of unclear tumor history, small and fewer primary spinal tumors, etc.

In this study, T2WI images of the spine were combined with radiomics to conduct a controlled study of malignant neoplastic VCFs and osteoporotic VCFs. The results showed that the model was effective in differentiating the two diseases, with the SPE, SEN, PPV and NPV being 0.97, 0.86, 0.97 and 0.87 in the training set and 0.87, 0.80, 0.86 and 0.81 in the validation set, respectively. Furthermore, MRI radiomics can be analyzed and compared through vertebral body morphology, bone destruction, intervertebral space changes, *etc*., so as to determine the type and severity of the patient's illness and classify and cluster the patient's image data, thus realizing individualized diagnosis and treatment. In recent years, most scholars [10-12] have used diffusion-weighted imaging (DWI) to study the osteoporotic and malignant neoplastic VCFs qualitatively and quantitatively. Sartoretti *et al*. [11] studied the diagnostic value of low to ultra-high b-values for benign and malignant vertebral fractures, and found that ultra-high b-values can also meet the needs of differential diagnosis. Hui *et al.* [12] reported that the AUCs of MRS, IVIM-DWI, and IVIM-DWI + MRS were 0.73, 0.88 and 0.94, respectively, indicating that the combination of IVIM-DWI and MRS has the highest SEN, SPE and ACC in differentiating osteoporotic and osteolytic metastatic vertebral fractures. All the preceding studies demonstrate the high differential diagnostic value of functional MRI. However, in clinical work, functional imaging is often limited by objective conditions, such as long examination time, magnetic field inhomogeneities, etc., as well as severe pain in most cases, poor cooperation and tolerance, which sometimes leads to the failure to obtain high-quality images that affect the result judgment.

Bacher *et al.* [13] used single-shot fast spin-echo T2 -weighted Dixon sequence to conduct qualitative and quantitative analysis of benign and malignant vertebral fractures and found that the AUC of qualitative diagnosis was 0.97-0.99 and that of quantitative diagnosis was 0.82-0.97, indicating that conventional T2WI has high value in judging benign and malignant vertebral fractures. Radiomics is an emerging discipline that has developed rapidly in recent years. It extracts a large number of features from radiation images with high throughput, and converts imaging data into minable spatial data with high resolution by using automatic or semi-automatic analysis methods, thus reflecting the changes of human tissues, cells and genes. The research object of radiomics is all kinds of imaging images and the quality of images and the amount of information will directly affect the effectiveness and accuracy of radiomics results. Li *et al*. [14] studied the value of CT-based ResNet50 deep learning in differentiating

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benign and malignant vertebral fractures and found that ResNet50 achieved high ACC. In addition, some studies have found that the combination of magnetic resonance images with high soft tissue resolution and radiomics can better extract the radiomics characteristics that reflect the biological nature of human tissues [15,16].

Of course, there are still some shortcomings in this study: (1) Given the retrospective design of the present study, we will conduct a prospective MRI radiomics study of vertebral fractures in the future. (2) In this study, only radiomics analysis of T2WI images is performed, and multi-sequence MRI based radiomics can be analyzed later to further improve the diagnostic efficiency of the model. (3) The sample size needs to be expanded to further validate the reliability of the model.

CONCLUSION

MRI radiomics has important application value in the differential diagnosis of osteoporotic and malignant neoplastic VCFs, which can improve the ACC and efficiency of imaging diagnostics and provide better support and guarantee for patients' diagnosis and treatment.

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Conflicts of interests: None.

Ethical consideration: Authors have no conflict of interest to declare.

Author contribution: Y.L. and H.Z. conceived and designed the project, and wrote the paper. Y.Q. and Z.G. generated the data. Z.H. and M.Z. analyzed the data. C.X. modified the manuscript. All authors gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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