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Predicting Lymph Node Metastasis of Ovarian Cancer by MSCT Radiomics

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Abstract

Purpose: To explore the value of radiomics preoperative enhanced Multislice Computed Tomography (MSCT) imaging in predicting Lymph Node Metastasis (LNM) of epithelial Ovarian Cancer (OC).

Materials and methods: Patients with epithelial OC confirmed by operation and pathology were retrospectively analyzed. Each patient underwent MSCT enhanced scan 2 weeks before operation, and the Region Of Interest (ROI) was obtained by manually segmenting CT enhanced scan venous phase images on Huiyihuiying scientific research platform. 1049 features were extracted from ROI, then the several dimensionality reductions were performed to select five optimal imaging features. A Support Vector Machine (SVM) classifier was used to construct a radiomics model for predicting LNM of epithelial OC. The imaging features were comprehensively selected to construct a combined model for predicting LNM of epithelial OC, and the effectiveness of the model was boosted by the verification method. Then, we evaluated it' s diagnostic value by the Area Under Curve (AUC), sensitivity, specificity, and 95% CI, and verified in the internal independent test set. Delong test was used to compare the prediction efficiency of the combinatorial model and the radiomic one.

Results: The included patients were randomly divided into training group (n=87) and test group (n=23). Multivariate regression analysis showed that the level of serum

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CA125, CT imaging evaluated lymph node status, and the location of the lesion were independent variables for LNM in epithelial OC (all P<0.05). Finally, five optimal imaging features of primary lesions of epithelial ovarian cancer were selected and constructed for the radiomics model, with the AUC in the training set and test set were 0.754, and 0.795. While, the AUC of the combined prediction model in training set and verification set were 0.849 and 0.813, respectively. Delong test results show that there is a significant difference in the predictive efficiency of the two models in the training set (P<0.05).

Conclusion: The radiomics model grounded on MSCT has a certain value in predicting LNM of epithelial ovarian cancer, moreover the combined model combined with clinical data, imaging qualitative and quantitative signs and imaging featuress has better diagnostic efficiency.

Keywords: Radiomics; Ovarian cancer; Lymph node metastasis; Prediction.

Abbreviation: LNM: Lymph Node Metastasis; MSCT: Multislice Computed Tomography; ROI: Region Of Interest; SVM: Support Vector Machine; ROC: Receiver Operating Characteristic Curve; AUC: Area Under The Curve; FIGO: Federation International Of Gynecology And Obstetrics; MRI: Magnetic Resonance Imaging; DICOM: Digical Imaging And Communications In Medical Data; PET/CT: Positron Emission Tomography Computed Tomography; GLDM: Gray Level Dependence Matrix; US: Ultrasonography; PACS: Image Archiving And Transmission System.

Introduction

Ovarian Cancer (OC) is one of the common gynecological malignant tumors, and epithelial ovarian cancer is the main cause of death [1]. Ovarian cancer accounts for about 4% of cancer morbidity and mortality among women worldwide, and the 5-year survival rate in most countries is only about 30% to 40% [2]. Lymph node status is listed as a crucial variable in the Federation International of Obstetrics and Gynecology (FIGO) ovarian cancer staging system [3]. OC patients with lymph node metastasis are divided into stage III or higher. Up to date, the traditional idea of surgical treatment of ovarian cancer is to achieve complete Cytoreductive Surgery (CRS), while removing enlarged or suspected lymph nodes [4]. However, there are still doubts about the need for lymph node resection in early stage I-II patients, patients who need to retain reproductive function, patients with low-grade serous cancer and patients with mucinous cancer, and for patients with advanced OC, the effect of retroperitoneal lymphadenectomy on its prognosis is still controversial [4,5]. The results of a prospective controlled study in 2019 showed that for patients who achieved complete CRS and had no enlarged lymph nodes before or during operation, pelvic and para-aortic lymphadenectomy not only did not achieve no survival benefit, but increased the risk of postoperative complications [6]. Therefore, it is obviously unwise to perform lymph node dissection on all patients with resectable ovarian cancer, nor is it in line with the current era of individualized cancer medicine.

Enhanced MSCT is one of the routine methods to evaluate the condition of patients with epithelial ovarian cancer before treatment. MSCT has superior advantages, including wide availability, good repeatability, and fast image scanning time [7]. However, the traditional interpretation of imaging images mostly depends on the professional knowledge of imaging doctors and the experience of imaging diagnosis. There may be great differences in the interpretation results of the same imaging data and different imaging doctors. In the process of traditional imaging interpretation, it is often difficult to interpret the metastatic lymph nodes of ovarian cancer due to the influence of pelvic mass and pelvic and abdominal metastatic foci. Inexperienced doctors, especially young imaging doctors are prone to misjudgment and omission. At present, as a developing new research field, radiomics aims to extract more complex feature information from traditional medical images, such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). These high-throughput objective image assembly features are extracted from the segmented ROI to achieve the transformation from images to quantitative data established clinical models, including diagnosis, prognosis and prediction models [7-11].

At present, in the field of radiomics, there are many related studies to predict the lymph node status of malignant tumors. In recent years, in the related research of pelvic tumors, there are many literatures about predicting lymph node metastasis of rectal cancer [12], cervical cancer [11] and endometrial cancer [13] based on radiomics imaging characteristics, and the diagnostic efficiency turns out to be good.

There have been several previous studies based on CT texture and neural network to predict the lymph node status of ovarian cancer. In 2019, some scholars studied the diagnostic value of LNM of ovarian cancer based on the lymph node texture analysis of multi-slice spiral CT images of ovarian cancer patients. Finally, the area under ROC of CT texture entropy was 0.83. However, it only analyzed the texture features of a single CT rather than a complete imaging analysis, without independent verification set verification [14]. In 2020, Liu et al [15] studied the clinical value of constructing pelvic and abdominal LNM assistant diagnosis system for ovarian malignant tumors based on depth neural network in enhanced CT images, and its AUC is 0.7664. But no related studies have been found to predict the LNM of ovarian cancer founded on complete radiomics.

The aim of our study is to construct a pretreatment prediction model of MSCT for epithelial OC founded on the imaging characteristics of preoperative LNM enhancement imaging in patients with epithelial ovarian cancer, so as to improve the accuracy of imaging evaluation of epithelial ovarian cancer before operation, and then assist clinical selection of appropriate treatment strategies, including the choice of adjuvant treatment, the feasibility of preserving fertility during surgical treatment, the determination of surgical scope and so on.

Material and methods

Research object

Patients with epithelial ovarian cancer confirmed by operation and pathology in the first affiliated Hospital of Guangxi Medical University from January 2015 to February 2021 were retrospectively analyzed. The review require approval by the Ethical Committee of First Affiliated Hospital of Guangxi Medical University.

Inclusion criteria: (1) patients was proved to be epithelial OC by operation and pathology, and there were pathological results of lymph node dissection, which included at least pelvic lymph nodes and para-aortic lymph nodes; (2) plain and enhanced MSCT scans of abdomen and pelvis were performed within 2 weeks before operation, and complete CT enhanced images were obtained, and the image quality met the requirements of post-processing; (3) there was no lack of clinical data and pathological information.

Exclusion criteria: (1) patients received preoperative radiotherapy, chemotherapy or other treatment, (2) patients with distant metastasis or complicated with other primary malignant tumors.

Information collection of patients enrolled in the group

(1) **General data:** Age, family history of tumor, menopausal history.

(2) **Laboratory examination parameters:** Serum CA125 level and CA199 level within one week before operation, for serum CA125 level, record its specific value, unit is U/ml; for serum CA199 level, record "0" = CA199 level is normal (<37 U/ml), "1" = CA199 level is increased (≥ 37 U/ml).

(3) **Pathological results:** All pathological results were reviewed and signed by two pathologists with more than 8 years experience in pathological diagnosis. Patients with multiple pathological results were subject to the last results or the pathological results of in-hospital consultation. According to the pathological results as the gold standard, if all the dissected lymph nodes of the patient did not show LNM, the patient was recorded as "0" = LNM negative; if one of the lymph nodes or more than two lymph nodes were metastasized, the patient was recorded as "1" = LNM positive.

Methods CT examination methods

All the patients in this study underwent multi-slice spiral CT plain scan and enhanced examination within 2 weeks before operation, and all the patients signed the examination consent form before the examination. During the examination, the patients were instructed to take the supine position and use a high-pressure syringe to inject the nonionic contrast agent iohexol 300 ng/ml (2.5-3.0 ml/kg) through the elbow vein with a dose of 3.0-3.5 mL/s. The contrast-enhanced MSCT images were obtained 60-80 seconds after injection of contrast medium. Scanning parameters: scan layer thickness and interval is 1.0 mm~2.5 mm, matrix is 512 x 512, tube voltage is 120 KV, and the tube current is automatically adjusted according to the patient's body shape (between 220~400 mAs). CT imaging equipment and scanning parameters are shown in Table 1.

Table 1: Inspection equipment and scanning parameters.

CT imaging device	Thickness	Tube voltage	Matrix
Siemens Force CT	1.0	120	512×512
GE Revolution CT	1.0	120	512×512
Siemens Sensation64	2.0	120	512×512
Siemens Dual Source	1.25	120	512×512
GE Light Speed VCT	2.5	120	512×512

Note: All CT scanning devices are multi-layer spiral CT; tube current automatically adjusted according to the body type of the patient.

Some studies have shown that there is no significant difference in the diagnostic efficiency of imaging modeling by selecting CT images with different thickness for ROI sketching [16]. More scholars obtain image data from multicenter institutions to analyze imaging characteristics for retrospective study [17-21].

Image and data processing methods

Analysis of qualitative and quantitative imaging data

The films were read by a radiologist with 3 years' experience and 5 years' experience in abdominal imaging diagnosis without knowing the results of operation and pathology. When there is a difference of opinion, discuss with another chief physician of abdominal imaging diagnosis to get the final interpretation result. When the lesions are bilateral ovarian lesions, the evaluation of the following [2] is based only on the largest lesions. Observe the following image features:

(1) Imaging evaluation of the location of the lesions, unilateral or bilateral ovarian disease, "0" = unilateral ovarian disease, "1" = bilateral ovarian disease.

(2) The two physicians evaluated the size of the tumor in the axial and sagittal plane, and after reaching agreement, they chose the same imaging orientation to measure, and calculated the average value of the maximum length and diameter of the tumor measured by the two physicians in the venous phase, from the outer edge of the lesion to the outer edge (including the capsule), avoiding the thickened blood vessels at the edge of the lesion, including the whole lesions, in cm, keeping one digit after the decimal point.

(3) With or without ascites, the presence or absence of ascites in the abdominal and pelvic cavity was observed in CT images. if there is a water-like density shadow in the abdominal and pelvic cavity, no matter how much it is, record "1" = ascites, and if there is no water-like density shadow in the abdominal and pelvic cavity, it is recorded as "0" = no ascites.

(4) The lymph node status was evaluated by CT. The enlarged lymph nodes in the abdominal and pelvic cavity were observed in the arterial phase and venous phase of CT enhancement. If the short diameter of the lymph node was ≥1 cm, liquefaction and necrosis were seen in the lymph nodes, and "1" = positive lymph node metastasis was recorded when the edge was circular enhancement, and "0" = negative lymph node metastasis was recorded if the short diameter <1 cm or fat and calcification in the lymph nodes.

Image segmentation

The venous phase enhanced CT images (DICOM) of each patient were downloaded from PACS and transmitted to Huiying big data artificial intelligence research platform of Huiyi. Without knowing the pathological results, the above two physicians were respectively on the venous phase MSCT enhanced axial thin slice (slice thickness of 1.0-2.5 mm) images of each patient. Manually delineate ROI of the primary lesion along the edge of the lesion on each continuous plane (Figure 1), carefully avoiding the thickened blood vessels, fat, and intestinal wall at the edge of the lesion. A month later, the same physician reconfirmed and adjusted the boundary of the lesions. The difference of the boundary of ROI was decided by two people through consultation, and the confusion was finally decided by reading the film with another chief physician of abdominal imaging diagnosis.

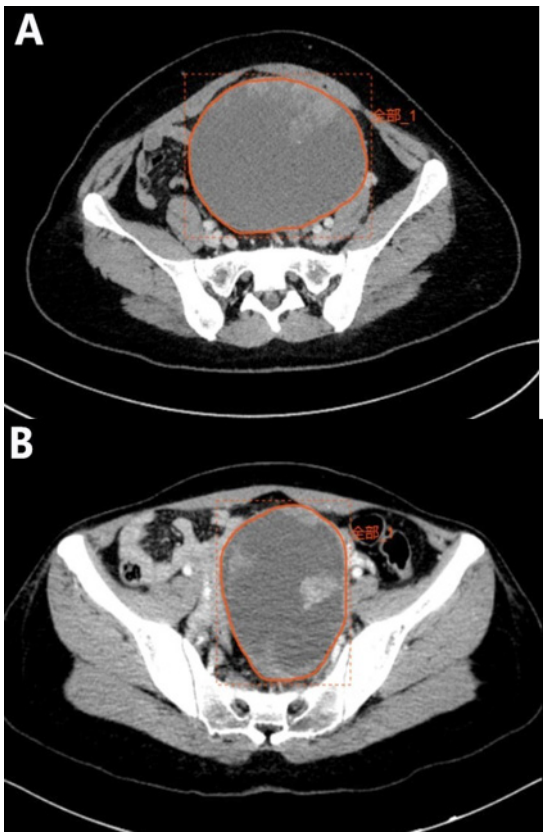

Figure 1: ROI sketch diagram.

Note: A and B are the CT enhanced venous phase images of two different patients, and the ovarian cancer tumor is delineated as ROI layer by layer on the axial images of each patient.

Feature extraction of image assemblage

Due to the image from different CT imaging devices, there are different scanning parameters, the Radcloud platform is used to pre-process the image before extracting the image features, so as to reduce the influence of different image parameters on the extraction of image features. Then a total of 1409 imaging features were automatically extracted from the segmented ROI on the Radcloud platform and were divided into three portions. The first portion (first-order statistical features) consists of 126 descriptors, which quantitatively describe the distribution of voxel intensity in MSCT images through common and basic metrics. The second portion (3D features) contains 14 3D features that reflect the shape and size of the region. The third portion (texture features), calculated from the gray running length and gray co-occurrence texture matrix, includes 525 texture features that can quantify regional heterogeneity.

Feature selection and model construction

The redundant features were successively reduced by the variance threshold method and Select K Best method, and the LASSO algorithm was processed to opt the optimal image features. For the frontmost method threshold is 0.8, so that the variance eigenvalues less than 0.8 are removed. As for Select K Best method threshold is 0.05 (P value), the features greater than 0.05 are removed. The cost function of LASSO model is L1 regularizer, which set 5 as the error value of cross-validation, and 1000 as the maximum number of iterations. Based on the selected characteristics of image group, this study uses support vector machine (SVM) to construct the prediction model of image group through machine learning. Then, the verification set and training set were randomly divided in term of the proportion of 2:8. After statistical analysis, the clinical data and CT imaging qualitative and quantitative data were selected, and the imaging parameters were integrated to construct a combined prediction model of lymph node metastasis of epithelial ovarian cancer. The validity of the model was verified in the internal independent test set. The diagnostic value of the model was evaluated by the area under the working characteristic curve (AUC), sensitivity, specificity and 95% CI. Then, verify its diagnostic performance in an independent test set.

Statistical analysis method

SPSS25.0 was used to analyze the data. Firstly, we performed the ShapiroWilk test to test the data normality. The unit of measurement satisfies the normal distribution, and the independent sample T test is used for univariate analysis. The measurement data do not meet the normality, and the comparison of different groups is expressed by nonparametric Mann-Whitney U rank sum test in the form of M (P25, P75). Chi-square test or Fisher exact test was used to compare the counting data, which was expressed in the form of n (%). The best critical value of serum CA125 level for predicting lymph node metastasis was obtained by ROC curve and Jordan index. The variables with significant differences were included in the multivariate analysis, and the multivariate binary Logistic regression analysis was used to determine the independent predictors. Delong test was performed in MedCalc software to compare the diagnostic efficiency of ROC curves of different models. All the statistically significant data turn out to be P value less than 0.05.

Results

Analysis of baseline data of patients in the group

Comparison of baseline data between training set and test set: A total of 110 patients with epithelial OC were enrolled according to the enrollment conditions (Figure 2). The average age was 48 ± 10.32, ranging from 23 to 70 years old.

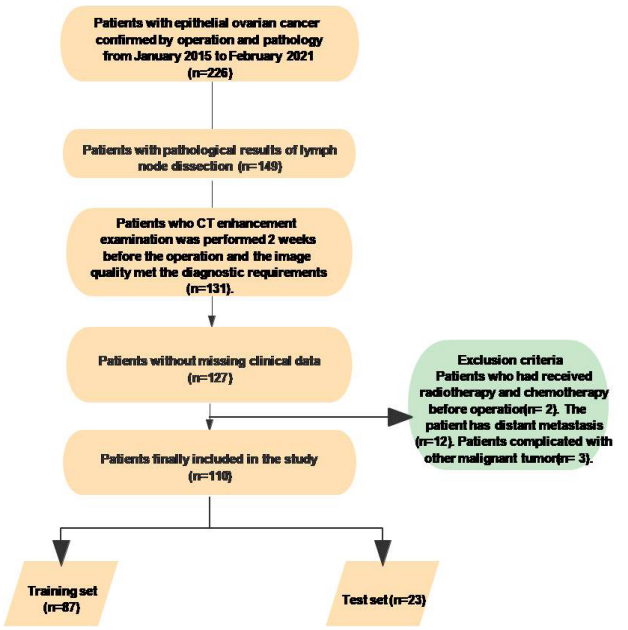

Figure 2: Case screening flow chart.

Table 2: Comparison of baseline data between training set and test set.

		Cases divided		
	Variables	**group**	***P* value**	
		Training (n=87)	test(n=23)	
Age	<45	31(83.7%)	6(16.3%)	0.389
	≥45	56(76.7%)	17(23.3%)	
Family history of cancer	yes	4(57.2%)	3(42.8%)	0.14
	no	83(80.6%)	20(19.4%)	
Menopause	yes	35(71.4%)	14(28.6%)	0.077
	no	52(85.3%)	9(14.7%)	
CA125 (U/ml)	≤297.8#	54(79.4%)	14(20.6%)	0.916
	>297.8#	33(78.5%)	9(21.5%)	
CA199 (U/ml)	<37	69(79.3%)	18(20.7%)	0.912
	≥37	18(78.2%)	5(21.8%)	
Lesion location	unilateral	67(77.9%)	19(22.1%)	0.563
	bilateral	20(83.3%)	4(16.7%)	
Ascites	yes	53(81.6%)	12(18.4%)	0.448
	no	34(75.6%)	11(24.4%)	
Size (cm)	<15	63(78.7%)	17(23.3%)	0.886
	≥15	24(80.0%)	6(20.0%)	
CT to evaluate LNM	Poc.	69(78.4%)	19(21.6%)	0.725
	Neg.	18(81.8%)	4(18.2%)	
LNM pathology	Neg.	60(81.2%)	16(18.8%)	0.956
	Neg.	27(79.4%)	7(20.6%)	

Note: #indicates that 297.8 U/ml is the best critical value of CA125 level for predicting lymph node metastasis verified by ROC curve and Jordan index. n is the number of cases.

Among the 110 patients with epithelial ovarian cancer, 34 cases were pathologically confirmed to be LNM positive, accounting for 30.9% of 76 cases with negative LNM, accounting for 69.13%. The training set (n=87) and test

set (n=23) of OC patients were randomly divided in term of the proportion of 8:2. The constituent ratio of patient baseline data between training set and verification set turn out to be no significant difference (Table 2).

Results of univariate analysis

The results showed that the P value of lesion location, CA125 level and CT evaluation of lymph node status in lymph node metastasis were all less than 0.05, but there were no significant differences in age, family history of cancer,

menopause, preoperative CA199 level, ascites and maximum line diameter (P>0.05). The sensitivity of CT in the assessment of lymph node metastasis was 41.2% (14/34) and the specificity was 89.4% (68/76).

Table 3: Results of univariate analysis.

		LNM			
Variables	**groups**	**Neg. (n=76)**	**Poc. (n=34)**	***P values***	
Age	<45 岁	29(78.3%)	8(21.7%)	0.133	
	≥45 岁	47(64.3%)	26(35.7%)		
Family history of cancer	yes	5(71.4%)	2(28.6%)	0.89	
	no	71(69.0%)	32(31.0%)		
Menopause	yes	32(66.7%)	17(33.3%)	0.441	
	no	44(71.2%)	17(28.8%)		
CA125 (U/ml)	≤297.8	55(78.9%)	13(21.1%)	**0.001**	
	>297.8	21(50.0%)	21(50.0%)		
CA199 (U/ml)	<37	60(61.5%)	27(38.5%)	0.956	
	≥37	16(87.6%)	7(10.4%)		
Lesion location	unilateral	65(74.7%)	21(25.3%)	**0.005**	
	bilateral	11(45.0%)	13(55.0%)		
Ascites	no	31(68.9%)	14(31.1%)	0.97	
	yes	45(69.3%)	20(30.7%)		
Size(cm)	<15cm	52(65.0%)	28(35.0%)	0.129	
		≥15cm	24(80.0%)	6(20.0%)	
	CT to evaluate LNM	Neg.	68(77.3%)	20(22.7%)	**<0.001**
		Poc.	8(36.3%)	14(63.7%)	

Note: If there is no special note, all the results are statistically significant (P<0.05).

Results of multivariate Logistic regression analysis

The variables with statistically significant differences in lymph node metastasis (lesions location, CA125 level, CT evaluation of lymph node status) were included in multivariate Logistic regression analysis, and multivariate analysis was carried out. Multivariate analysis using binary Logistic regression analysis showed that CA125 level (P<0.05), CT evaluation of lymph node status (P<0.05) and lesion location (P<0.05) were independent predictors of lymph node metastasis in patients with ovarian cancer, as shown in Table 4.

Table 4: Multivariate Logistic regression analysis results.

Variables	B	SE	Wald	P	OR*	95% CI
CA125	1.031	0.475	4.722	0.03	2.804	1.106-7.109
CT to evaluate LNM	0.936	0.54	8.404	0.004	5.022	1.687-14.954
Lesions location	1.174	0.557	4.731	0.03	3.234	1.123-9.109
Constant	-1.92	0.367	27.449	<0.001	0.147	

Note: * indicates the number of contrast, that is, a multiple concept index, with serum CA125 level ("0", that is, ≤ 297.8U/ml), CT evaluation of lymph node status ("0", that is, lymph node metastasis negative) and lesions location ("0", that is, unilateral) as control items.

Construction of radiomics model

Feature extraction and radiomics model construction: The dimensionality reduction analysis and machine learning of radiomics are carried out on the Radcloud platform. Firstly, the variance threshold method is used to select 398 features from 1409 features, and then 90 features are selected by select Kbest method. Finally, five optimal imaging features (Table 5, Figure 3) are selected by LASSO algorithm, which are represented by R1-R5, including three gray correlation matrix features (R1-R3) and two first-order statistical features (R4, R5).

Table 5: Lasso coefficient of image omics eigenvalues.

Radiomic feature	Radiomic class Filter	P value Lasso		
R1: Dependence Variance	gldm	wavelet-HHL	<0.001	0.05802
R2: Dependence Variance	gldm	wavelet-LHH	<0.001	0.05513
R3: Large Dependence Low	gldm	wavelet-LHH	0.005	-0.03292
Gray Level Emphasis				
R4: Skewness	first order	wavelet-LLL	0.002	-0.00175
R5: Skewness	first order	square	0.002	-0.05067

Notes: gldm: gray level dependence matrix; DV: Dependence Variance; LDLGLE: Large Dependence Low Gray Level Emphasis; Lasso coefficient: The negative value of indicates that there is a negative correlation between the feature and lymph node metastasis, while a positive value indicates that the feature is positively correlated with lymph node metastasis. The greater the absolute value, the greater the correlation.

Table 6: Diagnostic efficiency of the radiomics model.

Group	AUC	95% CI	Sensitivity	Specificity
Training set	0.754	0.65-0.86	0.74	0.7
Test set	0.795	0.65-0.86	0.71	0.69

Note: The results of ROC curve of training set and test set of radiomics model.

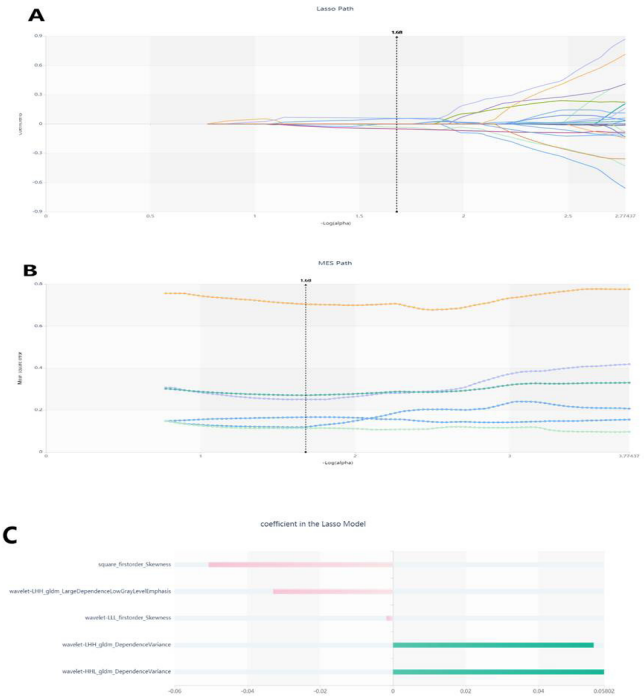

Figure 3: Radiomics feature values selected for constructing prediction model after LASSO algorithm.

Note: A: Lasso path represents the relationship between the independent variable regression coefficient and the Lasso penalty coefficient λ, and the best λ value corresponds to the log (λ) value of 1.68 × alpha MSEpath, that is, the corresponding mean square error when the alpha chooses different values; C: the coefficient of each radiomics feature most related to the prediction model in the Lasso model.

Evaluation and verification of radiomics model.

ROC curve analysis results of radiomics model are shown in Table 6 and Figure 4.

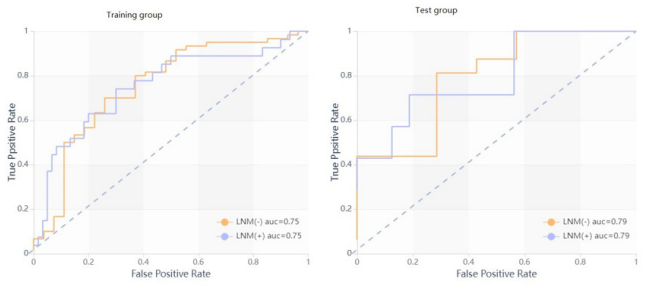

Figure 4: ROC curve of radiomics model.

Note: LNM: lymph node metastasis; the AUC value of imaging model training set is 0.75 and that of test set is 0.79.

Construction of combined model

Feature extraction and selection: On the Radcloud platform finally select the five optimal imaging features (R1~R5), which are the same as the imaging model, as shown in Table 5 and Figure 3.

Five imaging features selected from the statistically significant baseline data (CA125 level, lesions location, CT evaluation of lymph node status) were combined with SVM classifier to build a combined model, and the SVM parameters were consistent with the radiomics model parameters.

Evaluation and verification of combined model

ROC curve analysis results of combined model are shown in Table 7 and Figure 5.

Table 7: Combined model of clinical data, CT signs and imaging omics features.

Group	AUC	95% CI	sensitivity	specificity
Training	0.849	0.76-	0.81	0.8
Test set	0.813	0.76-	0.71	0.81

Note: The AUC value of combined model training set and test set is 0.85 and 0.81 respectively.

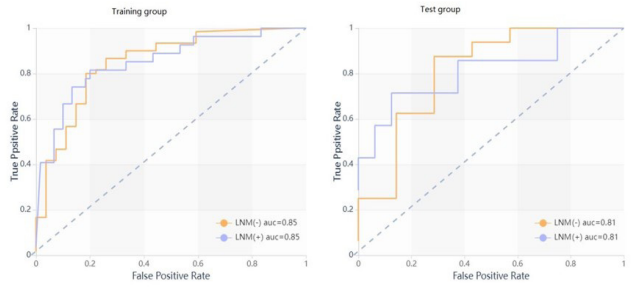

Figure 5: ROC curve of clinical data + CT signs + imaging features combined model.

Note: LNM: lymph node metastasis; the AUC value of combined model training set and test set is 0.85 and 0.81 respectively.

Comparison of prediction efficiency of different models.

The Delong test of the performance of the two models predicting LNMROC is shown in Table 8. The results showed that the AUC of the combined model for predicting ovarian cancer LNM in the training set and verification set was higher than that of the single radiomics model. There was a significant difference in the prediction efficiency of the two models in the training set (Table 8 and Figure 6).

Discussion

From now on, there are different methods to predict lymph node metastasis of tumor patients through imaging models. Based on different imaging images (CT, MRI, US, PET/CT, etc.), primary tumor, primary tumor and peritumoral structure, primary tumor and surrounding lymph nodes, regional lymph nodes are segmented as ROI, and then imaging features are extracted to establish LNM prediction models. There are a variety of feature

Table 8: Delong test results of ROC curve efficiency of both models.

	Models	AUC	SE	95% CI	*P* value
Training set	Radiomics model	0.754	0.060	0.65-0.86	**0.023**
	Combined model	0.849	0.047	0.76-0.94	
Test set	Radiomics model	0.795	0.109	0.65-0.86	0.719
	Combined model	0.813	0.114	0.76-0.94	

Note: The prediction efficiency of ROC curve of the two models was compared by Delong test, P < 0.05. The difference was statistically significant.

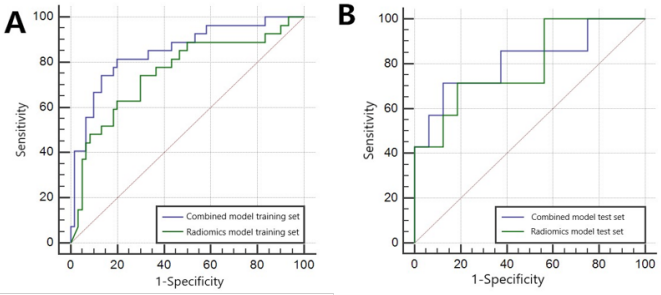

Figure 6: Comparison of ROC curve efficiency of two models by DeLong test.

Note: A is the ROC curve of the training set of the two models, and B is the ROC curve of the test set of the two models.

selection and modeling methods. However, there are few studies based on MSCT imaging in the field of ovarian cancer, and there are even fewer studies on the application of imaging model to predict the LNM of ovarian cancer. This study is based on MSCT imaging, using LASSO algorithm to select the best imaging features of LNM in MSCT, combined with traditional data related to ovarian cancer LNM, to explore the value of the model in predicting LNM of epithelial ovarian cancer.

Analysis of baseline data of enrolled

According to the relevant literature, the positive rate of LNM in ovarian cancer is about 44% to 60%, and the metastasis rate of patients with advanced ovarian cancer can be as high as 40% to 73.7%. The probability of LNM is also different due to different clinical stages, histopathological types, and degree of differentiation, while serous and clear cell carcinoma have a higher risk of LNM than other histological types of ovarian cancer [19,22-24]. In this study, there were 34 cases of LNM positive group (30.9%) and 76 cases of negative lymph node metastasis group (69.13%). Among the 87 cases in the training set, 27 cases were pathologically confirmed lymph node metastasis (31.0%), and 7 cases in the test set 23 cases (the metastasis rate was 30.4%). In this study, the results showed that the preoperative CA125 level of ovarian cancer patients with LNM positive was higher. This study showed that the rate of lymph node metastasis increased in serum CA125 >297.8 U/ml group, and the probability of lymph node metastasis in CA125 ≤ 297.8 U/ml group was 2.804 times higher than that in CA125 ≤ 297.8 U/ml group. Although the critical value is different from that of previous studies (the critical value of CA125 is 535 U/ml) [25], the results show that the level of CA125 is an independent risk factor for evaluating LNM in ovarian cancer. The

location of the lesions was an important risk factor for evaluating LNM in OC. The portion of lymph node metastasis in patients with bilateral OC was significantly higher than that in patients with unilateral (left or right) lesions, which was consistent with the results of other studies [14,26-28]. As a qualitative radiological feature, preoperative CT evaluation of lymph node status can be easily obtained. This study shows that CT evaluation of lymph node status is an independent risk factor for LNM.

However, our study showed that the age, family history of tumor, menopause, preoperative CA199 level, maximum tumor diameter and LNM in patients with OC with or without ascites are not independent variables. It is worth noting that the level of CA199 is an independent risk factor for LNM in patients with OC in previous research. Early diagnosis of retroperitoneal LNM of OC could be achieved by a combination of serum CA125, VEFG-C and CA199 levels, which has clinical predictive value [29]. On the basis of the univariate correlation between CA199 level and LNM in this study, it does not show sufficient predictive strength of CA199, which makes the exclusion of this variable a factor in the construction of a combined model. However, the rejection of important predictors may be the result of sample size, nuances in data sets, or be confused by other predictors. For these predictors, the non-significant statistical association with lymph node metastasis does not necessarily mean that CA199 levels are not important. The insignificance of other characteristics may be due to insufficient sample size or confusion among predictive factors, which need to be confirmed by further study.

Construction of radiomics model

Traditional human eye film reading is usually limited by a variety of subjective factors, but the emerging radiomics (Radiomics) breaks through these limitations to achieve the transformation from image to data, so as to obtain more information, and then improve the diagnostic efficiency. Its fast, non-invasive, low cost, high patient acceptance and other advantages promote its rapid development. As more and more variables are collected, high-dimensional data attract more and more attention in images. SVM, as a Machine Learning (ML) tool to deal with classification problems, has a good performance in the classification and prediction of high throughput data, even in ML tasks with limited samples [30].

In recent years, radiomics has a good performance in the classification and prediction of OC. In this study, based on MSCT images, the LNM predictive assembly model of epithelial ovarian cancer was constructed on the SVM classifier. The ROC results show that it has a certain diagnostic efficiency. Yu et al [14]. Studied the diagnostic value of metastatic lymph nodes of ovarian cancer based on multi-slice spiral CT image texture analysis, but only a single CT texture feature analysis rather than a complete imaging analysis, without independent verification set verification.

Combined model construction

In this study, univariate and multivariate Logistic regression analysis of 9 LNM-related clinical data and CT signs (age, family history of tumor, menopause, CA125, CA199, lesion location, tumor maximum diameter, ascites, and lymph node status assessed by CT) showed that three factors (CA125 level, lesion location and CT evaluation of lymph node status) were independent predictors of LNM in epithelial ovarian cancer. Combined with the selected five optimal imaging features, a combined prediction model is constructed. The combined model achieves good diagnostic efficiency, and the AUC of training set and test set are 0.849 and 0.813, respectively.

Some scholars have studied the preoperative serum CA125 level to predict the LNM of epithelial OC. The results showed that the ROC curve showed the best critical value (535 U/ml) of preoperative serum CA125 level, with a sensitivity and specificity of 70.0% and 83.1%, respectively. Imaging studies combined with preoperative serum CA125 levels showed the highest sensitivity (90.0%). Imaging studies alone showed the highest specificity for predicting lymph node metastasis (89.8%) [25]. It shows that the diagnostic efficacy of single factor or single sign in predicting LNM is lower than that of combining multiple factors and multiple factors. However, this study only analyzes the predictive performance in terms of sensitivity and specificity, and does not use other indicators to evaluate the predictive efficiency. This study combines multiple clinical data, CT signs and imaging features to construct a combined model. The AUC, specificity, sensitivity and 95% confidence interval are used to evaluate the prediction efficiency of the model, so as to improve and further increase the stability and credibility of the model. In 2020, Liu et al [31] studied the clinical value of the assistant diagnosis system of ovarian cancer pelvic and abdominal LNM based on depth neural network in enhanced CT imaging. The ROC curve analysis results show that the AUC is 0.7664, which is close to the diagnostic efficiency of the imaging model, but lower than our combined model.

Comparison of prediction efficiency of different models

The disease assessment needs to integrate clinical, pathological, imaging and other different aspects of information. In this study, it showed that the diagnostic efficiency of the combined model is higher than that of the single one. Studies have shown that the accuracy of CT in the diagnosis of pelvic lymph node and retroperitoneal LNM in patients with OC is 48.15% (13/27) and 41.67% (10/24), respectively, and its accuracy is low [32]. In this study, it turns out to be that simple CT signs have a certain rate of missed diagnosis of lymph node metastasis in patients with ovarian cancer. Moreover, the combined model can predict the LNM of patients with epithelial ovarian cancer with high sensitivity and specificity.

This study has the following shortcomings as follows: (1) The research object is a single center study, and the sample size is small. (2) This study is a retrospective study, the model is only verified in the internal independent test set, and there is no external verification and prospective verification. (3) There are few LNM-related baseline data collected and analyzed in patients with epithelial ovarian cancer. In addition to these characteristics analyzed in this study, epithelial ovarian cancer also has other risk factors for LNM. In addition, gene markers such as tumor suppressor gene P16 [33] and BRCA mutation [34] were not considered in this study. Further research is needed to explore the possibility of these factors adding to the comprehensive prediction model of LNM.

Conclusion

This study confirmed the correlation between preoperative enhanced MSCT imaging parameters and LNM in patients with epi-

thelial ovarian cancer, and established a preoperative combined prediction model of LNM of epithelial ovarian cancer based on MSCT imaging parameters and traditional baseline data (lesion location and CA125 level (297.8 U/ml), CT evaluation of lymph node status). The model achieved high diagnostic efficiency and was verified in the internal independent test set. This model has a certain value in improving the preoperative accuracy of ovarian cancer and guiding clinical decision-making.

Declarations

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