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Clinical Application of LCBP Risk Assessment Model in Risk Stratification of Pulmonary Nodules

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Abstract: ***Objective:*** ***To use the LCBP risk assessment model to evaluate tumor markers combined with imaging diagnosis, stratify the risk of pulmonary nodules, and predict the probability of disease malignancy in patients.*** ***Methods:*** ***A total of 80 patients with pulmonary nodules on lung CT examination in the Affiliated Hospital of Shaanxi University of Traditional Chinese Medicine from January 2020 to April 2021 were enrolled as the experimental group, and 60 patients without pulmonary nodules were selected as the control group. Blood samples were collected from patients without treatment, and ProGRP, CEA, SCC-AG and CYFRA21-1 serum biomarkers were determined by chemiluminescence immunoassay.*** ***Results:*** ***There were statistically significant differences in serological markers between the two groups (P<0.05), and the evaluation of the malignant probability of pulmonary nodules by imaging indicators and the presence or absence of burr signs were statistically significant (P<0.05). The AUC of the low-risk group was 0.761, the AUC of the intermediate-risk group was 0.749, and the AUC of the high-risk group was 0.804.*** ***Conclusion:*** ***The LCBP risk assessment model based on serological markers, imaging findings and clinical data has a good ability to distinguish the risk stratification of pulmonary nodules***

Keywords: Pulmonary nodules, Biomarkers, Imaging, LCBP risk assessment model.

1. Introduction

Pulmonary nodule is the presence of a distinct, imaging opaque, single or multiple pulmonary nodule ≤3 cm in diameter, completely surrounded by air-containing lung tissue in the lungs, not accompanied by pulmonary atelectasis, hilar enlargement, and pleural effusion [1,2]. The incidence of lung nodules has statistically increased from 8% to 51% [3], and with the gradual increase in people's health awareness, the number of small lung nodules found on annual physical examination has gradually increased. Benign lung nodules account for the majority of cases, and the proportion of malignant lung nodules is only 1.1%~12% [4,5]. Lung nodules are detected through health checkups, other disease visits, and clinical symptoms such as cough and haemoptysis. However, there are different sizes of nodules, and the smaller the diameter of the nodule, the more difficult it is to judge the nature of the nodule from the imaging characteristics, which affects the subsequent diagnosis and treatment.

At present, the main interventions for early lung nodules in major hospitals in China include regular follow-up with imaging, pathological testing and surgical treatment, and the choice of intervention depends on the risk stratification of patients with lung nodules. Therefore, a variety of lung cancer risk prediction models have been established internationally for determining the risk of lung cancer and improving the sensitivity and specificity of diagnosis. The models with high recognition abroad include the Mayo Clinic Model [6] and the Veterans Administration (VA) [7]. The People's Hospital Peking University (PKUPH) model [8] is more widely recognised in China, and a comparison of the three models revealed some limitations [9].

There are several differences in the criteria for the inclusion of data in several risk assessment models: 1) different imaging data, 2) different ranges of lung nodule diameters, and 3) different populations included in the samples. Due to the influence of geographic regions, demographic differences, testing instruments, and many other factors, the formulas of the various risk assessment models can not be completely unified and promoted for use, and there is an urgent need to establish a more standardised, comprehensive, and in line with China's actual situation, a more standardised, comprehensive, and in line with China's actual situation Based on this concept, we applied the LCBP lung nodule risk assessment model developed and recommended by the China Lung Cancer Consortium to assess and analyse the risk stratification of lung nodules, and to explore the value of early diagnosis of lung nodules in the model [10].

2. Objects and Methods

2.1 Study Subjects and Inclusion Criteria

Eighty patients with pulmonary nodules on lung CT examination who attended the Affiliated Hospital of Shaanxi University of Traditional Chinese Medicine between January 2020 and April 2021 who met the inclusion criteria were selected, including 52 males and 28 females, with an average age of (64.96±9.20) years. The control group consisted of 60 normal patients who had no pulmonary nodules detected by lung CT examination during the same period, including 31 females and 29 males, with an average age of (58.53±14.68) years. Clinical data (age, gender, smoking history, past medical history), pathological diagnosis, imaging manifestations (presence or absence of burr sign and nodule diameter) were collected. The general data of the two groups were compared statistically, and the gender composition and age of the experimental and control groups were compared ($\chi 2$ =3.906, P=0.0048 and $\chi 2$ =3.173, P=0.002).

Inclusion criteria: 1) male smokers (>=400 cigarettes/year), female smokers or non-smokers; 2) no history of lung cancer; and 3) no currently known extrathoracic malignancy. The nodule model required an additional inclusion criterion of

indeterminate lung nodules on chest CT. Exclusion criteria: 1) no histopathological diagnosis and 2) previous treatment with chemotherapy or surgery [9].

2.2 Study Content and Methods

2.2.1 Instruments and reagents

Serum biomarker indicators ProGRP, CEA, SCC-Ag and CYFRA21-1 were detected and analysed by using Abbott ARCHITECT i400SR chemiluminescence instrument, supporting the use of Abbott manufacturer's reagents, calibrators and quality control products, and the individual test items were detected and analysed in accordance with the requirements of the standard operating procedures for the samples. Imaging data were collected by 64-slice spiral CT (GE Discovery CT 750HD, GE Healthcare, Milwaukee, WI, USA) scanning equipment for enhancement-phase thoracic CT scanning for nodule size as well as the presence or absence of burr sign assessment.

2.2.2 Study methods

When untreated, 3ml blood samples were taken from patients using procoagulant tubes, centrifuged at 4000rpm for 10 minutes, serum was taken from patients, and the instruments were immediately used for the detection of blood biomarkers of ProGRP, CEA, SCC-Ag, and CYFRA21-1. The above detection indexes were under indoor quality control, and had passed the inter-room quality assessment of the ProCheck Centre of the National Healthcare Commission, and the results were accurate and reliable. The reference intervals were as follows: CEA: 0-5ng/ml, CYFRA21-1: 0-2.08ng/ml, ProGRP: 0-50pg/ml, and SCC-Ag: 0-1.5ng/ml; the imaging manifestations (presence or absence of burr sign and diameter of nodules) were collected, and the initial report was made by one imaging physician, and the report was reviewed by another, and the double report ensured that the maging results were accurate.

2.3 LCBP Risk Assessment Model - risk Assessment Formula for Lung Nodules

X=-5.6017 + (0.0264xAge) + (8.8539xSmoking History) + (0.1859xNodule Diameter) + (3.1865xHairpin Sign) + (-8.7109xSex) + (-0.00001xProGRP) + (0.0057xSCC-Ag) + (0.1686xCYFRA21-1) + (-0.00311xCEA). 0.00311xCEA), probability of malignancy = e^x/(1+e^x)

Formula description: e is the natural logarithm (2.71828); previous history of smoking, smoking = 1, no previous history of smoking, smoking = 0; presence of burr sign, burr sign = 1, absence of burr sign, burr sign = 0; sex is male, sex = 1, sex is female, sex = 0. Probability of malignancy ≤22% was considered low risk; probability of malignancy >22% and ≤94% was considered intermediate risk; probability of malignancy >94% was considered high risk.

2.4 Statistical Methods

SPSS25.0 statistical software was used for data processing. The data of each group were tested for normality, and the normally distributed measurements were expressed as t-test for inter-group comparison; the non-normally distributed measurements were expressed as M (P25, P75), and the two-by-two comparisons were made by Mann-Whitney U test. Count data were expressed as frequency and rate, and comparisons were made using the $\chi 2$ test. Differences were considered statistically significant at $P<0.05$. The sensitivity, specificity and accuracy of the model were calculated using the area under the subject operating characteristic (ROC) curve, AUC, as the discriminant criterion.

3. Results

3.1 Comparison of General Information between Experimental and Control Groups

The difference in gender composition (P=0.048) and age (P=0.002) between the experimental and control groups was statistically significant (Table 1).

Table 1: Comparison of general information between the two groups

	n	Gender [n(%)]		Age ($\bar{x} \pm s$)
		Male female	Female female	
Experimental group group l group (n=80)	80	52(65.0)	28(35.0)	64.96±9.20
Control group subjects (n=60)	60	29(48.3)	31(51.7)	58.53±14.68
$\chi 2$		3.906		3.173
P		0.048		0.002

3.2 Comparison of the Levels of Four Serological Markers between the Experimental Group and the Control Group

The differences between the experimental group and the control group were statistically significant for the serum tumour markers CEA, CYFRA21-1, SCC-Ag, and ProGRP (all $p<0.05$) (Table 2).

3.3 Comparison of the Relationship between Imaging Indicators and the Probability of Malignancy of Lung Nodules

The difference between imaging indicators of different nodule

sizes and the presence or absence of burr sign for the probability of malignancy of lung nodules was statistically significant ($p<0.05$) (Table 3).

Table 2: Comparison of the levels of four serological markers between the experimental and control groups ()

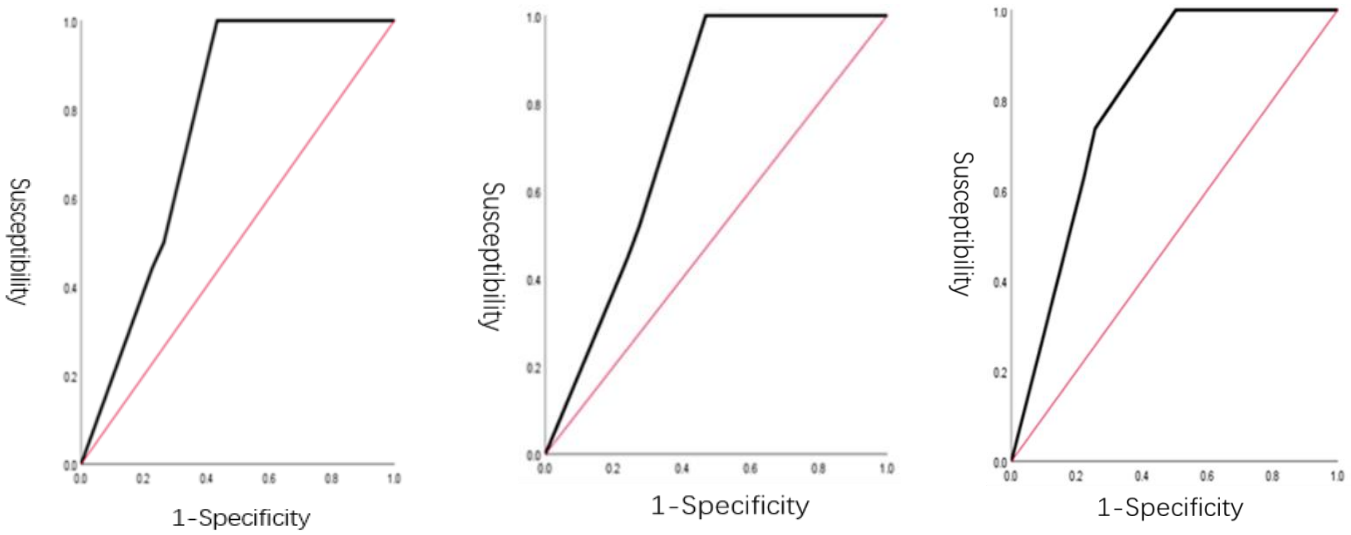
Group	n	CEA (0-5ng/ml)	SCC-Ag (0-1.5ng/ml)	ProGRP (0-50pg/ml)	CYFRA21-1 (0-2.08ng/ml)
Experimental group	80	7.73±9.44	1.68±4.46	161.24±9.25	3.91±7.72
Control group	60	3.10±5.01	0.86±0.28	37.76±8.71	1.41±0.51
t		3.047	4.589	3.01	7.734
p		<0.05	<0.05	<0.05	<0.05

Table 3: Comparison of imaging indices with the probability of malignancy of lung nodules

Imaging indicators	Malignant probability		
	≤22%	>22% and ≤94%	>94%
≥8mm, Hairy prick marks	0(0%)	3(3.7%)	34(42.5%)
≥8mm, Hairless prick sign	22(27.5%)	3(3.7%)	5(6.2%)
<8mm, Hairless prick sign	13(16.2%)	0(0%)	0(0%)
p	<0.05	<0.05	<0.05

3.4 Hazard Stratification According to Degree of Prediction and Degree of Diagnosis Using ROC Curves to Determine Accuracy of Prediction

The sensitivity and specificity of the malignancy probability and the degree of clinical diagnosis assessed by the model were validated, and based on the results of the analysis of the three ROC curves, it was shown that the area under the ROC curve (AUC), specificity and sensitivity, the AUC of the different stratification of the low-risk group was 0.761, the AUC of the intermediate-risk group was 0.749, and the AUC of the high-risk group was 0.804, and the LCBP model had a higher sensitivity and specificity of the LCBP model for different risk stratification (Figure 1).



Low-risk group (≤22%) Medium-risk group (>22% and ≤94%) High-risk group (>94%)

Figure 1: ROC curves for risk stratification of the probability of malignancy in lung nodules

4. Discussion

Lung cancer (lung cancer) is the malignant tumour with the highest incidence worldwide [11,12], for which early detection and early diagnosis and treatment strategies are mainly adopted, but there are many factors that lead to lung cancer not being screened at an early stage, such as failing to recognise abnormal imaging findings and misjudgement of pathology reports [13-15]. The popularity of low-dose spiral CT has led to a significant increase in the early screening rate of lung nodules, but the judgement of nodule benignity and malignancy by observing the size of the nodule, the presence or absence of the burr sign, and other imaging indexes, is easily affected by the subjective factors of doctors. In order to enable patients with pulmonary nodules to receive timely and effective treatment in the benign early stage, but also to reduce the over-treatment of patients with benign nodules, relying only on imaging diagnosis has a high rate of missed detection, which is not conducive to early screening. Pathological diagnosis as the gold standard for disease diagnosis, on the other hand, has high specificity, but it is an invasive means of examination, causing trauma to the patient's organism and low acceptance by the patient. Abnormal changes in the imaging characteristics of lung nodules are later than serum tumour markers, and their changes are relatively more obvious. Serological markers SCC, CEA, ProGRP and CYFRA21-1 are of great significance in the screening of lung nodules, and they can efficiently identify the nature of lung nodules in the early stage [16-19], and they are simple to operate, with good repeatability, and are more readily acceptable to patients. Combined use of CT, tumour markers, and patient history, the method has a low rate of missed diagnosis and high accuracy, and is generally applicable from tertiary hospitals to grassroots hospitals, which is more suitable for widespread promotion. However, tumour markers are not the only basis for the early diagnosis of lung cancer, and clinically there is a greater need to combine clinical symptoms, imaging and other means to comprehensively assess the stratification of lung nodules.

The advantage of the LCBP wind assessment model is that it is a risk assessment model that is in line with the actual situation in China, which not only incorporates clinical data, imaging data, but also serum markers of four lung tumours. Based on the current study, it is shown that the accuracy of imaging screening indicators has a great impact on the sensitivity and specificity of the LCBP model, and the diagnostic accuracy is subsequently improved. The ACCP guideline stratifies the risk from the location of the nodule, previous history of lung cancer, history of smoking, gender, age, and the diameter of the nodule by using the examination methods of (sputum cytology, PET scan, fluorescent bronchoscopy, and tumour marker In China, due to the high prevalence of tuberculosis, PET is not appropriate for screening lung nodules, and non-surgical biopsies should be used to confirm the diagnosis and for regular monitoring. In addition, the high prevalence of granulomatous and other infectious diseases in Asia should also be noted. In conclusion, guidelines for the evaluation of pulmonary nodules vary in different Asian countries Risk stratification is an integral part of the management process of pulmonary nodules. However, there are no good predictive models that can be used to assess the probability of malignancy of lung nodules present in

patients with an intermediate risk of malignancy. For the Chinese population at risk for lung nodules, the LCBP model has a better diagnostic compliance rate than the US ACCP model. In addition, for primary hospitals, the application of tumour marker profiles can improve the early diagnosis rate of lung cancer. As for general hospitals, the combination of tumour marker profiling and CT examination can make up for the shortcomings of the ACCP model diagnosis and further improve the sensitivity and specificity of the diagnosis of early lung cancer. Based on our study, we showed that there was a significant elevation of lung tumour markers in the lung nodule group compared with the control group, and the combined detection of serological markers, imaging indexes, and patient history had a high diagnostic value, and the assessment of malignant probability of patients' lung nodules using the model stratification had a better correlation, and the combination of the LCBP risk assessment model for the early stratification analysis of lung nodules was widely used in the clinic.

The combined detection of low-dose spiral CT examination and patients' serological markers has a high value for the early diagnosis of lung nodules, and is widely used in the clinic [20-23]. Imaging indicators such as nodule size, gross and fine burr signs, and vascular truncation signs can be used to assess the risk of lung nodules, and the study of new serological markers and imaging indicators of lung tumours is of great significance for early screening of lung nodules, and it will be of great significance to add new indicators in the future in order to improve the accuracy and sensitivity of the risk assessment model of lung nodules in the LCBP.

References

[1] ZHAO Mingwei. Differential diagnostic value of lung CT examination on the benign and malignant nature of ground-glass nodule-like lungs[J]. Sichuan Journal of Physiological Sciences, 2024, 46(4):849-851.

[2] CUI Xiaonan, YE Zhaoxiang. Predictive modelling of lung nodule pathology based on preoperative CT images [J]. Chinese Journal of Radiology, 2024, 58(2): 243-244.

[3] Shen Aijun, Li Hongjiang, Xia Ganlin, et al. CT imaging features of malignant isolated pulmonary nodules [J]. Chinese Journal of Practical Diagnosis and Therapy, 2013, 27(012): 1209-1211.

[4] HATT M, TIXIER F, PIERCE L, et al. Characterization of PET/CT images using texture analysis: the past, the present any future [J]. Eur J Nucl Med Mol Imaging, 2017, 44(1): 151-165.

[5] OHRI N, DUAN F, SNYDER B S, et al. Pretreatment 18F-FDG PET Textural Features in Locally Advanced Non-Small Cell Lung Cancer: Secondary Analysis of ACRIN 6668/RTOG 0235 [J]. J Nucl Med, 2016, 57(6): 842-848.

[6] PERANDINI S, SOARDI G A, MOTTON M, et al. Solid pulmonary nodule risk assessment and decision analysis: comparison of four prediction models in 285 cases [J]. Eur Radiol, 2016, 26(9): 3071-3076.

[7] WANG Xin, XU Yuehua, DU Ziyan, et al. CT imaging features of isolated pulmonary nodules and the establishment of benign and malignant prediction model [J]. Chinese Journal of Oncology, 2018, 40(002): 115-120.

[8] LI Y, CHEN K Z, WANG J. Development and validation of a clinical prediction model to estimate the probability of malignancy in solitary pulmonary nodules in Chinese people [J]. Clin Lung Cancer, 2011, 12(5): 313-319.

[9] AN Yang, LI Chunzhao, ZHAO Wei. Validation study of three lung cancer risk prediction models in patients with lung nodules [J]. Journal of PLA Medical College, 2020, 41(12): 2095-2097.

[10] YANG D, ZHANG X, POWELL C A, et al. Probability of cancer in high-risk patients predicted by the protein-based lung cancer biomarker panel in China: LCBP study [J]. Cancer, 2018, 124(2): 262-270.

[11] Jia Bo, Wang Zi Ping. Progress of emerging biomarkers for lung cancer treatment with immune checkpoint inhibitors[J]. China Cancer Clinics and Rehabilitation, 2023, 30(5):287-294.

[12] Yanyan Qiao, FU Enqing. Research progress of tumour-associated macrophages in lung cancer[J]. Chinese Journal of Lung Cancer, 2022, 25(1):34-39.

[13] SHIN K E, LEE K S, YI C A, et al. Subcentimeter lung nodules stable for 2 years at LDCT: long-term follow-up using volumetry [J]. Respirology, 2014, 19(6): 921-928.

[14] SINGH H, SETHI S, RABER M, et al. Errors in cancer diagnosis: current understanding and future directions [J]. J Clin Oncol, 2007, 25(31): 5009-5018.

[15] Bing Zhang, C G Hu. Three-dimensional CT bronchial angiography thoracoscopic segmental lung resection for T 1a~1bN 0M 0 stage non-small cell lung cancer [J]. Oncology Research and Clinics, 2023, 35(9):706-709.

[16] MAZZONE P J, SEARS C R, ARENBERG D A, et al. Evaluating Molecular Biomarkers for the Early Detection of Lung Cancer: When Is a Biomarker Ready for Clinical Use an Official American Thoracic Society Policy Statement [J]. Am J Respir Crit Care Med, 2017, 196(7): 15-29.

[17] Tingting Zhang, Yi Xiang, Yubing Lin. Predictive value of combined detection of tumor markers in the diagnosis of lung cancer[J]. Zhonghua Yu Fang Yi Xue Za Zhi, 2021, 55(6):786-791.

[18] Wu HY, Pan YY, Kopylov AT, Zgoda V, Ma MC, Wang CH, Su WC, Lai WW, Cheng PN, Liao PC. Assessment of Serological Early Biomarker Candidates for Lung Adenocarcinoma by using Multiple Reaction Monitoring-Mass Spectrometry[J]. Proteomics Clin Appl, 2020, 14(4):e-1900-1905.

[19] Gao J, Zhang L, Peng K, Sun H. [Diagnostic value of serum tumor markers CEA, CYFRA21-1, SCCAg, NSE and ProGRP for lung cancers of different pathological types]. Nan Fang Yi Ke Da Xue Xue Bao, 2022, 42(6):886-891.

[20] Wang R. Clinical value of low-dose spiral CT in lung cancer screening [J]. Imaging Research and Medical Applications, 2019, 3(18): 18-21.

[21] Huo Dandan. Analysis of the value of individual and combined detection of four lung cancer serum tumour markers in lung cancer diagnosis [J]. China Emergency Medicine, 2018, 038(0z1): 75-80.

[22] Wu H, Wang Q, Liu Q, Zhang Q, Huang Q, Yu Z. The Serum Tumor Markers in Combination for Clinical Diagnosis of Lung Cancer[J]. Clin Lab, 2020, 66(3):1905-1909.

[23] Huang J, Ren K. Detection of Changes in CEA and ProGRP Levels in BALF of Patients with Peripheral Lung Cancer and the Relationship with CT Signs[J]. Contrast Media Mol Imaging, 2023, 2(18):1421-1429.